St. Xavier's College (Autonomous), Kolkata

POSTGRADUATE & RESEARCH DEPARTMENT OF BIOTECHNOLOGY

CHIASMA 2024

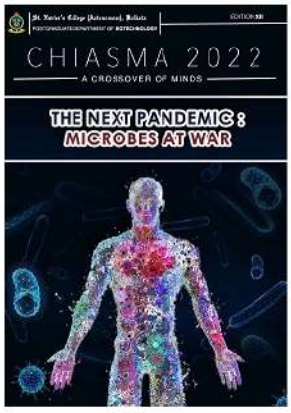
A CROSSOVER OF MINDS

BIOTECH HORIZONS

SHAPING TOMORROW'S HEALTH & ENVIRONMENT

EDITION XIV

Some Glimpses of our Departmental Activities



St. Xavier's College (Autonomous), Kolkata

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DISCLAIMER

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Although every effort has been made to ensure the accuracy of the material published in this magazine, the college and department accept no responsibility for the veracity of claims or the accuracy of the information provided by the contributor/ contributors.

The contents of the e-version of this magazine are available online at *chiasmabmbt.in*

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2024 CHIASMA

MESSAGE FROM
THE RECTOR

I am filled with a sense of profound joy at the publication of the fourteenth edition of "Chiasma 2024 - A Crossover of Minds", the departmental magazine of the Postgraduate and Research Department of Biotechnology, St. Xavier's College (Autonomous), Kolkata. This year's theme "Biotech Horizons – Shaping Tomorrow's Health and Environment" is based on a very contemporary issue. The environment is expected to play a major role in shaping the future health concerns of the world especially the developing countries. Biotechnological innovations have the potential of implementing the dual objectives of environmental sustainability along with significant improvement of the health perspective. I am confident that this edition of Chiasma 2024 has tried to address the various issues in this regard and the articles will not only enlighten but also inspire all who will read this magazine.

I am happy to learn that the tireless efforts of the students and faculty members of the Department of Biotechnology have culminated in this year's edition of Chiasma 2024. This magazine reveals the research orientation of the students and the research scholars through their well-researched scientific articles. This magazine is also a platform for the students to showcase their creative efforts.

I wish the students and faculty members of the Department of Biotechnology all the best and hope that their hard work and collective efforts will always lead them to achieve their goals in future too. Nihil Ultra!

Rev. Fr. Jeyaraj Veluswamy, SJ
Rector,
St. Xavier's College (Autonomous), Kolkata.

MESSAGE FROM
THE PRINCIPAL

It gives me immense pleasure to learn that the Postgraduate and Research Department of Biotechnology, St. Xavier's College (Autonomous), Kolkata, is launching the fourteenth edition of its departmental magazine, "Chiasma 2024 - A Crossover of Minds". This year's theme is "Biotech Horizons – Shaping Tomorrow's Health and Environment" which is extremely relevant in the present era of environmental sustainability with its implications on human lives and human health in a number of ways. This is a very contemporary issue as healthier environments and biotechnological innovations have the potential of reducing the global burden of disease.

This magazine is a fruit of months of tireless effort on the part of the students and faculty members of the Department of Biotechnology. This magazine serves as a forum for the young talents to ventilate their ingenious ideas on the aforementioned theme. The department is enriched with research-oriented endeavours on the part of the faculty members, research scholars and students and the articles in this magazine are a reflection of the same. It also dives deep to inculcate their literary skills along with their scientific efforts.

The Department has been instrumental right from its inception in July 2006, in imparting quality teaching, as reflected by the students' performance and by rigorous research work by the faculty, research scholars and students which has been acclaimed at both the national and international levels.

I wish to extend my heartfelt congratulations to the Department of Biotechnology for steadfastly setting and striving towards new goals of excellence, especially with regard to academic research and circulation of innovative ideas. I congratulate all the faculty members, and the students and research scholars of the Department and wish them success in their concerted efforts.

God bless you all. Nihil Ultra!

Rev. Dr. Dominic Savio, SJ
Principal,
St. Xavier's College (Autonomous), Kolkata.

MESSAGE FROM
THE VICE-PRINCIPAL (ARTS AND SCIENCE)

Chiasma, the annual publication of the Postgraduate Department of Biotechnology, is now in its fourteenth year. The continuity stands as a compelling testament to the department's unwavering dedication to scholarly pursuits, advanced research, and dissemination of knowledge. Beyond its scholarly focus, the magazine serves as a platform not only for academic articles within the discipline but also as a canvas for literary and artistic expression. This unique amalgamation positions Chiasma as a periodical ingeniously crafted to foster a comprehensive and all-encompassing growth in the department's students. I am sure this will serve as catalyst to inspire a many more students in the years to come.

I also appreciate the decision to enhance the publication's impact by introducing the digital version that has the potential to greatly amplify the magazine's visibility and extend its reach and influence.

Congratulations to the department on one more notable accomplishment.

Prof. Bertram Da' Silva

Vice-Principal (Arts and Science)

St. Xavier's College (Autonomous), Kolkata

MESSAGE FROM
THE DEAN OF SCIENCE

I want to offer my warmest congratulations to the Department of Biotechnology on the release of the fourteenth edition of their annual magazine, 'Chiasma'!

Chiasma has truly evolved into an outstanding platform that not only celebrates scientific inquiry but also nurtures collaboration and intellectual growth within our academic community. The unwavering commitment to organize this magazine exemplifies the remarkable spirit that drives the department's success. The publication beautifully encapsulates the multi-disciplinary nature of biotechnology through its rich array of articles.

I extend my heartfelt appreciation to the entire team behind Chiasma, whose tireless efforts have made this endeavour a resounding success. Your dedication to advancing knowledge in biotechnology is truly praiseworthy.

I am confident that the 14th edition of Chiasma will continue to enrich our scientific landscape and serve as a symbol of excellence in the field of biotechnology.

Dr. Indranath Chaudhuri

Dean of Science

St. Xavier's College (Autonomous), Kolkata.

MESSAGE FROM
THE DEAN OF ARTS

Chiasma – A crossover of minds with the theme for the 2024 issue "Biotech Horizons: Shaping Tomorrow's Health and Environment" reflects the profound connection that is shaping our future – the intersection of health and the environment. As we strive for sustainable living, we recognize that the health of our bodies is deeply tied to the health of our environment. When we care for our environment, we are also caring for ourselves. In this shared journey of understanding and action, we not only seek healing but the opportunity to thrive together, in harmony with the world around us. Let this crossover of minds inspire us to foster practices that ensure a better future for generations to come. I congratulate the Department of Biotechnology, all contributors, editors and readers for their commitment to this endeavor.

Farhat Bano

Dr. Farhat Bano

Dean of Arts

St. Xavier's College Autonomous), Kolkata

MESSAGE FROM
THE HEAD OF THE DEPARTMENT

It is with great delight that I herald the unveiling of the 14th edition of our departmental periodical, 'Chiasma'. This publication serves as a vibrant forum for the dissemination of scholarly and literary articles, penned by our students, research scholars and faculty, covering a broad spectrum of topics from biology to general interest.

I extend my profound gratitude to Rev. Dr. Dominic Savio, SJ, our esteemed Principal, for his unwavering encouragement, guidance and steadfast support. My heartfelt thanks go to the Vice Principal, Prof. Bertram Da' Silva, Dean of Science, Dr. Indranath Chaudhuri, and Dean of Arts, Dr. Farhat Bano for their relentless support.

I would like to express my deepest appreciation and gratitude to Dr. Aniruddha Banerji and Dr. Priyanka De, whose ceaseless guidance and tireless efforts have brought this magazine to fruition. I applaud the commendable efforts of our dynamic editorial board, whose dedication over the past few months has resulted in this year's edition, thereby continuing the decade long tradition of the Postgraduate Department of Biotechnology.

I extend my sincere thanks to our entire departmental faculty, research scholars and students for their valuable contributions and enthusiastic support, without which this endeavour would not have been possible. May our journey continue! Nihil Ultra!

Dr. Jhimli Dasgupta, M.Sc. Ph.D.

Associate Professor and Head,

Postgraduate and Research Department of Biotechnology,

St. Xavier's College (Autonomous), Kolkata

EDITORS' MESSAGE

It gives us immense pleasure to announce the release of the 14th issue of Chiasma, the annual departmental magazine of the Postgraduate and Research Department of Biotechnology, St. Xavier's College, (Autonomous), Kolkata. The theme of "Chiasma 2024 - A Crossover of Minds" is "Biotech Horizons – Shaping Tomorrow's Health and Environment".

This year's magazine tries to focus on various issues for protecting human health and environment in various settings. This is of pertinent importance in the current scenario as practical aspects of implementation of environmental protection is of utmost importance to safeguard people's health and safety. Biotechnology can play a very important role in shaping a better tomorrow with importance in the fields of private health, public health and also in the scenario of protecting health in the occupational settings. Biotechnology also has a substantial role to play in developing techniques which are environmentally sustainable, contributing to the sustainable growth of various countries in the fields of agriculture and industry. This magazine is an attempt to address the issues of sustainable environment and health in the future through the lens of various fields allied to Biotechnology.

The magazine incorporates thoughtful inputs in the concerned field contributed by eminent scientists and scientific articles contributed by students, research scholars and faculty members of our department on topics of both biological and general interest. It also tries to provide a platform for showcasing the creative endeavours of the students, research scholars and faculty members of the department. We express our heartfelt gratitude to Rev. Dr. Dominic Savio, SJ, our Principal, for his continuous encouragement, guidance and constant support. We also wish to thank, Rev. Fr. Jeyaraj Veluswamy, SJ, our Rector; Prof. Bertram Da Silva, our Vice Principal; Dr. Indranath Chaudhuri, our Dean of Science and Dr. Farhat Bano, our Dean of Arts, for their constant encouragement. We also take this opportunity to thank Dr. Jhimli Dasgupta, our Head of Department and all faculty members and support staff of the Department for their constant cooperation and support in this journey. We also wish to thank the contributors for sharing their valuable thoughts in this magazine.

Last but not least, a special word of appreciation for our Chief Editors and our Editorial, Design, Coordination and Finance Committees for their relentless hard work for the past few months, without which this magazine would not have been possible. Nihil Ultra!

Dr. Aniruddha Banerji
Associate Professor,
PG and Research Dept. of Biotechnology,
St. Xavier's College (Autonomous), Kolkata

Dr. Priyanka De
Assistant Professor
PG and Research Dept. of Biotechnology,
St. Xavier's College (Autonomous), Kolkata

EDITORIAL BOARD

FACULTY PROFILES

Dr. Jhimli Dasgupta
M.Sc., Ph.D.

RESEARCH INTEREST AND PROJECTS RUNNING IN THE LAB

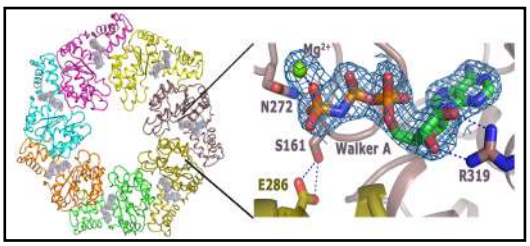
(1) Structural and functional insights of the molecular motors such as **σ**-54 dependent transcription activators, involved in flagellar gene transcription:

- Structural and functional aspects of the AAA+ ATPase FlrC that control flagellar synthesis and biofilm formation in motile bacteria.

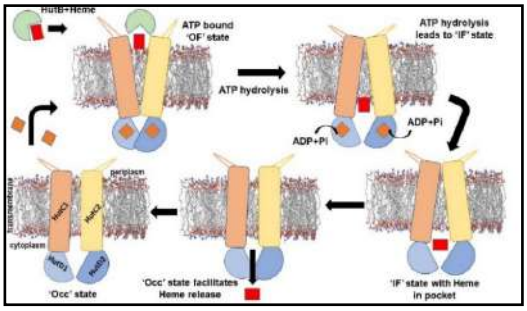
- FlrA, the master transcription regulator of flagellar synthesis in motile bacteria: Structural insights, oligomerisation, functional implications, and regulation by the second messenger c-di-GMP.

(2) Revelation of the sensory signal and mechanism of FlrB, a unique cytosolic sensor Histidine kinase playing a pivotal role in flagellar synthesis and motility of V. cholerae.

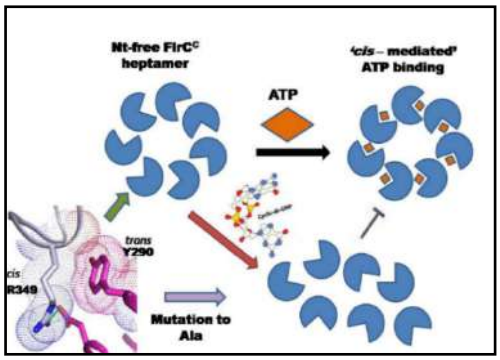
(3) Understanding the mechanism of nutrient uptake by pathogenic bacteria using ABC transporters to target 'Trojan horse mechanism' of drug delivery.



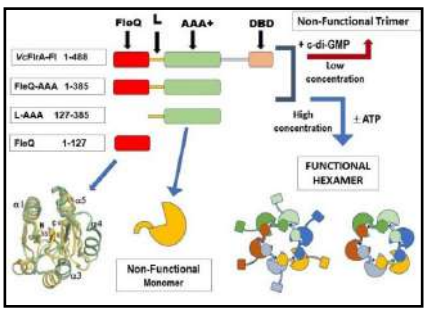
ATP binding to bEBP, FlrC



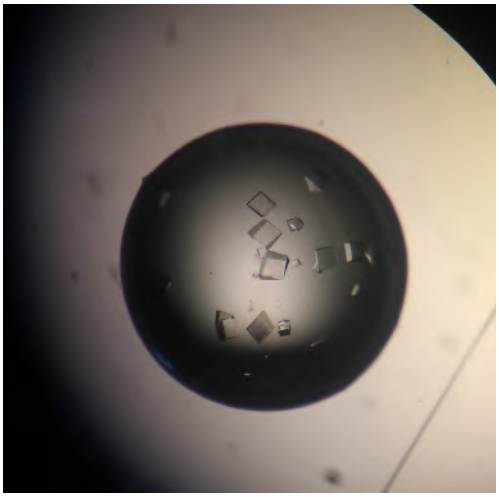
Heme transportation through ABC importer HutCD

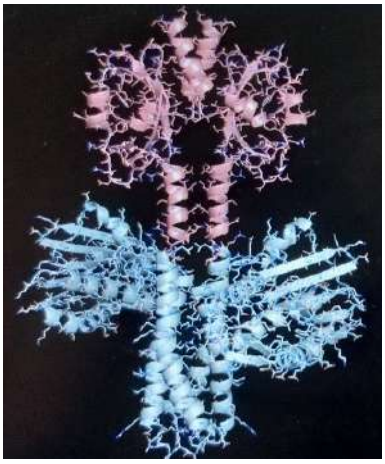


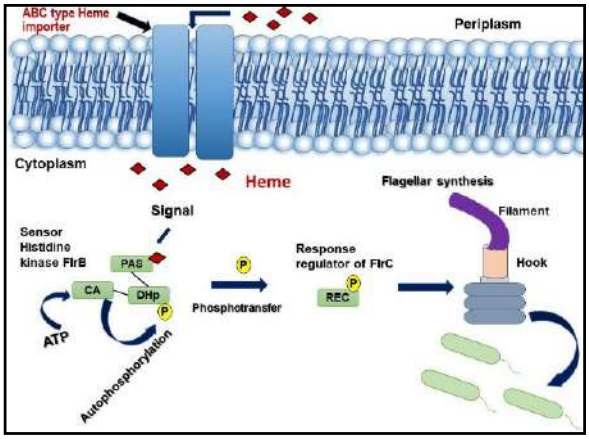
Modulation of bEBP, FlrC by ATP and c-di-GMP



c-di-GMP mediated regulation







Sensor histidine kinase FlrB involved in flagellar synthesis, binds heme as sensory signal

RECENT PUBLICATIONS (2023-24):

1. Indrila Saha, Biplab Ghosh, Jhimli Dasgupta. Structural insights into the atypical type-I ABC Glucose-6-phosphate importer VCA0625-27 of *Vibrio cholerae*. **Biochem Biophys Res Commun. 2024** Jul 5; 716:150030. doi: 10.1016/j.bbrc.2024.150030. Epub 2024 May 1.
2. Peeali Mukherjee, Shubhangi Agarwal, Sritapa Basu Mallick, Jhimli Dasgupta. PAS domain of flagellar histidine kinase FlrB has a unique architecture and binds heme as a sensory ligand in an unconventional fashion. **Structure. 2024** Feb 1; 32(2):200-216.e5. doi: 10.1016/j.str.2023.11.014. Epub 2023 Dec 28. **(This was COVER ARTICLE of February, 2024 issue).**
3. Shrestha Chakraborty, Shubhangi Agarwal, Arindam Bakshi, Sanjay Dey, Maitree Biswas, Biplab Ghosh, Jhimli Dasgupta. The N-terminal FleQ domain of the *Vibrio cholerae* flagellar master regulator FlrA plays pivotal structural roles in stabilizing its active state. **FEBS Lett. 2023** Sep; 597(17):2161-2177. doi: 10.1002/1873-3468.14693. Epub 2023 Jul 10.

Dr. Uma Siddhanta
M.Sc., Ph.D.

Fields of research experience:	Fields of Interest:
• Enzymology • Protein Structure-Function • Cell Signaling	• Immunology • Virology

Dr. Sudipa Saha
M.Sc., Ph.D.

Area of Research: Structure function studies of proteins.

RECENT PUBLICATIONS:

- Aparajita Chakraborty, Priyanka De and **Sudipa Saha**. "Structure-function relationship of α-crystallin in the context of vertebrate lens evolution and its role in eye disorders" (Review). Journal of Proteins and Proteomics, 2022. DOI: https://doi.org/10.1007/s42485-022-00101-5.
- Aparajita Chakraborty, Sayak Ganguli, Priyanka De and **Sudipa Saha**. "An insight in-to the structural analysis of α crystallin of habitat specific fish: a computational approach". Jour-nal of Proteins and Proteomics, 2022. DOI: https://doi.org/10.1007/s42485-023-00107-7.
- Aparajita Chakraborty, Sushmita Nandy, **Sudipa Saha** and Priyanka De. "An Insight on α-crystallin Interactions with Various Proteins in Systemic Disorders" (Review). Journal of Stress Physiology & Biochemistry, Vol. 19, No. 3, (2023), 35-46. ISSN 1997-0838.

Dr. Aniruddha Banerji
M.Sc., Ph.D.

Primary area of research interest: Cancer biology

Additional areas of research interest: Wildlife biology, Evolutionary biology, Environmental biology, Ecology and Epidemiology.

RECENT PUBLICATIONS:

JOURNALS (UGC-APPROVED JOURNALS)

1. I. Chakraborty, A. Roy, A. Banerji. Therapeutic Potential of Phosphatidylinositol 3' Kinase (PI3K) Inhibitors in Cervical Cancer. Science and Culture (2021) vol. 87(1-2) pp. 57-61.
2. A. Roy, I. Chakraborty, A. Banerji. Natural Compounds as Potential Regulators of the Phosphatidylinositol 3' Kinase (PI3K) Pathway in Breast Cancer. South Asian Journal of Experimental Biology (2021) vol. 11(5) pp. 524-538.
3. P. Ghoshal, A. Banerji. Looking at COVID-19 Pandemic Through the Lens of Epidemiological Transition Theory. Science and Culture (2023) vol. 89(1-2) pp. 27-32.
4. S. Sen, A. Biswas, A. Banerji. Analysis of Avian Diversity at Chintamoni Kar Bird Sanctuary: An Urban Forest Perspective. Uttar Pradesh Journal of Zoology (2023) vol. 44(12)pp. 7-15.

BOOK CHAPTERS:

1. **A. Banerji**. Endocrine Disrupting Compounds (EDCs): The Risks for Aquatic Fauna. Current Strategies in Biotechnology and Bioresource Technology Vol. 2, Ed. A. Alam, Pub: Book Publisher International (2020) pp.149-155. Print ISBN: 978-93-89816-88-4.
2. **A. Banerji**, K.K. Ganguly, A. Chatterjee. All-trans Retinoic Acid (ATRA), a Potential Inhibitor of Matrix Metalloproteinase-2 (MMP-2) and Tumour Invasion in Melanomas. Current Strategies in Biotechnology and Bioresource Technology Vol. 2, Ed. A. Alam, Pub: Book Publisher International (2020) pp.156-168. Print ISBN: 978-93-89816-88-4.
3. **A. Banerji**, P. Ghoshal. Agricultural Production and Climate Change: The Scope for Innovation in the Post-COVID 19 Scenario. Current Strategies in Biotechnology and Bioresource Technology Vol. 2, Ed. A. Alam, Pub: Book Publisher International (2020) pp.169-176. Print ISBN: 978-93-89816-88-4.
4. **A. Banerji**, P. Ghoshal. Agricultural Production and Climate Change: The Scope for Innovation in the Post-COVID 19 Scenario. Current Strategies in Biotechnology and Bioresource Technology Vol. 2, Ed. A. Alam, Pub: Book Publisher International (2020) pp.169-176. Print ISBN: 978-93-89816-88-4.
5. A. Majumder, S. Ray, **A. Banerji**. Phosphatidylinositol 3' Kinase (PI3K), A Crucial Regulator of

Epidermal Growth Factor Receptor (EGFR) Modulated MMP-2, MMP-9 and MT1-MMP Expression in Breast Cancer Cells. Recent Progress in Microbiology and Biotechnology Vol. 2, Ed. E.A. Makky, Pub: Book Publisher International (2020) pp. 165-174. Print ISBN: 978-93-90206-62-9.

6. P. Ghoshal, **A. Banerji**. Studies on Some Issues Specific to Demography during COVID-19 Pandemic. Issues and Development in Health Research Vol. 3, Ed. D.C. Sharma, Pub: Book Publisher International (2021) pp. 1-9. Print ISBN: 978-93-91595-14-2.
7. A. Roy, I. Chakraborty, **A. Banerji**. Determination of Phytochemicals as Potential Inhibitors of Matrix Metalloproteinases (MMPs) with Special Reference to Breast Cancer. Issues and Development in Health Research Vol. 5 (2021), Ed. W.M. Oo, Pub: Book Publisher International (2021) pp. 73-81. Print ISBN: 978-93-91882-30-3.
8. P. Ghoshal, **A. Banerji.** Agriculture in COVID-19 Pandemic: The Indian Perspective. New Innovations in Economics, Business and Management Vol. 8, Ed. M.D. Guillamon, Pub: Book Publisher International (2022) pp. 77-86; Print ISBN: 978-93-5547-510-7.
9. P. Ghoshal, **A. Banerji.** Forest Cover and Its Management: A Study in Indian Perspective. Novel Perspectives of Geography, Environment and Earth Sciences Vol. 9, Ed. H.L. Shrestha, Pub: Book Publisher International (2023) pp. 28-43; Print ISBN: 978-81-19491-52-0.
10. A. Roy, **A. Banerji.** Endogenous Regulators of Matrix Metalloproteinase Expression and Activity in Breast Cancers. Novel Research Aspects in Medicine and Medical Science Vol. 5, Ed. R.W. Sawadago, Pub: Book Publisher International (2023) pp. 37-49; Print ISBN: 978-81-19761-32-6.
11. I. Chakraborty, **A. Banerji**. Signalling Cascades in Melanoma: Understanding the Potential of Phytochemicals as Inhibitors. Research Perspectives of Microbiology and Biotechnology Vol. 1, Ed. E. Magiorkinis, Pub: Book Publisher International (2024) pp. 19-31; Print ISBN: 978-81-971580-1-8.

SELECTED PRESENTATIONS/ ACHIEVEMENTS FROM AB LAB

Poster Presentations:

1. A. Roy, A. Banerji. "Targeting EGFR-Mediated MMP-2 and MMP-9 Expression in Metastatic Breast Cancer Cells by Curcumin and ATRA" at 42nd Annual Conference of Indian Association for Cancer Research (IACR-2023) (International Conference) organized by Advanced Centre for Treatment, Research and Education in Cancer, Mumbai, Jan 2023.
2. I. Chakraborty, A. Banerji. "All-trans Retinoic Acid (ATRA) as an Inhibitor of Integrin α5β1 Mediated Signalling in the Murine Melanoma Cell Line B16F10" at 42nd Annual Conference of Indian Association for Cancer Research (IACR-2023) (International Conference) organized by Advanced Centre for Treatment, Research and Education in Cancer, Mumbai, Jan 2023.
3. A. Roy, A. Banerji. "Curcumin and All-trans Retinoic Acid (ATRA) As Inhibitors of Matrix Metalloproteinase Expression and Activity in Breast Cancer Cells" at Bio Colloq: One Day Conference on Inter-Disciplinary Biological Sciences (National Conference) organized by Ramakrishna Mission Vivekananda Centenary College (Autonomous), Rahara & Academy of Biodiversity Conservation, Jan 2024. **Awarded 1st prize for poster presentation.**
4. I. Chakraborty, A. Banerji. "Potential of All-trans Retinoic Acid (ATRA) For Inhibiting Cellular Signalling Pathways in Melanoma Cells" at Bio Colloq: One Day Conference on Inter-Disciplinary Biological Sciences (National Conference) organized by Ramakrishna Mission Vivekananda Centenary College (Autonomous), Rahara & Academy of Biodiversity Conservation, Jan 2024.
5. I. Chakraborty, A. Banerji. "The Role of All-trans Retinoic Acid (ATRA) as a Potential Inhibitor of Signalling Pathways in Cervical Cancers" at 8th World Cancer Congress-2024 (International Conference) organized at JNU Convention Centre, New Delhi, March 2024.

Oral Presentation:

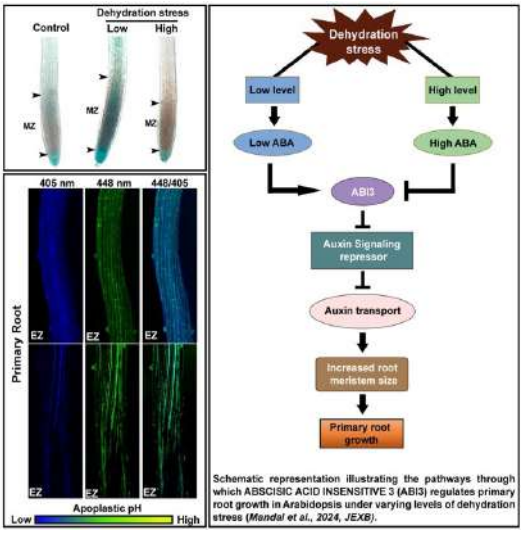
1. A. Roy, A. Banerji. "Synergistic Treatment with Curcumin and All-trans Retinoic Acid: Effects on Matrix Metalloproteinases (MMPs) in Metastatic Breast Cancer Cells" at 8th World Cancer Congress-2024 (International Conference) organized at JNU Convention Centre, New Delhi, March 2024.

Dr. Ronita Nag Chaudhuri
M.Sc., Ph.D.

RESEARCH INTEREST:

Investigating the genetic and epigenetic regulatory mechanisms involved in developmental and environmental signaling:

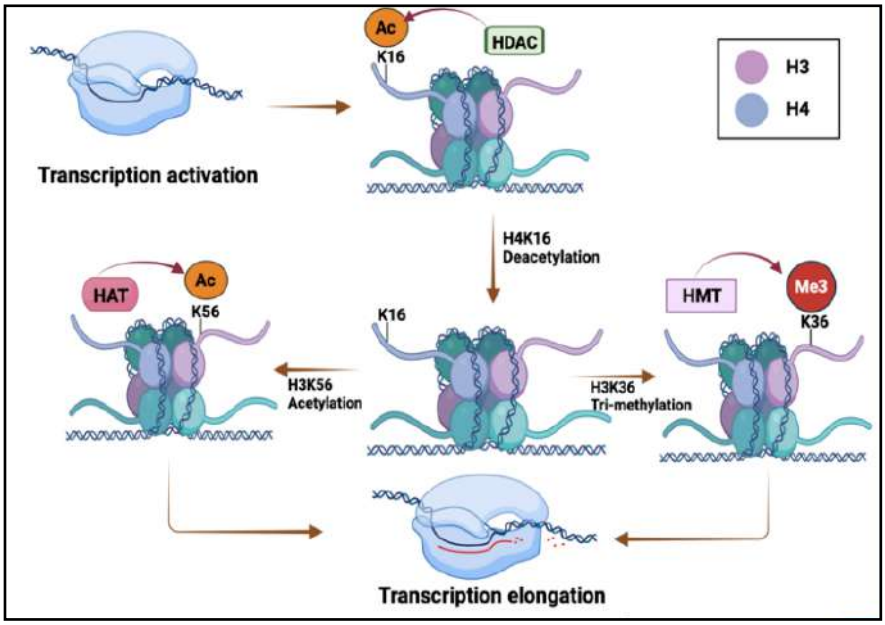
- Cross talk between hormone signaling pathways in modulation of root system architecture.
- Genetic and epigenetic regulation of root system architecture and its modulation in response to abiotic stress signals.
- Transgenic approach to improve quality traits for better adaptation to stress conditions.



Schematic representation illustrating the pathways through which ABSCISIC ACID INSENSITIVE 3 (ABI3) regulates primary root growth in Arabidopsis under varying levels of dehydration stress (*Mandal et al., 2024, JEXB*).

Investigating chromatin modifications during transcriptional regulation and DNA damage repair pathway:

- Decoding the crosstalk between acetylation of histone residues during DNA templated processes in-cluding transcription and DNA damage repair.
- Understanding the correlation between histone methylation and acetylation during transcription regu-lation and gene looping.



RECENT PUBLICATIONS:

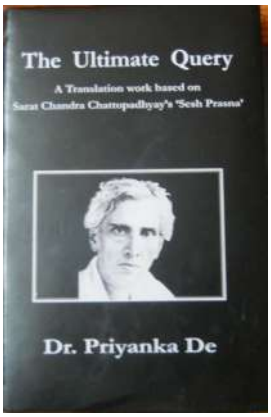
1. **ABI3 promotes auxin signaling by regulating SHY2 expression to control primary root growth in response to dehydration stress.** Drishti Mandal, Saptarshi Datta, Sicon Mitra and Ronita Nag Chaudhuri*. **Journal of Experimental Botany (2024)** DOI: 10.1093/jxb/erae237.
2. **RNA Polymerase II dependent crosstalk between H4K16 deacetylation and H3K56 acetylation promotes transcription of constitutively expressed gene.** Preeti Khan, Priyabrata Singha and Ro-nita Nag Chaudhuri*. **Molecular and Cellular Biology (2023)** DOI: 10.1080/10985549.2023.2270912.
3. **RAV1 mediates cytokinin signalling for regulating primary root growth in Arabidopsis.** Drishti Mandal, Saptarshi Datta, Giridhar Raveendar, Pranab Kumar Mondal and Ronita Nag Chaudhuri*. **The Plant Journal (2022)** DOI: 10.1111/tpj.16039.
4. **Acetylation of H3K56 orchestrates UV-responsive chromatin events that generate DNA accessi-bility during Nucleotide Excision Repair.** Preeti Khan and Ronita Nag Chaudhuri*. **DNA Repair (2022)** DOI: https://doi.org/10.1016/j.dnarep.2022.103317.
5. **DNA methylation and regulation of gene expression: Guardian of our health.** Invited Review as a part of Special Thematic Issue. Gaurab Aditya Dhar, Shagnik Saha, Parama Mitra and Ronita Nag Chaudhuri*. **The Nucleus (2021)**, DOI: 10.1007/s13237-021-00367-y.
6. **Deacetylation of H4 lysine16 affects acetylation of lysine residues in histone H3 and H4 promotes transcription of constitutive genes.** Anagh Ray, Preeti Khan and Ronita Nag Chaudhuri*. **Epigenetics (2020)**, DOI: 10.1080/15592294.2020.1809896.
7. **ABI3 plays a role in de-novo root regeneration from Arabidopsis thaliana callus cells.** Sourabh Sengupta and Ronita Nag Chaudhuri*. **Plant Signaling & Behavior (2020)** DOI:10.1080/15592324.2020.1794147.
8. **ABI3 mediated repression of RAV1 gene expression promote efficient dehydration stress response in Arabidopsis thaliana.** Sourabh Sengupta, Anagh Ray, Dristhi Mandal and Ronita Nag Chaudhuri*. **BBA Gene Regulatory Mechanism (2020)**, 1863(9):194582 DOI: 10.1016/j.bbagrm.2020.194582.

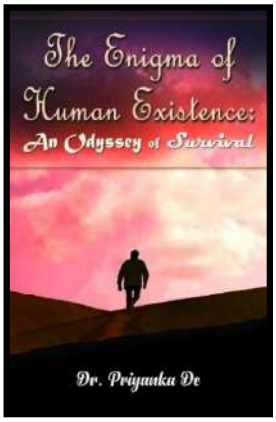
Dr. Priyanka De
M.Sc., Ph.D.

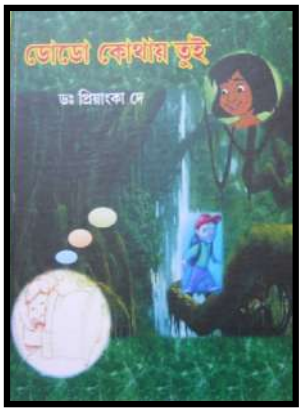
Area of expertise: Physiology, Animal Biology, Metabolism, Genetics, Ecology, Evolution & Behaviour.

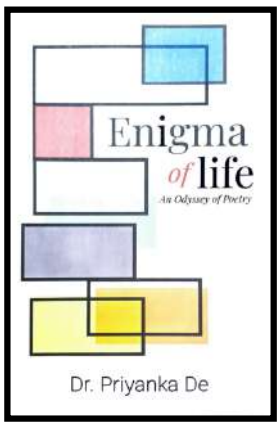
BOOKS PUBLISHED:

- 'The Ultimate Query', A translation work based on Sarat Chandra Chattopaddhya's Sesh Prasna (ISBN: 978-93-83548-89-7). January 2016.
- 'Dodo Kothai Tui', a Bengali storybook for Children (ISBN: 978-93-84184-41-4). December 2016.
- 'The Enigma of Human Existence: An Odyssey of Survival' (ISBN 978-81-940456-4-9). April 2019.
- 'Bigyaaner Antoraale', A collection of Bengali scientific articles (ISBN: 978-93-84184-87-2). August 2021.
- 'Enigma of life: An Odyssey of Poetry' (ISBN: 978-93-94035-83-6). January 2024.









Dr. Souvik Roy

M. Sc., M. Phil., Ph. D.

AWARDS & RECOGNITIONS:

- B.Sc. [1st Class 1st; Gold-Medalist]
- M.Sc. [1st Class 1st; Gold-Medalist]
- 'Microbiologist Society Best Teacher' & 'Bharat Jyoti Puraskar' Awardee [National-Level Awards].

PUBLICATIONS

PAPERS IN UGC-CARE APPROVED JOURNALS

1. **Roy, S.**, Mukherjee, P., Kundu, S., Majumder, D. & Raychaudhuri, V. (2024). Microbial Infections in Burn Patients. **Acute and Critical Care.** 39(2): 214-225. doi: 10.4266/acc.2023.01571. [ISSN (Print): 2586-6052; ISSN (Online): 2586-6060; Impact Factor = 1.7].

2. Das, M., Chakraborty, M., Das, P., Santra, S., Mukherjee, A., Das, S., Banyai, K., **Roy, S**., Choudhury, L., Gupta, R., Dey, T., Das, D., Bose, A., Ganesh, B. & Banerjee, R. (2024). System biology approach-es for systemic diseases: Emphasis on type II diabetes mellitus and allied metabolism. **Biocatalysis and Agricultural Biotechnology (Elsevier)** 58:103176. doi: 10.1016/j.bcab.2024.103176. [ISSN (Online): 1878-8181; Impact Factor = 4.0].

3. **Roy, S.**, Ray, D., Laha, I., & Choudhury, L. (2024). Human Mycobiota and Its Role in Cancer Progression, Diagnostics and Therapeutics: A Link Lesser-Known. **Cancer Investigation (Taylor & Francis).** 1-19. doi: 10.1080/07357907.2024.2301733. [ISSN (Print): 0735-7907; ISSN (Online): 1532-4192; Impact Factor = 2.4].

4. Bhattacharjee, A., Naga, R., Saha, M., Karmakar, S., Pal, A. & **Roy, S.** (2023). Viral inhibitory potential of hyoscyamine in Japanese encephalitis virus-infected embryonated chicken eggs involving multiple signaling pathways. **Archives of Virology (Springer)** 168:264. doi: 10.1007/s00705-023-05883-7. [ISSN (Print): 0304-8608; ISSN (Online): 1432-8798; Impact Factor = 2.7].

5. **Roy, S.** (2023). Assessing Public Health and Sanitation Status To Promote Preventive Healthcare In India. **International Journal of Biotechnology and Allied Fields** 11(10):105-116 [ISSN (Online): 2320-0774].

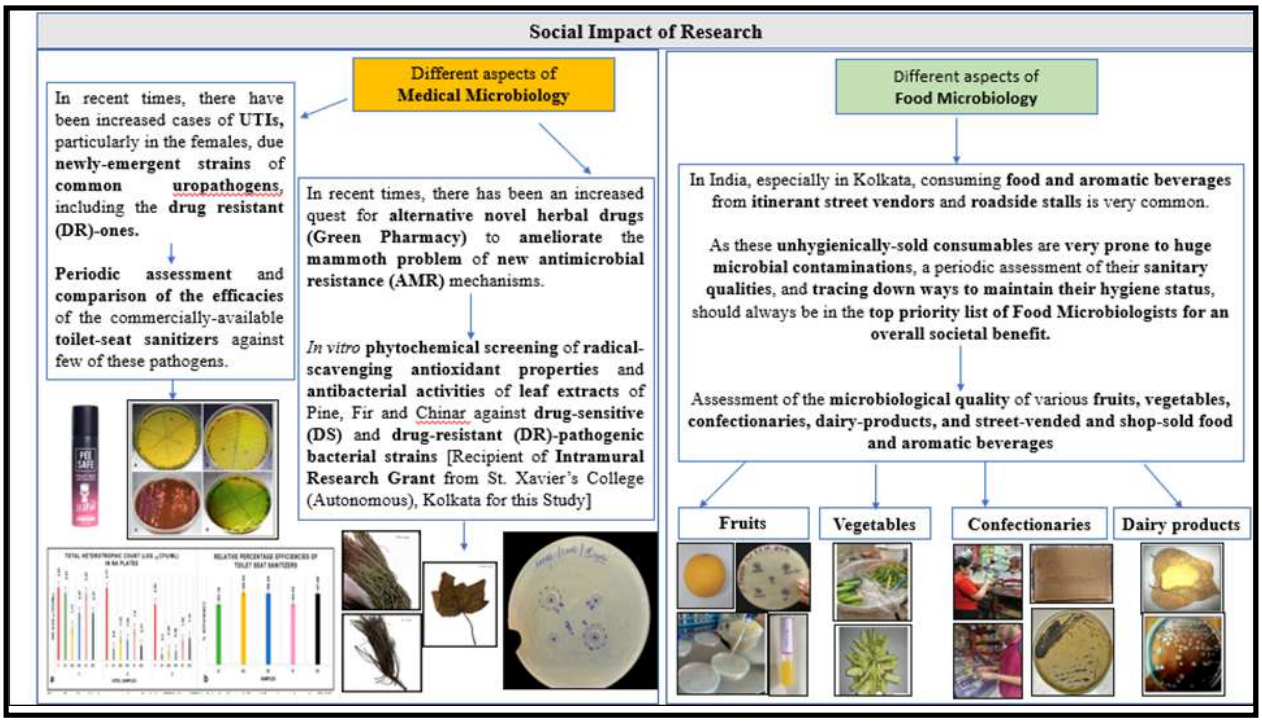
6. **Roy, S**., Majumder, S., Deb, A., & Choudhury, L. (2023). Microbial contamination of cosmetics and the pharmaceutical products, and their preservation strategies: A comprehensive review. *Novel Research in Microbiology Journa***l** 7(5):2116-2137 [ISSN (Print): 2537-0286; ISSN (Online): 2537-0294; Impact Factor = 1.3].

7. **Roy, S**., Manna, S., Chowdhury, S., & Choudhury, L. (2023). Improvement of Large-Scale Production of Lignocellulosic Bioethanol through Synthetic Biology Approaches: A Comprehensive Review. **World Journal of Biology Pharmacy and Health Sciences** 14:316-331 [ISSN (Online): 2582-5542].

8. **Roy, S**., Shaw, D., Sarkar, T., & Choudhury, L. (2023). Mycotoxins in fermented foods: A comprehensive review. *Novel Research in Microbiology Journal* 7(2):1897-1917 [ISSN (Print): 2537-0286; ISSN (Online): 2537-0294; Impact Factor = 1.3].
9. **Roy, S**., Chakrabarty, S., Pal, R. and Choudhury, L. (2023) Combating SARS-CoV-2: A Comparison between mRNA Vaccines and Killed Whole Cell Vaccines. **International Journal of Biology, Pharmacy and Allied Sciences** 12(4):1781-1798 [ISSN (Online): 2277-4998; Impact Factor = 1.892].
10. **Roy, S.**, Mullick, S., Chakrabarty, S. and Choudhury, L. (2023) Pathogen-based Molecular Mimicry and Autoimmune Disorders: A Close Look. International Journal of Biology, Pharmacy and Allied Sciences 12(4):1701-1716 [ISSN (Online): 2277- 4998; Impact Factor = 1.892].
11. **Roy, S.,** Banerjee, S., Bhowmick, P. and Choudhury, L. (2023) Psychobiotics: Deciphering its role in neuropsychiatry. World Journal of Biology Pharmacy and Health Sciences 13(01):457–464 [ISSN (Online): 2582-5542].

BOOK CHAPTERS

1. **Roy, S.**, Sarkar, S., and Choudhury, L. (2024) **"Bacteria & Cosmetics – the 'Industry' connect!"** Current Advances in Microbiology. **Vijaygarh Jyotish Ray College (in association with the Microbiologists Society of India)** (Ed. Saha Kesh Gargi). Pp 136-149 [ISBN (Print): 978-81-969267-6-2].
2. **Roy, S.**, Manna, S., Chowdhury, S., and Choudhury, L. (2024) Ways of Improvement: A step ahead towards improved cellulosic ethanol production. Biofuels: Scientific Explorations and Technolo-gies for a Sustainable Environment. **CRC Press, Taylor & Francis** (Ed. Banik Samudra Prosad & Bagchi Debasis). Edn 1. [ISBN 9781003350606, https://doi.org/10.1201/9781003350606].
3. **Roy, S.**, Bhowmick, P., Banerjee, S., Choudhury, L. and Mukherjee, A. (2024) Neuropsychiatric applications of psychobiotics. Developments in Applied Microbiology and Biotechnology, Microbial Essentialism. **Academic Press, Elsevier** (Ed. Sarsan Sreedevi) Pages 301-315 [ISBN 9780443139321, https://doi.org/10.1016/B978-0-443-13932-1.00002-7].



Outreach Activities

Dr. Sayak Ganguli
M. Sc., Ph. D

ACADEMIC INTERESTS:

I am a biologist, with background in Plant Biology, specialization in Plant Tissue Culture; Cytogenetics, Bioinformatics, Computational Biology, Genomics and Ethnomedicine.

ACADEMIC ACHIEVEMENT AND AWARDS [PERSONAL]

1. Aurobindo Guha Life Science Endowment (GOLD MEDAL) for Highest marks in B.Sc. Examination (2003).
2. DST Award for invited lecture at Next Generation Sequencing Congress Asia (2012) at Singapore.
3. Selected and participated as an Early Career Researcher in the Newton Bhabha Researchers Link Workshop titled "Building Ecological Resilience in Vulnerable Mangroves of the Indian Sundarbans: Sustainable and Equitable Management of Biodiversity and Ecosystem Services in the era of Climate Change" jointly orga-nized by WBSU, INDIA and NEWCASTLE UNIVERSITY, UK funded by DBT – GoI and British Council held in Indian Sunderbans from 2nd to 6th January 2022.
4. Served as Organizing Committee Member of the Professional Scientific Development Program, organised by St. Xavier's, College (Autonomous), from 23rd to 30th November 2022; under RUSA and DBT Star College Scheme.
5. Best Presenter Award (Science Group) in the FIP -12 conducted by UGC - HRDC, North Bengal University (3rd January to 6th February 2022).
6. Served as Course Coordinator for the two-day workshop on Gut Microbiome Analysis for Anthropological Survey of India, Government of India personnel on the 13th and 14th of June 2023.
7. Served as Convener for the first International Symposium on Biotechnology (ISBT 2023), organized by the Postgraduate and Research Department of Biotechnology on the 12th and 13th of October 2023.

ACHIEVEMENTS FROM SGLAB: [STUDENT ACHIEVEMENTS]

1. BEST POSTER AWARD (UG and PG students' category): Arunima Bhattacharya @ ICCCGC, Kolkata.
2. 3rd Prize in Poster (Research Scholar Category): Sarmishta Mukhopadhyay @ ICCCGC, Kolkata.
3. Second Prize in Young Researcher (s) Category: Nabarun Dawn and Souptik Ghosh @ ICCCGC,Kolkata.
4. Judges' Special Appreciation Award. "Creating a Mangrove endophyte bacterial collection for targeted genome editing. International Seminar and Workshop on CRISPR/Cas-based Plant Functional Genomics & Computational Modelling, organised by CSIR – North East Institute of Science and Technology, Jorhat, Assam (17th to 21st January 2023): Gaurab Aditya Dhar.

5. Souradip Basu presented a paper titled "Insights into the gut, dietary practices and subsistence patterns from an Indian foothill tribe at Students Conference on Conservation Science (SCCS2023) in University of Cam-bridge; 28th to 30th March 2023.

PUBLICATIONS (2023-2024):

1. Mukhopadhyay, S., Singh, M., Ghosh, M. M., Chakrabarti, S., & Ganguli, S. (2024). Comparative Genomics and Characterization of Shigella flexneri Isolated from Urban Wastewater. Microbes and environments, 39(2), ME23105. https://doi.org/10.1264/jsme2.ME23105.
2. Samanta, D., Das, D., Sinha, S., Mallick, B., Banerjee, R., Ganguli, S., & Roy, D. (2023). Transcriptome analysis reveals upregulated secondary metabolite pathways in micropropagated Lawsonia inermis L. Vege-tos, 36(3), 1130-1138. https://doi.org/10.1007/s42535- 023-00613-5.
3. Bhattacharya, A., Bhowmick, P., Ganguli, S., & Mitra, A. K. (2023). Evolutionary Insights into the Enzymes involved in the Biosynthesis of the Volatile Organic Compounds Isoprene and Pinene in Plants. Plant Sci-ence Today, 10(2), 253-262. https://orcid.org/0000-0001-5481-7436.
4. Bhowal, P., Roy, B., Ganguli, S., Igloi, G. L., & Banerjee, R. (2023). Elucidating the structure-function attributes of a trypanosomalarginyl-tRNA synthetase. Molecular and Biochemical Parasitology, 256, 111597. https://doi.org/10.1016/j.molbiopara.2023.111597.
5. Mukhopadhyay, M., Mukherjee, A., Ganguli, S., Chakraborti, A., Roy, S., Choudhury, S. S.,& Mitra, A. K. (2023). Marvels of Bacilli in soil amendment for plant-growth promotion toward sustainable development having futuristic socio-economic implications. Frontiers in microbiology, 14, 1293302. https://doi.org/10.3389/fmicb.2023.1293302.
6. Ganguly, K., Dutta, T., Ganguli, S., & Sengupta, M. (2023). Common structural attributes of tyrosinase variants are unlikely to determine differential retentions within endoplasmic reticulum: a homology model-ling study with 45 variants. Proceedings of the Indian National Science Academy, 89(4), 825-836. https://doi.org/10.1007/s43538-023-00196-4.
7. Das, D., Mallick, B., Sinha, S., Ganguli, S., Samanta, D., Banerjee, R., & Roy, D. (2023). Unearthing the inhibitory potential of phytochemicals from Lawsonia inermis L. and some drugs against dengue virus pro-tein NS1: an insilico approach. Journal of Biomolecular Structure and Dynamics, 1-18. https://doi.org/10.1080/07391102.2023.2298730.
8. Dhar, G. A., Chaudhuri, D., Mallick, B., & Ganguli, S. (2024). Insights into economically important endo-phytic and rhizospheric bacteria of true mangroves of Indian Sundarbans using high throughput mapping. In H. Sarma., S. Joshi (Eds.), Biotechnology of Emerging Microbes (pp. 299-325). Academic Press. https://doi.org/10.1016/B978-0-443-15397-6.00015-2.
9. Singh, M., Karmakar, R., Ganguli, S., & Ghosh, M. M. (2023). Metagenomics-Based Characterization of Microbial Diversity across Industrial Waste Dumping Sites. In S. Dey (Eds.), Biohydrometallurgical Processes: Metal Recovery and Remediation(pp. 90-107). CRC Press. eBook ISBN: 9781003451457.
10. Sarkar, M., Mondal, M., Bhattacharya, D., Basu, S., Mitra, A. K., & Ganguli, S. (2023). Computational modeling for exploring the therapeutic repertoire of lantibiotics. In S. Joshi., R. K. Kar., D. Lahiri., M. Nag (Eds.), Lantibiotics as Alternative Therapeutics (pp. 337-352). Academic Press. https://doi.org/10.1016/B978-0-323-99141-4.00012-6.
11. Chakravarty, D., Bhattacharya, D., Ganguli, S., & Ghosh, U. D. (2023). Targeting microbial biofilms using genomics-guided drug discovery. In H. Sarma., S. Joshi., D. Lahiri., R. R. Ray., M. Davoodbasha (Eds.), Microbial Biofilms: Challenges and Advances in Metabolomic Study (pp. 315-324). Elsevier. https://doi.org/10.1016/B978-0-323-95715-1.00020-0.

Dr. Arindam Bakshi
M.Sc., Ph.D.

RESEARCH INTEREST

Primary area of Research interests: Molecular Plant Virology:

1. Structure-function relationship of plant viral proteins and domains in viral replication, genome encapsidation and cell to cell movement.
2. Functional characterization of plant viral RNA dependent RNA polymerase (RdRp) in vitro and in vivo.
3. Use of proteomic approaches to identify interaction partners of viral RdRp and novel host factors in viral replication.

Additional area of Research interest:

1. Structural studies of Plant viral RdRp and its complexes using X-ray crystallography and cryo- electron microscopy.
2. Engineering of plant viral coat proteins as nano particles (VNPs) or virus like particles (VLPs) for intra-cellular delivery of therapeutic antibodies.
3. Subcellular localization of antibody tagged VNPs/VLPs inside mammalian cells and elucidation of bio-chemical pathways involved in antibody delivery.

RESEARCH EXPERIENCE

1. Postdoctoral Research Fellow in National Centre for Biological Sciences, Bangalore (May 2019-July 2019).
2. Postdoctoral Research Fellow in Iowa State University, USA (March 2020-Oct 2021).

PUBLICATIONS/BOOK CHAPTERS:

1. **Bakshi, A**., Sridhar, S., Sistla, S., Savithri, H.S., 2019. Interaction of the intrinsically disordered C-terminal domain of the sesbania mosaic virus RNA-dependent RNA polymerase with the viral protein P10 in vitro: modulation of the oligomeric state and polymerase activity. Archives of virology 164, 971-982. https://doi.org/10.1007/s00705-019-04163-7.
2. **Bakshi, A.**, Savithri, H.S., 2019. Functional insights into the role of C-terminal disordered domain of Ses-bania mosaic virus RNA dependent RNA polymerase and the coat protein in viral replication in vivo. Vi-rus Research 267, 26-35. https://doi.org/10.1016/j.virusres.2019.05.003.
3. Dev, B., **Bakshi A.** and B. Paramasivan (2022). "Prospects of utilizing seawater as a reaction medium for pretreatment and saccharification of rice straw." Chemosphere 293: 133528.
4. Wijeratne, S., **Bakshi, A.**, Talbert, J. (2022). Comparative Analysis of NanoLuc Luciferase and Alkaline

Phosphatase Luminescence Reporter Systems for Phage-Based Detection of Bacteria. Bioengineering 9, 479. https://doi.org/10.3390/bioengineering9090479.

5. Chakraborty S, Agarwal S, **Bakshi A**, Dey S, Biswas M, Ghosh B, Dasgupta J. (2023). The N- terminal FleQ domain of the Vibrio cholerae flagellar master regulator FlrA plays pivotal structuralroles in stabilizing its active state. FEBS Lett. doi: 10.1002/1873-3468.14693. Epub ahead of print.PMID: 37402215.
6. Dev, B., **Bakshi, A.**, Kar, S. et al. (2023). Evaluation of potent marine ligninolytic bacteria and its efficiency in seawater-based delignification. Biomass Conv. Bioref. https://doi.org/10.1007/s13399-023-04731-7.

MEMBERSHIP OF SCIENTIFIC SOCIETIES

- Graduate student member of the Protein Society (https://www.proteinsociety.org/).

Dr. Ditipriya Hazra

M.Sc., Ph.D.

AREA OF RESEARCH:

- Investigating the role of epitranscriptomic modulators in methylation dependent RNA degradation using X-ray crystallography.
- Structure guided drug designing and deciphering protein-drug interaction by molecular dynamics simulation

PUBLICATIONS (2020-2023)

- Ganguly, M., Gupta, R., Roychowdhury, A. and Hazra, D., 2023. De novo drug designing coupled with brute force screening and structure guided lead optimization gives highly specific inhibitor of METTL3: a potential cure for Acute Myeloid Leukaemia. Journal of Biomolecular Structure and Dynamics, pp.1-14.
- Manna, S., Samal, P., Basak, R., Mitra, A., Roy, A.K., Kundu, R., Ahir, A., Roychowdhury, A. and Hazra, D., 2023. Amentoflavone and methyl hesperidin, novel lead molecules targeting epitran-scriptomic modulator in acute myeloid leukemia: in silico drug screening and molecular dynamics simulation approach. Journal of Molecular Modeling, 29(1), p.9.
- Mitra, A., Manna, S., Kundu, R., Hazra, D. and Roychowdhury, A., 2023. Brute Force Virtual Drug Screening with Molecular Dynamics Simulation and MM/PBSA to Find Potent Inhibitors of METTL16. IEEE/ACM Transactions on Computational Biology and Bioinformatics.
- Hazra, D. and Roychowdhury, A., 2022. Protein-Based Nanostructures. Nanomaterials in Clinical Therapeutics: Synthesis and Applications, pp.269-283. (Book chapter)

DEPARTMENT AT A GLANCE

RESEARCH SCHOLARS

Peeali Mukherjee
DST-INSPIRE Fellow
PI: Dr. Jhimli Dasgupta

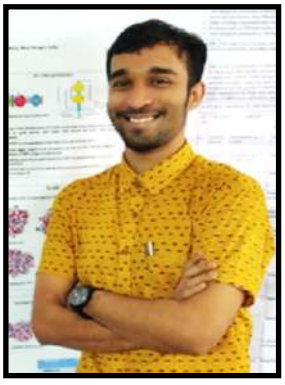
Indrila Saha
CSIR SRF
PI: Dr. Jhimli Dasgupta

Ruchira Das
DST-INSPIRE Fellow
PI: Dr. Jhimli Dasgupta

Arnab Pal
MHRD-STARS Fellow
PI: Dr. Jhimli Dasgupta

Sushmita Nandy
SVMCM Fellow
PI: Dr. Sudipa Saha
Co-PI: Dr. Priyanka De,
Dr. Srabani Karmakar

Aparajita Chakraborty
SVMCM Fellow
PI: Dr. Sudipa Saha
Co-PI: Dr. Priyanka De



Anirban Roy
SVMCM Fellow
PI: Dr. Aniruddha Banerji

Indira Chakraborty
SVMCM Fellow
PI: Dr. Aniruddha Banerji

Drishti Mandal
CSIR Direct Fellow, SRF
PI: Dr. Ronita Nag Chaudhuri

Saptarshi Datta
CSIR-Net Fellow, SRF
PI: Dr. Ronita Nag Chaudhuri

Priyabrata Singha
DBT Project Fellow
PI: Dr. Ronita Nag Chaudhuri

Sicon Mitra
SERB Project Fellow
PI: Dr. Ronita Nag Chaudhuri

Swarnavo Chakraborty
CSIR-NET Fellow, JRF
PI: Dr. Ronita Nag Chaudhuri

Sarmishta Mukhopadhyay
WB-DST Fellow
Thesis Submitted (2024)
PI: Dr. Sayak Ganguli
Co-PI: Dr. Santanu Chakrabarti

Souradip Basu
WB-DST Fellow
Thesis Submitted (2024)
PI: Dr. Sayak Ganguli,
Dr.Mahasweta Mitra Ghosh
Co-PI: Dr. Subrata Sankar Bagchi

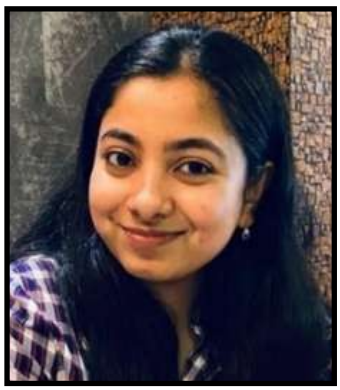
Rupsha Karmakar
PI: Dr. Sayak Ganguli, Dr. Mahasweta Mitra Ghosh

Wrick Chakraborty
IPCR Fellow
PI: Dr. Sayak Ganguli
Co-PI: Dr. Partha Sarathi Bhattacharya

Debava Chaudhuri
DBT-JRF
PI: Dr. Sayak Ganguli

RESEARCH SCHOLARS – Ph. D AWARDED (2018-2024)

Dr. Shubhangi Agarwal
PI: Dr. Jhimli Dasgupta
Ph. D Awarded: 2018
Current Position: Postdoctoral fellow, Weill Cornell Medicine, Department of Anesthesiology, NY 10065



Dr. Shrestha Chakraborty
PI: Dr. Jhimli Dasgupta
Ph. D Awarded: 2023
Current Position: Postdoctoral Research Associate, University of Cambridge, UK

Dr. Aheli Majumder
PI: Dr. Aniruddha Banerji
Ph. D Awarded: 2022
Current Position:
Guest faculty at Scottish Church College, Kolkata and Milli Al-Ameen College for Girls, Kolkata.

Dr. Sonia Bedi
PI: Dr. Ronita Nag Chaudhuri
Ph. D Awarded: 2018 Current Position: Genomic Informatics coordinator · Dartmouth Hitchcock Medical Center and Clinics. Bellevue, Washington, USA.

Dr. Anagh Ray
PI: Dr. Ronita Nag Chaudhuri
Ph. D Awarded: 2021
Current Position: Post-Doctoral Fellow, National Cancer Institute, NIH, Bethesda, MD, USA.

Dr. Sourabh Sengupta
PI: Dr. Ronita Nag Chaudhuri
Ph. D Awarded: 2022
Current Position: Post-Doctoral Fellow, Levy Lab, University of Wyoming, USA.

Dr. Preeti Khan
PI: Dr. Ronita Nag Chaudhuri
Ph. D Awarded: 2024
Current Position: Post-Doctoral Fellow, University of Texas Southwestern Medical Centre, USA

Dr. Meesha Singh
PI: Dr. Sayak Ganguli, Dr. Mahashweta Mitra Ghosh
Ph. D Awarded: 2023
Current Position: Postdoctoral Fellow, Jadavpur University, Kolkata

TEACHING FACULTY

SUPPORT STAFF

CHIASMA 2024 COMMITTEE

FIRST YEAR

SECOND YEAR

THIRD YEAR

FOURTH YEAR

FIFTH YEAR


Departmental
Diaries

STUDENT ACHIEVEMENTS

SEMESTER 3

1. Pramita Chatterjee: 1st in Innovation Hub, Sigma 2024; On campus Hult Prize 2024 Finalist.

2.Shreya Mukhopadhyay: 1st in Basketball tournament for XPL 2024.

3. Ritisha Chakraborty: 1st in Creative Writing in Literaria, Xavotsav 2024.

4. Ritoja Paria: 1st in Innovation Hub, Sigma 2024; On campus Hult Prize 2024 Finalist.

5. Adri Garai : 2nd in Digital poster making, Sigma'24; 3rd in Poster making, Bodhon 2024

6. Samadrita Shaw: 2nd in Table tennis (Mixed Doubles Event) in XPL 2024.

7. Prapti Gargari: 2nd in Digital poster making, Sigma 2024.

SEMESTER 5

1. Lajbarna Mandal: Solo vocals, first runner's up, Xavotsav 2024.

2. Saksham Arya Deo: 1st in Tug of War, Khel7 2024.

3. Srabonti Chattopadhyay: Publication in Pebbles (Ed.16) 2024

4. Shreyan Ghosh : Runners Up, MELAS quiz , Xavostav 2024; Third Position, Sports Quiz, Quizzophrenia 2024, IEM Kolkata; Runners Up, Enquesta 2024; MTIM'23, BioQuiz, Winner

5. Namit Ghosh: Cofradia 2024 (1st, Badminton doubles, 1st , Badminton mixed doubles, 1st , Table tennis singles, 1st, Table tennis doubles, 2nd, Tug of war.

6. Jishnu Chatterjee and Sayan Das: 2nd Runners up at Scientia Venari, Sigma 2024.

SEMESTER 7

1. Debdeep Chattopadhyay, Pratyusha Saha, Triyan Bhattacharjee, Srijani Roychowdhury: 1st Position at Inter College State Level Model Presentation at SN Bose Institute, Kolkata.

2. Debdeep Chattopadhyay: Best Poster, 1st Position at International Conference on Advancing Science and Technologies in Health Science (IEM-HEALS 2024)

3. Subham Sarkar, Dyutishmita Bhattacharjee and Heeya Gupta: Semifinalists, STHIRA Sustainable Food Innovation Challenge 2024,.

4. Saranya Dattaray, 3rd position : Mixed media art - fine arts, Xavostav 24

SEMESTER 9

1. Dattatreya Roy: Winner, PosterPedia (Poster Presentation), Sigma 2024; Journal Publication (Future Journal of Pharmaceutical Sciences), Feb 2024; Joint CSIR-NET All Indian Rank 122 (JRF qualified).

2. Dayeeta Bera: Winner, PosterPedia (Poster Presentation), Sigma 2024; Journal Publication (Future Journal of Pharmaceutical Sciences), Feb 2024.

3. Ranit Sarkar: Book chapter Publication (Enzyme Biotechnology for Environmental Sustainability, Elsevier); GATE XL All Indian Rank 130; Joint CSIR-NET All Indian Rank 164 (JRF qualified).

4. Nandini Jaiswal: Book chapter Publication (Enzyme Biotechnology for Environmental Sustainability, Elsevier)

5. Soham Mallick: Summer Research Fellowship program 2024, Indian Academy of Sciences.

6. Sakshi Angela John: Summer Research Fellowship program 2024, Indian Academy of Sciences.

7. Dibyanshu Shaw: 2nd prize, PosterPedia (Poster Presentation), Sigma 2024; 2nd prize in business pitch event Innovation Hub, Start-up idea 'Ecocast', Sigma 2024; 3rd prize in Model-Making Competition Eureka, Sigma 2024.

8. Tiyas Sarkar: 2nd prize, PosterPedia (Poster Presentation), Sigma 2024; 2nd prize in business pitch event Innovation Hub, Start-up idea 'Ecocast', Sigma 2024; 3rd prize in Model-Making Competition Eureka, Sigma 2024.

9. Vidhi Dhanuka: 2nd prize in business pitch event Innovation Hub, Start-up idea 'Ecocast', Sigma 2024; 3rd prize in Model-Making Competition Eureka, Sigma 2024.

10. Anindya Ghosh: 2nd prize, PosterPedia (Poster Presentation), Sigma 2024.

11. Abantika Samanta: 3rd prize in Model-Making Competition Eureka, Sigma 2024.

12. Koyena Nandi: 3rd prize in Model-Making Competition Eureka, Sigma 2024.

Industrial Visit to the Diamond Beverages (P) Limited

SEMESTER 3

Professors in charge

Dr. Souvik Roy and Dr. Arindam Bakshi

The Post Graduate and Research Department of Biotechnology, at St. Xavier's College (Autonomous), Kolkata had organized an industrial visit to the Diamond Beverages (P) Limited (DBPL), located in Taratala on 4th June, 2024. Ever since the establishment of Diamond Beverages Pvt Ltd in 1995, it serves as one of the leading bottling partners of The Coca-Cola Company in Kolkata. DBPL has established itself as a prominent player in India's beverage market since re-entering in 1993. With a team of over 1800 dedicated employees, DBPL has been committed to foster a culture of integrity, loyalty, and excellence. The company serves consumers through 50000 outlets. The company's constant effort and dedication enables them to move forward providing large varieties of soft drinks (like Coke, Thums-Up, Sprite, Fanta and Limca), water, juices (like Maaza and Minute Maid juices) and other hydration solutions. The organization has over 30 years of experience. It remains the most trusted by thousands of retailers and distributors in the city. We were highly obliged to have been provided the opportunity to experience and view the manufacturing of the beverages in front of our eyes. The manufacturing process starts with the water treatment. This is the most important step to prevent any contamination of the beverage. The next step is cleaning of the glass bottles or blow molding of the preforms of the desired design of the Polyethylene Terephthalate (PET) bottles. The next step is manufacturing of the beverage. This step is followed by the filling step. The bottles are labeled in the next step. They are plastic wrapped and these bottles are kept in the storage for two days for quality check. They are then released in the market. The company explained us about the concept of traceability. Traceability is the company's ability to trace back the products from the market in case of any problem.The visit played integral role as a practical platform for us to apply the theoretical knowledge we had acquired in the classroom. It bridged the gap between textbook learning and real-life applications within the beverage industry. This experience allowed us to comprehend the tangible implementation of the academic concepts, resulting in a comprehensive and profound understanding of the subject matter.The visit provided us a window for potential career paths. By directly observing the roles and responsibility of professionals in departments such as manufacturing, quality control, research and development, we gained valuable insights. This experience will help us make informed decisions regarding their future career paths.Throughout the visit, we confronted with real-life challenges and problem solving scenarios relevant to the Beverage Industry. By observing the efficiency of the production process, we students honed our problem-solving skills. These skills will definitely prove to be valuable in our professional careers. We were encouraged to pose questions and seek clarifications. These interactive sessions improved our understanding and enriched us with hands-on learning experience.The visit afforded students a unique opportunity to interact with industry experts, including departmental supervisors. This helped us to exchange knowledge and insights to create valuable networking opportunitiesfor securing internships, job opportunities and mentorship in the future.

Industrial Visit To The East India Pharmaceutical Works Limited, Kolkata

SEMESTER 5

Professors in charge

Dr. Souvik Roy and Dr. Arindam Bakshi

We, the students of Semester 5, got the wonderful opputunity to visit and experience the whole facility of East India Pharmaceutical Works Limited (EIPW), Kolkata on the 31st of August, 2024 for an industrial visit as specified in our curriculum. The aforementioned industry is one of the oldest pharmaceutical companies in India. This industry was established on 27th April, 1936 by Late Asoke Kumar Sen and he was

then later on accompanied by Late Hirendra Nath Duttagupta and together they laid the foundation of EIPW. The objective of the EIPW was "to develop, through private entrepreneurship, an organization to synthesize modern drugs from basic chemicals and cater to the needs of millions." Throughout all these years EIPW has proved its excellence in continuous research and its development and formulations of new medicines and products. They have been formulating new antibiotics, anti-fungal, analgesics, anti-pyretic and anti-diabetic, etc. formulations and slowly it also moved toward the formulation of ayurvedic medicines and products along with these. Some of the most popular products include Enteroquinol, Vitazyme, Locula, Bactiv, Tonoferon and Pyrigesic. The objective of our industrial visit to East India Pharmaceuticals was to have an in-depth understanding of the technological advancements and operational processes within the biotechnology and pharmaceutical sectors.

We started the tour firstly from the Microbiological Quality Control Department, where the quality of the product is checked in terms of raw material, water used for production as well as each and every finished batch of products is checked in terms of contamination level, that is in terms of bacterial count, fungal count and absence of pathogens as well as quality of the Active Pharmaceutical Ingredients(API) are checked here too and here all the testing processes follow the Indian Pharmacopia for Modern Medicine. After this we moved to see the Scale-up Operations where this serves as the pilot plant to the production unit. Here mainly medicine formulation and development is performed. The solid medicines such as capsules and tablets are prepared in 3 steps such as Dry granulation, Wet granulation and Direct compression. Next we moved to the Instrument Room where we saw many instruments which are required for the assay of the formulated products. We were told about High Pressure Liquid Chromatography (HPLC), UV-Visible Spectroscopy, Infrared Spectroscopy and their workings and how they are used for the assays of the different products. We then moved to the Biotechnology R&D Laboratory which works on biological molecules and cells. Some targeted products developed by this department include probiotic formulations and formulations with therapeutic enzymes in the segment of digestive and inflammatory disorders. Any kind of synthetic or chemical moiety is handled by the Biotechnology R&D department.

We were not able to see the production unit as it was not operating on that day hence, we all are looking forward to visit the EIPW again to view the production unit. The visit enhanced our insight into the process of formulations of the products which are manufactured in this industry. It was truly a valuable experience for all of us. We provide our sincere thanks to our Professors Dr. Souvik Roy and Dr. Arindam Bakshi and St. Xavier's College (Autonomous) Kolkata for extending this opportunity for us and we definitely thank the East India Pharmaceutical Works Limited (EIPW), Kolkata for their warm welcome, their acceptance of our visit and their guidance for sharing such wonderful information with all of us.

Educational Field Trip To Vivekananda Institute Of Biotechnology, Nimpith Kolkata

SEMESTER 7

Professors in charge

Dr. Sayak Ganguli and Dr. Arindam Bakshi

On 14th August, 2024, we, the students of Semester 7, went on an educational field trip to the Vivekananda Institute of Biotechnology, Nimpith, together with our Professors, Dr. Sayak Ganguli and Dr. Arindam Bakshi. The institution, established in 1991 is a branch institution of Sri Ramakrishna Ashram Nimpith and functions under the Core Support Program of the Department of Science and Technology, Government of India. It is extensively involved in the development, innovation, modulation and adaptation of appropriate rural technologies and in the transfer of some selected technologies to the farming community of the Sundarbans by providing proper training, building awareness and organising follow up programs frequently. For its continuous effort to unfold mysteries of science and the advancement of technologies for application at the grass root level, The Council for Advancement of People's Action and Rural Technology (CAPART) has entrusted Vivekananda Institute of Technology as Technology Resource Centre for Sundarban Areas.

We visited various departments such as the mushroom cultivation unit, the plant tissue culture unit, biofertiliser followed by biopesticides development units,

honey processing unit and finally the soil and health management unit. We learnt about the different types of edible mushrooms that are cultivated all year round in the mushroom cultivation unit such as oyster mushroom, milky mushroom, paddy straw mushroom and button mushroom, their growth conditions and the training provided to various personnel from nearby villages in order to cultivate and sell them. In the plant tissue culture unit, we were made to see several plantlets that had been grown in the lab and were informed about the various processes undertaken to grow a number of species such as banana and elephant foot yam. The biofertiliser, biopesticide development and soil health management units stressed on the importance of protection of the soil and its fertility by application of various methods to increase the same while also preventing the growth of any pest organisms in it. The biopesticide unit elaborated on the usage of organisms such as Trichoderma sp., Pseudomonas sp. in order to achieve this. We were also made aware of an ongoing project in the biofertilizer department titled "Isolation of Endophytic Diazotrophic Bacteria from Wild Rice" which aimed to explore how the bacteria in question, isolated from wild rice, could colonise cultivated rice roots and enhance nitrogen fixation under field conditions. We were also shown the common facility centre for the Sundarban bee keeping cluster and educated about the methods that are applied to process the honey from bees.

It was an extremely enriching experience for us to learn about the varied biotechnological aspects that were employed in order to carry out the above mentioned processes in different units and how these aided in the development and growth of rural areas as well as the people residing there.

Educational Visit To The Indian Museum, Kolkata: A Journey Through Knowledge

SEMESTER 9

Professors in charge

Dr. Jhimli Dasgupta and Dr. Priyanka De

On 13th of September 2024, as a part of our curriculum at St. Xavier's College (Autonomous), Kolkata, we visited the Indian Museum along with our professors Dr. Jhimli Dasgupta and Dr. Priyanka De. The Indian Museum is one of the oldest and most prestigious museums in the world. The visit exposed us to various galleries related to anthropology, evolution, ecology, and biotechnology, providing a well-rounded educational experience. Each section enriched our understanding of history, science, and the environment, helping us connect theoretical learning with tangible artifacts and exhibits.

Anthropology and Cultural Insights

We began our exploration with the Bharhut, Gandhara, Archaeology, Coin, and Egypt Galleries, which offered fascinating insights into ancient civilizations. The Bharhut and Gandhara Galleries showcased Buddhist art, with Bharhut sculptures illustrating early symbolism, while Gandhara art highlighted a unique Greco-Buddhist fusion. The Archaeology Gallery displayed ancient tools and artifacts, emphasizing the development of human civilizations. In the Coin Gallery, we saw coins from various dynasties, reflecting ancient trade practices and political histories. A highlight of this section was the Egypt Gallery, which featured a real mummy and provided an engaging cross-cultural comparison between Egyptian and Indian civilizations.

Evolutionary Study: Tracing Life's Origins

The galleries dedicated to evolution were equally captivating. In the Insect and Invertebrate Fossil Galleries, we explored the diversity of invertebrates, which also comprised ancient marine fossils, learning how life evolved over millions of years. Moving on to the Vertebrate section, we visited the Fish, Mammal, and Human Evolution Galleries. The Fish Gallery highlighted the adaptations of aquatic species, while the Mammal Gallery displayed preserved specimens of extinct and endangered mammals, emphasizing the importance of conservation. In the Human Evolution Gallery, we traced humanity's evolutionary journey, gaining a clearer understanding of anatomical changes over time.

Ecology and Environmental Awareness

The Ecosystem Gallery offered insights into the interconnectedness of life forms and ecological processes. Through detailed displays, we learned about food chains, biodiversity, and the importance of maintaining ecological balance. This section also emphasized the role of sustainable practices in protecting ecosystems from threats like human interference and climate

change. Our visit also coincided with World Ozone Day celebrations, during which we participated in interactive quiz sessions related to environmental awareness. These activities helped us understand the significance of protecting the ozone layer and other critical ecological challenges. The quizzes added a fun and engaging element to the trip, reinforcing the importance of individual responsibility toward environmental conservation.

Biotechnology and Industrial Applications

In the Industrial Botanical Gallery, we explored the economic roles of plants in biotechnology and industry, learning how they contribute to the production of textiles, medicines, food, and other essential goods. Alongside plants, the museum also showcased the economic roles of animals, such as lac insects and silkworms. The detailed models of lac cultivation and sericulture demonstrated how these animals contribute to industries like dye production and silk weaving, emphasizing the interplay between animals, industry, and biotechnology. This section provided us with valuable insights into how biological resources, both plant and animal, are harnessed sustainably for economic growth. It showcased how traditional knowledge and modern biotechnology work together to promote environmental and industrial sustainability.

Conclusion: A Holistic Learning Experience

The trip to the Indian Museum was an enriching experience that broadened our perspectives across multiple disciplines. Each gallery provided valuable insights into anthropology, evolution, ecology, and economic biotechnology. The visit deepened our appreciation for cultural heritage and the natural world, while also highlighting the importance of scientific research and conservation. This interdisciplinary exposure allowed us to connect academic concepts with real-world artifacts and specimens, fostering a deeper understanding of the subjects we study. We left the museum with a sense of responsibility toward preserving our cultural and natural heritage, making the experience both educational and inspiring.

International Symposium on Biotechnology (ISBT) 2023

Convener: Dr. Sayak Ganguli

Co-convener: Dr. Ditipriya Hazra, Dr. Arindam Bakshi

The Postgraduate and Research Department of Biotechnology, St. Xavier's College (Autonomous), Kolkata held the first International Symposium on Biotechnology (ISBT) on 12th and 13th October, 2023. Dr. Sayak Ganguli (Convener), Dr. Arindam Bakshi and Dr. Ditipriya Hazra (Co–Conveners), Dr. Souvik Roy (Treasurer) and Dr. Jhimli Dasgupta (Head of the Department) formed the integral organizing committee, who worked efficiently as a team to make the conference a success.

The inaugural address was delivered by Reverend Father Dr. Dominic Savio SJ, Principal, St. Xavier's College (Autonomous), Kolkata. The 13th edition of the annual department magazine, Chiasma 2023 and the Conference Proceedings of ISBT 2023 were also released during the inaugural session. This was followed by insightful lectures by the keynote speaker, Dr. Partha Pratim Majumder (National Science Chair, Science and Engineering Board, Government of India), Dr. Arun K Shukla (Indian Institute of Technology, Kanpur), Dr. Sangram Bagh (Saha Institute of Nuclear Physics, Kolkata) and Dr. Gautam Sethi (National University of Singapore, Singapore) on 12th October.

On 13th October, engaging lectures were delivered by Dr. Utpal Nath (Indian Institute of Science, Bengaluru), Dr. Souvik Mukherjee (National Institute of Biomedical Genomics, Kalyani), Dr. Marc Graille (Ecole Polytechnique, Paris) and Dr. Ranjan Sen (Indian Association for the Cultivation of Science, Kolkata).

In addition to these enlightening lectures, there were oral presentations from faculties and research scholars of more than twenty different institutions. Poster presentations by students, research scholars and professors from various prestigious institutions were also held on both the days. A colourful cultural program, directed by Dr. Priyanka De concluded the first day. The second day concluded with a valedictory session in which prizes and certificates were awarded to the winners of the various categories.

The International Symposium on Biotechnology was successful in creating interest among the attendees on the various topics in biotechnology and awareness about the ever-expanding scope of science.

GUEST ARTICLES

Biotechnology's Dawn: Shaping a Healthier and More Sustainable Future

Dr. Dhriti Banerjee

Director

Zoological Survey of India

It is with great pleasure that I extend my warmest greetings to all the participants of Chiasma 2024.

Today, as we stand on the brink of a new era in healthcare and environmental stewardship, biotechnology offers us unparalleled opportunities to shape a healthier and more sustainable tomorrow. In this evolving narrative, biotechnology is not merely a tool for discovery but a powerful agent for reshaping our relationship with health and the environment. It is in the fusion of biology and technology that we are witnessing transformative solutions to the most pressing challenges of our time - those that affect both human health and the environment.

At the dawn of the 20th century, life expectancy was significantly lower than it is today. Infants and children faced high mortality rates, and diseases such as cancer were largely untreatable and poorly understood. The groundbreaking work of Crick, Watson, and Franklin in the 1950s, which unveiled the double helix structure of DNA, was a turning point in our understanding of genetics. Fast forward to today, the landscape of human health has transformed dramatically. Advances in medicine, including antibiotics, chemotherapy, vaccines, and innovative diagnostic tools, have increased life expectancy. Conditions that once led to significant mortality are now manageable, and the horizon for the future of medicine is even more promising.

Indeed, biotechnology is at the heart of this transformation. The advances we see today in healthcare are not mere enhancements but are fundamentally reshaping our approach to patient care. Personalized medicine, once a distant dream, is now becoming a reality. We are moving away from the one-size-fits-all treatments toward tailored interventions based on individual genetic profiles. Today, the cost of sequencing a human genome has decreased substantially, creating new opportunities for precision medicine. This progress holds immense promise for reducing healthcare costs and improving patient outcomes.

The strides in cancer therapy further exemplify the impact of biotechnology. Immunotherapies and monoclonal antibodies are now at the forefront of treating previously incurable cancers. Engineered gut micro-biomes offer innovative approaches to combat metabolic and autoimmune diseases. One of the most exciting developments in this field is the advent of micro-RNA (miRNA) therapies. These small, non-coding molecules regulate gene expression and have become invaluable diagnostic agents. The global success of mRNA vaccines against SARS-CoV-2 has reignited interest in RNA-based therapies, setting the stage for further advancements in miRNA-based cancer immunotherapy. CRISPR-Cas9 gene-editing technologies and stem cell therapies are pushing the boundaries of what is possible. These tools are not just improving healthcare but are reimagining it. The potential of biotechnology to address genetic issues through advanced editing technologies is immense. The integration of artificial intelligence (AI) into drug discovery and development is another significant leap forward. AI is believed to streamline the process by accurately predicting protein structures and reducing drug development costs. This integration is also anticipated to shorten the average 13-year drug development timeline, bringing life-saving drugs to market faster and more affordably.

As we contemplate the future, the quest for extending human life and improving its quality is becoming more tangible. The breakthroughs, while still in their early stages, offer the potential to extend life expectancy and improve overall health outcomes. If successful, these could also contribute to greater health equity and economic growth.

While biotechnology is dramatically transforming healthcare, offering personalized treatments and novel therapies, its potential extends far beyond the medical field. The innovative principles of biotechnology are now being applied to address some of the most urgent environmental challenges of our time. Biotechnology is revolutionizing our approach to environmental stewardship, offering solutions that can restore ecosystems, reduce pollution, and combat climate change.

According to reports, the challenges posed by climate change and pollution are urgent and profound. In 2023, global carbon dioxide levels reached a record high of 419.3 parts per million - a significant 50% increase since the Industrial Revolution. This increase is contributing to accelerating climate change, with far-reaching effects on ecosystems, communities, and industries. Biotechnological innovations offer promis-

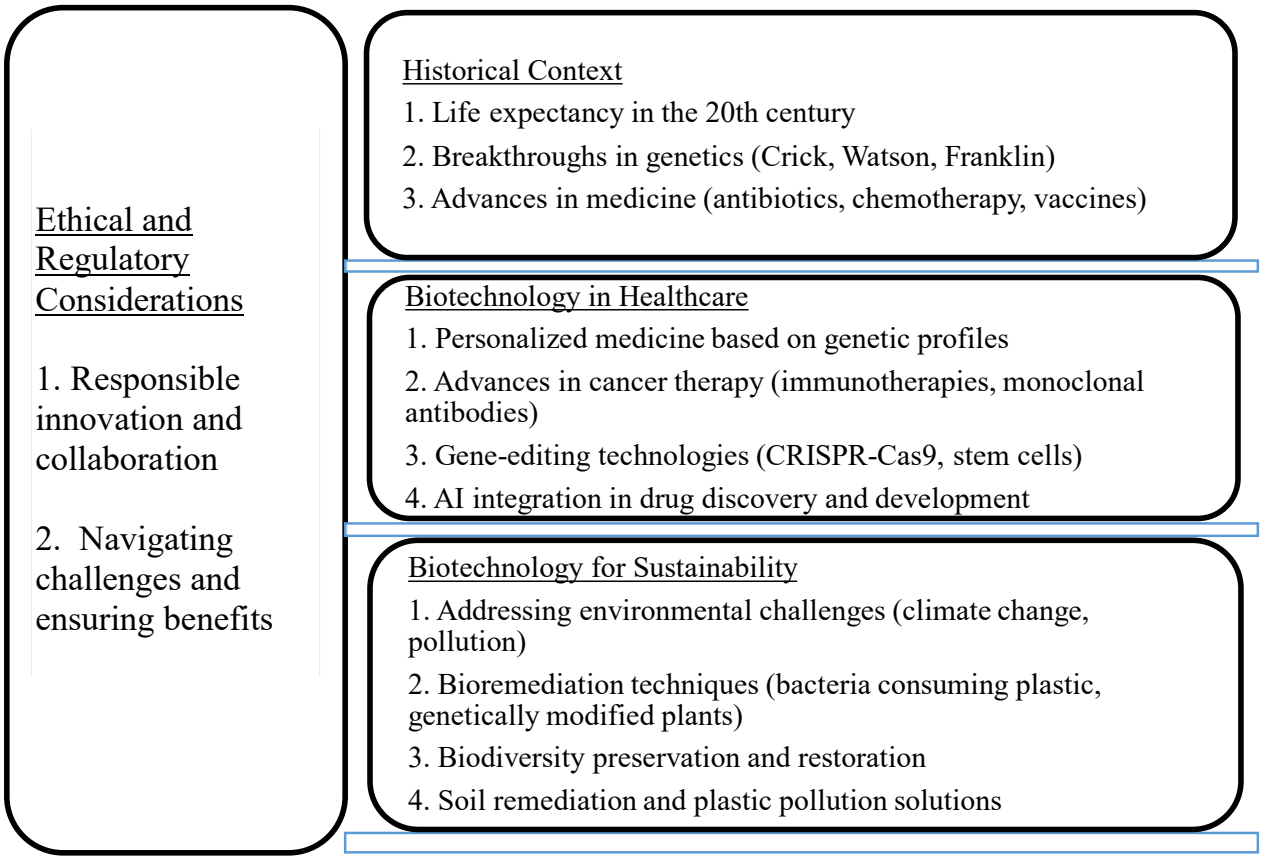
ing solutions to these challenges.

Bioremediation, which utilizes living organisms to eliminate pollutants and restore environmental health, is gaining momentum. Innovations such as bacteria that consume plastic are on the brink of making significant commercial impacts. For instance, genetically modified plants that improve air quality by reducing atmospheric pollutants and greenhouse gases are becoming a reality. In addressing biodiversity, biotechnology also holds the key to saving endangered species and probably even reintroducing extinct ones. Soil remediation is another critical area where biotechnology is making strides. Researchers are using hyper-accumulator plants to clean sites contaminated with metals like lead and cadmium. The challenge of plastic pollution, projected to outweigh the mass of all ocean fish by 2050, is being addressed through innovative solutions.

Overall, Biotechnology holds immense potential to restore and enhance the natural environment. It offers solutions to repair damage from human activity and improve resilience. However, sustainable living practices must accompany these technological advancements to ensure meaningful progress. As we look to the future, biotechnology could transform our relationship with the planet, potentially even surpassing milestones such as the space race. According to studies, it has been even envisioned that integrating humanity with nature through synthetic biology may become one of the most profound transformative leaps in the coming centuries.

So, as we stand on the cusp of a new era driven by the extraordinary potential of biotechnology, it is imperative that we address the ethical and regulatory concerns that accompany such powerful technologies. The rapid advancements in this field not only promise significant benefits but also pose profound challenges that must be navigated with care and foresight. Collaboration between different sectors is very essential to foster responsible research and development.

Thus, in order to shape tomorrow's health and environment; let us move forward with a commitment to responsible innovation, ensuring that the benefits of biotechnology are realized in a manner that is ethical, equitable, and inclusive. Together, we can embrace the horizons of biotechnology to create a future where its promises are fully realized for the well-being of all.



Momordica charantia : An Useful Plant for the Treatment of Diabetes

Prof. Sarmistha Raychaudhuri

Former Professor,

Department of Biophysics, Molecular Biology & Bioinformatics,

University of Calcutta, Kolkata.

Introduction

The bitter melon *Momordica charantia* (also commonly known as bitter gourd, mara ki nok, karella or uchhe) is a tropical perennial vine belonging to Class Magnoliopsida and Family Cucurbitaceae. *Momordica charantia* is found in various regions of the world including India, China, Thailand and other parts of Southeastern Asia, Mexico, Brazil, Cuba, Trinidad, Panama, Peru and part of Africa. The fruit is edible when harvested green and cooked and has a bitter taste (hence the names of bitter melon and bitter gourd). The fruits are low in calorie (19 kcal/100gm) and rich in polynutrients, dietary fibers, minerals, vitamins and antioxidants. Bitter melon is rich in vitamin A and vitamin C and in comparison to bananas, has twice the potassium content. Although the seeds, leaves and vines of bitter melon can all be used, the fruit is the safest and most prevalent part of the plant used medicinally.

The fruit, fruit juices and extracts (oral, hot water extracts, oil extracts) have been used for treatment of diabetes mellitus, jaundice, piles, leprosy, rheumatism, gout and malarial fevers and also as antivenin, anti-helminthic and abortifacient in humans. Bitter melon, like many bitter-tasting herbs in traditional herbal medicine, is considered to stimulate digestive function, and improve appetite. Also, a number of constituents present in bitter melon appear to have blood-sugar lowering potential which can be of benefit for treatment of diabetes mellitus.

Phytochemistry and Medicinal Properties of Indian Varieties

Fruits and leaves of *Momordica charantia* contain two alkaloids including momordicine. The plant has also been reported to contain a saponin-like substance, a glucoside, an aromatic volatile oil, an unpleasant tasting resin and a mucilage. The seeds contain an alkaloid (with melting point 236°C) and an antihelminthic compound. The seeds also contain urease.

The fruit of *Momordica charantia* contains ascorbigen. Ascorbigen is a bound form of ascorbic acid which can be released by heating with water in an atmosphere of nitrogen or carbon dioxide. Certain types of *Momordica charantia* bear larger sized fruits which are richer in ascorbigen than small fruits borne by other types which are cultivated. Free amino acids present in the fruit of *Momordica charantia* include serine, threonine, alanine, aspartic acid and glutamic acid. The fruits also contain γ-amino butyric acid and pipecolic acid and the green fruit contains luteolin. The principal pigment present in the carpels is carotene while lycopene is present in the red aril. Fruits and seeds of *Momordica charantia* also contain a polypeptide with a melting point of 240°C, p-Insulin, which was considered to be similar to bovine insulin.

The varieties found in India are *Momordica charantia* var. *charantia* Linn. with large fusiform fruits and *Momordica charantia* var. *muricata* Linn. with small, round fruits. Several parts of the plants of these Indian varieties show medicinal importance with the leaves having purgative and anti-bacterial properties, the fruits having hypoglycaemic, anti-mutagenic, anti-leukaemic and anti-diabetic properties as well as the capacity of healing malignant ulcers and the seeds having anti-HIV and anti-helmintic properties.

Role in Blood Sugar Management

Some clinical trials have confirmed bitter melon is beneficial for treatment of people with diabetes mellitus. Studies indicate three different groups of constituents present in *Momordica charantia* have blood-sugar lowering actions which can be of potential benefit for treatment of diabetes mellitus. These constituents include charantin (a mixture of steroidal saponins), certain alkaloids and the insulin-like peptides. However, it is still unclear as to which of these three is most effective, or whether all three work together.

The standardized extract of *Momordica charantia*, contains charantin. Charantin, which was first identified by Lolitkar & Rao (1960), is a hypoglycemic agent, a 1:1 mixture of beta-sitosterol-beta-D-glucoside and 5,25 stigmadien-3-beta-ol glycoside. Charantin is whitish, crystalline, neutral and tasteless, melting at 266-268°C. It is soluble in ether, ethanol and methanol but sparingly soluble in water and highly polar solvents as well as

in apolar solvents like hexane.
Vicine, charantin and polypeptide–P increase glucose uptake and glycogen synthesis in the liver, muscle and adipose tissue, improve glucose tolerance in humans and animals, cause reduction in glucose- 6-phosphatase and fructose–1, 6-bisphosphatase activity and cause increased glucose oxidation by G6PDH pathway in mice. They also show cytotoxic activity against leukemic cells in vitro (acting as guanylate cyclase inhibitor).

Conclusion

Studies highlight the importance of *Momordica charantia* (bitter melon) as a plant having anti-diabetic activity. Thus, *Momordica charantia* could be a herbal alternative for management of blood sugar levels, particularly for non-insulin dependent diabetes mellitus. In this regard, an extract of bitter melon which is standardized for all the active principles would have proven efficacy. Extracts from *Momordica charantia* could be useful for making polyherbal formulations and for further biotechnological applications in this regard. The use of Charantin in herbal medicine may lead to new drug discovery for management of diabetes.

An ode to "Karella" (Bitter Melon)

Oh Karella! With "Bumpy skin"!
You belong to the family of Pumpkins!
Storehouse of phytochemicals, even when green!
Taste bitter, because of "Momordicine".
Rich in minerals, folate and vitamins,
Excellent source of beta-carotene!
Contain the wonder drug "Charantin",
That lowers blood sugar like Insulin!!
The fight against diabetes, we are sure to win!
To cure all men,
With "Advancement of Learning".

New Tricks of an Old Drug

Prof. Urmi Chatterji

Cancer Research Lab, Department of Zoology

University of Calcutta

When Mary Poppins belted out 'a spoonful of sugar helps the medicine go down', the concern was entirely about consumption of the medicine, not the medicine itself. Yet through years, diseases have prevailed, medications have been discovered, implemented, discarded, and diseases have persisted. As the nature and intensity of several diseases changed with time, the need for more effective and easily accessible medicines have become imperative. Drug discovery, therefore, became both a flourishing science and business for several years.

Drug discovery is a multidisciplinary and multivariate optimization endeavor. Compounds derived from natural products, synthetic drugs, in silico screening tools, small molecule designing and computer-aided drug designing have been practiced over several decades, with the aim of developing safe, inexpensive, and specific medicines with reduced side effects. Recently, non-invasive diagnostics and targeted drug delivery using nanoformulations are also in vogue. However, the usual time taken to bring a drug to the market is about 10 to 15 years, since it is a complex and time-consuming process that involves identifying molecules that can interact with specific molecular targets in the body to treat diseases. Traditionally, this process has been carried out through "trial and error", which can be costly and time-consuming. Optimizing the process of drug discovery is thus of great interest to the pharmaceutical industry, as the efficient identification and selection of suitable drug candidates can have a dramatic impact on the cost and profitability of new medicines.

In this respect, the application of AI can help accelerate the drug discovery process by using algorithms to analyze large volumes of data and identify potential drug candidates more quickly and accurately. One of the most promising applications of AI in drug discovery is prediction of drug-target interactions. AI algorithms can analyze large chemical and biological data databases to predict which molecules are most likely to interact with specific targets in the body. This can help identify potential drug candidates more quickly and accurately than traditional methods. Another promising application of AI in drug discovery is the design of new drug molecules. AI algorithms can generate and evaluate millions of potential drug molecules, considering factors such as target specificity, drug metabolism, and toxicity. This can help identify molecules that are more likely to be effective and safe, reducing the risk of failure in clinical trials.

Nevertheless, the process of bench-to-bedside delivery of novel drugs still poses a major challenge. The steps, as defined by the Food and Drug Administration (FDA), include (i) discover and development, where research for a new drug begins in the laboratory; (ii) preclinical research, for drugs to undergo laboratory and animal testing to answer basic questions about safety; (iii) clinical research, where drugs are tested on people to make

sure they are safe and effective; (iv) FDA review, as review teams thoroughly examine all of the submitted data related to the drug or device and make a decision to approve or not to approve it; and finally (v) FDA post-market safety monitoring, where FDA monitors all drug and device safety once products are available for use by the public. Despite cutting-age technologies, the entire process is lengthy, laced with uncertainties and increased failure rates, and costly with high attrition rates. Our hope, therefore, is that one day it will become possible to rapidly design inexpensive, more specific, more effective, non-toxic, and personalized drugs, which will be patient-friendly.

More recently, in order to counter-intervene the issue, the concept that existing drugs have potentially beneficial off-target effects or new usefulness has led to the design of more intentional drug repurposing strategies to identify promising drug candidates. Drug repurposing, also known as drug repositioning, is a strategic attempt encompassing the identification of novel therapeutic applications for already existing pharmaceuticals. This itself is a highly advantageous strategy due to its cost-effective nature and ability to save time in the drug discovery process, while mitigating the risks of failure.

As a rejoinder to the concern that promising drugs are commonly shelved either due to insufficient efficacy or poor market prospects, more research is needed on the current value of repurposing in drug development and how to better facilitate resources to support it. In addition, legal expertise to negotiate intellectual property agreements in multi-partner collaborations need to be delineated. Some reports state that about 30–40% of new drugs and biologics approved by the US FDA between 2007 and 2009 can be considered repurposed or repositioned products. Similarly, a study found that 35% of transformative drugs approved by the FDA between 1984 and 2009, defined as drugs that were both innovative and had groundbreaking effects on patient care, were also considered as repurposed products.

Several experts claim re-purposing drugs can be faster, cheaper, less risky and carry higher success rates than traditional drug development approaches, primarily because researchers can bypass earlier stages of development that establish drug safety, as they have already been completed earlier. In lieu of the above, exactly how much time, risk and money are actually saved is debatable. Some reviews state about 30% of repurposing efforts are successful and result in a product approved for marketing, in comparison to about 10% for new drug applications. However, others conclude contradictorily that repurposed agents do not necessarily succeed more often than new agents, with efficacy typically being the limiting factor rather than safety. Albeit reports indicate de novo drug discovery and development can be a 10-to-15-year process, repurposed drugs are generally approved within 3 to 12 years, and at about half the cost.

Drug repurposing has, therefore, become the need of the hour to hasten the drug discovery process and find quicker solutions to the over-exerted healthcare scenario and drug needs. Drug repurposing involves (i) identifying the drug, (ii) evaluating its efficiency using preclinical models, and (iii) proceeding to phase II clinical trials. Identification of the drug candidate can be made through both computational and experimental approaches. This approach usually utilizes public databases for drugs, data from primary and translational research, clinical trials, anecdotal reports regarding off-label uses, and other published human data information. Scientists use artificial intelligence algorithms and other bioinformatics tools, and systematically try to identify the interaction between drugs and protein targets. This is then combined with genetic data, clinical analysis, structure (molecular docking), pathways, signatures, targets, phenotypes, binding assays, and artificial intelligence to get an optimum outcome in repurposing.

Today, drug repurposing is an extremely advantageous technique in the field of pharmaceutical research because it capitalizes on the unintentional off-target effects of extant medications. By utilizing pharmaceuticals that have previously been approved, drugs that have been declared ineffective in clinical trials, and drugs that have been removed from the market for a variety of reasons, are now under consideration for different diseases. By venturing into the realm of drug repurposing, researchers can unlock a vast reservoir of therapeutic potential that has hitherto remained untapped.

A typical question posed by several researchers and patients is whether any drug that has been repurposed has actually received approval for their new indications. The case of thalidomide, the drug infamously recognized as a sedative and curative for morning sickness, returned to the medical world for the treatment of leprosy, and, subsequently, multiple myeloma, possibly as a serendipitous occurrence, and recounted in the book Dark Remedy. In this tale, a physician administered the only sedative available in the hospital's pharmacy, which had not been previously attempted, to a suffering leprosy patient. Astonishingly, the drug had a dramatic and unexpected effect on the patient's condition. This is a perfect example of repurposing a medicine that was authorized and then abandoned to treat a completely different ailment. Another example of drug repurposing is sildenafil, which is also commonly known as Viagra. Initially, this medication was prescribed for the treatment of arterial narrowness, hypertension, and heart diseases in both humans and

animals. However, it was fortuitously discovered that sildenafil has beneficial effects on erectile tissue dysfunction in male genital organs. On approval by US FDA in 1998, sildenafil has brought about a significant transformation in the management of erectile dysfunction and has a positive impact on the overall well-being of men.

Despite the numerous obstacles and unsuccessful attempts, there have been instances of drug repurposing that have achieved success. Notable examples include the utilization of zidovudine as a therapeutic agent against human immunodeficiency virus (HIV) and the repurposing of tocilizumab for the treatment of COVID-19. The practice of repurposing drugs has demonstrated its effectiveness in the development of therapeutic strategies for various diseases and holds promise in addressing rare and difficult conditions. This approach entails a combination of experimental and computational methods, leveraging existing safety data and redirecting the application of drugs based on validated target molecules. Through the optimization of the therapeutic potential of already existing drugs, drug repurposing enhances the likelihood of attaining successful outcomes and offers a means to promptly identify effective treatments. Thinking deeply, we can conclude that the development of repurposed medications requires creativity and innovation in designing the development program, as the body of evidence varies for each individual case and does not rely solely on chance.

The process of drug repurposing has a number of drawbacks, such as the pharmaceutical industry's restricted focus on diseases that provide more financial rewards, lowering the amount of repurposing chances for orphan diseases and neglected tropical disorders. Furthermore, there are legal concerns which may surround repurposed medications, including restricted patent coverage. Despite the inherent advantages of this technique, such as cheaper costs and faster time frames, comprehensive analysis of these challenges and limitations must precede the pursuit of drug repurposing strategies. However, there is promising potential for drug repurposing to forecast the effectiveness of repurposed medications in phase III clinical trials, thereby streamlining the process. Finally, it is important to acknowledge Sir James Black, Nobel laureate in Physiology and Medicine (1988) for drug development, for his farsighted vision and for astutely predicting that "the most fruitful basis for the discovery of a new drug is to start with an old drug".


SCIENTIFIC
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Precision Pesticides

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The Menace of the Colorado Potato Beetle

One of the most destructive pests to potato crops is the Colorado potato beetle (*Leptinotarsa decemlineata*), which is renowned for its capacity to quickly adapt to and withstand chemical pesticides. This pest, which was once native to the United States, has spread throughout the world and resulted in large financial damages. Due to its ability to become resistant to a variety of pesticides, the beetle presents a difficult challenge to both farmers and agricultural scientists.

Fundamental Features of the Colorado Potato Beetle:

1. Quick Reproduction: Female beetles can produce up to 800 eggs in a single season, which quickly builds up vast populations.
2. High Mobility: Crops can be consumed and destroyed by both adult and larval stages, with larvae being especially
3. Development of Resistance: Conventional pest control methods are less successful owing to the beetle's resistance to over 50 different kinds of insecticides.

The Demand for a Novel Approach

Innovative pest management techniques that are sustainable and effective are desperately needed, as traditional pesticides have several drawbacks.

The drawbacks of conventional pesticides

1. Development of Resistance: As the Colorado potato beetle has shown, pests can easily acquire resistance, making chemical treatments useless.
2. Environmental Impact: Ecosystems and biodiversity may be impacted by chemicals discharged that contaminates soil and water.
3. Damage to Non-Target Species: Broad-spectrum insecticides may unintentionally cause harm to beneficial insects and other non-target organisms.

A Hopeful Substitute

An innovative method of controlling pests seems to be the use of RNA-based precision insecticide. By targeting particular genes in pest species and using the natural mechanism of RNA interference (RNAi), this method successfully silences those genes and interferes with vital biological processes. Important biological functions like feeding, reproduction, and survival can be interfered with by silencing essential genes, which can efficiently manage the pest population.

Development of Pesticides Based on RNA

Target genes that are essential to the pest species' survival or reproduction are identified in order to build RNA-based insecticides. Researchers have concentrated on the genes that control eating behaviour and larval development in the Colorado potato beetle.

Procedures for Creating RNA-Based Insecticides:

1. Target Gene Identification: Researchers locate and choose genes that are critical to the life or procreation of the pest.
2. dsRNA Synthesis: Target gene sequences are matched to create synthetic dsRNA molecules.

Table 1: Comparison of Traditional Pesticides and RNA-Based Precision Pesticides

Aspect	Traditional Pesticides	RNA-Based Precision Pesticides
Target Specificity	Low; broad-spectrum	High; specific to target pest
Environmental Impact	High; potential pollution and runoff	Low; minimal impact on environment
Resistance Development	High; rapid resistance evolution	Lower; specific targeting reduces resistance potential
Non-Target Effects	High; affects beneficial organisms	Low; minimal impact on non-target species
Regulatory Challenges	Moderate; established regulatory frameworks	High; new regulations needed for RNA-based approaches

3. Delivery Techniques: A range of delivery techniques are evaluated to guarantee that the ds-RNA is efficiently absorbed by the pest. These may consist of bait assimilation, root uptake, or foliar spraying.
4. Field Testing: To assess the effectiveness and safety of RNA-based insecticides for non-target organisms, field testing is conducted.
5. Target Specificity: By focusing on particular genes in the pest species, RNA-based pesticides might lessen the possibility of harming non-target organisms such as humans, animals, and beneficial insects.
6. Environmental Safety: RNAi pesticides naturally break down and do not stay in the environment like chemical pesticides do, which lowers the danger of contaminating soil and water.
7. Decreased Resistance Development: The possibility of resistance development is decreased by employing species-specific sequences or targeting numerous genes, which increases the effectiveness of the management strategy.

Future Challenges:

Although RNA-based pesticides hold great promise, there are challenges that need to be addressed:

1. Regulatory Barriers: The introduction of RNA-based pesticides requires a new regulatory framework to assess safety and efficacy.
2. Delivery Efficiency: Ensuring that dsRNA reaches the target pest in sufficient quantity remains a challenge, especially under field conditions.
3. Public understanding: As with any new technology, public acceptance depends on understanding the benefits and safety of RNA-based pesticides.

Conclusion

RNA-based precision pesticides offer a targeted, eco-friendly alternative to traditional chemicals, utilizing RNA interference to minimize harm to ecosystems and non-target organisms. This approach could transform agricultural pest management significantly. Agricultural organizations and companies are attempting new ways to bypass the digestive and immune system of the Lepidopterans. For example, a company named Agrospheres are on the verge of patenting a technology where they are using engineered bacteria to synthesize cell wall based dsRNA and protective shells around them. They reported a commercially viable control of the cabbage disease caused by diamondback moth. Trillium Ag has developed aptamer guided packaging using lipids or proteins for their small RNAs and currently field trials are underway against fall armyworm and a few other pests. Future directions for RNA-based treatments involve expanding their application to additional pests and plant diseases, integrating them into Integrated Pest Management strategies alongside biological and chemical methods, and ongoing research to overcome challenges related to delivery, regulation, and approval processes in agriculture.

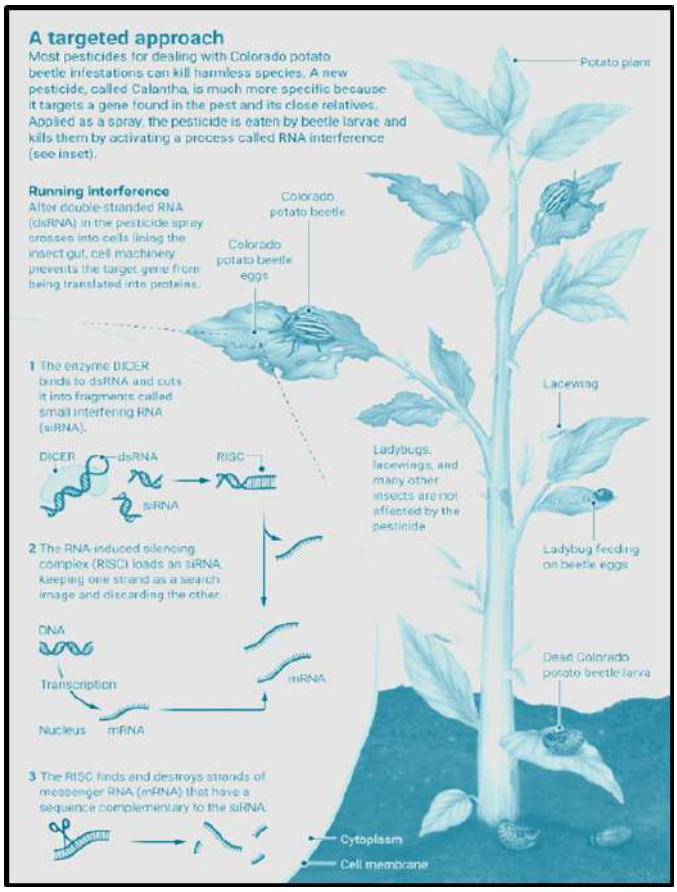

Figure 1: The science behind precision pesticides [Image Source: doi: 10.1126/science.zb5lj7d]
Benefits of RNA-based pesticides

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Cancer Therapy: Recent Advances and New Challenges

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Introduction

Cancer is a disease caused by abnormal cellular proliferation, leading to the formation of tumours (neoplasms). Cancer cells exhibit almost unlimited replicative potential, insensitivity to growth inhibiting signals and contact inhibition, the capacity to metastasize and invade adjacent and distant tissues, the ability to evade apoptosis, changes in cellular signalling pathways and the abilities to promote angiogenesis (by secreting growth factors) and degradation of the extracellular matrix (by secreting proteases). Traditional treatments for cancer include radiation therapy, surgery and chemotherapy. Radiation therapy seeks to destroy malignant cells by the medical use of ionizing radiation, surgery seeks to removes tumours while chemotherapy uses anticancer drugs (which includes alkylating agents like Busulfan, anti-metabolites like Fluorouracil or topoisomerase inhibitors like Etoposide) to inhibit cell proliferation and to reduce tumour invasion. Although these therapies have appreciably improved rates of survival in cancer patients, metastasized cancer still remains largely incurable. Chemotherapy and radiotherapy also exhibit a wide range of side effects including nausea, vomiting, hair loss, myelosuppression and anaemia. The search thus continues for a therapeutic method which would show good efficacy in treatment of both primary and metastatic tumours as well as minimal side effects. Modern advances in this field include the use of molecular methods for improved diagnosis and treatment and the use of natural phytochemicals for therapy.

Molecular Methods for Cancer Treatment

Circulating tumour cells (CTCs) are tumour cells which have split from the primary tumour and are found singly or in clusters in the patients' peripheral blood circulation. CTCs move through blood to reach potential sites for formation of secondary tumours. Analysis and identification of CTCs (by distinguishing them from other cells in the blood like leucocytes) can provide valuable information about a patient's condition. Various techniques are used for detection of CTCs including isolation on the basis of size and surface charges, separation using immunological techniques (by targeting specific protein biomarkers expressed on the surface of CTCs by their complementary antibodies) and fluorescence flow cytometry.

MicroRNAs (miRNAs) are small non-coding RNAs which, by complementary base pairing, can control expression of many genes at the post transcriptional level. Studies indicate miRNAs can play important roles in regulation of various biological processes including cancers. For example, miR-21 is overexpressed in several cancers including breast, colorectal and gastric cancers and promotes rapid cell growth and tumour progression, thus acting as an oncogene, while the miRNA Let-7 acts as a tumour suppressor in breast and lung cancers by targeting oncogenes like Myc. MiRNA based therapies involve two basic approaches: inhibition of oncogenic miRNAs (thereby restoring expression of the tumour suppressing genes they target) and restoring expression of tumour suppressing miRNAs (thereby inhibiting the oncogenes that they target). Techniques used to target oncogenic miRNAs involve the use of anti-miRNA oligonucleotides (single-stranded oligonucleotide sequences complementary to the target miRNA) or miRNA sponges (inhibitors with multiple binding sites for target miRNAs) which prevent interaction of miRNA with their targeted gene transcripts. Resto-

ration of tumour suppressing miRNAs expression levels involves the use of miRNA precursors or miRNA mimics (small, chemically modified RNA molecules which mimic endogenous miRNAs).

One of the challenges of cancer therapy involves delivering drugs to tumour sites in adequate concentrations without causing toxicity to healthy organs. **Aptamers**, short single-stranded oligonucleotide sequences can play an important role in cancer therapeutics due to their low immunogenicity and high targeting ability. Aptamers can be used to deliver chemotherapeutic drugs to cancer cells, inhibit target molecules and stimulate immune receptors in lymphocytes. Aptamers can be synthesized by cell-free chemical synthesis and show superior tissue penetration compared to antibodies. These potential advantages make them a possible alternative to conventional antibodies for therapy.

Photoimmunotherapy is a new form of cancer therapy involving the use of near infrared (NIR) light. Photoimmunotherapy uses an antibody to which a photo-absorbing chemical is attached. The antibody-photo absorber conjugate is injected into the patient's bloodstream. The conjugate binds to specific cancer cell receptors, allowing the photo-absorbing chemical to be activated by near-infrared light causing damage to the cell membrane, swelling and necrosis by releasing cellular contents. This highly specific treatment does not appear to damage nearby normal cells and is currently under clinical trials.

Nanotechnology also holds promise for cancer treatment and diagnosis, offering targeted drug delivery, early detection through molecular diagnostics, and improved surgical resection by guiding and improving the removal of tumours, thereby reducing systemic toxicities and improving patient outcomes. **Nanomedicine** involves the production of miniature-sized particles for the delivery of drug molecules to specific cells, thus seeking to provide better bioavailability and decreased toxicity. The process of formulation and encapsulation of compounds in these carriers and easy deliverance into tumour sites with lesser premature degradation, high aqueous solubility and enhanced pharmacological ability has the potential to increase the efficiency of cancer therapy.

Phytochemicals in Cancer Therapy

Many recent studies have revealed that several compounds from natural plant sources have significant potential for use in cancer therapy. Various classes of phytochemicals like flavonoids, polyphenols and terpenoids have been studied extensively for their cytotoxic, antioxidant and apoptotic capabilities. Cancer cells exhibiting multi drug resistance (MDR) can increase efflux of drug molecules or alter drug targets (reducing sensitivity to anti-cancer drugs), or acquire an increased ability to repair DNA damaged by radiation therapy or chemotherapy. Some recent studies have indicated the ability of natural phytochemicals to reverse MDR in various cancers including breast, lung and colon cancers and leukemia.

Flavonoids: Apigenin, a tri-hydroxy flavone which is present in a number of fruits, vegetables and medicinal herbs, can promote apoptosis, induce cell cycle arrest and suppress cell invasion on various human cancers by inhibition of cellular signalling cascades like the PI3K/ Akt signalling pathway. Apigenin also inhibits P-glycoprotein-1 and breast cancer resistance protein (BCRP), increasing cellular uptake of anti-cancer drugs such as Doxorubicin in MDR cells. Wogonin, a methoxyflavone, increases sensitivity of breast cancer cells to sorafenib and doxorubicin, induces apoptosis and has the potential to reduce tumour growth. Kaempferol, a yellow-coloured flavonoid found in fruits, flowers and leaves of different plants including beans, broccoli, cabbage, cauliflower and garlic has anti-inflammatory and anti-tumour activities. Kaempferol can induce apoptosis by suppression of Bcl-2 and upregulation of the tumour suppressor protein p53 (which induces apoptosis and cell cycle arrest in cells with DNA damage) and promote cell cycle arrest at the G2/M phase.

Polyphenols: Polyphenols like resveratrol, curcumin and epigallocatechin gallate (EGCG) show significant anti-tumorigenic properties. Resveratrol, a natural polyphenol found in grapes (*Vitis vinifera*) and peanuts (*Arachis hypogaea*) regulates formation of ROS, stimulates apoptosis by inhibition of anti-apoptotic proteins such as Bcl-2 and activation of pro-apoptotic proteins such as Bad and Bax. Resveratrol inhibits expression of human epidermal growth factor receptor 2 (HER2), inhibits cellular signalling through the p38MAPK, Jnk and PI3K/ Akt pathways and downregulates expression of pro-angiogenic molecules like vascular endothelial growth factor (VEGF) in various cancers. Epigallocatechin gallate (EGCG), a phenol found in green tea (*Camellia sinensis*), has been shown to possess anti-tumorigenic potential against a number of cancers including oestrogen receptor positive (ER positive) breast cancers. EGCG inhibits signalling through focal adhesion kinase (FAK) and nuclear factor kappa-β (NF-κβ) pathways. EGCG can reduce cell viability and promote apoptosis in a number of cancers via activation of mitochondrial pathways. EGCG also reduces expression of VEGF, thus inhibiting tumour angiogenesis. Curcumin, a polyphenol present in rhizome of turmeric (*Curcuma longa*), possesses potent anti-inflammatory, anti-tumorigenic and anti-oxidant properties.

Curcumin inhibits chemical induced carcinogenesis and suppresses growth and proliferation of various types of cancer cells. Curcumin has been reported to inhibit multiple cellular signalling pathways including NF-kβ, MAPK, FAK and integrin mediated signalling pathways, thus inhibiting proliferation and invasion of cancer cells. Curcumin can inhibit epithelial mesenchymal transition and secretion of proteases in cancer cells, thereby inhibiting tumour invasion and metastasis.

Terpenoids: Terpenoids like sesquiterpene have been shown to inhibit metastasis, cell survival and prevent chemoresistance in cancer cells.

Conclusion

Studies regarding the use of modern molecular methods and phytochemicals in cancer therapy indicate that these could have extremely good therapeutic potential and may lead to development of effective clinical strategies to meet the challenges of cancer therapy. Molecular techniques currently under study appear to have potential to improve molecular diagnosis and treatment of cancers. Many of the phytochemicals under study and their plant sources are already a part of human diet; therefore, using these compounds may help in reducing side effects of treatment. A combination of molecular methods and the use of phytochemicals may further increase efficacy of cancer treatment. For instance, encapsulation of natural compounds in molecular carriers could promote easier delivery to tumour sites with high aqueous solubility and enhanced pharmacological ability.

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The Looping Enigma: A Secret Orchestra of Transcription

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Keywords: Gene loop, Transcription memory, Chromatin loop, Transcription factory

In the bustling core of a living cell, where instructions of life are inscribed in the elegant script of DNA, there exists a remarkable gathering place known as the "chromatin". Electrostatic interactions between negatively charged DNA and positively charged basic proteins called histones enable DNA to be packaged into chromatin. Here, the expression of genes, like storytellers, weave the backdrop that governs every function of a cell or group of cells. The chromatin is a milieu of genetic and epigenetic codes where past events are recorded not in ink, but in molecular marks. Have you ever imagined that genes might remember their past activities? Yes, genes exhibit a fascinating phenomenon known as "transcription memory." In simple terms, these genes retain a "memory" of their previous transcriptional activity, which persists even when transcription is repressed. When the cell receives a signal to restart transcription, it uses this molecular memory to resume gene expression immediately. As a result, after successive cycles of induction and repression, these genes can initiate transcription more rapidly, than they did during the initial round. Several chromatin modification marks act as "memory tools" that remain intact even when transcription is repressed, keeping the promoter "primed" for quick reactivation.

Gene looping acts as a transcriptional 'memory tool', much like epigenetic modifications, by facilitating the physical interactions between apparently distant genomic regions [1]. To promote multiple rounds of transcription, genes can bend their linear stretch of DNA to form 'gene loops'. This looped conformation brings the gene promoter and terminator into close physical proximity and enables the transcription machinery to swiftly relocate from the terminator to the promoter region. Let's put forth a question- if you have back-to-back trips, would you rather not unpack your bags after the first round of trip? The cell follows the same strategy during multiple rounds of transcription. Several transcription factors including RNA Polymerase II assemble in the promoter region through an ordered interaction to form a pre-initiation complex (PIC). A subset of the pre-initiation complex (PIC) acts as a scaffold at the promoter after initiation of the first round of transcription. These factors join the rapidly relocating RNA Polymerase II to form a re-initiation complex without having to re-organize from scratch. These loops even retain a memory that makes genes ready to snap back into action the moment it is needed. Studies have revealed that after the first round of induction, inducible genes may remain in looped conformation even after transcription shuts down so that the next round of transcription can be initiated rapidly upon induction [1]. It is worth noting from earlier research that transcription-associated chromatin modifications are integrally associated with gene loops [2]. Moreover, intragenic loops work towards maintaining transcriptional directionality, especially from bi-directional promoters that may initiate transcription in both the sense and antisense directions. Disruption of gene loops often results in repositioning of RNA Pol II on the promoter leading to increased production and accumulation of divergent non-coding RNAs (ncRNAs) [3].

The genome content is identical in every cell of an organism, whether it is a neuron in the brain or a hepatocyte in the liver. Yet, somehow each cell seems to have its unique characteristics attributed to the expression of specific sets of genes at specific times. This fact raises the question, 'how is gene expression regulated in a spatio-temporal manner?' While gene looping regulates the rate and pace of gene expression, the spatio-temporal fidelity of gene expression is affected by chromatin looping. The dynamic nature of chromatin loops allows transcription activation and repression of the genes according to the needs of a cell. This flexibility plays a key role in the "spatio-temporal control" of transcription. Incidentally, this dynamic yet very stringent regulation of chromatin looping is carried out by proteins like Cohesin, CTCF (CCCTC binding factor), and WAPL (Wings Apart-like Protein homolog) in mammalian cells [4,5,6]. According to the "Loop extrusion hypothesis" by Alipour and Marko, the chromatin threads through the ring-like cohesin protein complex continuously forming a larger loop until it reaches CTCF proteins bound to a specific sequence called insulator sequence, in a convergent

head-to-head orientation [7]. That's how CTCF acts as the insulator protein and defines the boundary of chromatin loops. Additionally, WAPL helps to release chromatin looping after the need for transcription is over. Now an obvious question that comes to mind is what is the requirement of this CTCF-mediated regulation of chromatin looping? To answer that we can look into an example (Fig 1).

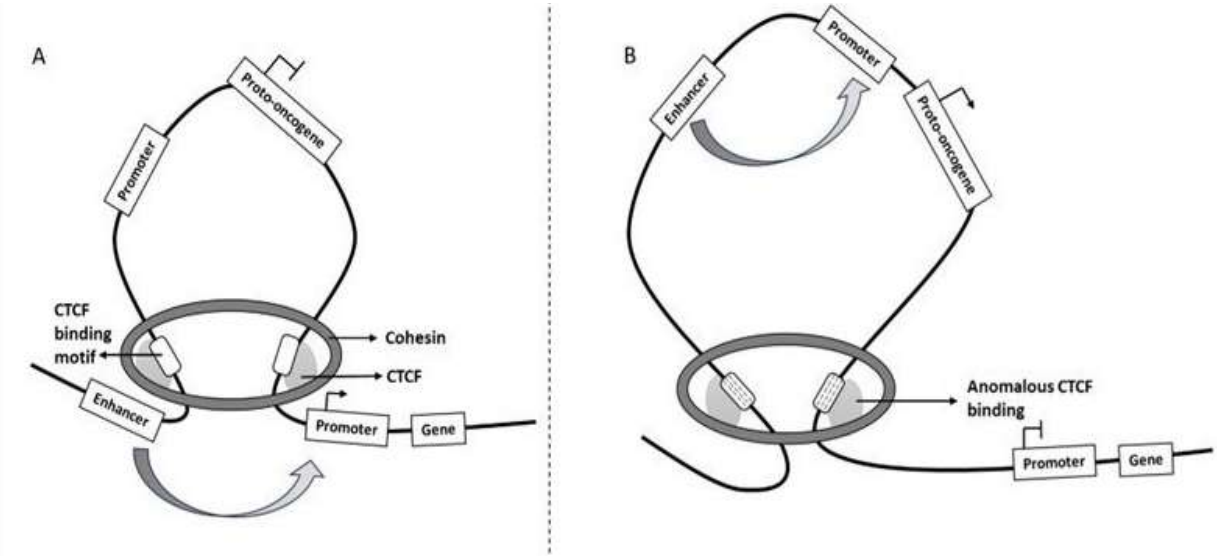

Fig 1: Transcription regulation by Cohesin and CTCF: A) CTCF binding to its respective insulator sequence to repress protooncogenes. B) Enhancer element comes in proximity to the promoter of the proto-oncogene and activates transcription as a result of anomalous binding of CTCF.

In the above image, Figure 1A depicts the binding of CTCF to the correct CTCF binding motif, the enhancer element and the promoter of the gene required to be transcribed come in close contact enabling the initiation of transcription. On the other hand, the promoter of the proto-oncogene is insulated from the enhancer by gene looping. While in Figure 1B, due to the anomalous binding of CTCF and its failure to define the boundary of the chromatin loop correctly, the enhancer element comes in close contact with the promoter of the proto-oncogene and this, in turn, activates its transcription. The activation of a proto-oncogene which is supposed to remain transcriptionally silenced can lead to predisposition to cancer. From this example, we can understand the significance of this stringent regulation mediated by CTCF in defining the boundary between transcriptionally active and repressed or silenced chromatin regions. Cells organize these chromatin loops in such a manner that the preferential long-range promoter-enhancer interactions are kept together and insulated from transcriptionally repressed or silenced regions. These domains with preferential long-range interactions are called Topologically Associated Domains or TADs [8]. CTCF proteins define the boundaries of these TADs by limiting the promoter-enhancer interaction within each TAD. If the spatio-temporal regulation of transcription is impaired due to TAD boundary disruption during development, limb malformations like synpolydactyly (production of supernumerary, fused digits), and Cooks syndrome may occur [9].

RNA Polymerase II along with factors involved in transcription activation and mRNA processing assemble to form "transcription factories" [10]. These are discrete and specialized sites of transcription that are accessed by chromatin loops through strict regulation. Two or more genes, that are remotely located, tend to share common transcription factors from the same transcription factory for gene expression. Upon transcription activation, both the gene loop and the chromatin loop, referred to as the "transcription loop", engage with transcription factories. These loops reel through the elongating RNA Pol II as it synthesizes nascent RNA [10]. Thus, the combinatorial effect of transcription factory and three-dimensional chromatin loops co-regulates multiple genes simultaneously making a particular signalling or developmental pathway possible. Thus, whether it is the preservation of the memory of previous transcription or orchestrating spatio-temporal gene expression, transcription loops serve as essential guardians of genome function. Thanks to such architectural looping- the secret orchestra of transcription that enables our genes to tell the tales of their journey towards maintaining cellular harmony and systemic fidelity.

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Brain goes Underground: Mystery of the subterranean organ system

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Keywords: root system, subterranean brain, plant neurobiology

Ever imagined in your wildest dreams that an organism can have its brain buried underground? Take a breath and unleash your imagination. No, you are probably not guessing it right- it is not an earthworm or any member of the animal kingdom that we are talking about, it is actually the plant system! Plants are a unique kind of organisms that has been speculated to possess a subterranean brain. While it is quite fascinating to think about an underground brain system, the obvious question that arises is what could be the precise seat of this hidden brain within the plant body. It might sound impossible, but the tip of the radicle acts as the brain of a plant. The radicle tip is equipped with the sensitivity to govern movements of the adjoining plant organs (Baluska et al., 2009). Remarkably, the role of the plant root tip closely mirrors that of the brain in lower animals, endowed with the ability to perceive and control body movements.

The basis of this concept can be traced back to Charles Darwin, who first speculated about the possibility of root tips acting as a plant's "brain" in his book "The Power of Movement in Plants" (1880). Charles Darwin and his son Francis Darwin observed that the root tip could detect and respond to various stimuli such as gravity, moisture, and light guiding the growth and orientation of the entire plant system. The tip of the radicle is perhaps the most remarkable structure in the plant body, regarding its functionality. Research findings indicate that the root apex can perceive the difference between slightly harder and softer objects if simultaneously pressed on opposite sides and in turn orient itself towards the softer side (Baluska et al., 2009). However, if such a similar constraint is applied to the radicle in a zone above the root apex, the influence is not transmitted to the adjoining organs. It has been further observed that the root cap, that is known to protect the root apical meristem, when removed induces faster root growth - but the root fails to exhibit gravitropism (Kutschera and Niklas, 2009). Thus, gravity sensing seems to occur primarily through the root cap. The accelerated growth

exhibited by the root when de-capped seems to be an escape mechanism, against biotic and abiotic assaults. Hence, originated the concept that the plant root apex serves as a 'brain-like' organ bestowed with the ability to sense the surroundings and curate consequent responses accordingly.

In all non-plant multicellular organisms, the anterior pole typically houses the brain or a brain-like organ and possess the ability to acquire nutrition; while the posterior pole bears excretory apparatuses, sexual organs and locomotory structures (Barlow, 2006). In comparison, if we try to think deep and differently then it becomes apparent that the root system working as the anterior end of the plant is equipped with brain-like functions and sensory attributes, along with the responsibility of procuring optimum nutrients. The aerial plant parts, on the other hand are comparable to the posterior pole in animals and display tropic movements, bear reproductive organs and perform excretory functions in the form of transpiration through leaves. Although plants do not exhibit locomotion, it is evident that their active root growth guided by the root tip enables them to explore soil niches for nutrients, water and microbiome interactions (Baluska and Mancuso, 2009). Thus, the root apices serve not only as sites of nutrient uptake but also as points of progressive movement much like the anterior poles of multicellular animals. Parasitic plants offer compelling evidence that roots are essential, while shoots can be dispensable. In cases where nutrition is obtained heterotrophically, the plant is reduced to a haustorial system derived from roots, specialized for absorbing organic nutrients. For instance, in holoparasitic plants like ***Rafflesia***, the aboveground green part is entirely absent (Barkman et al., 2004). It is known to one and all that the root system is an indispensable part of the plant and serves as a crucial regulator of its growth. But how do root apices function as the "brain" of the plant? The initial indication of root apices functioning as a "brain-like" organ comes from the observation that it remains safeguarded by the root cap, mimicking the role similar to that of the skull in multicellular organisms. Another key observation is that upon sensory perception root apex can transmit signals to other parts of the plant, influencing their behaviour. For instance, when the root tip encounters an obstacle or a gradient in moisture or nutrients, it can send signals to the shoot, adjusting its growth patterns accordingly (Baluska et al., 2009). This communication occurs through chemical signalling molecules, such as auxin, cytokinin and other phytohormones. Plants also possess synapses that utilize vesicular recycling processes for cell-to-cell communication, similar to neuronal synapses. Plant synapses are F-actin supported adhesive domains located at cellular endpoles (cross-walls) between adjacent cells (Baluška et al., 2001). These structures facilitate the transport of auxin and other chemical signals across the plant body. Auxin, functioning similar to a neurotransmitter, is transported along the anterior-posterior axis in a light and gravity-dependent manner (Baluska et al., 2009) The root tip located at the anterior-most end of the plant works as the major sink for polar auxin transport and harbours the command centre of the plant body.

So, plants have cell-to-cell communications through plant synapses but what about long-distance regulations? Do plants have "neurons"? It is apparent

that the vascular strands of plants serve the role of plant "nerves" (Baluska et al., 2004). In roots the vascular tissue constitutes a major portion of the organ and further extends into the stem and leaves, forming a complex vascular network. Vascular tissue, as we know is comprised of xylem and phloem. Phloem acts as the "axon-like" channel which connects root and shoot apices (Mancuso, 1999). It is further specialized for rapid transportation of RNA molecules, similar to axons in higher organisms.

It is amazing to realize how much plants resemble the animal system in certain unexpected ways. Recent advances in plant biology have reached a new milestone, revealing that plants are "intelligent" beings capable of learning and making decisions in response to environmental challenges. Plants can emit Volatile Organic Compounds (VOCs), bestowed with a wide range of ecological functions. VOCs can be grouped into terpenoids or isoprenoid plant volatiles, oxygenated plant volatiles and a few furanocoumarin derivatives and sulfur compounds, based on their chemical structure and biosynthetic origin (Berenbaum and Zangerl, 2008). Interestingly, VOCs are largely species specific with different plant lineages adopting different plant volatiles to tackle the same threat. Roots release VOCs which play an essential role in plant interactions with biotic and abiotic agents. Additionally, a recent scientific finding indicates that roots can detect chemical signals originating from their neighbours (Ninkovic et al., 2019). VOCs induced by biotic threats can enhance resistance and trigger defence mechanisms in neighbouring plants (Jin et al., 2023). This phenomenon is often termed as "eavesdropping", since the receiving plant tends to benefit from the VOCs emitted by the affected neighbouring plant. VOCs released by a plant into the rhizosphere have been seen to modulate the germination and growth of neighbouring plants. They tend to improve photosynthesis, nutrient uptake via regulation of phytohormonal homeostasis leading to better survival and increased yield of the plant community. Root-derived VOCs are known to aid in the recruitment of beneficial rhizospheric microbes thereby positively affecting plant

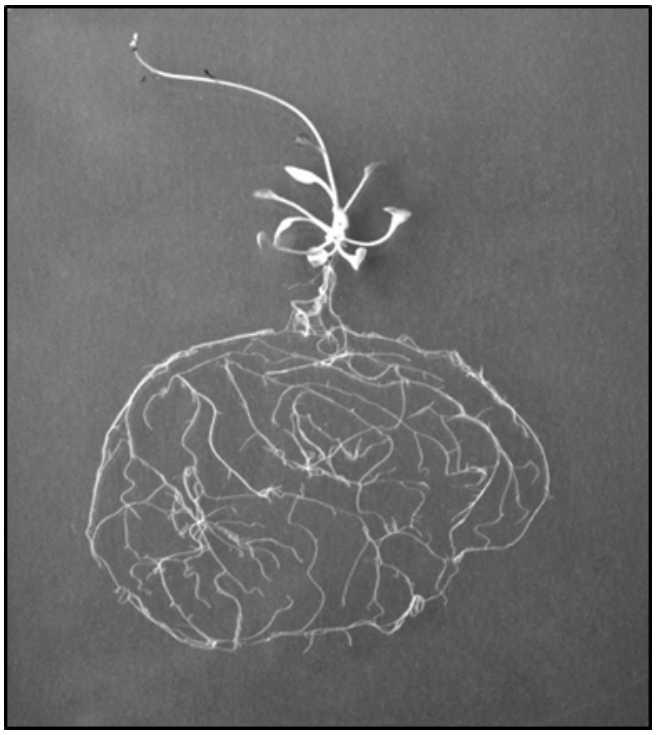

Figure 1: An illustration depicting the root system architecture of *Arabidopsis*, resembling the intricate network of an animal brain.

growth and health (Hammerbacher et al., 2019). Interestingly, plants are smart beings who display the ability to retain memory of stressful environmental and ecological experiences. They can further call upon the memory of the previous trauma for making quick decisions that modulate their future activities. Hence, plants are often considered to be more sophisticated than animals in terms of their behaviour and adaptive responses. However, this unique potential of plants has been obscured, particularly because plant activities demand longer time scales to display response, unlike animals that often exhibit more rapid and visible responses. Such comparable attributes of the plant and animal community possibly evoked the famous statement made by T. H. Huxley (1853) - "The plant, then, is an animal confined in a wooden case...".

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The Balancing Act: Root Growth Decisions for Stress Avoidance and Stress Tolerance

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Keywords: Root system architecture, Drought stress, Primary root.

Water is crucial for plant life, playing a central role in processes like photosynthesis, nutrient transport, and cellular metabolism. The availability of water in the soil directly impacts plant growth and development, influencing the yield of crops as well as the natural ecosystem. With climate change intensifying drought conditions globally, understanding how plants respond to varying water levels is becoming crucial for both basic plant science and its application in agriculture. This knowledge can help develop strategies to maintain crop health and productivity under suboptimal water conditions. Drought stress requires plants to adapt and reorganize their transcription, metabolism, and resource allocation. While drought is traditionally seen as detrimental, moderate water stress can promote beneficial responses, especially in root system development. This demonstrates the complexity of plant-environment interactions and the adaptive strategies plants have evolved through the ages.

Plants like *Arabidopsis thaliana*, adapted to various environments, offer insights into how plants balance drought tolerance with growth. Depending on drought severity, plants may adopt either a tolerance or an avoidance strategy. The root is the primary organ responsible for absorbing water and nutrients from the soil. Root system architecture (RSA) encompasses various traits, including rooting depth, root growth angle, root-to-shoot ratio, root diameter, root length density, surface area, volume, distribution, tip frequency, and root hair development. RSA is highly plastic and can adapt to changing environmental conditions. Under mild drought stress, plants resort to an avoidance strategy, characterized by elongation of the primary root to access deeper soil layers where water may still be available. This elongation is vital for maintaining water uptake as surface soils dry, especially in arid and semi-arid regions where deeper soils retain moisture longer. In severe drought conditions, plants may inhibit primary root growth to conserve energy and resources, shifting to a tolerance strategy (Mandal et al., 2024). Thus, despite lacking canonical sensory organs, plants exhibit sophisticated responses to environmental stimuli. Under drought conditions, the root system detects water deficits and triggers adaptive responses like root elongation. While roots may continue to grow under mild stress, shoot growth is typically suppressed. Such adaptive strategies that have developed over a long evolutionary span, allow plants to survive and adapt to different environmental pressures, ensuring their survival under changing conditions. The critical question that surfaces here is - how do plants decide whether to tolerate or avoid a form of stress, drought stress for example? The answer lies in the complex network of plant hormones that regulate these adaptive responses. Phytohormones such as auxin, cytokinin, gibberellic acid, abscisic acid (ABA), jasmonic acid, ethylene, and strigolactone play significant roles in modulating growth and development under stress conditions (EL Sabagh et al., 2022)

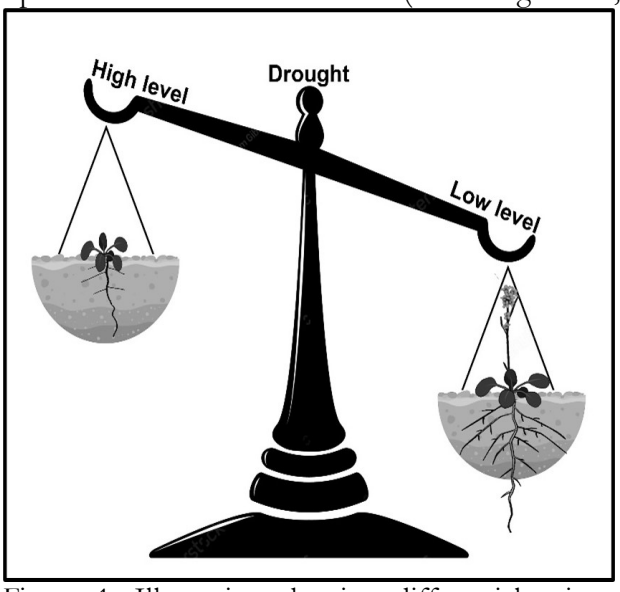

Figure 1: Illustration showing differential primary root growth under varying levels of drought stress.

ABA is one of the most crucial hormones involved in response to drought stress and plays a complex role in balancing both shoot and root growth under such conditions.

It works towards sustaining plant growth when water availability is limited, but inhibits growth when drought stress reaches severity. Research findings indicate that

low levels of exogenous ABA stimulate root growth, whereas high concentrations inhibit it. This biphasic response is paralleled by the effect of drought stress itself: low-stress levels promote root elongation, while high stress dampens it (Miao et al., 2021). Auxin, long known for its role in promoting plant growth, has been recognized for its function in stress responses, including the regulation of root meristem activity during drought (Rowe et al., 2016). Auxin works by controlling cell division and elongation in the primary root and alterations in auxin gradients can significantly affect plant's ability to adapt to drought stress. Interestingly, scientific findings indicate interactions between auxin and ABA, with ABA inhibiting auxin biosynthesis under specific conditions to regulate root growth. Cytokinin, on the other hand, has an opposing role compared to auxin and ABA in drought stress response (Nguyen et al., 2016). Under osmotic stress, plants typically reduce cytokinin levels, which enhances root growth and increases drought tolerance. Cytokinin is considered a negative regulator of drought adaptation, and mutants lacking functional cytokinin receptors show enhanced resilience to drought. The ABA-cytokinin antagonism is another layer of complexity in the plant's hormonal response to water deficit, where reduced cytokinin signaling is necessary for the plant to activate its drought-adaptive mechanisms. Such an overlapping network of interactions highlights the complexity of hormone-mediated responses to drought, where both hormones can act synergistically or antagonistically depending on the stress intensity.

In addition to hormonal regulation, drought stress profoundly impacts the expression of various genes in plants, enabling them to adapt and optimize growth under adverse conditions. Transcription factors, as key regulators of gene expression, play a pivotal role in orchestrating stress response pathways, ensuring the plant's survival and resilience. Key transcription factors such as ABSCISIC ACID INSENSITIVE 3 (ABI3) and ABSCISIC ACID INSENSITIVE 5 (ABI5) are pivotal in regulating ABA signaling pathways (Lopez-Molina et al., 2002). These transcription factors are part of the core ABA signaling machinery and play a role in both developmental processes and stress responses. Interestingly, ABI3 can function as both a transcription activator and transcription repressor (Bedi and Nag Chaudhuri, 2018). While ABI3 is known to positively regulate the expression of a cassette of downstream genes in response to water scarcity, it negatively regulates the expression of another transcription factor, RELATED TO ABI3/VP1 1 (RAV1) under similar conditions (Bedi et al., 2016, Sengupta et al., 2020). Repression of RAV1 expression enhances primary root meristem size by dampening cytokinin signaling (Mandal et al., 2023). Such interaction between ABI3 and RAV1 underscores the complex web of hormonal cross-talk that governs primary root growth under conditions of water dearth (Sengupta et al., 2020).

The primary root of *Arabidopsis*, which consists of distinct zones (meristematic, transition, elongation, and maturation zones), is highly sensitive to hormonal regulation. Under favourable growth conditions, cytokinin regulates root meristem function by controlling the expression of *SHORT HYPOCOTYL 2* (*SHY2)*, a key inhibitor of auxin signaling. SHY2, in turn, represses the expression of auxin transporter protein PIN-FORMED 1 (PIN1), which regulates auxin distribution (Ruzicka et al., 2009). Maintenance of auxin gradient helps in restricting primary root meristem size and growth. As mentioned before, under conditions of mild water stress where plants opt for stress avoidance, cytokinin signaling is inhibited, leading to increased auxin transport and consequently resumed growth of primary root in search of water. However, under severe drought conditions, ABA antagonizes auxin signaling by repressing PIN1 expression, effectively stalling primary root growth. Transcription factor ABI3 has been shown to regulate primary root growth by modulating *SHY2* expression in response to drought stress and consequent ABA levels (Mandal et al., 2024). Under mild stress when ABA levels are low, ABI3 expression increases leading to reduced SHY2 activity and resultant enhanced primary root growth. However, at higher stress levels when ABA levels are high as well, ABI3 expression decreases, leading to increased SHY2 activity and impaired primary root growth. This dynamic regulation of primary root growth by ABA and auxin is thus fine-tuned by ABI3 through expression regulation of SHY2, PIN1, and other downstream genes (Mandal et al., 2024). Interestingly, this gives us a picture of how plants critically control primary root growth in response to varying intensities of drought stress. The regulation of primary root meristem size and cell division rates under different levels of drought stress highlights the plasticity of root growth as a well-orchestrated adaptive mechanism exhibited by plants. This intricate balance ensures that the plant can adjust its root growth in response to fluctuating water availability, optimizing its ability to survive and thrive under adverse conditions.

In conclusion, it is pertinent to state that the dynamic relationship between water stress and root growth highlights the intricate adaptive mechanisms that plants employ to cope with drought conditions. Root system architecture, driven by a complex web of hormonal regulation plays a pivotal role in determining whether a plant adopts a stress avoidance or stress tolerance strategy. Under mild drought conditions, plants enhance root elongation, enabling them to reach deeper water sources and maintain growth. In contrast, severe drought often

triggers a shift toward growth arrest and stress tolerance, conserving resources for survival. The balance between these responses is coordinated by intricate hormone signaling networks that integrate environmental cues with growth decisions. Understanding these adaptive mechanisms not only deepens our knowledge of plant-environment interactions but also holds promise for agricultural innovations. By harnessing the insights gained from model plants like *Arabidopsis thaliana*, we can potentially develop crops with optimized root systems that are more resilient to water scarcity. Such advances can potentially improve crop productivity and food security in drought-prone regions, making the study of root responses to water stress crucial for both basic scientific understanding and its future agricultural applications.

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SCIENTIFIC ARTICLES

FROM STUDENTS

Breaking the Cycle: How Stress Fuels PCOS Symptoms

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Keywords: PCOS, Lifestyle, Stress, Androgen, Hormonal Imbalance

Introduction

Polycystic Ovarian Syndrome or Disease (PCOS/PCOD) is now a global epidemic which affects almost 1/5 of adolescent Indian females and premenopausal women worldwide. This complex endocrine disorder is characterized by hyper serum androgen level, irregular menstruation, cystic appearance on ovaries and consequent epidermal manifestations such as acne, alopecia and hirsutism followed by an increased risk of insulin resistance, obesity and their associated diseases including comorbidity and infertility related difficulties in conception. The complicated interplay of genetic predisposition, environmental influences and lifestyle are proposed to be correlated with the susceptibility of this lifestyle-oriented metabolic syndrome. PCOS is not only increasing healthcare burdens across countries but also posing impactful physical and most importantly psychological load on females due to characterizing hormonal imbalance-oriented symptoms (Benjamin et al., 2023) (Qureshi et al.,2023) (Steegers-Theunissen et al., 2020).

However, evolutionarily, researchers suggested that ancestral traits resembling PCOS have favored both non-primates as well as early human ancestors. PCOS-like phenotypes which have been reported in primate non-human ancestors like rhesus macaque, were beneficial for cooling purposes in African environments of the Oligocene before ancestors of humans diverged. The contemporary most adapted genome that was selected during the late Pleistocene age of hunters-gatherers humans, revealed that the PCOS-resembling traits may have served as ancient metabolic adaptations advantageous under additional selection pressure for the survival of humans during food deprivation period. But now, PCOS predisposes individuals to metabolic-endocrine-reproductive dysfunction especially in today's obesogenic calorie-surplus age (Dumesic, Abbott and Chazenbalk, 2023).

Genome-Wide Association Studies (GWAS) have inferred multiple genes and genetic loci involved in steroid hormone receptors, steroidogenesis, insulin action, chronic inflammation etc. Multiple SNPs of Fat Mass Obesity (FTO) genes and Epigenetic modifications including dysregulation of microRNAs can also be correlated with PCOS predisposition (De Leo et al., 2016).

However, the proper gene-phenotype correlation and heritability of PCOS are still sparse and matters of grave interest(De Leo et al., 2016). Gestational or maternal hyperandrogenism during fetal development and later exposure to Endocrine disruptors are also determined as causative factors of PCOS onset in daughters (Kshetrimayum et al., 2019).

Nonetheless, lifestyle modification and most importantly stress management are advised to reverse PCOS. Unfortunately, PCOS and mental health problems are emerging as two sides of the same coin as both influence and aggravate each other. Apart from genetic factors, psychological and physiological stress stands out to be potential contributors to PCOS-oriented hormonal discrepancies and therefore, understanding the stress-mediated molecular pathways holds immense importance in proper understanding of the pathogenesis of this disease that is now affecting substantial female populations in different aspects. Therefore, the article particularly emphasizes the role of chronic stress conditions that induce and exacerbate PCOS phenotypes as demonstrated in multiple studies.

Psychological Stress

Women suffering from the syndrome are more likely to suffer from psychological issues like anxiety, depression, OCD, and even PTSD and bipolar disorder compared to same-age women. Notably, a study on Indian women has found that PCOS-diagnosed females have elevated serum cortisol (stress hormone) and DHEA levels compared to their healthy counterparts delineating its pathogenesis as a stress response (Benjamin et al., 2023). This indicates the perturbation in the Hypothalamus-Pituitary-Adrenal (HPA) axis and results in the disturbed release of FSH and LH thereby promoting ovarian androgen production (Quirishi et al.,2023). Stress indeed causes reproductive dysfunction and hormonal imbalance leading to the manifestation of this syndrome and perturbed body composition (Basu, Chowdhury

and Saha, 2018). Steegers-Theunissen et al postulated that PCOS is induced by psychological distress and episodes of overeating and/or dieting (eating disorders) during puberty and adolescence which are periods of body dissatisfaction and emotional distress. Psychological stressors common in young females include hardships at school or home, low self-esteem, victim of bullying, premenstrual dysphoric disorder etc. This potentially dysregulates the Hypothalamic-Pituitary-Gonadal (HPG) axis, elevating androgen levels (Steegers-Theunissen et al., 2020). Not only that, it is noted that occupation-related psychological stressors also act as intensifiers of PCOS manifestations (Arefi et al., 2022).

Henceforward, lifestyle modifications and additional activities that reduce stress should be implemented in PCOS patients. An important but subtle change in the day-to-day life of women having PCOS is proposed to be implemented by understanding and rectifying the anxious and insecure attachment style and maladaptive coping strategies like societal withdrawal and distress conditions. Therefore, understanding respective attachment styles will assist individuals in developing adaptive coping habits to deal with PCOS symptoms while the former requires more caregiver support and the latter needs the introduction of breathing exercise routines (Simon et al., 2021).

Physiological Stress

PCOS imparts metabolic stress and pro-inflammatory responses to the overall system due to multifaceted hormonal imbalance. Apart from that oxidative stress markers which are common in PCOS patients irrespective of obesity, successively subscribe to proinflammatory states and; therefore lead towards repercussions like hyperandrogenism and insulin resistance, especially in visceral adipose tissue (Kshetrimayum et al., 2019). Endoplasmic Reticulum (ER) stress is now connected with higher androgen levels in PCOS. The protein misfolding phenomenon at ER switches on Unfolded Protein Response (UPR) and maladaptive UPR in granulosa cells (GCs) of ovarian follicles due to increased androgen results in apoptosis and follicular growth arrest. ER stress also promotes the TGF-β1 signaling pathway which drives fibrosis in various tissues leading to ovarian fibrosis during the pathophysiology of PCOS. ER stress in the pancreas, liver, muscle, and adipocytes induces Insulin resistance and compensatory hyperinsulinemia directly contributes to elevated androgen and ovarian dysfunction (Koike et al., 2023).

Conclusion

The article highlights the vicious loop of stress and PCOS symptoms and vice-versa. Although the psychosomatic stress-influenced induction of PCOS is still a matter of research. Physicians should consider the implications of underlying chronic psychological distress and the etiology of PCOS and therefore, suggest ideal stress management mechanisms or psychiatric therapies along with the prescription of optimization of weight, intake of proper nutrient-enriched diet and physical activities. The ER stress response pathway reveals promising therapeutic targets which can be subjected to clinical investigations. The metabolic perturbations leading to physiological distress due to PCOD could be managed by medications and intentional lifestyle changes. Altering the genetic tendency of disease development is not possible, nonetheless, the adolescent must understand the importance of medications as well as the tremendous impact of reducing psychological burdens instead of shame-induced social withdrawals which can lead to further mental and metabolic complications later.

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Pray and Mimic: Mastering the Art of Deception

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Keywords: Batesian Mimicry, Myrmecomorphy, Praying Mantis, Adaptation, Predator-prey dynamics

It dates back to one sunny afternoon in Hyderabad when I was bored and observing the ants on the Neem tree adjacent to our lab complex. My lab senior Rishiddh pointed at the ants, asking if anything about them looked peculiar. As I focused my camera to take a picture, I was taken aback. One of the "ants" was actually a mantis! I stared back at Rishiddh in surprise as he nodded with approval. I was overjoyed to discover another fascinating yet unobvious and subtle example of mimicry in nature. One species evolving to mimic another, usually to fool predators or prey, is known as mimicry. This phenomenon is widespread in the animal kingdom and plays a crucial role in the evolutionary arms race between predators and prey. Among the most intriguing examples of mimicry are ant-mimicking praying mantises, which have evolved to resemble ants in both appearance and behaviour.

Ant-mimicking praying mantises, such as *Euantissa pulchra* and *Odontomantis planiceps*, are remarkable examples of Batesian mimicry, where a harmless species mimics a harmful one to avoid predation. These mantises have evolved to look and move like ants, which are often avoided by predators due to their aggressive nature and chemical defences. The mantises' slender bodies, elongated legs, and ant-like movements help them blend seamlessly into ant colonies, providing them with protection from predators.

Figure1: Ant-mimicking mantis

The success of ant-mimicking mantises lies in their morphological and behavioural adaptations. Morphologically, these mantises have developed body shapes and coloration that closely resemble ants (as can be observed in Picture A). Their bodies are often narrow and segmented, with a constricted "waist" that mimics the petiole of an ant. Behaviourally, they exhibit ant-like movements, such as jerky walking patterns and frequent antennal grooming, which further enhance their disguise. Work done at Harvard suggested a similar pattern in movement trajectories of ant-mimic spiders compared against normal spiders (refer complementary material through QR code). Research has shown that these adaptations are highly effective in fooling predators. For instance, a research examining a praying mantis's distinct reaction to ant-mimicking spiders found that predators are less likely to attack spiders that mimic ants than those that do not. This demonstrates the significant survival advantage conferred by mimicry.

Ant-mimicking mantises play a unique role in their ecosystems. By mimicking ants, they can infiltrate ant colonies and exploit the resources within, such as prey items or shelter. This mimicry also affects predator-prey dynamics, as predators that avoid ants will also avoid the mantises, reducing predation pressure on them. The evolutionary history of mimicry is complex and influenced by various genetic and environmental factors. Studies on ant mimicry in other species, such as jumping spiders and beetles, provide valuable insights into the evolutionary pressures that drive the development of mimicry.

Not only is mimicry fascinating from an evolutionary standpoint, but it is also essential to conservation efforts. Studying mimicry can help identify key spe-

cies interactions and the ecological roles of different organisms. This knowledge is essential for developing effective conservation strategies, particularly in ecosystems where mimicry plays a significant role in maintaining biodiversity. For example, preserving the habitats of ant-mimicking mantises and their ant models can help maintain the delicate balance of predator-prey interactions and ensure the survival of these unique species. Additionally, understanding the mechanisms of mimicry can aid in the development of biomimetic technologies, where principles from nature are applied to solve human challenges.

The importance of mimicry extends beyond academic curiosity; it has significant implications for conservation. By studying mimicry, scientists can gain insights into the complex interactions within ecosystems and the roles different species play. This understanding is crucial for developing effective conservation strategies, especially in habitats where mimicry is a key factor in maintaining biodiversity. For instance, protecting the habitats of ant-mimicking mantises and their ant counterparts can help preserve the intricate balance of predator-prey relationships, ensuring the survival of these unique species. Furthermore, the principles of mimicry can inspire biomimetic technologies, where nature's strategies are applied to solve human challenges, such as creating more efficient camouflage materials or developing new methods for pest control.

Ant-mimicking praying mantises are a testament to the incredible adaptability and ingenuity of nature. Through morphological and behavioural adaptations, these mantises have evolved to blend seamlessly into ant colonies, gaining protection from predators and access to resources. Their mimicry not only highlights the complexity of evolutionary processes but also underscores the importance of studying and conserving these fascinating organisms. As we continue to explore the natural world, the lessons learned from mimicry can inspire new approaches to conservation and innovation.

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For supplementary video and GIF, please visit: https://drive.google.com/drive/folders/1amgkYAgFviQjXu-3wFYh3Db0GHLDrCwzl

Environmental risk factors influencing orofacial cleft

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Keywords: Orofacial clefts, Maternal nutrition, Tobacco and alcohol use, Folic acid deficiency

Introduction

Orofacial cleft lip and palate are one of the most common congenital developmental disorders that have affected millions worldwide. This deformation results from a disruption in the normal fusion of the lip or palate during fetal development.
Globally, approximately 1 in 700 births is observed to be affected by orofacial clefts, where prevalence in variation in regions and populations is significant and specific [1]. The global incidence of orofacial clefts is approximately estimated at 270,000 cases annually, with the highest prevalence in Asia and Africa. As per the records of the Centers for Disease Control and Prevention (CDC), approximately 2,650 cases have been reported annually in the United States itself, thus highlighting the widespread nature of the condition [4].
Developmentally, the critical period for formation of cleft lip and palate occurs between the 4th and 12th weeks of intrauterine life. While cleft lip forms between the 4th and 8th weeks, cleft palate formation occurs between the 8th and 12th weeks [15]. This narrow developmental window means that any disruptions, including environmental ex-

posures, maternal nutritional deficiencies, or genetic mutations during pregnancy, may lead to orofacial clefts. It is therefore important to understand the severity and causes of the anomalies for better treatment and management of such patients. Typically, cleft lip and palate (CLP) are categorized according to their anatomical location and severity. A common classification is as follows:

1. *Cleft Lip (CL)*:

a) Unilateral Cleft Lip: A cleft that affects only one side of the upper lip.
b) Bilateral Cleft Lip: A cleft that impacts both sides of the upper lip.
c) Complete Cleft Lip: Cleft that extends from the upper lip through to the base of the nostril.
d) Incomplete Cleft Lip: The cleft is limited to the upper lip and does not reach the nostril.

2. *Cleft Palate (CP)*:

a) Soft Palate Cleft: It involves only the soft part of the palate.
b) Hard Palate Cleft: It involves the hard portion of the palate and may extend to the soft palate.
c) Submucous Cleft Palate: A cleft that is covered by the mucosal layer, thus making it less visible, although it still affects [illegible]

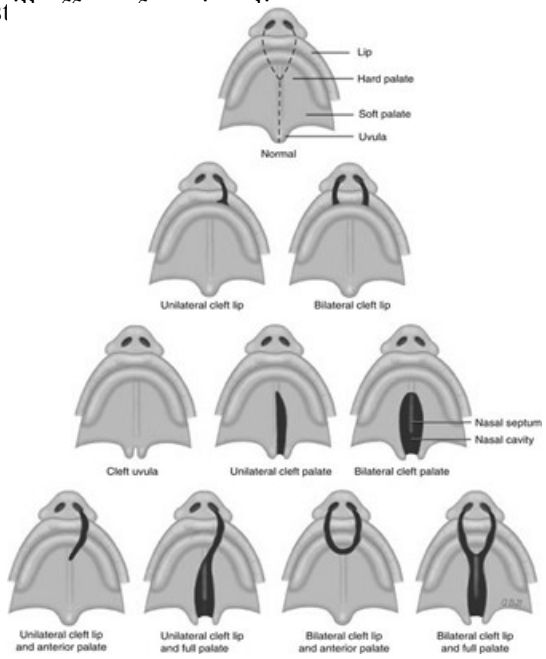

Figure 1: Classification of cleft lip and palate (Source: Haug et al., 2012 www.uptodate.com), Banerjee, M., & Dhakar, A.S. (2013). Epidemiology-clinical profile

3. *Cleft Lip and Palate (CLP)*:

This condition presents a combination of both cleft lip and cleft palate.

Etiology

Genetics plays a crucial role in the development of orofacial clefts. Studies suggest that orofacial clefts, particularly non-syndromic cases (those not associated with other anomalies), result from the interaction of multiple genes and environmental factors. One of the key genes implicated in the development of non-syndromic orofacial clefts is the *TGF-β3* gene, which influences cell signaling and tissue development. Genetic studies in Indian populations have shown the significance of *TGF-β3* polymorphisms in increasing susceptibility to non-syndromic cleft lip and palate [10]. Other genes, such as *CDH1*, involved in cell adhesion, have been studied for their role in craniofacial development.

Research has also identified several other genes, including *IRF6*, *MSX1*, *MTHFR*, and those in the FGF family, contributing to orofacial clefts [12] [9]. The *MSX1* gene is implicated in mediating epithelial-mesenchymal interactions during craniofacial development. Polymorphisms in *MSX1* have been associated with increased risk of cleft lip and palate, further highlighting the genetic heterogeneity of this condition. Although the genetic component is significant, environmental factors and gene-environment interactions also play a pivotal role in the manifestation of orofacial clefts.

Empirical Risk Factors

Several environmental factors contribute to the development of orofacial clefts. These include maternal nutrition, exposure to environmental toxins such as pesticides, smoking, alcohol consumption, and socioeconomic status.

Nutrition And Maternal Health

Folic acid deficiency during pregnancy has been strongly associated with an increased risk of orofacial clefts. Studies have demonstrated that maternal folic acid supplementation during the periconceptional period significantly reduces the risk of cleft lip and palate [5]. Conversely, deficiencies in other nutrients, such as vitamin B12 and selenium, have been proposed as potential risk factors, although their role is less well-established. Hyperhomocysteinemia, resulting from folate deficiency, has been implicated as a potential mechanism for orofacial clefts, with higher homocysteine levels observed in mothers of affected children [13].

Pesticide Exposure

It is seen that exposure to pesticides, especially from the agricultural fields, has been linked to an increased risk of orofacial clefts. Studies indicate that maternal exposure to pesticides, such as organophosphates and pyrethroids, during pregnancy correlates with higher incidences of cleft palate and cleft lip [3] [14]. Women living near agricultural areas or working in fields or areas with frequent pesticide exposure are at increased risk of giving birth to children with orofacial clefts.

These findings highlight the potential teratogenic effects of pesticide exposure during critical periods of fetal development.

Tobacco And Alcohol Use

Maternal smoking has been consistently associated with an increased risk of orofacial clefts. Studies suggest that maternal smoking, particularly during the first trimester, significantly increases the likelihood of cleft lip and palate development [3] [7]. Smoking increases the risk of bilateral clefts and interacts with genetic susceptibility factors, such as polymorphic variants of detoxification enzymes in the fetus, exacerbating this risk [7].

Consumption of alcohol during pregnancy is a potential risk factor for orofacial clefts. High levels of alcohol intake, particularly binge drinking episodes, have been linked to an increased risk of various cleft phenotypes [11]. However, findings are inconsistent, with some studies reporting no significant relationship between alcohol consumption and orofacial clefts [6].

Socioeconomic Factors

Socioeconomic status (SES) is another significant determinant in the risk of orofacial clefts. Lower SES has been associated with a higher prevalence of orofacial clefts, likely due to factors such as poor maternal nutrition, limited access to prenatal care, and increased exposure to harmful substances [2]. In India, for instance, disparities in healthcare access between urban and rural populations exacerbate the challenge of treating orofacial clefts. Families in lower-income areas may lack the resources for adequate prenatal care and postnatal surgery, leading to poorer outcomes for children with orofacial clefts [8].

Conclusion

Orofacial cleft lip and palate represent a complex congenital anomaly that is influenced by a multifactorial combination of genetic and environmental factors. While advancements in surgical interventions have improved its treatment, preventing the disorder from occurring has remained a significant public health challenge. Genetic studies have led to the identification of several key genes involved in craniofacial development as well as maternal factors such as nutrition, pesticide exposure, smoking, alcohol consumption, and socioeconomic status, which are seen to play critical roles in the manifestation of orofacial clefts. Preventive measures, including adequate folic acid intake by the mother, reduced exposure to pesticides, complete stop to smoking and drinking, and access to healthcare, could help mitigate the risk.

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Nature's pause button: The surprising link between Hibernation and Longevity

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Keywords: : Hibernation, Metabolic Rate, Oxidative Stress, Longevity, Telomere Shortening, Reactive Oxygen Species.

Endothermic animals can function regardless of ambient temperatures (Ta) because they generate heat through metabolism, which keeps their body temperature (Tb) high. Since most enzyme-mediated processes take place at their best in a small temperature range, thermoregulation is crucial. Endothermic animals can therefore maintain biological processes over a broad range of environmental temperatures. Nevertheless, there are substantial energy expenditures associated with maintaining these high metabolic rates.

The body's temperature setpoint (Tset) is significantly reduced during hibernation, and the body temperature (Tb) frequently approaches the ambient temperature (Ta) by 1°C. Tb can go as low as -2.9°C in exceptional circumstances, but for the majority of hibernators, it varies from 2°C to 10°C. As a result, biological processes slow down to a tiny portion of their typical rates. Less than 1% of the resting metabolic rate can be reached during hibernation. For example, the average heart rate of hibernating Gould's long-eared bats (Nyctophilus gouldi) can drop to as low as 5 beats per minute, whereas their resting heart rate averages 228 beats per minute. The respiratory rate also drastically decreases during hibernation, and some people have protracted episodes of apnea, in which their breathing is momentarily stopped. Many tiny mammals and certain birds enter a state known as torpor, which is characterized by a decreased body temperature and metabolic rate. The classifications Aves and Mammalia contain species that are capable of torpor, or heterothermy. Among them are marsupials, hummingbirds, nightjars, rodents, bats, and even some primates.

According to a study by Turbill et al. (2011a), hibernating bats have the longest lifespans of all small animals, but even non-bat hibernators had considerably longer lifespans than non-hibernators. The maximum lifespan of a normal 50-gram hibernator, for instance, is 50% longer than that of a non-hibernator of the same size, indicating that the rate of aging in hibernators is roughly halved. Additionally, the analysis showed that hibernation affects other important life history traits: in comparison to similarly-sized non-hibernators, little hibernators typically reproduce more slowly, mature later, and have longer generation durations. The co-evolution of characteristics indicative of sluggish life histories is associated with the enhanced survival rate of hibernating mammals. Latitude was examined in the study; however, the final models did not show it to be a major explanatory variable. This implies that the evolution of sluggish life histories is not largely driven by the short breeding season at high latitudes, where most hibernators are found.
Rather, "bet-hedging"—distributing reproductive events over several active seasons with different environmental circumstances—might be a significant selective factor influencing these characteristics. Unlike shorter-lived, non-hibernating seasonal breeders, hibernators can schedule the birth of their progeny to coincide with ideal food and climate conditions due to their increased survivability and capacity to spread reproductive bouts. Nevertheless, smaller species with shorter life spans may be compelled to reproduce at less favourable periods throughout the active season, even among hiberna-

tors, primarily due to their own birth timing.
The beginning of hibernation seems to be an underlying reaction to photoperiod and is somewhat impacted by other environmental parameters, such as the amount of food available on the terrain and individual condition, that diminish predictably before the hibernating season.

Increase in the ratios of [ADP]:[ATP] and [NAD+]:[NADH] indicate metabolic stress, which is brought on by reductions in the availability of food. Two major features of hibernation are a decrease in metabolic rate and an increasing reliance on lipolysis for ATP synthesis as a response of the cell to decreasing concentrations of energy substrates.
Hibernators may invest in senescence-delaying mechanisms only if they have high rates of survival during the dormant stage (though it's unclear if these mechanisms are indeed products of the torpid state). Lyman et al. (1981) conducted a study in Turkish hamsters that showed a positive corelation between longevity and time spent in hibernation, evidently suggesting that hibernation delays aging. This is consistent with the "rate of living theory" (ROL), a theory that states that decreased energy use during hibernation delays aging and increases lifespan. Reactive oxygen species (ROS) generated by mitochondria are known to cause oxidative damage to DNA and macromolecules, which is frequently associated with aging (Kregel and Zhang, 2007). Minor oxidative stress can boost the maintenance and repair mechanisms that decrease aging, even while ROS can damage cells (Ristow and Schmeisser, 2011). Arousal is one of the hibernation periods when ROS generation may rise, although higher antioxidant levels counteract this (Brown et al., 2011). Overall, by avoiding ROS bursts during wakefulness and reducing ROS generation at low body temperatures, hibernation probably lessens oxidative stress and may even lengthen life (Brown et al., 2011).
Telomere shortening, which is associated with worse survival rates, can be accelerated by oxidative stress (Monaghan, 2010). This is likely true for the species that undergo deep hibernation as well. Hibernation is linked to lower rates of telomere shortening, as shown in Djungarian hamsters during daily torpor (Turbill et al., 2011c). According to Koizumi et al. (1992), two variables that probably lessen telomere shortening are a reduction in ROS-induced damage, a decrease in oxidative stress during hibernation, and a slowdown in cell division processes at low temperatures. Hibernation is therefore linked to slower aging and a state of increased somatic maintenance (Turbill et al., 2011c).

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Bridge RNA: The Successor of in Genome Editing

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Keywords: : Genome editing tool, Molecular Biology, DNA Recombination, DNA transposition

Introduction

With improvement in molecular biology tools, the discovery of genome editing tools can be marked as a milestone, and several years of evolution in that field have resulted in the extensive use of tools like CRISPR-Cas9 for genome editing. A recent study talks about the discovery and functionality of bridge RNAs (brRNA), which facilitate programmable recombination of target and donor DNA through a novel mechanism involving non-coding RNA (ncRNA) associated with the IS110 family of mobile genetic elements. These genomic rearrangements, including insertions, deletions, and inversions are typically mediated by various enzymes involved in DNA repair and transposition.

Mechanism

Researchers found that IS110 elements express a structured ncRNA that binds specifically to their encoded recombinase. This bridge RNA features two internal loops that can independently base-pair with the target DNA and the donor DNA (the IS110 element itself). This modularity allows for the reprogramming of the target-binding and donor-binding loops, enabling sequence-specific recombination between two DNA molecules. The study highlights that this system expands the repertoire of nucleic-acid-guided systems beyond existing technologies like CRISPR and RNA interference. The IS110 family, characterized by minimal autonomous mobile genetic elements, utilizes a recombinase that allows scarless excision of itself from the genome, generating a circular form that integrates into specific genomic target sequences. The research reveals that the bridge RNA plays a critical role in mediating recombination by bridging the donor and target DNA through direct base-pairing interactions.

Experiments were conducted to demonstrate that the bridge RNA is essential for in vitro recombination, showing that the combination of the ncRNA, recombinase, target DNA, and donor DNA is sufficient to produce the expected recombination products. The bridge RNA was named for its dual role in binding both target and donor DNA, with distinct loops for each. Experiments were also done to check the programmability of the bridge RNA, demonstrating that the target-binding loop can be reprogrammed to direct target site specificity for DNA recombination. A two-plasmid recombination reporter system was designed, confirming that reprogrammed bridge RNAs could abrogate recombination with wild-type targets while enabling high rates of recombination with cognate target sequences. Findings also suggest that the bridge RNA allows for flexible programmability of both target and donor DNA recognition.

Advantages Of Bridge RNA Over CRISPR-Cas 9

The unique mechanism of Bridge RNA offers several advantages that make it a complementary or even superior alternative to CRISPR-Cas9 in certain applications. Some of the potential advantages of brRNA over CRISPR-Cas9 are as follows:

1. *Increased Targeting Flexibility*

One of the standout features of bridge RNA is its modular design that allows for seamless programmability in targeting DNA at multiple sites. Unlike CRISPR-Cas9, which requires the design of a unique guide RNA (gRNA) for each target sequence, bridge RNAs can be reprogrammed by simply altering specific loops responsible for DNA binding. This flexibility enables rapid adaptation of the system to target different sequences without the extensive re-engineering typically associated with CRISPR protocols.

2. *Reduced Off-Target Effects*

Off-target activity presents a significant concern with CRISPR-Cas9, where unintended cuts at non-target sites can result in deleterious mutations. The precise base-pairing capabilities of bridge RNA allow for more accurate targeting, potentially reducing off-target activity. Each component of the bridge RNA framework can be finely tuned, allowing for enhanced specificity and lower risks of unintended genome modifications. Consequently, bridge RNA systems could lead to safer applications in therapeutic contexts, particularly in clinical treatments

3. *Scarless Recombination*

CRISPR-Cas9 typically leads to double-strand breaks in the DNA, which necessitates repair mechanisms

that can result in insertions or deletions (indels), sometimes with unwanted consequences. In contrast, bridge RNA facilitates scarless recombination, allowing for the precise insertion or excision of genetic material without leaving behind disruptive sequences. This ability makes bridge RNA a more appealing option for applications requiring pristine genomic alterations, such as the correction of genetic disorders or in scenarios where precise gene additions are necessary.

4. *Simplicity of Design and Use*

The design and implementation of CRISPR-Cas9 systems can be relatively complex, requiring careful optimization of both the gRNA and the Cas9 endonuclease. In contrast, the bridge RNA system permits easier assembly and deployment by using an organized structure of loops to guide specific sequences.

5. *Enhanced Delivery Mechanisms*

Bridge RNA's unique structure and function may enable more efficient delivery mechanisms for targeted genome editing—both in vivo and in vitro. While CRISPR-Cas9 often faces challenges in penetrating cellular pathways and can evoke immune responses, bridge RNA's smaller size and less complex composition may enhance its stability and ease of cellular uptake. This potential increases its feasibility in gene therapy applications where delivery to specific tissues poses a significant hurdle.

6. *Broad Applicability in Genomic Rearrangements*

Bridge RNA is not limited to simply cutting and pasting genomes; it offers extensive versatility concerning genomic rearrangements, including inversions and duplications that CRISPR-Cas9 does not readily accommodate. The inherent design of bridge RNA makes it especially suitable for more complex genetic modifications that require precise manipulation of genomic architecture, enabling applications in synthetic biology and complex trait engineering.

7. *Adaptation to Different Organisms*

CRISPR-Cas9, while robust, was originally derived from bacterial immune systems and can sometimes face compatibility issues in more complex eukaryotic systems. Bridge RNA, on the other hand, may exhibit greater universality across different organisms due to its foundational mechanism being based on mobile genetic elements, which operate within various biological contexts. This adaptability could help bridge RNA gain traction as a tool in diverse fields, from agriculture to human health.

8. *Potential for Multi-Target Editing*

The configuration of bridge RNA permits concurrent targeting of multiple sites in a single reaction. Unlike CRISPR-Cas9, where multiplexing requires careful design to minimize interference and eliminate off-target effects, bridge RNA may streamline multi-target editing by synergistically binding to multiple target sites simultaneously with a single construct. This feature opens up new avenues for genome-wide studies and complex engineering projects that demand precise alterations at several loci.

While CRISPR-Cas9 has undeniably transformed the landscape of genome editing with its profound applications and effectiveness, the emergence of bridge RNA as a powerful tool presents numerous advantages that can complement and extend the capabilities of existing technologies. As research continues to explore this innovative RNA mechanism, it holds the promise of advancing the fields of biotechnology and therapeutic applications, enhancing our capacity to manipulate genome with unprecedented precision and efficacy.

Conclusion

In conclusion, IS110 bridge recombination system has the potential to enable precise control over DNA rearrangements, including insertion, excision, and inversion, with implications for genome design and engineering, and the discovery of bridge RNAs has caused a significant advancement in the field of genetic engineering, offering a unified mechanism for manipulating DNA sequences in a programmable manner.

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Role of Endophytes in Camptothecin Synthesis under Abiotic Stress, and its In-Vitro Production

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Keywords: endophytes, abiotic stress, Camptothecin, anti-cancer properties, in-vitro production

Introduction:

Secondary metabolites are mainly associated with the defense and protection of the plant from potential threat factors that they encounter daily. In the past, such metabolites have been studied to understand how the secretions help the species survive. For example, some phenolic metabolites with specific volatile residues have been effective in repelling herbivores and protecting the plant.

We are aware of the fact that organisms often tend to be in a mutualistic or symbiotic association with entities of other species for their benefit. Such a phenomenon is also observed in the flowering plant *Opphiorhiza mungos*, where it is associated with the fungus *Fusarium solani* in an endophytic relationship. Endophytes are bacteria or fungi in a symbiotic relationship with plants, wherein they receive shelter and nutrition from the plant, provide protection against infection, and help the plant perform other metabolic processes. They can hence help the plant in the production of various secondary metabolites and also influence their production.

In recent studies, it has been understood that under abiotic stress conditions like water or thermal stress, the action of these endophytes is enhanced, which in turn produces secondary metabolites, which ultimately help the plant to survive. One very important pentacyclic alkaloid, Camptothecin, is found in the plant *Ophiorrhiza mungos*, a member of the coffee family, and one that is found prevalently in the Western Ghats of India, has broad-spectrum anti-cancer effects, and can be used for chemotherapy to make these services approachable to every person afflicted by cancer.

Body:

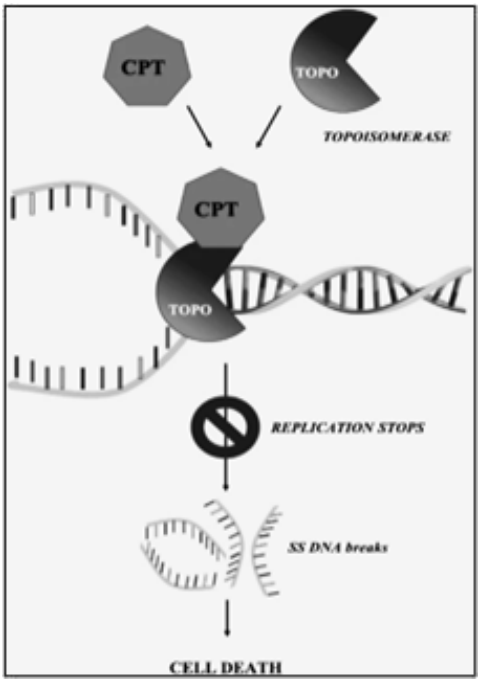
What triggers the production of camptothecin by endophytes?

The production of metabolites is related to the existence of certain factors. Such factors are either caused by internal or external factors and create a stressful condition for the plant.

Stress conditions can be related to nutrition limitations, changes in pH, or even temperature fluctuations. These collectively are called abiotic stress. Abiotic stresses can be classified as stresses that are caused by external stimuli. Such a condition causes the plant to develop different pathways to sustain itself. One such development is the production of secondary metabolites mainly associated with defense. One such metabolite is camptothecin.

For this to happen, the host plant or some neighboring molecules produce signaling molecules. The interplay between the plant and the endophyte is important, as the plant often produces certain precursor molecules that help in the biosynthesis of camptothecin. Moreover, different inducible genes present in the genome of the endophytic organism that are regulated only in the presence of such environmental cues are responsible for its production. However, this process is largely based on an adaptive mechanism where the plant needs to have a strong defense mechanism to save itself from herbivores and pathogens and, in turn, enhance the endophyte.

Activity of Camptothecin:



In the figure above, CPT stands for camptothecin-

the metabolite, and topoisomerase I is the enzyme.
Topoisomerase is an enzyme whose activity lies predominantly in DNA replication, transcription, and repair. It nicks one of the strands of the double helix, allowing it to rotate around the other intact strand and, in turn, reducing the torsional stress caused by supercoiling. This enzyme, being one of the most crucial enzymes that manages supercoiling, is also one whose actions are repressed by the secondary metabolite camptothecin.
Camptothecin, a potent inhibitor of this enzyme, Topoisomerase I, is useful in providing its chemotherapeutic properties to patients who are either prone to cancer or are afflicted by it. Topoisomerase nicks one strand, causing a single strand to break, and then unwinds the helix and finally seals this nick. However, when this exact phenomenon is taking place, camptothecin goes and binds to the Topoisomerase I-DNA complex right before the nick is sealed, thereby preventing the nick from getting sealed, ultimately leading to single-stand breakage. Due to this binding, the cleavage complex is stabilized, leading to the accumulation of the broken strands and preventing the resealing of the strands.

In-vitro extraction and preparation:

If conditions are mimicked in the lab and the plant is subjected to stressful conditions, oxidative stress can be induced upon the plants, which causes the accumulation of Reactive Oxygen Species (ROS) in the plants and hence an increase in the synthesis of the secondary metabolites, which, when extracted by percolation, maceration, etcetera, can be used by humans.

Culturing the microbes:

To culture endophytes in the lab, natural conditions need to be mimicked. These conditions include maintaining a proper pH, and temperature, and providing sufficient nutrients to promote the growth of the host and, subsequently, the endophyte to promote the production of the metabolite. To facilitate this, at times certain inducers or precursors are added to the medium to promote synthesis. When the growth is facilitated and a certain mass has been reached, the culture is harvested.

As per the industry, when preparing a condition where a maximum amount of metabolite is desirable, the strain is subjected to improvement to produce a HYS (high-yielding strain).

Extraction of the metabolite:

The metabolite is synthesized extracellularly and is present in the culture broth. To extract it, organic solvents like methanol are used to separate it from the microbial biomass. Upon centrifugation, the metabolite is present in the supernatant, and the pellets contain the cellular mass. The supernatant is then evaporated, and further separation of this metabolite from other extracts is done by liquid-liquid or solid-phase extractions.

Lastly, it is purified by chromatographic techniques, and its concentration is measured by UV-Vis or NMR.

Conclusion:

This metabolite, shows a promising influence on cancerous cells. Production of such a compound in the lab not only increases opportunities to manipulate and use it according to our needs but also helps us attain a sustainable and scalable alternative.

Future aspects are related to understanding and, hence, optimizing the different pathways, increasing production to facilitate drug delivery mechanisms, and finally exploiting and developing metabolites or enzymes that share this common function.

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Mutation in Centrosomal Protein 135 can lead to Microcephaly Type 8

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The centrosome is a cellular organelle involved in association and regulation of the microtubule network, especially during cell division. The centrosome contains a pair of centrioles, which are cylindrical structures composed of microtubules. Each centriole is made up of nine- triplet microtubules arranged in a pattern. Surrounding the centrioles is an amorphous matrix of proteins known as the pericentriolar material (PCM), which aids in microtubule nucleation and anchoring.

The centrosome acts as the primary microtubule-organizing centre (MTOC) in animal cells, essential for maintaining, polarity, intracellular transport and cell shape in the cell. During cell division, it also organizes the mitotic spindle, which ensures the accurate segregation of chromosomes into the daughter cells.

The centriole duplication cycle:

During cell division, a new centriole, called the procentriole, assembles orthogonally to the proximal region of each parent centriole once per cell cycle. This process ensures that each daughter cell inherits a centrosome, thereby maintaining cellular organization and function. The centrosome cycle is tightly coordinated with the cell cycle.

1. *G1 Phase (Gap 1 Phase):* The cell grows and prepares for DNA replication here. The centrosome consists of a pair of centrioles, known as the mother and daughter centrioles, linked through a flexible structure that connects the proximal end. They are surrounded by pericentriolar material (PCM).

2. *S Phase (Synthesis Phase):* The centrosome duplicates in coordination with DNA replication. The procentriole begins to assemble orthogonally to each of the existing (parental) centrioles.

3. *G2 Phase (Gap 2 Phase):* The procentrioles continue to elongate and mature. Toward the end of G2, the flexible connection between the two parental centrioles is severed, allowing the two centrosomes, each containing a centriole pair, to separate and direct the assembly of the bipolar mitotic spindle.

4. *M Phase (Mitosis Phase):*

Prophase: The centrosomes move to opposite poles of the cell, and microtubules begin to form the mitotic spindle, for chromosome segregation.

Metaphase: The mitotic spindle attaches at the kinetochore and aligns the chromosomes at the cell's equatorial plate.

Anaphase: The sister chromatids are pulled apart towards the centrosomes at opposite poles.

Telophase: The cell begins to divide, and the centrosomes help re-establish the interphase microtubule network in each daughter cell.

Cytokinesis: As the cell completes its division, each daughter cell contains one centrosome with a pair of centrioles.

CEP135

Centrosomal Protein 135 is a crucial protein of the centrosome and plays a pivotal part in the assembly and stabilization of centrioles. It is essential for the proper conformation of the nine-fold symmetrical structure of centrioles. By interacting with the other centrosomal proteins, CEP135 helps in organizing and anchoring microtubules, contributing to the integrity and function of the centrosome as MTOC.

CEP135 plays a key role in the precise timing and regulation of centriole duplication and separation, which is critical for accurate cell division and mitotic spindle formation. It contains several coiled-coil domains, which facilitates its interaction with other centrosomal proteins. Its C-terminal region is crucial for its localization to the centrosome.

Cep135 (or its equivalent, Bld10p in some organisms) is evolutionarily important because it plays a key role in the formation and structural integrity of centrioles, which are essential for cell division and the formation of cilia and flagella. Across different species, the function of Cep135 varies, but it generally contributes to the stability and proper assembly of centrioles.

Without proper Cep135 function, centrioles can have structural defects. For example, in Chlamydomonas, the loss of the Cep135 homolog Bld10p results in the centrioles lacking key components such as the cartwheel structure, which is crucial for centriole assembly and stability. In human cells, depletion of Cep135 leads to a significant reduction in the number of cen-

trioles, which can impair processes like cell division and cilia formation. Cep135 is involved in connecting the cartwheel spokes to the pinhead within the centriole, thus, it's mutation can lead to defective centriole assembly.

Hence, mutations in this protein can lead to various disorders, including microcephaly and ciliopathies, which indicates its significance in cell division and developmental processes.

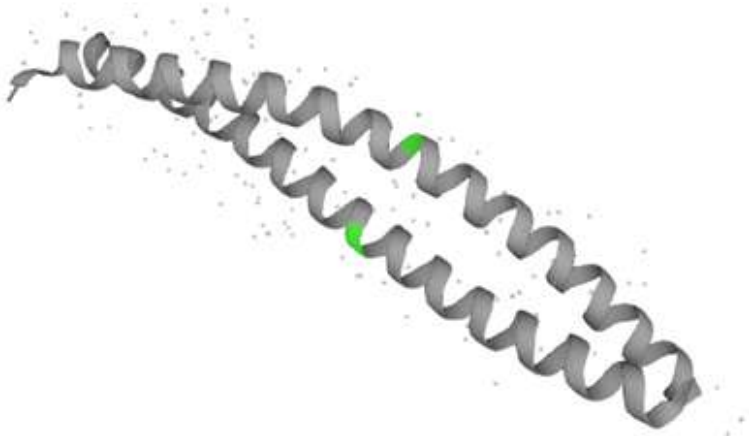

Figure: CEP135, Homodimer, coiled-coil structure

Source: https://www.uniprot.org/uniprotkb/Q66GS9/entry#structure

Microcephaly Type 8

Autosomal-recessive primary microcephaly (MCPH) is a rare congenital disorder characterized by intellectual disability and a reduced size of the brain and head. MCPH is a heterogeneous condition, and the genes associated with its seven known loci encode centrosomal proteins. A homozygous frameshift mutation in the CEP135 gene located on chromosome 4q, which encodes the 135 kDa centrosomal protein is observed in children suffering from this disease.

The disorder follows an autosomal recessive inheritance pattern. Some affected individuals may experience seizures. Diagnosis is confirmed through genetic testing that identifies mutations in the CEP135 gene. These mutations often result in a loss of function or a significant reduction in the function of the Cep135 protein. And may lead to defects in centriole duplication, spindle orientation, and chromosome segregation during mitosis. As a result, this causes cell cycle arrest, apoptosis, or abnormal division of neural progenitors, all contributing to the reduced brain size as seen in microcephaly.

Role of Cep135 in Microcephaly Type 8

Understanding the role of Cep135 in microcephaly through genetic testing may offer insights into potential therapeutic approaches to mitigate the effects of the disorder, although such treatments are still in the research phase.

To help diagnose and to study its effects, a patient-specific mutation in the centrosomal protein 135 gene sample is taken, and the following experiments are done.

1. Mutation is expressed in cells with Cep135 Knockout (in U2-OS cells), which is done by employing CRISPR-Cas9–based genome engineering technology and Lentiviral transduction method (using single guide DNA plasmids, Cas9 enzyme plasmids, transfected in HEK293-T cells along with lentiviral packaging and envelope plasmids to produce the viral particles).

2. Patient-specific mutation is generated by site-directed mutagenesis in the Cep135 cDNA construct (plasmid).

3. The plasmid also consists of a Green fluorescent tag- GFP along with an ampicillin antibiotic resistance gene and restriction enzyme sites for respective recombinant DNA technologies such as bacterial transformation in DH5α competent cells, screening of positive clones, plasmid isolation, immunofluorescence (the cells are viewed in a Zeiss LSM 700 confocal microscope)

4. Centriole Duplication Assay is used to study the process by which centrioles duplicate during the cell cycle. This assay can help identify defects in centriole duplication due to genetic mutations or the disruption of specific proteins like Cep135.

5. Hydroxyurea Treatment is done to arrest the cells in S-phase to stress the centriole duplication machinery and reveal the defects.

6. Fluorescence microscopy is used to visualize and count the centrioles in each cell.

Ideally, each centrosome should contain one or two centrioles before duplication, and four centrioles after duplication. Cells with aberrant centriole numbers (indicating duplication failure) or with abnormal centriole structures and the presence of monopolar spindles could indicate defects in centriole duplication and is linked to the patient specific mutation in Cep135 that was generated.

Analysis of spindle assembly using fluorescence microscopy to detect abnormalities in spindle structure or chromosome segregation can be done as well.

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Effect of Pharmaceuticals on Aquatic Life through Behavioral Alterations

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Keywords: pharmaceuticals, aquatic system, pollution

1. Introduction

Substances identified as environmental contaminants that can have harmful effects on ecosystems and humans are known as emerging pollutants. An example of emerging pollutants is effluents from pharmaceutical industries, which are present in various aquatic systems worldwide dTue to their widespread and continuous use. When these pharmaceutical products enter water bodies, they can significantly impact aquatic organisms by altering their behavior, causing reproductive issues, and even death. These substances are also persistent and are foreign to the environment, resulting in prolonged exposure of aquatic organisms and humans who consume contaminated water.

The effect of various pharmaceuticals has been analyzed by assessing pharmaceutical pollution in freshwater environments, conducting a thorough examination of studies on the impact of them on fish behavior, and exploring the potential ecological consequences of pharmaceuticals through changes in fish behavior.

The use of standardized behavioral tests in ecotoxicity studies, especially those involving behaviors known to be of direct and indirect ecological importance (Fig 1), may improve the understanding of pharmacologic effects on wildlife. Examples of behaviors with obvious direct ecological effects include food intake, mating success, and parental care, changes in which can affect individual fitness (i.e., an individual's future reproductive potential). There are other behaviors where change is less obvious but still have a direct impact on fitness (Fig 1).

For example, in most animal species, avoiding predators is important, and individuals often adjust their behavior accordingly. Essentially, avoiding predators includes a reduction in activity to minimize the frequency of meetings with potential predators. However, reduced activity often leads to reduced nutrition and growth, and therefore reduced fitness.

The ability of potential prey to correctly assess predation risk is therefore essential for fitness. Dispersal and migration are also examples of behaviors that directly affect population stability, especially under conditions of rapid environmental change as bold and/or antisocial behaviors tend to be more likely to disperse or migrate.

Finally, among fishes, shoaling, a behavior closely related to sociality, is of direct importance. Shoaling is important because it confuses predators and thereby increases the chances of survival of each individual. Thus, several variable behavioral patterns have a direct impact on the fitness of individuals throughout the animal's life.

Consequently, external factors, such as pharmaceutical pollution that changes selection pressure will probably have separate consequences at the individual level as well as the level of the ecosystem.

Behavioural Traits	Direct Ecological Effects	Indirect Ecological Effects
activity	cooperation	community structure
aggression	dispersal/migration	cross-boundary effects
boldness	feeding rate	ecosystem function
exploration	mating success	feedbacks
sociality	parental care, predator avoidance	population dynamics, trophic cascades

Fig 1. Environmentally relevant behavioral characteristics essential for assessing the sublethal effects and potential downstream effects of pharmaceutical exposure. Each indirect effect can potentially result from changes in any of the direct effects.

2. Effects of various pharmaceuticals:

i. Antidepressants

Selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) are widely used antidepressants and they work by acting on the serotonin and norepinephrine reuptake transporters and influencing other aspects of the serotonin system. Serotonin levels have an impact on the physiology and behavior of various organisms, including fish, and they play a crucial role in activities, aggression, and reproductive behaviors. This is demonstrated by a negative association between serotonin levels and aggression levels. As a result, antidepressants have been found to decrease territorial aggression in coral reef fish and reduce locomotion and aggression in Siamese fighting fish.

The presence of Citalopram, another SSRI, did not have any impact on rainbow trout, even when present at concentrations, a thousand times higher than those in the earlier studies. This emphasizes the substance-specific effects and the species-specific responses to SSRIs.

In addition to treating depression, SSRIs are also employed for managing obesity in humans, as serotonin is crucial for regulating appetite. This suggests that exposure to SSRIs could potentially alter feeding behavior. Studies have demonstrated that fluoxetine decreases the feeding rate in both white and striped bass, as well as in goldfish. Although these effects were observed at relatively high concentrations exceeding 1 mg per liter, other studies have reported reduced feeding rates in fathead minnow and hybrid striped bass following **exposure to 3.7 mg per liter of fluoxetine and 250 mg per liter of venlafaxine, respectively.**

following exposure to 3.7 mg per liter of fluoxetine and 250 mg per liter of venlafaxine, respectively.

ii. Psychiatric drugs

In human medicine, certain psychiatric drugs have effects on behavior, which may also affect wildlife that is exposed to them. Benzodiazepines, which act on the g-aminobutyric acid (GABA) receptor found in various vertebrate species, have been gaining attention for their potential impact on wildlife. These drugs depress the central nervous system and are commonly used to treat anxiety, insomnia, and muscle spasms. Studies have shown that Diazepam, a widely used benzodiazepine, can increase activity in zebrafish and pumpkinseed sunfish at concentrations of micrograms per liter. Additionally, exposure to micrograms per liter of diazepam has been found to increase boldness in larval zebrafish. A similar effect, i.e. increased activity and affinity to light, has been demonstrated in zebrafish, exposed to benzodiazepines. In addition, haloperidol, a drug used to treat acute psychosis, aggression, and acute delirium, was found to increase dominance in male fathead minnows.

iii. Other pharmaceuticals

Research has explored the impact of various pharmaceuticals on fish behavior due to their potential effects on wildlife. For example, beta blockers, commonly used to treat hypertension, act on beta receptors to

inhibit the effects of adrenaline and noradrenaline, which leads to reduced stress and diminished fight-or-flight responses.

However, studies have shown no significant effects of beta blockers on fish activity, boldness, or reproductive behavior. Another category of pharmaceuticals that may influence wildlife behavior is antihistamines. While primarily used to treat allergic reactions, some antihistamines can also affect serotonin levels and have anticholinergic properties. In experiments, fathead minnows exposed to microgram per liter concentrations of diphenhydramine demonstrated a decrease in feeding rates due to the drug's effect on serotonin levels. Similarly, Japanese medaka fish exhibited reduced feeding rates and/or activity when exposed to Carbamazepine, an antiepileptic medication, and Diclofenac, a non-steroidal anti-inflammatory drug.

Consequently, external factors, such as pharmaceutical pollution that changes selection pressure will probably have separate consequences at the individual level as well as the level of the ecosystem.

3. **Conclusion:**

While the effect of pharmaceuticals is species specific, it is essential to keep in mind the delirious consequences such substances may pose to the aquatic ecosystem. In their study, Brodin et al has shown that some drugs may not have effect on the selected set of species. However, it would be wrong to conclude from this that they have no negative effect at all on the aquatic wildlife.

Pharmaceutical industries must take great care while disposing wastes and releasing effluents to minimize the harm. Even at seemingly low concentrations, such drugs may pose prolonged threats to aquatic ecosystems. These effects may persist across generations and may lead to endangerment or even extinction of species over a long period of time. Longitudinal studies, investigating several generations of a particular species may provide more insights on the same.

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Fertility Preservation through In Vitro Gametogenesis in Oncofertility: Present-Day Challenges and Future Applications

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Keywords: In Vitro Gametogenesis (IVG), Somatic Stem Cells (SSCs), Induced Pluripotent Stem Cells (iPSCs), Hematopoietic Stem Cells (HSCs), Oncofertility

Reproductive endocrinologists and fertility specialists are increasingly focused on fertility preservation, a vital issue, especially for cancer patients. In the US, over 1.9 million cancer diagnoses occur annually, with improved survival rates. However, treatments like radiation, chemotherapy, and surgery can significantly reduce fertility, particularly among young patients. Current female fertility preservation methods include oocyte and embryo cryopreservation, but these may delay cancer treatment or be unsuitable for some individuals. Male patients face similar challenges, with sperm banking only available for those past puberty. Many patients, due to insufficient counselling or financial constraints, do

not pursue fertility preservation. Advances in medical science, particularly in vitro fertilization (IVF), have opened doors for assisted reproductive technologies (ART), enabling infertile individuals to have genetically related children. Further developments have expanded options to include same-sex couples and even the possibility of male pregnancy.3. CEP135

1. Introduction to In Vitro Gametogenesis

The remarkable advancements in science continue, particularly in germ cell development, which involves complex genomic regulations for genetic and epigenetic inheritance. In the last decade, significant progress has been made in in vitro gametogenesis (IVG), a cutting-edge technique that facilitates the creation of gametes outside the body. This process converts somatic cells (46XX or 46XY) into oocytes or sperm, which can then be fertilized to form embryos. IVG has considerable potential in reproductive medicine, especially in oncofertility and non-gamete-dependent reproduction through induced pluripotent stem cells (iPSCs). Additionally, IVG may enable enhanced genetic screening for undesirable traits, offering promising solutions for infertility challenges and attracting interest from biotech companies.

2. Technology of IVG

Early IVG studies, constrained by human embryology research restrictions, primarily utilize mouse models to test oocyte in vitro maturation (IVM) for developing healthy offspring. Continued research on IVG could deepen our understanding of assisted reproductive technology (ART) and improve outcomes for infertile patients. This advancement may also enable the use of primordial follicles from cryopreserved ovarian tissue to create embryos in vitro, thereby minimizing the risk of reintroducing cancerous cells.

Human IVG presents a promising option for cancer patients facing reduced reproductive lifespan due to treatment. Once clinically available, it could allow patients to concentrate on their cancer therapies without additional procedures. A pre-treatment skin biopsy could later restore reproductive potential, particularly beneficial for prepubertal patients, as traditional fertility preservation methods have limitations. For males, semen preservation is ineffective, and prepubertal testicular tissue preservation remains experimental. In females, oocytes do not respond to maturation medications. IVG's ability to replicate germ cell development from pluripotent stem cells offers renewed hope for fertility preservation post-cancer treatment.

Adult stem cells (ASCs), or somatic stem cells (SSCs), found in differentiated tissues, aid in cellular regeneration. A key example is hematopoietic stem cells (HSCs), used in bone marrow transplants to replace diseased blood cells. ASCs can be reprogrammed into pluripotent stem cells (PSCs) by transferring their nucleus into an oocyte cytoplasm, as in the cloning of Dolly the sheep. Somatic cells can also be converted into induced pluripotent stem cells (iPSCs) and guided to become gamete precursors, later maturing into eggs or sperm in the lab. This, combined with cryopreservation, expands iPSC use in treating patients undergoing gonadotoxic chemotherapy.

In mouse models, reprogramming involves upregulating oncogenes Myc and Klf4 while downregulating p53, potentially increasing the risk of mutations and cancer. In 2011, researchers successfully produced mouse haploid oocytes and sperm from iPSCs in vitro. However, progress in generating gametes from pluripotent stem cells has been limited by gaps in understanding germ cell characteristics and necessary developmental signals. A breakthrough occurred when Morohaku et al. matured mPGCs into fertilization-competent MII oocytes in vitro, successfully producing healthy offspring. This was achieved by optimizing in vitro differentiation (IVDi), growth (IVG), and maturation (IVM), recreating the complete oogenesis process.

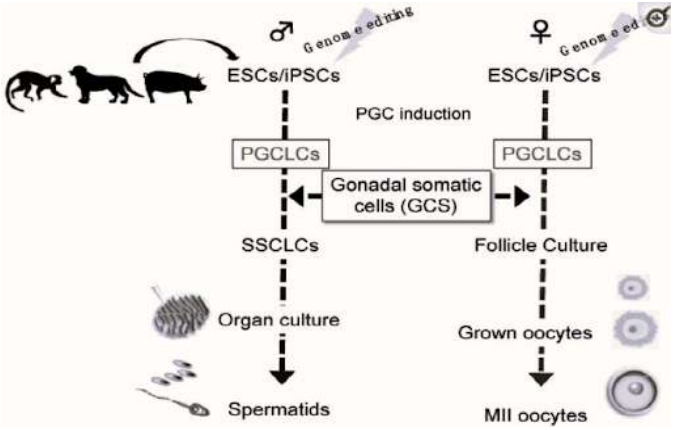
In male germline research, spermatogonial stem cells (SSCs) were shown to self-renew and produce sperm throughout life. In 2016, mPGCLCs cultured with fetal testicular cells generated germline stem cell-like cells (GSCLCs), which, after transplantation, completed spermatogenesis and produced fertile offspring. Another study reported successful production of spermatids from mPGCLCs. However, further research is needed to confirm the absence of epigenetic defects and ensure the robustness and reproducibility of these findings for potential human application.

Human IVG research has not advanced as far as in mice, but scientists have created cells from human ESCs resembling primordial germ cells with mature germ cell markers. Recent stem cell developments suggest IVG may be possible without human embryos. Dedifferentiating adult stem cells into "haploid spermatogenic cells" could result in induced pluripotent stem cells. While human oocytes have yet to be produced, mouse studies have successfully generated both sperm and eggs, suggesting human IVG could eventually achieve the same. However, extensive research is still needed to assess the potential for healthy offspring from human IVG.

3. Future of IVG: Possible Implications for Oncofertility and Beyond

Oncofertility, a vital area of ART, stands to benefit significantly from IVG by enabling timely fertility

preservation, especially for patients needing urgent gonadotoxic chemotherapy or radiation. Current options, like oocyte and ovarian tissue cryopreservation, are invasive, costly, and labor-intensive, requiring ovarian stimulation medications that can delay treatment and carry risks such as ovarian hyperstimulation. These techniques are limited to post-pubertal females and may involve the risk of reimplanting malignant cells during ovarian tissue transplantation. IVG offers a potential solution by restoring fertility after chemo-radiation without these risks.



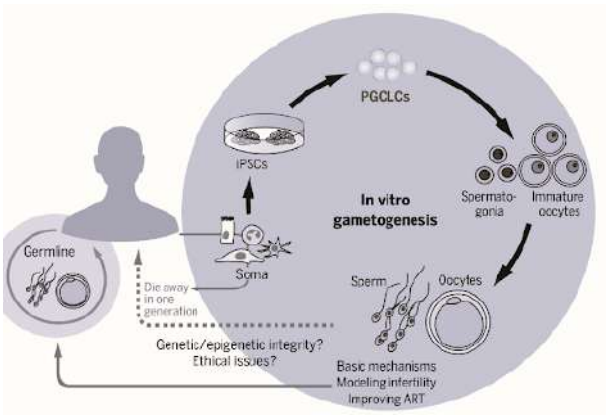
By Yoshimatsu et al. 2022

A unique future application of IVG is the ability to genetically modify hiPSCs from patients with inherited genetic mutations, preventing transmission to offspring, particularly useful for cancer survivors. Even without CRISPR, IVG could generate a larger pool of embryos than current IVF methods, potentially helping women beyond their reproductive years create healthy, genetically related embryos.

The most revolutionary aspect of IVG is its potential to redefine reproduction, eliminating the need for one male and one female to create life. IVG could allow same-sex couples to have biologically related children and enable "multiplex" parenting, where more than two individuals—regardless of gender—could procreate together, producing children with shared genetics. It could also lead to "solo IVG," where a single individual can procreate without another's genetic contribution. While mouse models have demonstrated success using male gametes for live births, similar work with female gametes is ongoing. Although IVG offers immense clinical potential, it raises significant ethical concerns regarding its use in humans.

4. Key Challenges of implementing IVG

Currently, IVG lacks biological safety data, and there is no evidence that oogonia derived from hiPSCs can produce healthy offspring. The field is still developing, and it remains unclear what genetic testing will be necessary to ensure the safety of these gametes and avoid significant anomalies in resulting foetuses.



By Saitou et. al 2021

Consequently, preliminary studies in animal models are underway. Another concern with IVG is the relative ease of obtaining skin biopsies compared to oocyte retrieval or semen collection, which could encourage individuals to sell their skin or lead to non-consensual harvesting. The risk of consanguinity may increase if a single, highly sought-after source can produce numerous offspring by multiplying stem cells without differentiation.

Regulatory measures would need to establish who can utilize these stem cells, and the procedure is likely to be costly, limiting access to only those who can afford it. Additionally, the widespread use of IVG could potentially impact the natural reproductive capabilities of individuals. These ethical, legal, moral, and technical barriers must be addressed as IVG technology advances.

5. Conclusion

IVG holds great promise for addressing reduced reproductive potential, especially among cancer survivors. While ethical, legal, and regulatory hurdles exist, experts predict IVG may become available in 10 to 20 years. Encouraging mouse model results and ongoing human research using skin fibroblasts drive excitement in the field. IVG could not only preserve fertility but also deepen our understanding of embryonic development, implantation, and genetic influences. However, significant scientific challenges remain, such as developing viable human gametes, ensuring genetic integrity, and assessing embryo quality. Despite unresolved ethical concerns, IVG has the potential to benefit many, particularly reproductive-age cancer survivors.

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All That Glitters is not Gold but it might be Plastic!

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Keywords: microplastics, biomagnification, textile, marine organisms, human health, ecosystem

1. Introduction

Microplastics are integrated into the smallest aspects of our environment including animal physiology. They are found in most running waters and thus are ingested by almost all marine animals. Biomagnification[1] increases the levels of microplastics as well as any harmful additives from the zooplankton[2] to humans. Microplastics are defined as fragments smaller than 5 mm[3] which are of high interest due to their ready intake throughout the food web over much larger particles. The sheer volume of plastic and the amount already in our bodies and all the fauna around us is astounding. The probable inputs of the microplastic and the present scenario of where these particles have been found in marine and human bodies have been discussed here.

2. Main body:

Microplastics are present not only in the usual water bodies but also in glaciers[4] in a significant amount with a mean amount of 74.4 ± 28.3 (SE) items per kg of sediment. Along with rainwater [5] as shocking as it sounds, the mean microplastic fluxes (MPs/m2/day) were 1959.6 ± 205.0 and 1320.4 ± 126.0 in urban and peri-urban areas, respectively. This level of intertwining with nature by microplastics is usually attributed to their small size which also adds to their persisting nature allowing for ease of transportation by wind[6] or water. Thus, the level of microplastic via rainwater depends on the trajectory of the winds.

Microplastics might be generated from the breakdown of larger plastic debris[7], the release of packaging materials[8] and textiles - fibres from synthetic clothing[9] are the common sources. Textiles sound like an unlikely source of microplastics. However, with the advent of fast fashion and the landfill created by textile industries along with the dyes (most notably glitter, sequins and little beads for ornamentation) and the effluents from these textile industries, the waste created is magnanimous. The fibres from washing of clothes[9] are a possible source of microplastics as well. Another source of microplastics in our effluent water is cosmetic products[10]. The extensive use of microplastics (size up to 500 μm in diameter) marketed as scrubbers are released after daily use without any treatment or screening making these microplastics available to the external environment.

Along with these, another problem arises from the unknown substances that accompany microplastics such as heavy metals and other toxic chemicals. One would think that microplastics are inert in nature since there are no enzymatic ways of degrading plastic. However, in reality, it is a different scenario. These unknown additives attached to the microplastics are the ones that pose the greatest danger to the entirety of the ecosystem. Along with this, persistent organic pollutants (POPs)[11] pose a danger as well. Initially, one might say that the microplastics help in the accumulation of these POPs providing a superficial cleaning of the marine water. However, ingesting these microplastics will make these POPs bioavailable, causing the problem it could have curbed, but in a higher and immeasurable manner.

Ingestion of microplastics is common due to their presence in all the water and air sources. Thus,

there have been cases of discovering microplastics in phytoplanktons, small crustaceans (e.g. zooplankton), amphipods, polychaete worms, tubifex worms, molluscs, echinoderms[12] as they are more likely to encounter microplastics that are denser than water and thus ingest them and assimilate them in their systems. Birds, fish[13] and mammals can also ingest microplastics directly and indirectly. Fishes, in particular, are important organisms to screen for the presence of microplastics since it is one of the staple food items worldwide. Thus, any contamination in fishes, crustaceans, mussels, barnacles etc. will lead to disaster due to biomagnification. A study has shown that 83% of Norway lobsters, Nephrops norvegicus collected in the Clyde Sea had plastic ingested including monofilament lines and fragments of plastic bags[14].

In humans, microplastics have been identified in the gut lining[15], lung tissues[16] and surprisingly in human breast milk[17]. Microplastics have been detected in human feces and colon biopsies thus proving that they have travelled through the gastrointestinal tract. Microplastics when in the GI tract act like clumping agents and may form knots which could be hazardous if they block feeding appendages or hinder the passage of food. If they are accumulating in high numbers in the intestines of smaller animals, they may have the same effect as that of debris of larger sizes and clog digestive systems. The gradual accumulation of debris in the digestive tract may cause a false sense of fullness leading to decreased food consumption and thus nutrient depletion and eventual death. A recent investigation observed that microplastics and their toxic substances lodge themselves into the delicate alveolar epithelium, leading to localized inflammation. Thereafter, they are transported throughout the entire circulatory system, invoking the generation of pro-inflammatory factors, thus causing inflamed conditions. The removal of microplastics from the human body is nearly impossible, though through continued efforts one can theoretically flush themselves free from microplastics. However, in reality, there is continuous intake of microplastics from various sources making it unlikely to ever be completely free from the ubiquitous microplastics.

3. Conclusion:

The distribution of microplastics has reached levels beyond human control and its impact is severe and of unknown danger. The stochasticity of these particles and their effects pose a deep fear. There is ongoing research on this topic to try and shed some light in this pit of darkness. Nonetheless, there are a lot of unpredicted areas that pose a looming danger just over the horizon not only for all of humanity but all of the ecosystem. If there is no drastic change in the screening of the amount of plastic made, there is no use in capping the output generated. From medical waste, plastic wrapping, polystyrene cups and plates, plastic bags, unethical fishing nets, unnecessary plastic boxes, and microbeads for cosmetics - all of these should be eradicated as soon as possible and in its place other biodegradable items should be used or at the very least, a standard or maximum limit should be incorporated to reduce overproduction.

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Genomic Personalised Medicine

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Keywords: genomics, personalised medicine, pharmacogenomics, tailored treatments, pharmacokinetics, system biology, translational genomics, GWAS(Genome Wide Association Studies), WGS(Whole Genome Sequencing), metabolomics

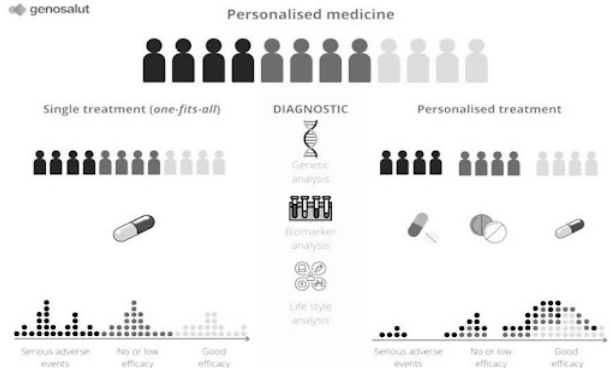

Image Source: https://www.genosalut.com/en/news/healthy-lifestyle/what-is-personalised-medicine/

1. Introduction

Over the past decade, there has been a growing adoption of genomic and personalized medicine among senior government officials, industry leaders, healthcare providers, and the general public. As medicine increasingly adopts genomic tools for more accurate disease prediction and treatment—such as comprehensive analysis of genomic sequences, gene expression, proteins, and metabolites—the core principles of genomic and personalized medicine will necessitate the creation, standardization, and integration of essential tools. DNA-based risk assessment for common complex diseases, molecular signatures for cancer diagnosis, genome-guided therapy and dose selection are among the few important examples.

- What is genomic medicine?

Genomic medicine involves using information from genomes—both human and other organisms and their by-products like RNA, proteins, and metabolites to inform medical decisions. Additionally, gene

expression patterns are being searched, across the whole genome, for more detailed insights into health and disease states.

- What is personalized medicine?

Personalized medicine is a dynamic and expanding area of healthcare that tailors treatment based on each individual's unique clinical, genetic, genomic, and environmental information. It relies on multidisciplinary healthcare teams to enhance health and wellness, educate patients, and provide comprehensive care.

2. Origin of personalized medicine

It's one of the main promises of the Human Genome Project (HGP) initiated three decades ago. It marked the end of an era in which drugs developed for broad patient groups, were withdrawn due to risks posed to a small subset of patients, despite their benefit to the majority. It also signified the move away from trial-and-error approaches. It started with the sequencing of the human growth hormone (*hGH*) locus, which provided proof of principle for HGP-inspired personalized medicine with the development of a test for detecting patients who would benefit from its administration and the first personalized diagnostic test was the companion test for Herceptin, created four years before the invention of the HercepTest® (registered as the first companion diagnostics ever developed).

3. **Fundamentals**

i. Translational Genomics -

It helps to delineate the complex interactions among genes, gene products, and the environment. It has driven researchers to develop advanced DNA sequencing technologies. With advancements in next-generation sequencing (NGS) techniques, has greatly improved the detection of genetic diseases. Different sequencing options, such as exome sequencing, RNA-seq, ChIP-seq, and whole-genome sequencing (WGS), are available depending on the type of sample under question and the region of interest in the genome. This has led to the development of pharmacogenetics. It's a field that combines pharmacology and genetics to study how genetic variations affect individual responses to medications in clinical and laboratory settings. These can alter the expression and function of drug-metabolizing enzymes and proteins involved, resulting in varied drug plasma levels and therapeutic outcomes.

ii. Informatics -

Systems biology is a field of study that uses math and computation to model and analyse complex biological systems. It's a holistic approach to studying the natural world and one of its disciplines, proteomics has a major role.

- Data Integration: An amalgamation of genomic, transcriptomic, and proteomic information, helping a comprehensive understanding of a patient's health.
- Genomic Analysis: Advanced algorithms and software for the analysis of next-generation sequencing (NGS) data, identifying genetic variants associated with diseases and tailoring treatments.
- Predictive Modelling: To assess a patient's risk for specific diseases based on their genetic makeup
- Drug Development: By analysing genetic variations affecting drug metabolism and efficacy, designing targeted therapies
- Clinical Decision Support: For devising treatment plans—Biomarker discoveries for diagnosis, prognosis, and monitoring treatment responses

iii. Basics -

- DNA Sequencing for Detection of Human Genome Variation: Technologies, such as Sanger sequencing and next-generation sequencing (NGS). These methods identify variations like SNPs, insertions, deletions, and structural variants. This can pinpoint genetic factors contributing to health and disease.
- Genome-Wide Association Studies (GWAS): GWAS are research approaches that scan the entire genome for associations between genetic variants and specific traits or diseases. GWAS can identify SNPs associated with diabetes, heart disease, and cancer.
- SNP Genotyping Arrays
- PCR-based Methods: Techniques like TaqMan and allele-specific PCR, are used to identify specific SNPs.
- Whole Genome Sequencing (WGS)
- Copy Number Variation (CNV) and Human Health: CNVs are structural variations in the genome where segments of DNA are duplicated or deleted. They can influence gene dosage and contribute to various diseases, including neurodevelopmental disorders and cancer.
- DNA Methylation Analysis: DNA methylation is an epigenetic modification that can affect gene expression without altering the DNA sequence. Changes in methylation patterns are detected with techniques like bisulfite sequencing providing insights into disease mechanisms and biomarkers.
- DNA Microarrays: DNA microarrays allow simultaneous analysis of thousands of genes,

helping study gene expression patterns, identify disease-associated genes, and classify tumors based on genetic profiles.

- Proteomics: involves the large-scale study of proteins, including their functions, structures, and interactions. By analysing the proteome, researchers can understand how genetic variations manifest at the protein level.
- Comprehensive Metabolic Analysis: Metabolomics is the study of metabolites in biological systems. It helps understand the biochemical pathways involved in disease states. This identifies biomarkers and monitor disease progression.

iv. Areas of impact: Cardiology -

a. Genetic Profiling:

- Risk Assessment: Genetic testing can identify predispositions to cardiovascular diseases (CVD) such as hypertension, coronary artery disease, and familial hypercholesterolemia.
- Targeted Therapies: Specific genetic variants may influence the efficacy of certain medications, allowing for more effective treatment choices.

b. Pharmacogenomics (Medication Response): metabolizm of drugs can guide them to make choices in medications, such as statins or anticoagulants, reducing adverse effects and improving outcomes.

c. Lifestyle and Environmental Factors: Personalized medicine considers lifestyle factors such as diet, exercise, and stress management, enabling customized prevention and treatment plans.

d. Innovative Technologies -Wearable Devices: Continuous monitoring through wearables provides real-time data on heart rate, activity levels, and other vital signs, facilitating personalized adjustments in treatment plans.

e. Research and Clinical Trials -Precision Trials: Ongoing research and clinical trials focused on specific populations help validate personalized approaches, leading to evidence-based practices in cardiology.

v. Oncology -

- Genomic Profiling -Tumor Sequencing: Analysing the genetic makeup of a tumor helps identify specific mutations that drive cancer growth, allowing for targeted therapies.
- Targeted Therapies -Precision Drugs: Medications like tyrosine kinase inhibitors or monoclonal antibodies specifically target cancer cell pathways, minimizing damage to normal cells and reducing side effects.
- Biomarkers -Predictive Indicators: Identifying biomarkers can help predict how a patient will respond to certain treatments such as immunotherapy or chemotherapy. Personalized approaches in immunotherapy focus on using a patient's immune profile to develop treatments that enhance the body's ability to fight cancer.
- Pharmacogenomics (Drug Understanding): genetic variations that affect drug metabolism can help tailor chemotherapy regimens, improving efficacy and reducing toxicity.
- Comprehensive Treatment: with a Multidisciplinary Approach, personalized medicine often involves a team of specialists (oncologists, genetic counsellors, surgeons, etc.), creating a comprehensive treatment strategy.

v. Neurological Diseases

Considering one disorder like Parkinson's disease (PD) aims to tailor treatment and management strategies based on individual patient characteristics. Here are the key components:

- Genetic Testing -Identifying Risk Factors: Genetic testing can identify mutations linked to familial forms of Parkinson's, such as mutations in the SNCA, LRRK2, and PARK7 genes, helping to assess risk and guide treatment options.
- Biomarkers -Diagnostic Tools: Researchers are exploring biomarkers, such as alpha-synuclein aggregates or neuroinflammatory markers, to aid in early diagnosis and monitor disease progression.
- Pharmacogenomics (Optimizing Medication Choices): selecting the most effective medications, like levodopa, and minimize side effects.
- Tailored Therapies
- Lifestyle and Environmental Modifications

Personalized medicine focuses on understanding individual patients by examining various factors, including genetic, biochemical, and behavioural traits. This understanding helps tailor treatments to each patient, which is crucial because significant differences in how individuals respond to treatments have been observed and will continue to arise.

Recent advancements in biomedical technologies, have made it easier to identify these variations, underscoring the need for a more personalized approach to healthcare.

Looking ahead, the challenges will involve improv-

ing how we characterize patients and enhancing the development and testing of personalized therapies to ensure they are effective. Although traditional blockbuster drugs that work for many patients should still be considered, finding such widely effective treatments may become increasingly challenging in the future.

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Why Do Birds Matter?

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Keywords: Biomimicry, influential invention, innovation, ecosystem, messengers

Birds are interwoven in our lives in a much more intricate manner than most other animals. If that is not reason enough, the Earth is for us to share and keep, and not colonise and thrive all by ourselves. Yet we kill, cage and disrupt their natural ways for our own reasons, forgetting that their true beauty is only when they are free in the open with the blue sky as their background. Birds are an inherent part of our ecosystem and livelihood, there are multiple examples of such. For this article however, I'll be writing in detail about only a few namely, biomimicry, plant propagation and carrier pigeons as messengers.

Biomimicry is the design and production of materials, structures, and systems that are modelled on biological entities and processes. Birds have been role models for a lot of the structures that we use and see every day. A great example is the Shinkansen Bullet Train. In the 1900s, the fast trains in Japan were facing a major problem, whenever they sped up there was a loud booming noise which disturbed many in the neighbourhood of the train stations. This was because an envelope of air was formulating at the front of the train, thus, when the train sped, the air formed at the front was vanishing with a loud boom noise. To find a solution to this problem, engineers looked towards birds once again. One of the engineers noticed a Kingfisher diving into the water at high speed but not causing much of a splash in the water. Hence, the bullet train was formed by changing the front of the train and making it look like the beak of the kingfisher. Thus, birds once again contributed to innovation, helping to improve our lives manifolds and furthering technological advancements.

Birds were also a source of inspiration for an influential invention - the aeroplane. Without the invention of the aeroplane, our world would be vastly different, shaped by limited mobility and slower progress. Even as children, many of us have looked up to birds and wondered about their magical ability to fly and soar through the sky. This fascination has led to the development of the flying contraption as we know today. It is one of the most used forms of transportation in our fast-paced civilisation.

Birds are also a big part of our ecosystem. Some examples of birds who help in the process of pollination are spider hunters, sunbirds, honeycreepers and honeyeaters. Hummingbirds are tiny birds with immense speed and ability (their average time for flapping wings is 90 flaps per second). They flit from one flower to another seeking the sweet nectar and also helping in the process of pollination as the pollen grains get stuck on their feathers and are transferred. Another bird - the honeyeater is extremely similar to the hummingbird and serves for pollination as well. However, they cannot travel as far and wide as the hummingbirds. Nonetheless, with their highly developed brush-tipped tongue they can easily reach the nectar, while at the same time serving as a pollinator. Birds are not known for pollinating food crops, however without birds, a lot of beautiful plant species would have been long extinct.

Additionally, birds help propagate the seeds from their parent plants and hence help in the dispersion of seeds. For instance, birds consume seeds and then they proceed to fly. During their flights, they discharge their faecal matter along with the seeds they had previously ingested. As a result, they disperse the seeds very effectively and over a wide area. One particular plant to benefit from this is the Banyan Tree (*Ficus benghalensis*) whose seeds are commonly ingested by frugivorous birds such as the coppersmith barbet

and the common myna.

As can be expected, birds have been messengers for mankind since the beginning of time. Whether it be pigeons or eagles or owls, they have played a significant role in passing messages before the time of technology. In particular, carrier pigeons have played a major role as messengers and as war heroes for their unique sense of direction. Pigeons have a unique homing ability by which they can find their way back to their nests from 1300 miles away, even when they are transported in isolation. Sports fans in ancient Greece were said to have used trained pigeons to carry the results of the Ancient Olympics. Carrier Pigeons (*Columba livia domestica*) played a crucial role during both the World Wars. All the rival nations had in possession huge flocks of pigeon messengers. These avians delivered critical updates which saved thousands of human lives amidst all the other destruction. One such bird named Cher Ami completed a mission which led to the rescue of 194 stranded U.S soldiers, hence we can imagine the multitude by which pigeons have helped us during the time of wars.

The pigeons surround us everywhere we look, especially in the metropolitan cities. There is a lot of wonder behind pigeons which are one of the most hated birds, and are also known as 'rats with feathers'. However, after their use was finished with us, we resigned them to their fate and turned our backs on them to fend for themselves in an unnatural habitat - the concrete jungle.

To conclude, birds matter because they have been a part of our ecosystem and have lived on Earth for ages. From the age of the dinosaurs, birds have existed and continue to exist through multiple adaptations on Earth. Birds matter simply because they exist on earth and coexist among us. It is reason enough for us to respect and continue to keep the Aves from danger. Why must we find more reason rather than accepting the beauty of the different birds that live among us? Birds matter because of who they are and will continue to matter even as time transcends further through another assortment of future generations.

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Obligate Chimerism In Yellow Crazy Ants: An Insight Into One Of The Most Invasive Species On Earth

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Keywords: Reproduction, Chimerism, Haplodiploidy, Invasive Species

1. Introduction

The genotype of living organisms is the full complement of their genetic information Multicellular organisms, growth begins as a single fertilized egg, and so consist of cells with identical genotype. If an organism has cells with more than one distinct genotype, then it is said to be a Chimera. This is derived from the mythical Chimera of Greek lore. Chimerism may occur naturally in some species, or even might be induced by humans. However, there is only one known case of obligate chimerism in the animal world- in yellow crazy ants, uncovered by a team of scientists in 2023. This article is an attempt to shed light on this amazing discovery.

The Yellow Crazy Ant (*Anoplolepis gracilipes*) is originally native to West Africa, although it has been introduced to many areas around the tropics. Its epithet 'crazy' is due to their erratic behaviour when disturbed. Like other species of the Insect order Hymenoptera, sex determination in ants occurs by a

unique mechanism. Males develop from eggs that are unfertilized, producing haploids, while females develop from fertilized eggs and hence are diploid. [2] In this particular species of Ant, however the haploid males were found to be obligate chimeras of lineages derived both paternally and maternally.

2. Methodology

Field Samples of *Anoplolepis gracilipes* were collected from 14 different locations across South East Asia.

Genotyping studies indicated two very different genetic groups -the R and the W lineages. The queens which were sampled from the field had an R/R genome and the workers showed an R/W genome. In ants males have a unique mode of genotype determination -they are generally haploid. Thus, both R and W males were present in the population, explaining the different genotypes of the queen and worker ants.

Flow cytometry technique was used to confirm the ploidy of the males. Irrespective of the genetic lineage, all males showed half the DNA content of the workers, proving their haploidy. A change in fluorescent intensity (along X axis) was observed with increasing nuclear count (along Y axis). All the males (n=30) showed haploid nuclei, with precisely half the amount of DNA of the diploid workers (n=15).[1] In Figure A, the main peak corresponds to the ploidy and additional peaks due to both mitotic divisions or from endoreduplication events.

When Single Cell Genotyping was performed for the workers and males separately,

i)A diploid R/W genotype was present in all workers.

ii)In R/W males ,50% of the nuclei showed an R genome,45% had only W genome and 5% had alleles from both genetic lineages, possibly due to cross contamination between different samples.[1]

In situ hybridization assays (DNascope assay) were also performed, and clusters of cells in different organs showed only R or only W staining, as indicated in the figure. R nuclei stained pink, while W nuclei stained blue. In **Figure C**, a) represents Longitudinal section with the head facing left, while b-g) represent magnified views of different tissues.

3. **Conclusion**

There are two different linages of sperms-one with the R genome and one with the W genome. When an R sperm fuses with an oocyte (oocyte always has R lineage) a diploid R/R queen is produced. When a W lineage sperm fuses with the R oocyte, there can be two distinct possibilities. Fusion of these pronuclei from sperm and egg produces a diploid worker (with a R/W genotype). If they do not fuse ,haploid males that are chimeras of R and W lineages are produced. These results have been summarized in **Figure B.**

4. Discussion

This is the first known example of obligate Chimerism in the animal world. Competition and Natural Selection are the key factors at play-such chimeras are selected over normal counterparts because they cannot inbreed. This in turn helps these ants to proliferate in unfamiliar environments. These are thus naturally selected. Out of many theories, their unique reproductive cycle could be one of the reasons for its success as an invasive species, i.e it can detrimentally affect any new environment where it is introduced. As an invasive species, these ants have wreaked havoc on Australia, with estimates that it could cost their economy 3 billion dollars, besides the loss of biodiversity [3]

The largest supercolonies of the species are on Christmas Island, an Australian External Territory in the Indian Ocean. These ant populations have almost completely wiped out the native Christmas Island Red crab, a very important keystone species.[4]

Thus, we see how the key to understanding the impact of invasive species on the environment lies in the basics of genetics. Further studies in this discipline may help in identifying key areas of the genome to target which might prevent the proliferation of invasive species. Such genetic manipulations may have enormous impacts on the natural environment.

Humanity has reached the point where it we could claim of creating life itself. However, every time we think that we know all there is to know -nature comes up with something so blissfully new that shakes the very pillars of our science. And there we stand, stupefied.

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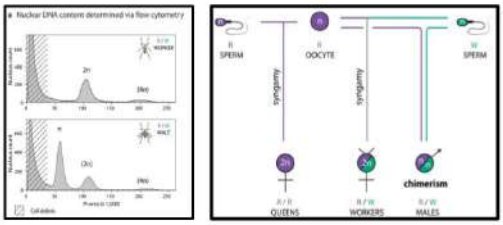

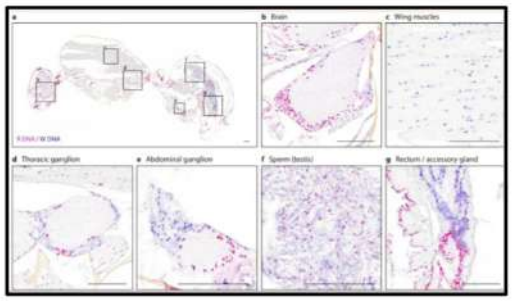

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Death Note: What Harbingers of Death (Scavengers) can teach us in our fight against Antimicrobial Resistance

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Keywords: antimicrobial resistance, microbiota, defence, antimicrobial peptide, scavenger

Antimicrobial Resistance a growing global concern

Antimicrobials, such as antibiotics, antivirals, antifungals, and antiparasitics, are frequently used in medicine to treat and prevent infections in humans, animals, and agricultural crops.However, the effectiveness of conventional antimicrobials is now jeopardised as many microorganisms have developed resistance against the drugs. The World Health Organization (WHO) identifies antimicrobial resistance (AMR) as one of the top 10 global health threats. AMR endangers human and animal health, environmental safety, food and nutrition security, economic development, and social equity.

Compounds from natural sources exhibit antimicrobial activity

Attempts have been made to synthesize new antimicrobials by synthetic chemical methods in the industry, but it has often failed to prove as a source of novel drugs effective against resistant pathogens. A significant proportion of the novel drugs therefore are compounds obtained from natural sources or their derivatives thereof. Natural products exhibiting antimicrobial activity in-vitro, function as antibiotics in nature. Microbes produce these chemical "weapons" to participate in interference competition within their specific ecological niche and fortify their defences. Sometimes the competition and defence compulsions extend to interspecies symbiotic relations. In fact, the strongest evidence for natural products functioning as antibiotics is often seen in symbiotic relationships, where microbes contribute to boost the defence of a multi-species ecosystem.

Scavengers and their defence strategies

It is in this context that we explore the idea of natural products derived from scavengers-more appropriately called necrophages and their associated microbiota- their capacity to function as innovative drugs against antimicrobial resistant pathogens and other biotechnological applications in health and food security. Scavengers feed on dead and often decaying matter- carrions or carcasses which would be expected to contain a high pathogenic load thus exposing them to the threat of infections.

But scavengers have developed unique mechanisms to ward off pathogenesis caused by microbes in their food. This holds promise for designing novel therapies drawing on their defence strategies. There are a few things which make carrions a high-risk food, with considerable microbial load- organisms dead from infectious diseases harbouring the causative agent in their bodies, proliferation of soil and airborne bacteria on the carcass and lastly the interaction of several scavengers some of which such as blow flies and muscid flies are often themselves carriers of pathogenic bacteria.

To expand on the subject of defence mechanisms that these necrophagic species have developed, the preliminary technique is based on behavioural ecology. Wolves have been found to avoid carcasses exposed to the sun for prolonged hours and ravenous birds prefer carrions killed by a predator to those that have died from unknown causes. The physiological defences that scavengers have evolved are also particularly fascinating. For instance, wolves can retain food in their stomachs for up to 12 hours—almost twice the time in humans— the increased periods of exposure to gastric acids serves to significantly reduce bacterial load. In dermestid beetles and other insects, the gut is shielded by a unique lining made of chitin, a material with natural antibacterial properties. From an immunological standpoint, scavengers have developed a diverse repertoire of antimicrobial molecules with certain chemical modifications, to bolster their defences and these often outnumber the antimicrobial molecules occurring in non-scavenging species. Hence from an anthropogenic perspective, successful identification, isolation and screening of these antimicrobial molecules hold promise for the discovery of new therapeutics in treatment of infections caused by AMR pathogens. Active research in this area has already been set in motion in Germany, China, USA and other countries.

Biomolecules from scavengers exhibiting antimicrobial properties

One of the many biomolecular defences present in scavengers are antimicrobial peptides (AMPs). The AMP-pathogen surface interactions are mediated through electrostatic or hydrophobic forces to initiate various methods to eliminate bacteria though lysis, disruption of microbial homeostasis, membrane permeabilization and rupture, inhibiting protein synthesis or inducing reactive oxygen species synthesis causing cellular death .The larval secretion of blowflies (*Sarconesiopsis magellanica*) was found to contain an AMP-Sarconesin-II with a conserved ATP synthase domain that binds to DNA, causing filamentation in bacterial cells, inhibiting cell repair, and killing bacteria. Griffon vultures (*Gyps fulvus* subspecies *fulvus*) are known to harbour gut microbiota which are the source of bacteriologically produced AMPs-bacteriocins synthesized by lactic acid bacteria. In a study among the several isolates from a griffon vulture gut, *Enterococcus faecium* was identified as producer of enterocin HF (EntHF), which exhibited remarkable antimicrobial activity and spiked interest for its use as a natural food preservative. The gut of burying beetles (*Nicrophorus vespilloides)* which occupy a unique ecological niche by feeding and reproducing on carcasses, have microbially secreted compounds with antibacterial and nematostatic activity and could contribute to the control of both bacteria and phoretic nematodes in the gut. Antibiotics in animal feed can potentially be replaced with antimicrobial lipids, such as monoglycerides and medium-chain fatty acids obtained from mutualistic bacteria in insects. Lauric acid and its monoglyceride derivative have the strongest antibacterial properties among medium-chain fatty acids. Black soldier flies (*Hermetia illucens)* due to their high content of lauric acid and bioactive compounds serve as an important source of livestock and poultry feed. Scientific investigations are also on to utilize scavenger derived AMPs for disease resistance in crops, for example, the antimicrobial peptide gene Sarcotoxin-IA is being probed for resistant crop development.

A gleam of hope

In conclusion, scavengers are frequently exposed to infectious microbes through both their diet and interaction with other participating partners as well as the environment. Thus they have evolved numerous strategies to defend themselves which could serve as an inspiration for new and innovative discoveries for therapeutic purpose. Natural selection acts on all living organisms and the presence of bacterial competitors or pathogens in an environment can favour the evolution of antimicrobial adaptations as has been elucidated in cases of many necrophages. Research efforts are already underway to harness these natural defence apparatus for the development of new antimicrobial products in the continuing fight against rising AMR. With over 90% of scavenger species still largely unexplored and understudied, it's safe to assume many novel, beneficial and interesting defence mechanisms are yet left to be uncovered. Thus, quite contrary to the traditional epithet given to scavengers as "harbingers of death", they could actually give a ray of hope in the dark abyss of mounting antibiotic resistance plaguing the human society.

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A Link to the Past: A Study of Ancient Glacial Microorganisms

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Keywords: Glaciers, Microorganisms, Antibiotic resistance, Integrons

Introduction

In recent times various human activities like excessive burning of fossil fuels, deforestation have led to a gradual increase in overall temperature of the planet. This has resulted in accelerated melting of the polar ice caps and glaciers all over the world. Glaciers are large bodies of dense ice from which rivers originate and they can also be found floating in the seas of the Artic and the Antarctic. Microorganisms that have been trapped in these ice for thousands of years are getting thawed and are mixing into the oceans. An estimation states that 10^{17} to 10^{21} viable microbes are released into water annually from melting ice caps and glaciers. It gives us a wonderful opportunity to study the ancient DNA of microorganisms from the past. They survive in the subglacial lakes beneath the ice sheets despite the harsh environment in the pitch black and near freezing lakes. In an expedition in 2018 Ryan Venturelli, a paleoglaciologist at the Colorado School of Mines in Golden, along with his team of researchers, after drilling a kilometre into ice, collected and analysed the lake water and sediment samples from the lake bed. Although no photosynthetic planktons were revealed, they found 6000 years old C-14 a form of element that's made in the atmosphere and falls back to earth. They concluded that ocean water had flowed into the ice presenting nutrients from microorganisms to consume and grow and even in present day it is recycled by their descendants for food as determined by presence of C-14 in water samples and sediment.

Detection of the Microorganisms

Skidmore et al. carried out a study to check the presence of microbial life beneath high artic glaciers. They used basal ice samples and glacial (supraglacial or surface) ice samples from John vans Glacier on Eastern Ellesmere Island Nunavut, Canada. Samples were collected and examined across 3 years from 1996 to 1998. It was seen from the 1996 samples that viable microbes were present in both supraglacial and subglacial environments, with their activity increasing with increased suspended sediment concentration as found in basal or subglacial water. The 1997 water samples were incubated in both aerobic and anaerobic conditions and which confirmed presence of culturable aerobes and anaerobes including heterotrophs, nitrate and sulphate reducers and even methanogens. The 1998 samples were incubated under conditions as close to in situ conditions as possible. The respiration rates

were studied which confirmed their ability to grow in conditions as present under the base of ice. It was also concluded that microbes present in glacier ice live in more nutrient limited conditions compared to basal ice. This study might help in determining presence of living organisms in the polar ice caps of Mars.

The Ross Ice Shelf holds a particular significance in many of the studies done on microbes trapped in ice. It is the largest ice shelf in Antarctica about the size of France and several hundred metres thick. It has been studied extensively and it was found that the ecosystem under Ross Ice Shelf was large sustained by dark carbon fixation. Mostly, chemolithotropic process is the main driving force in sustaining and maintaining the viability of the microbial world under the ice shelf. The emergence of such microorganisms also poses a question on the effect of these microorganisms, especially if they are pathogens, on humans when they come in contact with them due to the disappearance of the natural ice barrier. Even though most of the organisms are present in a metabolically dormant state in the ice, they remain viable and can start growing when exposed to favourable conditions. The ability of spore formation and cyst production also enables them to survive in harsh conditions. *Cryptococcus,* yeasts, bacterial colliforms and emerging pathogens like *Aureobasidium melanogenum, Naganishisa albida* and *Rhodotorula mucilaginosa* have been isolated from Artic environments in Greenland and Svalbard. While these pathogens are related to modern microbial strains, some very ancient, potentially pathogenic microbes have been found in very old ice samples by a Russian group of researchers led by Sabit. S. Abyzov. Several eukaryotes like amoeboids, protozoans ciliates etc. have been found.

Special Characteristics of the Microorganisms

These bacterial populations in glaciers are also seen to harbour antibiotic resistance genes, several of which are unknown. These microbes have been able to survive in high concentrations of antibiotics in vitro. Mindlin et. al collected bacterial samples from Eastern Siberian Permafrost sediments and showed that many strains harboured resistance genes against several known antibiotics like chloramphenicol, tetracyclin, kanamycin etc. Particularly relevant (and worrying) was the presence of integrons. These are special genetic elements that possess an attI site which allows insertion of gene cassettes via site specific recombination using enzymes like integrase. These integrons can be transferred horizontally by becoming components of other mobile genetic elements like plasmids and transposons. Presence of transposons conferring resistance to several antibiotics was found in *Pseudomonas sp*. Isolated from 15000 to 40000 year old permafrost by Petrova et. Al. in 2011.This was considered the first example of its kind in the pre antibiotic era. Makowska in 2020 detected resistance integrons in bacteria isolated and cultured from two Arctic and two Caucasian glaciers.

Effect of Glacial Pathogens in our Ecosystem

It is extremely worrying to think about the consequences such ancient microbes can have on the current ecosystem. Ancient genes especially resistance genes can be acquired by contemporary microbes resulting in genome turnover. The theory that glacial pathomes can be deemed as a potential threat to the ecosystem received unforeseen support in the *Bacillus anthracis* outbreak that wreaked havoc in Yamal, Russia, in 2016, killing the entire population of reindeer, one child and forcing hospitalization of more than a hundred pastors. This strain was recognised to be identical to other strains of *Bacillus anthracis* that had been discovered in tissues of dead animals trapped in the Siberian permafrost for centuries until they thawed due to global warming.

These microbes may alter the existing biogeochemical cycles on Earth after being thawed. They can release more carbon dioxide and other greenhouse gases in the atmosphere accelerating global warming. Also the rapid influx of microbes in the ocean waters can lead to depletion of oxygen resulting in reduction in fish population.

Conclusion

Thus we can conclude that microorganisms are indeed present in viable conditions under the ice shelves across the world. These microorganisms act like a fascinating snapshot to the past, enabling us to understand how the genomes have evolved throughout the ages by comparing them with present day microorganisms. Thus they are very helpful in learning about the ancient DNA and how life, as we know it, evolved. However the major concern is how the pathogenic organisms after being thawed and entering the ecosystem from its natural barrier, will affect it. Already reports of diseases caused by such ancient microbes have been seen. The transfer of antibiotic resistance genes may result in creation of a super microbe not affected by any of the regular antibiotics which might result in complete extinction of the current species. More studies need to be undertaken regarding such ancient microorganisms, especially pathogens, and their effects in the current ecosystem and methods need to be devised to counter harmful effects of these microorganisms.

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Birth Reimagined: The Artificial Womb Era

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Keywords: Ectogenesis, artificial womb, Bioengineering, Neonatal care, Stem cell research, human reproduction, Medical ethics, Future of Parenting

Motherhood is a profound journey, it starts from the very day of conception to the first cries of the newborn in the delivery room, it is about the years that follow. For some it's a journey of endurance - hoping, praying, and waiting for a child to come into their lives. Now if someone asks you to grow a baby outside a mother's body, maybe in a pot, you will feel it's nothing but a fantasy. We all know about the story of Gandhari's hundred and one children from the great Indian Epic – *Mahabharata*. Gandhari cut

a lump of flesh (which she gave birth to after being pregnant for two long years) into hundred and one pieces and placed them into pots with ghee which produced a hundred sons called *Kauravas* and a daughter named Dussala. But in 2024, this thinking is no longer a fantasy, scientists are working on it to make it a reality!

What is Ectogenesis?

Ectogenesis is the process of the development of mammalian embryo in an artificial environment. The World's first artificial womb facility allows infertile couples to become biological parents. In other cases, if a woman has undergone hysterectomy (surgical removal of the uterus) or a health problem that would otherwise worsen due to pregnancy, such women can still produce fertile ova which can be recovered using laparoscopy or any other such surgical technique. It also reduces the risk of miscarriages and issues of low sperm count in males. This Revolutionary Concept of Artificial Womb Technology was revealed recently by Hasheem Al Ghaili, a biotechnologist, which will produce 30,000 lab-grown babies outside the mother's womb in an artificial environment. It is designed to help nations that are suffering from low populations.

Historical Aspect of Ectogenesis

The idea of Ectogenesis is certainly not a new concept. In the sixteenth century, Paracelsus, A Swiss Physician, provided a recipe for creating a *homunculus* or a little man. Paracelsus suggested that if the semen of a man is sealed in a glass flask with horse dung and fed with man's blood, after forty weeks it will become a true and living infant. In those days people used to think that sperms were thousands of little humans who were swimming throughout the semen and the woman's womb was an incubator where the sperms develop into human beings. The concept of Ectogenesis was also explained by J.B.S Haldane, geneticist and physiologist in the 1900's in his book *Daedalus* where he explained that the development of ectogenesis would be one of the most pioneer discoveries in the history of mankind.The first successful ectogenesis experiment was performed in 1996. Scientists took 14 fetuses of goats and placed them in an artificial womb which was a plastic box filled with their artificial amniotic fluid and they were

able to deliver at least one of those offspring. Hashem Al Ghaili envisaged it on a human scale and revealed the first Artificial Ectogenetic Setup.

Design

The facility has 75 well-equipped labs. Each lab can house up to 400 artificial wombs or pods. Each pod is designed n such a way that it mimics the exact conditions conditions found inside the uterus, providing the fetus with an infection-free sterile medium. This is done by adding a lab-made amniotic fluid. Natural Amniotic fluid consists mainly of water, nutrients, hormones, antibodies, and the baby's urine. This natural amniotic fluid is replaced by Lactate Ringer's Solution which has a composition very similar to Amniotic Fluid.

Each pod has 360º cameras installed that will monitor the growing fetus 24*7, each major and minor change taking place in the growing fetus will be recorded by those cameras which can be viewed as a timelapse video on a smartphone. There will be three different types of sensors attached to the baby – a bioimpedance sensor that will send a weak current to measure the amount of water and muscle mass present in the body of the fetus; an electrocardiogram that will take account of the heart rate of the fetus and lastly photo-plethysmography that will measure the blood volume variations and arterial oxygen saturation of the fetus. Also, there will be an Artificial Intelligence generated system to monitor all physiological processes taking place in the body of the fetus and report any potential genetic abnormality in real-time. The AI System will continuously match the DNA of the newly dividing cells with the parental DNA and wherever it finds an anomaly, the AI system will repair the damage.

All the pods will be connected to two large tanks or bioreactors present at the center – the Nutrition Tank that will provide nutrients, oxygen, and other essential fluids and the Waste Management Tank that will collect wastes from the baby and recycle them – via pipelines. Wastes collected will be broken down anaerobically and enzymatically by different microbes releasing only oxygen and water.

The Artificial Womb Technology allows the parents to customize the baby's traits – such as eye colour, skin tone, height, level of intelligence, etc. If a family has a history of a fatal genetic disease that may appear in the upcoming generation, it can be genetically engineered which ensures a healthy life for the baby. In developing nations, approximately 20 million premature and low birth weight infants are born every year and 4 million die within one month. Ectogenesis minimizes the infant mortality rate on a bigger level. On the completion of development, just by pressing a button, the baby can be delivered. This omits the issues of C-sections and reducing maternal mortality rates.

Downsides

The development of Ectogenetic Technology raises questions about the ethics of artificial reproduction and the implications for parental roles and societal norms. Artificial Womb Technology seemingly ends the role of women in society. Women may start to lose their respect in the society. It will empower men to have children without the assistance of women. Artificial Womb seems to be fundamentally against the natural reproductive order. It may increase the debates on abortion rates. The absence of Strict Laws regarding Ectogenesis may lead to misuse of the technology. Last but not least, these baby-making factories will end the divine bonding between a mother and her child.

Conclusion

As of now, Artificial Womb Technology remains a concept and is not yet in widespread use. It represents a potential future direction for reproductive technology but has not been implemented in practice. This ex-utero gestation technique will be a great alternative to conventional Neonatal intensive care. The downsides of the technology should be kept in mind for further processes in research and development. The concept embodies significant advancements in reproductive technology, but its practical application and broader implications are still subjects of ongoing research and debate. Hoping the advancements in this technology may play a pivotal role in the medical field so that more couples can become parents of a healthy child.

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Genetic Risk Factors of Schizophrenia: A Systematic Review

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Keywords: Schizophrenia, 22q11 locus, cognitive impairment, Proline Dehydrogenase.

Introduction: Cognitive impairment is a major determinant of functional outcomes in schizophrenia. Impaired working memory, attention and other such ailment in cognitive function can have a major impact on a person's ability to socialize; eventually leading to conditions like schizophrenia.

"A global deficit of cognitive is characteristic of schizophrenia with evidence indicating greater impairment for specific cognitive domains such as executive function, attention, episodic memory and motor speed." [1]

Understanding the genetics and the biological mechanisms underpinning the cognitive dysfunction is thus of utmost importance.

The overlaps between latent cognitive factors and schizophrenic symptoms have already been explored and they contribute to our understanding of the condition.

1. Inheritability of Schizophrenia:

Cognitive ability and thus schizophrenia are inheritable. An important discovery of family and twin studies shows the proportional increase in risk for disease with the degree of genetic relationship to a person suffering from schizophrenia.

"The risk is approximated at 2% for third-degree relatives, 9% for first-degree relatives, 27% for children of two affected parents and 50% for monozygotic twins." [2].

Even though the genetic component of schizophrenia is quite high, much of its genetic structure remains unknown – schizophrenia is a multifunctional disorder that encompasses the interplay of various susceptible genes, and epigenetic processes.

Twin studies reveal that schizophrenia has higher heritability in monozygotic twins than in dizygotic twins. Genome-wide association studies (GWAS) have identified over 100 genetic loci (E.g.- C4 gene in synaptic pruning and immune system involvement) associated with the disorder.

Table 1 :

Risks to relatives of those with schizophrenia

Relation	Risk (%)
Identical twins	57.70
First-degree relatives	
Parents	4.40
Brothers and Sisters	8.50
Children	8.20
Second-degree relatives	
Uncles and aunts	2.00
Nephews and nieces	2.20
Grandchildren	2.80
Half-brothers and Sisters	3.20
Third-degree relatives (first cousin)	2.90
Risk of offspring of 0-2 schizophrenic parents	
Neither parents schizophrenic	8.20
One parent schizophrenic	13.80
Both parents schizophrenic	36.60
General population	0.86

A Table showing the risk of relatives of those with Schizophrenia with respect to the type of genetic relation between them.

2. Polygenic Risk Score:

Polygenic Risk score (PRS) is the estimate of an individual genetic risk for some trait, and it is obtained by aggregating the effects of multiple genetic variants across the genome, weighted by their effect sizes and frequencies.

Evidence on the association between schizophrenia polygenic risk score (SZ PRS) and clinical presentation has been inconsistent – PRS is especially sensitive to positive symptoms, while a study on an adolescent group found that the SZ PRS predicted negative symptoms and anxiety [3].

Moreover, although symptoms course is a crucial factor of the diagnostic criteria for schizophrenia, the relationship between the SZ PRS and symptom trajectories in psychotic disorders is still unknown. In comparison with relations with symptoms, the association of SZ PRS with neurocognitive deficits has been stronger.

3. Linkage Studies:

Coupling studies is one of the first molecular genetic approaches. It resides in the concept that genetic traits located close to each other are more prone to be inherited together compared with traits farther apart.

Several chromosomal regions – like 6p23.2 ('p' arm of chromosome 6 which has a size of 23.2 million base pairs), 13q32-34, and 22q11 – have been found to be linked with schizophrenia through multiple studies. Other chromosomal regions in chromosome 1,2,5 and 8 have also been identified to be linked to schizophrenia.

A recent large-scale linkage study showed the disruption in schizophrenia 1 (DISC1) gene (gene involved in brain development and function) resulted from a 1q42 translocation and previously described as a segregating with psychopathology in a large Scottish family [4].

4. Genetic Mechanism of Schizophrenia:

No single gene is necessary or sufficient to determine the disorder, rather a combination of risk genes with small effects describe the highly heterogeneous genetic basis of schizophrenia [5].

The gene for Proline Dehydrogenase (mapping on the 22q11 chromosome) codes for an enzyme that metabolizes L-Proline, an amino acid that may be directly involved in glutamatergic transmission, which in turn is one of the core pathways associated in schizophrenia [6]. Through fine mapping of the 22q11 locus, overexpression of haplotypic variants (specific genetic variations inherited together on the same chromosome) at the 3' end of the gene has been identified. This finding has been confirmed in two independent studies evaluating a large (528) group of Chinese families, as well as 274 Ashkenazi Jewish origin families [7][8].

In another study on 360 Iranian subjects (175 schizophrenic and 185 controls) 3 polymorphisms of the ProDH (Proline Dehydrogenase) gene were associated with an increased risk of schizophrenia [9].

Rare variants of the gene have shown to reduce the activity of the enzyme (a neurotransmitter regulator). In an animal-model study on mice involving the ProDH gene variants, abnormal plasticity of glutamatergic synapses and dopamine dysregulation in the frontal cortex have been identified. The dysregulation of dopamine generates increased levels of transcripts of the cathecol-O-methyltransferase (COMT) gene, located on the 22q11 chromosome. This seems to be a triggered compensatory response to the glutamate dysregulation.

Glutamate dysregulation leads to phenomenons like over activation and consequent death of neurons, causing reduced grey matter volume [10][11].

Conclusion:

The heritability of schizophrenia estimates highlights significant familial transmission. PRS have provided a framework for quantifying the cumulative effect of common genetic variants while linkage studies have been pivotal in identifying the key genetic loci that contribute to its pathopsychology.

ProDH encodes for Proline Dehydrogenase, an enzyme involved in neurotransmitter regulation, and certain polymorphisms in this gene are associated with altered brain function and thus an increased risk of schizophrenia. This may even lead to cognitive and psychiatric symptoms like working memory deficits, attention and executive problems, social withdrawal, hallucinations, etc. – common symptoms of schizophrenia.

From these evidences we see that Schizophrenia has a strong genetic basis and thus are subjected to a great number of genetic risks.

Continued research will eventually unravel a more genetic architecture of schizophrenia.

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When Defense Turns Dangerous: Autoimmunity's Link to Cancer

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Keywords: Autoimmune diseases, Chronic inflammation, Macrophage migration inhibitory factor (MIF), Cancer risk, p53 suppression

Introduction

Our immune system protects us from infections and abnormal cells, including cancerous ones. However, when this system turns against itself, as seen in autoimmune diseases, it can lead to chronic inflammation and potential development of malignancies. It is a strange paradox that the system meant to defend the body can become a driver of cancer through immune dysfunction and chronic inflammation.

Understanding Immune Dysregulation in Autoimmunity

Autoimmune diseases like rheumatoid arthritis, lupus, and multiple sclerosis arise when the immune system confuses its own tissues for invaders. This confusion leads to chronic inflammation, driven by immune cells like T cells and macrophages.

In a healthy body, these cells work together to eliminate threats. But in autoimmunity, they attack healthy tissues instead, leading to long term damage. This immune dysregulation not only harms tissues but also interferes with the body's natural DNA repair mechanisms thus creating a breeding ground for cancer by fuelling inflammation and genetic instability.

The Role of Chronic Inflammation in Cancer Development

Chronic inflammation, a hallmark of autoimmune diseases, is a well- known cancer risk factor. Prolonged inflammation keeps immune cells, like the macrophages and lymphocytes, activated which further secretes cytokines, chemokines and growth factors meant to help repair tissues. Overtime, however, these molecules can cause more harm than good, especially in tissues exposed to prolonged inflammation.

Inflammatory cells also release reactive oxygen (ROS), which damages DNA over time. This continuous DNA damage can lead to mutations, a key driver of cancer. Simultaneously, the tissue repair process encourages rapid cell growth which combined with weakened immune checkpoints, gives mutated cells a chance to survive and proliferate. These conditions together increase the risk of oncogenesis. Inflammation thus acts like a slow burning fire, damaging tissues and setting the stage for cancer in autoimmune conditions.

MIF and p53: The Dangerous Pathway

A key player in this link between inflammation and cancer is the macrophage migration inhibitory factor (MIF), a cytokine released by immune cells. In autoimmune diseases, MIF amplifies tissue damage and plays a direct role in cancer development.

MIF interferes with one of the body's most important tumour suppressors: p53. Normally, p53 plays a vital role in DNA repair, halting cell division in response to genetic damage and inducing apoptosis (programmed cell death) in severely damaged cells. MIF, however,

inhibits p53 by suppressing its transcriptional activity. This suppression allows cells with DNA damage to bypass the checkpoint that would normally halt their proliferation or initiate their death.

This chronic bypass of p53's regulatory function can lead to the survival of cells harbouring genetic mutations. These mutations accumulate over time, particularly in tissues already exposed to chronic inflammation, further increasing the chances of cancer development. The MIF-p53 axis represents a dangerous pathway through which chronic autoimmune inflammation directly fuels the accumulation of oncogenic mutations, fostering the environment for cancer initiation and progression.

Autoimmune Diseases and Their Cancer Risks

Several autoimmune diseases come with an increased risk of specific cancers, showing how chronic immune dysfunction can create a cancer-friendly environment:

1. Systemic Lupus Erythematosus (SLE): SLE increases the risk of blood cancers like lymphoma and leukemia, as well as solid tumours, such as lung cancer. The chronic immune activation in lupus leads to more cell turnover, raising the chance of cancer.

2. Inflammatory Bowel Disease (IBD): Diseases like Crohn's and ulcerative colitis increase the risk of colorectal cancer, with long-term inflammation in the gut lining driving genetic mutations and tumour growth.

3. Multiple Sclerosis (MS): Although MS mainly affects the nervous system, it's linked to higher risks of cancers in the urinary tract, breast, and digestive system, likely due to chronic inflammation and immune mis regulation.

4. Type 1 Diabetes Mellitus: Individuals with Type 1 diabetes, an autoimmune disease where the immune system attacks insulin-producing beta cells in the pancreas, have an increased risk of developing pancreatic cancer. Chronic inflammation in the pancreas, along with immune system-mediated damage, contributes to a pro-cancerous environment, making pancreatic cancer a notable concern for people with long-term.

How Inflammatory Cells Can Fuel Tumour Growth

While inflammatory cells are essential in defending the body, they can also encourage the growth of tumours. In the early stages of cancer, these cells release cytokines and growth factors that help create a tumour friendly environment.

Inflammatory cells also promote genetic instability, speeding up mutations in cancerous cells. They also stimulate angiogenesis by supplying tumours with oxygen and nutrients that they need to grow. This further creates a feedback loop where cancer cells take advantage of the very immune system that is supposed to protect the body.

As tumours develop, they exploit immune processes to their advantage. Neoplastic cells hijack immune cell functions like matrix metalloproteinase (MMP) production and selectin-ligand interactions to facilitate their invasion and metastasis. This shift in the immune system reveals how, over time, the very cells meant to protect us can end up helping cancer grow. These inflammatory cells, once our body's defenders, gradually turn into unwitting accomplices, supporting cancer's development instead of stopping it.

A path to new therapies

The connection between autoimmunity and cancer shows how the body's own defense system, which is designed to keep us safe from disease, can sometimes turn against us. Instead of protecting the body, this system can, under certain conditions, become a major contributor to illness. In autoimmune disorders, chronic inflammation from an overactive immune system doesn't just hurt healthy tissues, it also sets the stage for cancer to grow more easily. The constant inflammation harms DNA, weakens the body's ability to maintain genetic stability, and nurtures a microenvironment where tumours can grow and spread more freely. Proteins like macrophage migration inhibitory factor (MIF) play a key part in this damaging cycle. They interfere with crucial tumour-suppressing mechanisms, such as the p53 gene, which normally prevents dangerous mutations. When p53 is disrupted, cells are more likely to gather harmful mutations, increasing the risk of cancer. Even the immune cells, which should be defending the body, can unintentionally help cancer grow. By studying these intricate relationships, scientists are uncovering new treatments aimed at targeting inflammatory pathways. These therapies bring hope not only for easing the difficult symptoms of autoimmune diseases but also for lowering the risk of cancer in people dealing with these conditions.

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mRNA Vaccines: A Paradigm Shift in Prophylactic Medicine and Immunity Development against SARS-CoV-2

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Keywords: mRNA vaccines, antigen synthesis, SARS-CoV-2, spike glycoprotein, immunogenicity.

Introduction: Understanding the Virulence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus responsible for the global COVID-19 pandemic, exhibits several distinctive biological features that contribute to its high virulence and transmissibility. A hallmark characteristic of SARS-CoV-2, as with many coronaviruses, is the presence of spike (S) proteins that play a crucial role in viral entry into host cells, initiating infection.

The RNA genome of coronaviruses, with a median length of 29 kb, is the longest among known RNA viruses. This extensive genome encodes essential proteins, including the viral replicase and structural components necessary for viral assembly and function. The three main proteins that make up the SARS-CoV-2 viral envelope are the spike (S) protein, which are essential for invading host cells, the envelope (E) protein, and the membrane (M) protein.

Features of the Spike (S) Protein:

- The S protein is a large, highly glycosylated type I transmembrane fusion protein, consisting of 1,160 to 1,400 amino acids depending on the coronavirus species.
- Unlike the M and E proteins, which primarily function in viral assembly, the S protein is responsible for viral fusion with host cell membranes, allowing viral entry.
- The spike-shaped protrusions on the viral surface are formed by the S proteins, a feature integral to the virus's ability to infect host cells.

Targeting the Spike Protein in SARS-CoV-2:

SARS-CoV-2 needs the S protein in order to attach to host cell receptors and start an infection.Given its indispensable role in viral entry, the S protein has emerged as a critical target for vaccine development and antiviral therapeutics. Disrupting the interaction between the S protein and host cell receptors offers a promising strategy to prevent viral infection and propagation.

This marks a pivotal point where scientists can leverage their expertise in molecular biology to inhibit the synthesis of the S protein, thereby fostering immunity against the virus through the development of mRNA vaccines.

Historically, most vaccines, including those for measles,

polio, and yellow fever, were developed using killed or weakened forms of the entire virus. Producing whole virus-, protein-, and vector-based vaccines requires large-scale cell culture, a process that is resource-intensive and constrains the ability to rapidly produce vaccines in response to emerging outbreaks and pandemics. Consequently, researchers have sought to develop alternative vaccine technologies independent of cell culture, which is undoubtedly challenging.

With the use of the body's own cellular machinery, mRNA vaccines provide a fresh method to immunization by producing antigens and inducing an immune response. This technology has gained considerable attention due to its rapid development and demonstrated efficacy, notably exemplified by the COVID-19 pandemic. The foundation of mRNA vaccines lies in their ability to synthesize and deliver genetic material encoding antigens. The process involves the identification of target antigens, mRNA synthesis, and encapsulation in lipid nanoparticles for efficient delivery. The modular nature of mRNA allows for swift adaptation to emerging pathogens.

Mechanism of Action

Upon administration, mRNA is taken up by host cells, and ribosomes translate it into viral or bacterial proteins. These proteins act as antigens, stimulating the immune system to mount a robust response. Due to the flexibility of mRNA vaccines, antigens that are specifically designed to trigger particular immune responses can be created.

The Scientific Breakthrough

In the early 1990s, mRNA synthesized in the lab (in vitro) was prone to instability and difficult to deliver, leading to significant inflammatory responses. This necessitated the creation of advanced lipid-based delivery systems to stabilize and transport the mRNA. During this period, Dr. Weissman, a postdoctoral researcher at NIAID, investigated the role of dendritic cells and their response to mRNA. He identified that the interaction between mRNA and dendritic cells triggered adverse inflammation. To address this issue, Dr. Weissman partnered with Dr. Karikó, an assistant professor, to explore solutions. Drs. Karikó and Weissman discovered in their research that dendritic cells interpreted in vitro mRNA as a foreign material, leading to inflammation. However, this impact was absent with mRNA derived from mammalian cells.

RNA comprises four nucleotide bases: adenine (A), uracil (U), guanine (G), and cytosine (C), which pair with uracil (U), adenine (A), cytosine (C), and guanine (G) in DNA, respectively. Drs. Karikó and Weissman noted that while mammalian cell RNA undergoes various chemical modifications, in vitro transcribed mRNA does not. They hypothesized that this lack of modification could be contributing to the inflammatory responses observed. To test this, they created several mRNA variants with specific chemical alterations in their nucleotide bases and introduced them to dendritic cells. Their findings were profound: incorporating these modifications nearly eliminated the inflammatory response, leading to a fundamental shift in our understanding of how cells perceive and react to different mRNA forms.

The researchers found that introducing chemical modifications to the mRNA synthesized in the lab effectively eliminated the inflammatory response. Published in 2005, this finding significantly changed our knowledge of how cells recognize and react to different types of mRNA.

Conclusion: The Future of mRNA Vaccines

The 2023 Nobel Prize in Physiology or Medicine was awarded to Katalin Karikó and Drew Weissman for their pivotal contributions to the development of mRNA vaccines. Their groundbreaking work on nucleotide base modifications has overcome significant challenges in mRNA vaccine technology, particularly by mitigating inflammatory responses and enhancing protein expression. This achievement has transformed the landscape of vaccine development, particularly in the context of the COVID-19 pandemic. Karikó and Weissman's innovations have not only paved the way for effective COVID-19 vaccines but also set the stage for mRNA technology to address a broader spectrum of health issues. The success of these vaccines underscores the potential of mRNA to be adapted for targeting specific viral proteins, such as the spike protein of SARS-CoV-2. Researchers are now exploring the possibility of developing standardized mRNA-based agents to inhibit the binding and fusion of this protein, which could enhance our ability to prevent and treat COVID-19.

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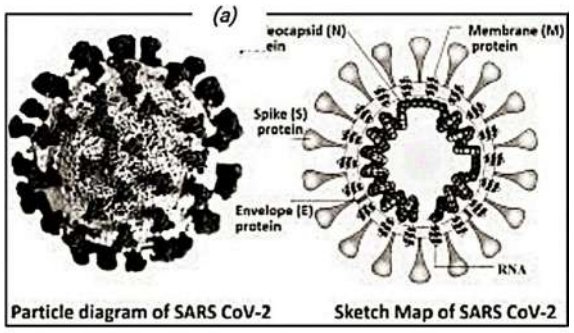
(a)



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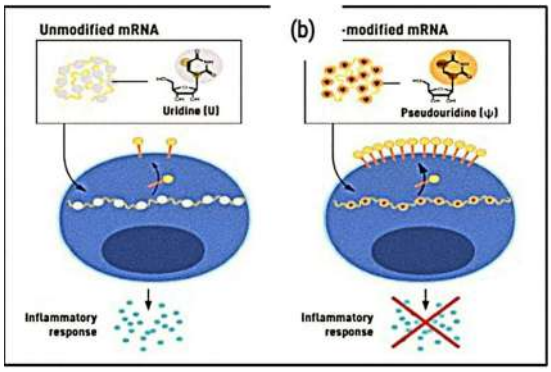

Disease/Condition	Current Successes	Vaccine Names	Future Applications	Key Dates
COVID-19	Rapid vaccine development and deployment.	Pfizer-BioNTech, Moderna	Updates for variants and long-term efficacy.	Emergency use Dec 2020
Influenza	Early-stage mRNA vaccine development.	Moderna Influenza, Pfizer-Flu (in development)	Rapid updates to match strains.	Trials began 2023
Sickle-Cell Disease	Initial research into gene editing therapies.	mRNA therapies (under development)	Gene correction and improved outcomes.	Studies started 2021
Multiple Sclerosis	Research on modulating autoimmune responses.	mRNA treatments (under development)	Potential treatments to halt or reverse disease.	Trials began 2022
Cancer	Personalized mRNA cancer vaccines in trials.	BioNTech's, Moderna's cancer vaccines	Tailored treatments for individual tumors.	Trials started 2021
Emerging Infectious Diseases	Adaptability for new pathogens.	mRNA vaccines for Zika, Ebola (in development)	Rapid response to new threats.	Research ongoing 2022

(c)

Figure 1: (a)Particle Diagram Of SARS-CoV-2 (Image Reference: https://molmed.biomedcentral.com/articles/10.1186/s10020-024-00855-2);(b)"mRNA contains four different bases, abbreviated A, U, G, and C. The Nobel Laureates discovered that base-modified mRNA can be used to block activation of inflammatory reactions (secretion of signaling molecules) and increase protein production when mRNA is delivered to cells." - The Nobel Committee for Physiology or Medicine. Ill (Image Reference: https://www.nobelprize.org/prizes/medicine/2023/press-release/); (c)Table: Overview of mRNA Vaccine Success and Applications (Original)

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Advancements in Vaccine Delivery Technologies: Toward More Efficient Immunization

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Keywords: Vaccine efficacy, Microneedles, Nanoparticles, Vaccine stability, Personalized vaccine.

Introduction

Vaccination is a cornerstone of public health, but traditional delivery methods face challenges related to efficacy, safety, and patient adherence. Effective vaccine delivery is crucial for ensuring high immunization coverage and robust protection against diseases. Conventional needle-and-syringe methods, while proven, often encounter issues such as pain, needle phobia, and suboptimal antigen stability. Infection risk (e.g., HIV, hepatitis) if needles are reused, limited accessibility in resource-poor areas, cold chain requirements for storage and transport, limited scalability in mass vaccination scenarios are some major drawbacks of traditional vaccine delivery methods. Innovations in vaccine delivery technologies aim to overcome challenges by improving antigen delivery, enhancing immune responses, and increasing patient compliance. The latest developments in vaccine delivery technologies such as microneedle arrays, nanoparticle-based systems and controlled-release formulations and the potential for integrating these technologies lead to addressing of the global health needs.

Microneedle Arrays

Microneedle arrays consist of tiny needles that penetrate only the outermost layer of the skin, minimizing discomfort and avoiding nerve endings. These arrays deliver vaccines directly into the dermal layer, which contains numerous immune cells. Microneedles can be designed as solid, coated, or dissolvable types. Solid microneedles create micro-channels in the skin, while coated microneedles have vaccine antigens on their surface, and dissolvable microneedles release the vaccine as they dissolve. The primary advantages of microneedles include their ability to improve vaccine stability, reduced pain, ease of administration, and potential for self-administration. Additionally, microneedles can enhance the uptake of vaccines by targeting skin's immunological sites and provide an alternative to conventional needle-based methods. Recent innovations include the development of microneedle patches that are user-friendly and can be applied by patients themselves. For instance, dissolvable microneedle patches for influenza and COVID-19 vaccines have shown promise in clinical trials. Studies have demonstrated that these patches can effectively deliver vaccines and generate strong immune responses with high patient acceptance.

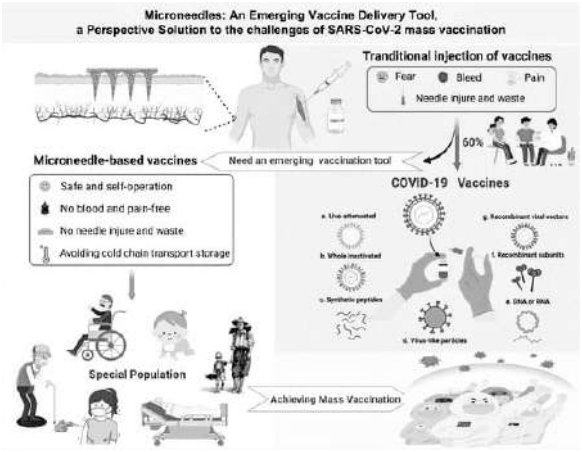

Figure 1 : Microneedles: An Emerging Vaccine Delivery Tool and a Prospective Solution to the Challenges of SARS-CoV-2 Mass Vaccination by Ya-Xiu Feng 1,Huan Hu 1,Yu-Yuen Wong 1,Xi Yao 1,* and Ming-Liang He Source/Image Reference : https://www.mdpi.com/1999-4923/15/5/1349

Nanoparticle-Based Delivery Systems

Nanoparticle-based delivery systems involve encapsulating antigens in nanoparticles made of materials such as lipids, polymers, or proteins. These nanoparticles enhance vaccine stability, protect antigens from degradation, and facilitate targeted delivery to immune cells. Nanoparticles can be engineered to provide controlled release, improving the duration of the immune response. Nanoparticle systems offer several advantages, including improved antigen stability, enhanced cellular uptake, and potential for targeted delivery. For example, lipid nanoparticles used in mRNA vaccines protect the mRNA from degradation and ensure efficient delivery into cells, leading to robust immune responses. The success of lipid nanoparticles in mRNA vaccines, such as those developed for COVID-19, represents a significant advancement. These nanoparticles have proven effective in enhancing vaccine stability and efficacy. Research is ongoing into other types of nanoparticles, such as gold and silica nanoparticles, for

their potential use in vaccine delivery.

Controlled-Release Formulations

Controlled-release formulations are designed to release vaccine antigens gradually over time, providing a sustained immune response and reducing the need for multiple doses. These formulations can be achieved using technologies such as polymeric microspheres and hydrogels. The primary advantages of controlled-release formulations include improved compliance, as they reduce the frequency of doses, and enhanced immune responses due to prolonged antigen exposure. These systems can simplify vaccination schedules and improve patient adherence. Recent advancements include the development of biodegradable polymeric microspheres that encapsulate vaccines and release them slowly. These systems are particularly useful for vaccines requiring booster doses and have shown potential in enhancing immune responses and providing longer-lasting protection.

Oral and Nasal Vaccines

Alternative delivery routes, such as oral and nasal vaccines, are also being explored to improve vaccine accessibility and patient compliance. Oral vaccines, which are administered via the gastrointestinal tract, offer the advantage of being needle-free and easier to administer. However, challenges remain in ensuring the stability of the vaccine antigens in the harsh gastrointestinal environment. Nasal vaccines, which are administered via the nasal mucosa, provide a non-invasive alternative and have the potential to induce mucosal immunity, which can be beneficial for protecting against respiratory pathogens. Recent advancements in nasal vaccine formulations have improved their efficacy and stability, making them a viable option for widespread use.

Future Directions

• Integration of Technologies : Combining different delivery technologies may offer synergistic benefits. For example, integrating nanoparticles with microneedles could provide controlled and targeted vaccine release, potentially enhancing both efficacy and patient compliance. Research into these integrated systems is ongoing and holds promise for improving vaccine delivery.

• Personalized Vaccine Delivery : Advancements in genomics and biotechnology may lead to personalized vaccine delivery systems tailored to individual immune profiles. Personalized approaches could optimize vaccine responses and minimize adverse effects, making vaccines more effective and safer for diverse populations.

• Addressing Global Health Needs : Innovative delivery technologies have the potential to improve vaccine access in low-resource settings. Technologies that are easier to use, require less refrigeration, and are cost-effective could significantly impact global vaccination efforts, particularly in underserved regions.

• Regulatory and Manufacturing Considerations : The successful implementation of new vaccine delivery technologies requires addressing regulatory and manufacturing challenges. Ensuring that new technologies meet regulatory standards and can be produced at scale is essential. Collaboration between researchers, manufacturers, and regulatory agencies will be crucial in advancing these innovations.

Conclusion

Advancements in vaccine delivery technologies represent a significant step forward in enhancing immunization practices. Microneedle arrays, nanoparticle-based systems, and controlled-release formulations each offer unique benefits and address specific challenges associated with traditional methods. While these technologies hold great promise, addressing associated challenges such as cost, manufacturing, and regulatory approval will be critical for their successful implementation. Continued research and development, coupled with a focus on overcoming these challenges, will be essential in leveraging these innovations to improve global health outcomes.

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The Athlete's Heart: Pathology behind sudden Cardiac Death

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Keywords: Athlete's heart, Exercise-induced arrhythmogenic right ventricle cardiomyopathy, Exercise-induced arrhythmias, Phidippides cardiomyopathy.

Phidippides And Sudden Cardiac Death:

Have you ever heard the story of Phidippides? In 490 BC, during the Greco-Persian war, the Persian king Darius I commanded his army to attack the Greeks, whom they outnumbered greatly. In this face of attack, a 40-year-old Athenian herald, Phidippides, was ordered to run about 75 miles through the mountainous terrain to Sparta to request military support. Although the Spartans had agreed to assist the Greeks, they somehow could not immediately due to some religious obligations, so Phidippides continued his journey back to Marathon, completing 150 miles in less than 2 days. On arrival at Marathon, to his disbelief, the Greeks had defeated the Persians. Phidippides was then again sent 26.2 miles to Athens from marathon to spread the news of their impressive victory with the other Greeks. Upon his arrival in Athens, after running 26.2 miles, he stretched out his arms and exclaimed happily, "We are victorious!" After that, he simply collapsed and died! His death was the first report of sudden cardiac arrest death in a long-distance runner. Numerous such deaths in athletes during marathons were reported after his demise.

Sudden Death Due To Exertion:

There has been much confusion regarding the aetiology of the sudden death that has been recorded following extreme exertion. Greater significance has been given to hypertrophic cardiomyopathy, anomalous coronary arteries, acute myocardial ischemia and premature coronary artery disease; however, as per recent studies, continuous cardiac exertion in any form can lead to cardiomyopathy. It has been known that endurance athletes have cardiac chamber enlargement, left ventricle hypertrophy, and increased rates of ventricular and atrial arrhythmias.

How Healthy Were The Arteries Of Phidippides?

With advancing age, there is pervasive vascular disorder that with time, manifests as stiffening of the greater arteries as well as augmented pressure from wave reflections. This contributes to subclinical target organ damage, like impaired vascular reactivity due to endothelial damage and increased left ventricular pressure, contributing to cardiac hypertrophy. In fact, each of these is an indicator of future cardiovascular events. Although habitual physical exercise and moderate intensity endurance training are known to have positive effects on our body, some of them paradoxically can have opposite effects on the body. Thus, there appears to be a U curve with respect to exercise and vascular function. Inactivity is detrimental for the body but too much high intensity training can prove to be equally detrimental for the body.

Studies reveal that marathon runners have increased central artery stiffness. It has been suggested that exercise-induced bradycardia causes a compensatory increase in stroke volume to maintain the cardiac output. Increased load on vasculature may cause elastin fatigue and fragmentation, thereby contributing to a loss of arterial compliance. Interestingly, exercise-induced bradycardia and increased stroke volume can also cause increased pressure from wave reflections and increased central pulse pressure. With each cardiac ejection, a pressure wave is generated that traverses the aorta. Arriving at areas of impedance mismatch, this pressure is reflected back to the heart, adjoining a newly generated pressure wave. Thus, the central blood pressure and the overall pulse pressure are due to forward and reflected waves. With a heart rate reduction as is seen in chronic exercise training, systolic ejection duration is increased, altering the pressure wave temporal associations, such that the reflected wave has reflected wave has more time to arrive during systole than during diastolic decay. Studies have shown that the same reduction in heart rate causes an increase in pressure in persons with stiffer vessels as compared to people with more compliant vessels, a fact of concern for bradycardic marathon runners with stiff arteries.

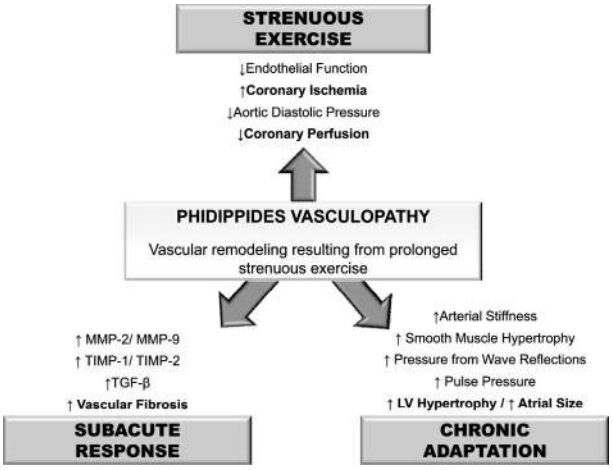

Fig: Acute and chronic changes in systemic vasculation structure and function with marathon training (Source/ Image Reference: https://onlinelibrary.wiley.com/cms/asset/6ec197f0-ff1b-43cc-b512-55a0bfc87b6c/mfig001.jpg)

Following completion of a marathon, there is a large reduction in pressure from wave reflections, aortic pulse pressure and aortic diastolic pressure. This is medically relevant because aortic diastolic pressure is a very significant determinant of coronary perfusion pressure and subendocardial viability. This can often lead to peripheral vasodilation and peripheral venous pooling. Myocardial ischemia is a prime arrhythmogenic substrate which increases the risk of SCD.

Running a marathon reduces femoral-artery flow mediated dilation, suggesting endothelial damage. Besides, studies have revealed that marathon running causes release of novel angiogenic peptides that have systemic endothelial regulatory actions, such as soluble FMS-like tyrosine kinase-1 and endoglin. Coronary ischemia causes release of sFlt-1 that impairs endothelial function by causing a reduction in nitric oxide bioavailability and causing apoptosis of the endothelial cells and sensitizing them to pro-inflammatory factors. Endoglin affects LV filling pressures and is associated with LV disfunction.

Conclusion:

In conclusion, it is thus proposed herein that repetitive and elevated rates of cardiac output in individuals for several hours cause fatigue in the elastin fibres, stimulate resident macrophages and fibroblasts, thereby causing stiffening of the arteries. This, together with bradycardia and augmented pressure resulting in the forward waves, ultimately increases the pressure and leads to downstream damage to the endothelial cells and ultimately damage to the target organ. The article proposes that Phidippides cardiomyopathy may extend beyond the chambers of the heart and should be rightfully placed under cardiovascular disease and should be treated like one.

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Chronicles of chimera: the reality of human-animal hybrids

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Keywords: Chimera, Nakauchi, Salk Institute, human-animal hybrid, stem cells, and organ harvesting

We all grew up reading stories about superheroes like Spider-Man and Ant-Man. The idea of a human-animal hybrid has always seemed fascinating, and with the development of various scientific theories and methodologies, the prospect seems even more fascinating. But how much of this is actually possible? And how far are we from recreating the pages of a comic book into reality? One may think that it should

be pretty simple.

For one, we have successfully hybridized mammals and created mules, ligers, beefalo, wholphins etc. Moreover, we're all made of different combinations of the same amino acids and proteins. Much of the blueprint, such as our genes and DNA, is shared between species. For example, humans and mice share over 90% of their DNA, while we share approximately 35% of our genes with the basic roundworm. A human-animal hybrid should not be much of a problem considering this information.

But that is where things start getting a little complicated. The need for a human-animal chimera (mosaic animals) first emerged for medical purposes. Human-animal chimera research has potential benefits for physiological modeling, neural analysis and organ harvesting, the last of which is particularly relevant for the organ donor market in almost any country.

But the quest for creating a chimera or a hybrid animal was not an easy task.

In 2010, Japanese scientist Nakauchi successfully generated adult mouse-rat chimaeras by injecting rat pluripotent stem cells (stem cells with an ability to rise to several different cell types) into mouse blastocysts. When mouse embryos - unable to make their own pancreases - were supplemented with rat pluripotent stem cells, the adult animals were found to have a functioning pancreas comprised of rat cells. Similarly, in March 2013, Nakauchi demonstrated that pig pluripotent stem cells could develop a pancreas in a pig that had been genetically designed to be incapable of producing one on its own.

With the initial series of successes, Nakauchi attempted to introduce human cells into embryos of pigs, cow and rat. Though the chimeras were successfully created, they never made it to full term and died within a few days.

Embryo of human-monkey chimera as published by Nature Magazine.

In 2017, researchers at Salk Institute, California, confirmed the viability of human pluripotent stem cells surviving and proliferating in pig cells. The size of these embryos was smaller than normal due to the limited contribution of its human counterpart. This model was discarded as well.Although we have successfully generated a number of human-animal chimeras, neither of them has been able to survive more than 14-20 days.

The main reason for this problem has been identified to be the incompatibility of animal genes with that of human. The 'evolutionary distance' between human and other animals currently hinders creation of true human chimeras [2].

In 2021, however, a human-monkey chimera was created by injecting human cells into stem cells of monkeys, as a joint project between the Salk Institute in the US and Kunming University in China. Though this chimera looked promising, it was terminated due to ethical and moral reasons.

Ethical conflict is one of the major obstacles of chimera-scientists today. Not only is the sanctity of the human nature interrupted, but also issues extend as far as questioning the ethics concerning human dignity, disregard for interspecies mixing and the moral confusion regarding the species formed.

Several countries banned the experiments and trials necessary for the development of a successful chimera.Another problem that the human animal chimera brings are cross-species diseases like H5N1 influenza A and the infamous HIV/AIDS [3].

It is safe to say at this junction that the lines of evolution are blurring. Today we face moral complications regarding the life of the chimera. It would only be a matter of years when full-grown chimeras will be a common sight.

We may have rats with the cognitive power of a human.We may have cows with a long furry tail.

We may even have humans climbing up walls like spiders.These assumptions are only for the future.

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Celestial genetics: unraveling the genetic challenges of space travel

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Keywords: cosmic radiation, microgravity, CRISPR-Cas-9, genetic engineering.

Subjected to the advancements made by space organizations and astronauts as attempts to unravel the ambiguity of the universe, the constant weightlessness poses huge physiological adversities.

Muscle atrophy, space osteopenia, amplified cancer risks, cardiovascular dysfunction and vision impairment are some of the key anomalies that comes with long term space expeditions. However, genetic engineering and modifying strategies inculcate extensive technologies to cure the damages induced by microgravity and cosmic radiations.

1.Physiological effects of spaceflight

The acronym 'RIDGE' (i.e., "space radiation, isolation and confinement, distance from Earth, gravity fields, and hostile and closed environments") is used by NASA to describe the aberrations experienced during space travel. To affirm that, the NASA Twins Study was carried out with two monozygotic twin astronauts and gene expression changes were reported in the astronaut that spent a 340 day-mission onboard the International Space Station when compared with his Earth-bound twin.

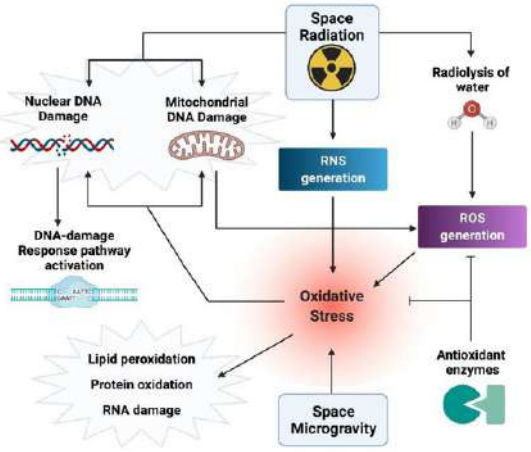
Based on the observations made by the Human Space Program (HSP) of NASA, it is to be concluded that cosmic radiations and micro gravity contribute synergistically to the harm incurred.

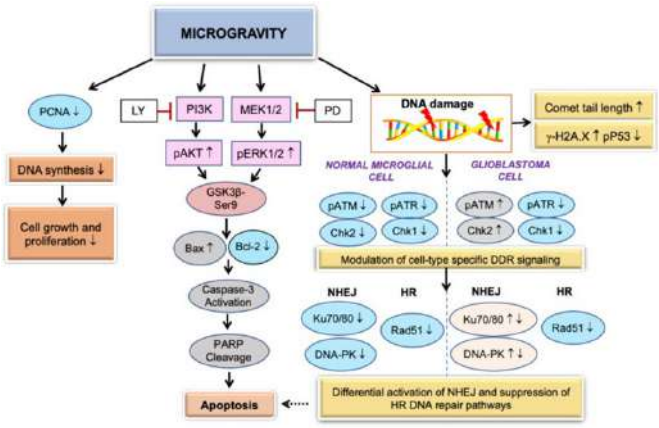
A.Cosmic radiation: In the Lower Earth Orbit (LEO), astronauts encounter protons trapped in Earth's geomagnetic field, and some high energy Galactic Cosmic Rays (GCR) and large Solar Particle Events (SPE) that are able to penetrate to LEO. Nucleotide modifications and mutations due to radiations heighten the risk of cancer, neurodegenerative and cardiovascular diseases.

1. DNA breaks: Cell's exposure to such amplified ionizing power sustains single-strand breaks (SSBs) and double-strand breaks (DSBs) in the DNA molecules. When radiation creates DSBs in the cell, the upstream signalling protein kinase called Ataxia Telangiectasia Mutated (ATM) gets activated. This initiates chromatin remodelling and onsets a series of protein phosphorylation events known as the DNA-Damage Response (DDR). This DDR pathway relies on proteins which when phosphorylated by the ATM, participate in detecting and transmitting the DNA damage signal to effector proteins, which take care of the repair pathway. However, DNA repair mechanisms might become faulty in the space environments, introducing errors in the sequences and thus lead to larger scale genetic damages.
2. Reactive Oxygen Species (ROS): Since the cells are mainly composed of water, ROS might get generated on radiolysis of cells. High levels of such toxic, free radicals lead to increase in oxidative damage to lipids, proteins and nucleic acids. Purines and pyrimidines are damaged by ROS, leading to oxidized pyrimidine derivatives such as thymine glycol (Tg) and 5,6-dihydrouracil (DHU), that can block DNA and RNA polymerases. Moreover, presence of ROS leads to creation of oxidized base-derived apurinic/apyrimidinic sites and SSBs. ROS, thus can cause mutations by damaging DNA bases, leading to faulty DNA replication or repair.
3. Radioactive Nitrogen Species (RNS): Early activation of nitric acid synthetases produces RNS, which modify protein in the form of tyrosine nitration and S-nitrosylation of cysteine, that alter the normal activity of proteins.

B.Microgravity:

1. Base repair impairment: The lack of gravity in space impairs the repair pathways increasing the effects of radiation-induced damage. Genomic instability mostly in the microglial and glioblastoma cells occurs on exposure to microgravity. Study on HL-60 cells (human leukemia cell line) reveals microgravity inhibited the activation of single strand DNA break repair pathways including base excision repair (BER), nucleotide excision repair (NER) and mismatch repair (MMR).
2. Physical consequences: The lack of mechanical stress leads to substantial loss of bone and muscle mass in astronauts. Deterioration of cardiovascular system, changes in fluid distribution and loss of proprioception occur. In October 2018, researchers found that extended space travel, such as trips to





Figures 1 and 2: showing the genomic damage of cosmic radiations and microgravity, respectively.
Image Source:
Figure 1 - https://www.mdpi.com/1422-0067/22/19/10507;
Figure 2 - https://www.sciencedirect.com/science/article/abs/pii/S0167488924000223?via%3Dihub

Mars, may severely damage astronauts' gastrointestinal tissues and brains, leading to premature aging.

CRISPR-Cas9 Technique and Remediation

CRISPR-Cas9, short for clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9, is a gene editing technique. Scientists implement this to insert, delete or alter genetic material at specific locations in the genome.

CRISPR-Cas9 was adapted from an inherent genome editing mechanism used by bacteria as an immunological defence mechanism. Bacteria that are virus-infected seize and incorporate tiny fragments of the virus' DNA into their own to form CRISPR array segments. The bacteria are able to recall the viruses thanks to this CRISPR arrays. The bacteria employ the CRISPR arrays to make RNA segments that can connect to specific DNA sequences on the viruses in case they re-attack. Thereafter, the bacteria use the Cas9 enzyme to break apart the DNA, rendering the virus inoperable. The mechanism of CRISPR-Cas9 can be comprehended through Figure 3.

This immune defence system can be reprogrammed to edit genomic DNA in humans. A small piece of RNA with a short guide sequence is created which binds to specific target sequence in a cell's DNA, similar to the RNA segments bacteria produce from the CRISPR array. This guide RNA attaches to the Cas9 enzyme. When introduced into cells, the Cas9 enzyme breaks DNA at the desired spot after the guide RNA identifies the desired DNA sequence. Once the DNA is cut, researchers use the cell's own DNA repair machinery to add or delete pieces of genetic material or to modify by replacing an entire sequence with a customized

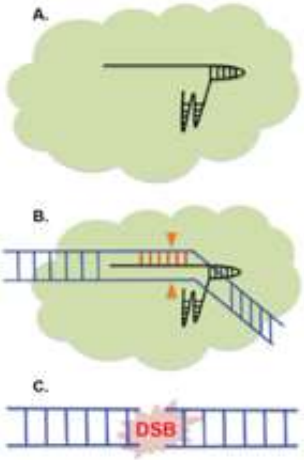


Figure 3: CRISPR-Cas9 mechanism

DNA sequence.

CRISPR-Cas9 has a wide potential to mitigate various physiological effects faced by astronauts.

i. *Biallelic mutations:* CRISPR results in efficient biallelic modifications through Non-Homologous End Joining (NHEJ) and Homology-Directed Repair (HDR) to repair the double strand breaks to create whole genome knockout libraries. Knockout libraries allow researchers to address questions regarding cellular functions. Figure 4 shows the DNA repair ability of CRISPR.

ii. *Enhanced resilience:* Genetically engineered organisms are subjected to a myriad of weightlessness and radiation exposure studies to assess the impact of these conditions on bone density, cognitive function, cancer incidence and more. So, if an astronaut were genetically engineered to have more muscle mass, stronger bones, an improved immune system and higher levels of circulating radioprotectant molecules they would

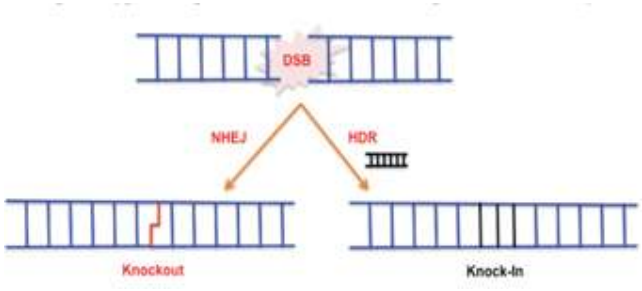


Figure 4: CRISPR repairs DNA through NHEJ and DBR

certainly be in a much better position to survive a long-term space voyage.

iii. *Long term health monitoring:* CRISPR could also be used to develop new methods for monitoring astronauts' health by creating biosensors or diagnostic tools that provide real-time information about their genetic and physiological status. A program called 'Genes in Space' by NASA studied the impact of space conditions on DNA repair through CRISPR-Cas9 and affirmed the viability of this strategy.

Conclusion

The health challenges thus posed by long-term space travels can jeopardize substantial missions and astronauts' well-being. With the development of CRISPR/Cas9 being a slam-dunk exclamation point, brilliant technological progress is witnessed by allowing precise genetic modifications to enhance DNA repair mechanisms, boost immunity, and maintain muscle and bone health. By harnessing CRISPR's potential, scientists could mitigate many of the biological harms of space travel, improving astronauts' resilience and ensuring safer, longer missions in space.

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Pleiotropic effect of thyroid hormone in metamorphosis of clownfish

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Keywords: Clownfish, Metamorphosis, Thyroid Hormone, Vision, Metabolism, Lipid synthesis, Transcriptomic data, Nanostring Technology

Metamorphosis is a biological process in which an organism undergoes structural changes after birth to give rise to an adult, via abrupt changes in organism's physiology, biochemistry and behaviour. This is accomplished by cell growth and differentiation. In lower vertebrates this post embryonic transformation takes place under regulation of Thyroid hormone.

The false clownfish Amphiprion ocellaris is used as the model organism. The fish lives in coral reefs in symbiosis with the sea anemone. Their larvae are dispersed in oceans for 10-15 days after birth. When they reach their pelagic phase, they transition to small juveniles by metamorphosis. The light pigmentation, elongated body of larval stage is transformed into conspicuously pigmented ovoid miniature adult body. This change is believed to be regulated by TH. It also contributes to transition of energy production pathway.

Reproductively active pairs of Amphiprion ocellaris are chosen and the larvae are allowed to rear in every 2-3 weeks. The stages of development in the organism are

divided into 7 distinct stages. 3 larvae per stage are sampled which are euthanized in a solution of MS222 and then photographed for identification, followed by RNA extraction. Quantity and integrity of RNA is analyzed with an Agilent 2100 Bioanalyzer. For sampling RIN value > = 8 is chosen.

To determine whether there's a shift in visual perception a three compartment and dual choice aquarium is build with plexiglass on each side, larvae in it then subjected to a shorter wavelength light (blue) and longer wavelength light (orange) on either side of central chamber after giving few minutes to acclimatized and colour panels were inverted in a time interval to notice the colour preference by larvae of stage 2 and stage 5.

To check the effect of TH hormone in metamorphosis, the larvae were exposed to mixture of different concentrations of T3 hormone (10^(-8)M, 10^(-7)M, 10^(-6) M) and a constant iopanoic acid(stops the degradation of T3 and activity of deiodinases) and preserved in DMSO (dilution: 1:1000) larvae were subjected in a time interval of 12h, 24h,48h,72h for gene expression using nCounter technology in Nanostring at -20°C.

Stage 3 larvae were taken as samples and treated with DMSO and LXR antagonist SR9243 at 10^(-7). Specific designed primer sequence is used for gene expression by RT-qPCR. Two housekeeping genes such as rpl7, rpl32 are used for normalization.

Results :

Behavioural Shift In Vision:

The effects of TH on the 8 identified visual opsin genes were studied. The short-wavelength opsins and mid-wavelength opsins were highly expressed at the larval stage, but downregulated after S4. The expression of long-wavelength opsin (opnlw) was poor at the larval stage, but sharply increased from S4 onwards and remained high throughout metamorphosis. The study using a dual-choice chamber exhibit the shift in perception. The S2 larvae spent more time in the blue compartment while the S5 larvae stayed in the orange compartment. The opnsw2B gene was highly expressed at S2 but only slightly expressed at S4 and S6. Gene expression analysis by the Nanostring process revealed that T3 and the rescue treatment (with T3+MPI) upregulated the expression of opnlw gene and downregulated the opnsw2B .

Th Regulated Metabolic Transition:

The metabolic gene expression of TH was studied in the Glycolysis, TCA, Lactic acid Fermentation, Fatty Acid β-oxidation pathways. At the Larval Stage (S1 to S3), the Glycolytic genes and lactic acid fermentation genes were highly expressed due to surge of the enzymes pfkma and pfkmb at S3 and then during metamorphosis, the expression decreased till S7. Contrastingly, the TCA Cycle genes (cs, dlst2 idh3A) and the fatty acid β-oxidation genes (acetyl CoA dehydrogenase, cpt1aa, cpt1b and cpt2) were expressed at lower rates at the larval stage and their expression increased during metamorphosis (sharp increase at S3 and S4). Based upon experimental results, it was observed that the Glycolytic genes and Lactic acid fermentation genes were downregulated by the action of T3. MPI treatment upregulated their expression. Hence, it was found that T3 exerts its regulation according to the developmental expression pattern. This indicated that TH controlled the switch from glucose based aerobic energy production (Glycolysis and Lactic acid fermentation pathway in larval stage) to fatty acid based anaerobic energy production (TCA cycle and fatty acid β-oxidation pathways in juvenile stage).

Complexification Of Lipids:

The fatty acid β-oxidation pathway functions as the major energy pathway in clownfish during Metamorphosis. Lipid biosynthesis requires the transport of citrate from mitochondria to cytosol by the carrier protein slc25A1. This leads to the formation of acetyl CoA, which is later converted to malonyl CoA (starting substance for fatty acid biosynthesis). From the transcriptomics data, it was observed that the slc25a1 expression decreased steadily from S1 to S6, with a slight increase in S7. The expression of other genes in the pathway were either increased (in acacb) or remained constant (in acaca, and fasn).

On TH treatment, slc25a1, acacb, fasn, me2 and me3 expression decreased, while MPI treatment increased their expression. Hence it was concluded that TH does not favor de novo fatty acid biosynthesis during metamorphosis. It was also established that dietary fatty acids serve as the primary fuel source for β-oxidation.

During metamorphosis, the genes involved in fatty acid desaturation and elongation were mostly upregulated. The polyunsaturated fatty acids and highly unsaturated fatty acids, involved in many biological processes serve as precursors of key signalling molecules . These are generated by the action of front-end desaturases (FADS) and Elongase (elovl).

On analysis of TH control, it was observed that TH exposure caused an increased expression of fads2, elovl1a and elovl8b genes along with the major transcriptional regulators of desaturases and elongases. MPI treatment cause their downregulation. Based upon results, it was concluded that clownfish utilized free fatty acids as a major energy source and the dietary lipids as substrates for the synthesis of numerous molecules that serve in

FA transport or as membrane constituents and signaling molecules.

Lipid X Regulator (Lxr) Modulation:

The LXR modulation links metabolic transition to metamorphosis of clownfish. On experimental analysis, the larvae treated with SR9243 (a selective LXR antagonist) exhibited accelerated metamorphosis compared to the Control larvae (treated with DMSO). The progression of metamorphosis is indicated by the presence of white bars. In the T3 and SR9243 treated larvae, a higher proportion of individuals showed white bars on trunk and head. SR9243 stimulates metamorphosis by upregulating the duox and trb gene expression and downregulating the dio3a and dio3b expression, to increase TH levels in target organs. On further research, it was observed that T3 and SR9243 regulate lipid metabolism and cause the downregulation of genes involved in vision development (in phototransduction cascade)

It is concluded that TH controls and coordinates a major ecological transition: metamorphosis of pelagic coral reef clownfish larvae to benthic reef-associated juveniles. Hence, it affects various processes like white bar appearance, visual preference shift, metabolic transition, etc. Several evidences from studies during post-embryonic stages show that these developments are homologous to metamorphosis of other

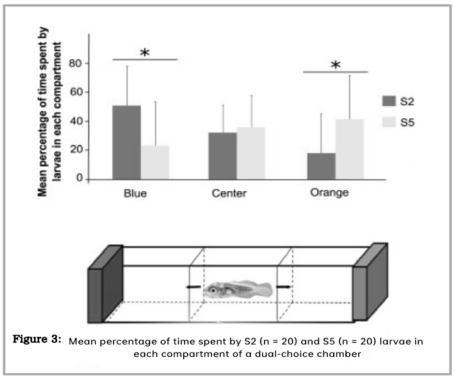


Figure 3: Mean percentage of time spent by S2 (n = 20) and S5 (n = 20) larvae in each compartment of a dual-choice chamber

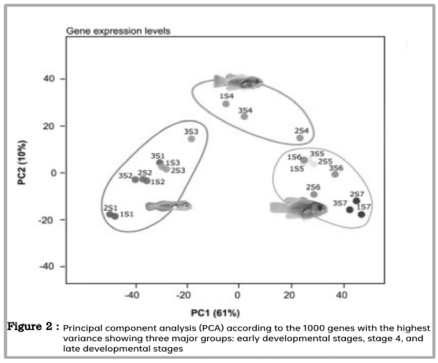


Figure 2 : Principal component analysis (PCA) according to the 1000 genes with the highest variance showing three major groups: early developmental stages, stage 4, and late developmental stages

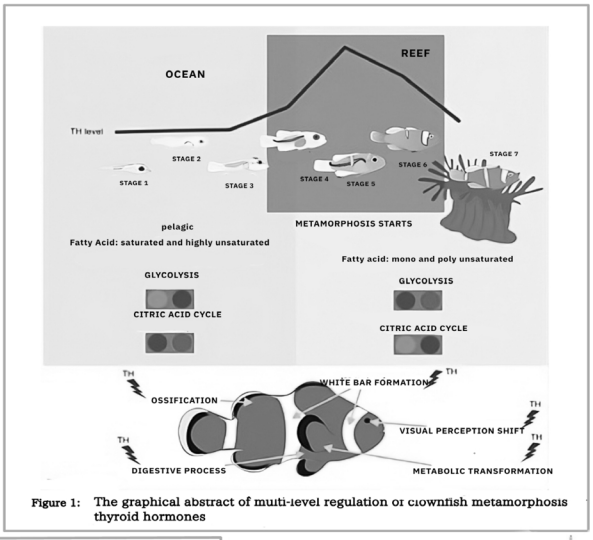
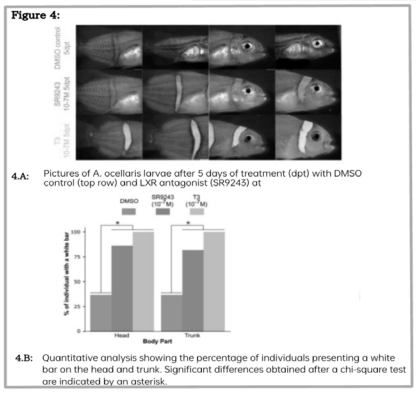
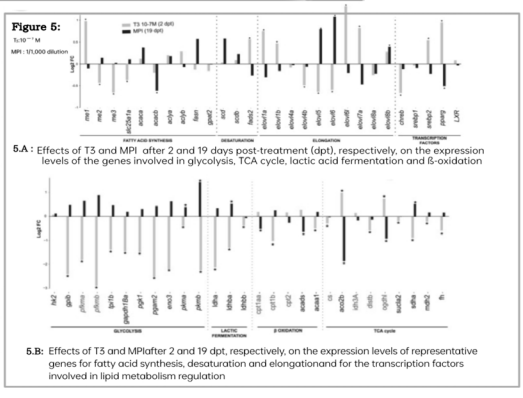


Figure 1: The graphical abstract of multi-level regulation of clownfish metamorphosis thyroid hormones



4.A: Pictures of A. ocellaris larvae after 5 days of treatment (dpt) with DMSO control (top row) and LXR antagonist (SR9243) at

4.B: Quantitative analysis showing the percentage of individuals presenting a white bar on the head and trunk. Significant differences obtained after a chi-square test are indicated by an asterisk.



5.A : Effects of T3 and MPI after 2 and 19 days post-treatment (dpt), respectively, on the expression levels of the genes involved in glycolysis, TCA cycle, lactic acid fermentation and ß-oxidation

5.B: Effects of T3 and MPIafter 2 and 19 dpt, respectively, on the expression levels of representative genes for fatty acid synthesis, desaturation and elongationand for the transcription factors involved in lipid metabolism regulation

Source: https://www.researchgate.net/publication/369198369_The_multi-level_regulation_of_clownfish_metamorphosis_by_thyroid_hormones

teleosts. Results from transcriptomics data reveal that bone mineralization and digestion also change during metamorphosis. A recent study of A. melanopus larvae demonstrated that physiological changes are related to hypoxia tolerance. Thus, this detailed analysis of various biological processes clearly illustrate the pleiotropic TH action during metamorphosis.

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The Role of Microparticles in Drug Delivery Systems:

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Keywords: Biocompatibility, systemic delivery, Drug delivery systems, Targeted therapy, Bioavailability, Lipid-based microparticles.

Microparticles

Microparticles are tiny solid particles, typically in the micrometer range, used in drug delivery systems. They serve to encapsulate medications, providing protection from degradation and ensuring controlled release. Additionally, they can be tailored to target specific areas in the body. These particles, made from a variety of materials, offer improved efficiency in drug absorption, distribution, metabolism, and excretion due to their small size and large surface area.

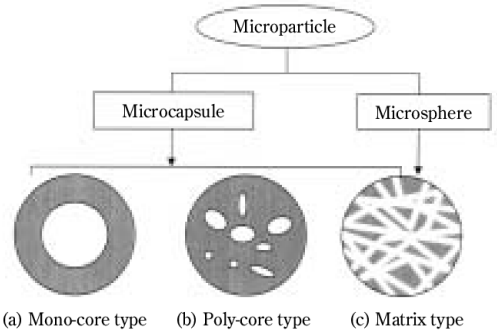

Figure: Classification of microparticles from their morphology

Source: https://www.researchgate.net/figure/Classification-of-microparticles-from-their-morphology_fig1_270559244

Fate After Injection

Microparticles tend to remain at their injection site, as demonstrated by 60 mm polymeric particles observed at the sciatic nerve 8 weeks after injection. Larger particles can block vessels of similar size, which can be beneficial in procedures like chemoembolization. However, when used intravenously, large particles can become lodged in the pulmonary vasculature or peripheral circulation, potentially leading to necrosis. The specific particle size that causes embolism is still unclear. (Kohane et al, 2002). For example, it is found that large quantities of 4 to 5 mm particles could be injected directly into the carotid arteries of mice without causing detectable problems except if enormous quantities were delivered (Kohane et al.,2002). Hydrophobic nanoparticles such as unmodified liposomes will be cleared rapidly from the bloodstream by the reticuloendothelial system. The circulation time of such particles can be greatly increased by surface modification, such as rendering the surface hydrophilic by PEGylation (Harris et al., 2001).

Crossing Barriers

Microparticles, by virtue of their smaller size, can cross such barriers, although exactly what size is necessary and what barriers can be crossed and under what conditions is often a matter question. The ability to cross barriers can be enhanced by disease or by deliberate disruption. As examples, the endothelia in solid tumors are leakier than normal, and the blood-brain barrier can be loosened by osmotic disruption. These factors can also be used as a form of passive targeting: since injected particles can leave affected vascular beds more easily than the general circulation, they will tend to accumulate there preferentially.

Entering Cells

Particles enter cells by a collection of processes termed endocytosis, which includes phagocytosis and pinocytosis. Phagocytosis, 'cell eating', is a method by which material up to 10 mm in diameter and bigger can be taken up (Tabata and Ikada, 1988). This is the special function of only a few types of cells, so-called 'professional' phagocytes, such as macrophages, neutrophiles, dendritic cells, etc. Pinocytotic ("cell drinking") uptake mechanisms can be done by all cell types, and take up sub-micron material and substances in solution. Microparticles are mainly delivered to phagocytic and pinocytic cells, and some researchers use them to passively target antigen-presenting cells.

Lately, the focus has shifted to studying what happens to these particles inside cells, especially how intracellular transport, their final destination in organelles, and exocytosis influence the effectiveness of the delivered payload.

Tissue Reaction

Particle size gets in the way of migration of these materials and affect their degree of phagocytosis at the injection site. Such high concentrations may induce a stimulatory effect that provokes an immediate chemical response in the body involving macrophages and neutrophils. In 7-14 days persistent inflammation with lymphocytes and macrophages sets in, more so, if particles are still there.

Numerous particles are taken by macrophages into its cytoplasm and the foreign body giant cells can also surround few small particles as well leading to the compartmentation of the region.

Advantages of Microparticle based Drug- Delivery Systems

1. *Controlled Release :* One of the most significant advantages of microparticles in drug delivery is their ability to provide controlled and sustained release of drugs. By encapsulating drugs in microparticles, the release profile can be tailored to deliver the drug over a specific period, reducing the need for frequent dosing and improving patient compliance.
2. *.Targeted Delivery:* Microparticles can be engineered to target specific tissues or cells, enhancing the effectiveness of the drug while minimizing off-target effects. This is particularly important in cancer therapy, where targeting tumor cells while sparing healthy tissue can reduce side effects and improve therapeutic outcomes.
3. *Improved Bioavailability:* Many drugs, particularly those that are hydrophobic, face challenges in absorption and bioavailability. Microparticles can encapsulate these drugs, enhancing their solubility and protecting them from degradation in the gastrointestinal tract thus ensuring a larger proportion of the drug to reach the systemic circulation and improve its therapeutic effect.
4. *Reduction of Side Effects:* Microparticle-based systems help in minimizing the exposure of healthy tissues to the drug, by means of controlled release and targeted delivery. This reduces the risk of systemic side effects, which are common with traditional drug delivery methods, especially for potent drugs like chemotherapeutics.
5. *Protection of Sensitive:* Drugs made of peptides and proteins, are affected by sensitive to harsh conditions in the body and are also subjected to enzymatic degradation. Microparticles can protect these drugs, allowing them to reach their target site intact. This is particularly important for

biologics, which can lose their therapeutic activity if degraded prematurely.

Applications of Microparticles in Targeted Therapy

1. *Cancer Therapy:*

Microparticle-based drug delivery systems can be engineered to target tumors specifically, using surface modifications or external triggers. This approach helps minimize damage to healthyengineered to target tumors specifically, using surface modifications or external triggers. This approach helps minimize damage to healthy cells while improving the effectiveness of chemotherapy by reducing overall systemic toxicity.

2. Vaccines:

Microparticles in vaccines play a key role in boosting immune response. They do this by regulating the release of antigens, protecting them from breaking down, and ensuring that these antigens are delivered directly to immune cells. This targeted approach leads to a more robust and longer-lasting immunity.

3. Gene Therapy

Gene therapy involves using microparticles to transport DNA or RNA directly to specific cells. This method not only shields the genetic material but also enhances its ability to enter cells. By precisely targeting, it can treat genetic disorders, cancer, or infections while minimizing unwanted side effects on non-target cells.

4. Anti-inflammatory Therapies

In chronic inflammatory diseases such as rheuor inflammatory bowel disease, microparticle-based drug delivery can help reduce inflammation by delivering anti-inflammatory drugs directly to the inflamed tissues. This delivery being localized helps in minimizing the systemic side effects and also improves the therapeutic outcome.

Challenges and Future Directions

Although microparticle-based drug delivery systems provide numerous advantages, they still run into obstacles like instability in biological fluids, inability to control drug release from the implantable form or scaling to clinical practice. Interactions with the immune system are an important aspect to consider, since some materials can cause unwanted immunogenic response leading to washout before the delivery to the disease site. There will be restoration of encouraging mutations and modifications to enhance targeting and exploring new biocompatible materials as well as combination therapies for increased potent and precise delivery.

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Regenerative medicine – stem cell therapy

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Keywords: Stem Cells; Totipotent; Organoids; Tissue Engineering; Gene Editing; Personalized Medicine

1. **Introduction:**

The approach of regenerative medicine to heal or replace damaged tissue and organs, allowing the body to restore normal physiological function, is now revolutionizing healthcare across all areas. At the core of this new discipline is stem cell therapy, which harnesses the regenerative potential and ability to differentiate into other types of cells that are intrinsic to stem cells, making them perfect for healing damaged tissues. Stem cell use as an intervention to ameliorate a breadth of disorders including auto-immune diseases, neurological conditions and heart disease

is possible through their inherent plasticity. Stem cell therapy can enable patient-specific, tailored treatments beyond that of conventional therapeutic modalities. As such regenerative medicine is ushering in a new era of personalized medicine where the body's regenerative capacity is harnessed, promising to fundamentally reshape the future of medical treatment and chronic disease management.

2. Types of stem cells:

Based on the trans differentiation potential stem cells can be divided into 4 types: unipotent, multipotent, pluripotent, and totipotent. The zygote is the only totipotent cell in our body capable of giving rise to whole organism through transdifferentiation. Cells from the inner cells mass (ICM) of the embryo are pluripotent and differentiate into the three germinal layers but are not capable of differentiating into the extraembryonic tissues. Stemness and transdifferentiation potential of the various types of stems cells (e.g. ESCs, ASCs etc.) depend on the functional status of pluripotency factors like OCT4, cMYC, KLF44, NANOG, SOX2 etc.

There are two broad categories of stem cells that can be used in regenerative medicine:

1. Embryonic Stem Cells: These are derived from the early-stage embryos and can develop into any cell type in the body hence making them "pluripotent". However various ethical concerns limit their use
2. Adult Stem Cells: These cells are multipotent i.e.they can develop into a limited range of cell types related to their tissue of origin and found in tissues like bone marrow and fat. ASCs like hematopoietic stem cells (for blood) and mesenchymal stem cells (for bone, cartilage, and fats) have already been used in treatments like bone marrow transplants.

Another emerging type of stem cell is the induced pluripotent stem cells (iPSCs) which are adult stem cells that have been genetically re-engineered to act like embryonic stem cells without the ethical concerns associated with embryonic cells. At present the basis of regenerative applications stem cells can be categorized into 6 classes, 'embryonic stem cells (ESCs), tissue-specific progenitor stem cells (TSPSCs), mesenchymal stem cells (MSCs), umbilical cord stem cells (UCSCs), bone marrow stem cells (BMSCs), and iPSCs.'

3. How stem cell therapy works:

Developing organoids for organ repair in regenerative stem cell medicine, past the focus on tissue engineering involving combinations of cell transplantation-material science-micro engineering in creating organoids to replace tissues and organs that are damaged. It uses biodegradable 3D scaffolds with cell adhesive properties, matched mechanical properties to tissue of interest, and support for blood vessel formation that is non-immunogenic. 'Stem cell number in tissue transplant impacts upon regenerative outcome in that case

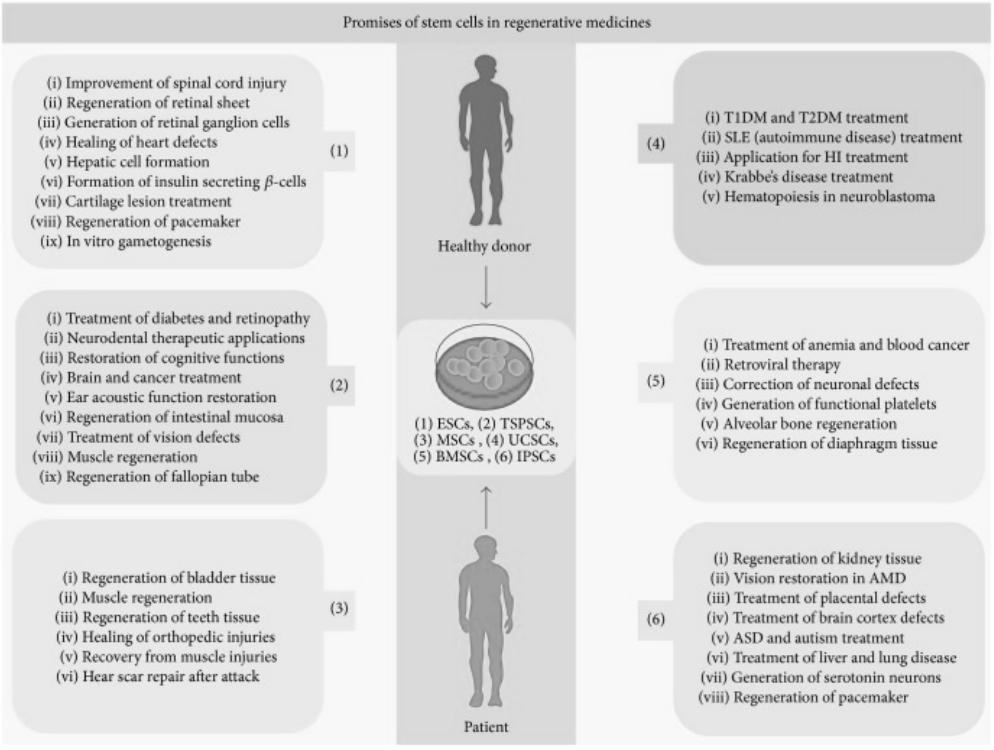

FIG.1 Promises of stem cells in regenerative medicine
Source: http://www.ncbi.nlm.nih.gov

prior ex vivo expansion of transplantable stem cells is required'. For regeneration to be successful, transplanted stem cells must survive, grow, differentiate, and connect with the host's circulatory system. The transplantation of stem cells can be autologous (patient's body), allogenic (from the donor), and syngeneic (from an identical twin) for induction of tissue regeneration and ammonolysis of pathogen or malignant cells. With allogeneic transplants, the cells must match closely enough with that of your immune system. In the case of allogeneic donors, to avoid host-graft rejection matching human leukocyte antigen using tissue typing is often recommende

Application:

1. Cardiovascular Diseases: Stem cells like mesenchymal stem cells are used in regenerating heart cells, forming new blood vessels, reducing scarring, and improving heart functions. Recent trials show great improvement in improving heart conditions which otherwise would have been fatal.

2. Neurodegenerative Diseases: By potentially replacing lost neurons and restoring neurological function, stem cell therapy provides hope to various patients suffering from neurodegenerative diseases like Parkinson's, Alzheimer's, or MS. Researchers are exploring the use of stem cells to produce 'dopaminergic neuron'-the type of cells lost in Parkinson's disease. In spinal cord injury stem cell therapy often helps regenerate damaged neurons and severed neural connections which improve mobility and functionality in paralyzed patients.

3. Diabetes: In the case of Type-1 diabetes stem cells could regenerate insulin-producing cells. Research involving iPSC-derived beta cells could eliminate the need for insulin injections and long-term diabetes management

4. Liver Disease: Mesenchymal stem cells, and hepatic progenitor cells in particular, are integrated into therapeutic efforts to regenerate liver tissue and restore liver function to potentially decrease the need for transplants.

5. Bone and Cartilage Repair: Mesenchymal stem cells are under assessment regarding their ability to regenerate cartilage in osteoarthritis and repair bone fractures. Such treatments would revolutionize orthopaedics, just by reducing some joint replacement procedures and improvements in recovery.

Future prospects:

The possibilities for treatment through stem cells are enormous. Scientists are working on ready to use off shelves stem cell therapies – this means that pre-prepared stem cells will always be kept handy whenever there is a need without any market having to fetch and grow particular patients' cells, therefore, reducing the ordeal of collecting as well as growing cells from patient or donor. They are also trying to bioengineer organs like kidneys, and livers which can be constructed in the laboratory using stem cells. The field is still very much in its infancy but promises that in such a specific future, patients will not need to wait long periods on donor organ waiting lists anymore.

At the same time, the search for gene functions and the changing of genes in stem cells using gene editing technologies such as CRISPR are gradually increasing.

Genetic defects may be corrected in the stem cells prior to their application into therapy using genetic engineering methods. It would be one of the essential objectives in treating patients with genetic abnormalities, which will revolutionize safe, precise, and effective stem cell therapy from the current development.

Conclusion:

In the present situation, donated tissues and organs cannot meet the transplantation demands of the diseased population which has given a thrust to the search for alternatives. Stem cells with their unique ability and indefinite cell division and development into diverse tissues and organs have provided a suitable alternative. Stem cells pave the foundation for the development of all tissue and organ systems in our body along with regulating various roles in disease progression, development, and tissue repair processes in the host. Despite the challenges that still exist, the advancements in stem cell research signal a future where medicine shifts from merely addressing symptoms to offering real cures. This evolution is set to transform healthcare and improve patient outcomes in ways that were unimaginable just a few decades ago. The future of regenerative medicine is not only promising—it is poised to redefine the very fabric of therapeutic interventions.

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What danger lies underneath the ice?

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Keywords: Cryosphere microbes, permafrost, pathogens

Introduction:

The immediate thought that arrives to us as soon as we think of Earths cryosphere melting is it being an effect of global warming. But do we ever wonder what the effects of cryosphere melting can be? Permanently frozen environments are claimed to be a natural reservoir of immense amounts of microorganisms including human pathogens, though in a dormant phase. The presence of viral and bacterial pathogens in glaciers worldwide and the anthrax disease outbreak in reindeer herds of Siberia prove the claims of lurking danger of rise in epidemics due to cryosphere melting. This becomes extremely concerning when we consider that approximately $4x10^{21}$ of microorganisms are released annually from these frozen layers to enter natural ecosystems.

Survival of microorganisms in cryosphere:

The myriad of microorganisms found in glaciers, permafrost (soil and rocks held together by ice at a temperature well below 0° C for two or more consecutive years) are mostly metabolically active and multiply at a very low rate. They are limited to the small veins formed between ice crystals. They benefit from the liquid water and sufficient nutrients present there for their basal metabolism. Some microorganisms exist such that they do not multiply and are metabolically active. These reactivate when the environment becomes more suitable in permafrost; fungi mainly exist in form of spores. Microorganisms in cryosphere have adapted to upregulate cell membrane and cell envelope biogenesis and increase expression of proteins related to membrane fluidity, nutrient transport in comparison to their warmer climate habiting counterparts. The gene expressing extracellular structure of flagella are down regulated. Bacteria can exist in their dormant phase due to their sporulate form.

Pathogens found in cryosphere:

The frozen environments of cryosphere are habitat for microorganisms, which are dormant but viable. In different regions, melt water runoff and ice core have been detected to consist of *Cryptococcus* yeast and bacterial coliforms. From the Arctic regions of Greenland and Svalbard emerging pathogens such as *Aureobasidium melanogenum* (cause infections in humans, especially in immunocompromised people), *Naganishisa albida* (can cause pneumonia, encephalitis, keratitis), and *Rhodotorula mucilaginosa*. These yeast exhibit virulence-associated traits such as hemolytic ability, resistance to antifungal agents and production of siderophores. Numerous studies report presence of potentially pathogenic microorganisms in ancient ice samples. Culturing them in laboratory under controlled condition has reactivated many of these microorganisms. Highly diverse viable bacteria have been found in the ancient ice cores in several kilometer depth of Lake Vostok. In Batura Glacier of Karakoram Mountains, 14 genera of fungi including *Penicilium*, *Cladosporium* and *Geomyces* were isolated from the ice. Analysis of Guliya Ice Cap in Qinghai Tibet Plateau, 254 bacterial genera were found and 118 species were classified to 32 known genera including *Janthinobacterium, Polaromonas* and *Flavobacterium.* Microbial compositions were reported to vary according to the depth of the ice layers, indicating to environmental variations in different periods. Permafrost is an important habitat for microorganisms have cell density of about 105-108 cells/mL. The recent outbreak of Anthrax in Russia in 2016 was caused by the release of *Bacillus anthracis* from a 70-year-old reindeer carcass in melting permafrost. Abundant viral resources have also been discovered in multiple cryosphere environments. Large number of DNA and RNA viruses were detected in Lake Limnopolar (Antarctica); most with genomic features different from known viruses. Numerous bacteriophages, algal viruses and giant viruses infecting amoebae were detected in Antarctic soil. In Antarctic and Arctic, viruses including bacteriophages, circular ssDNA viruses, dsDNA viruses, phycoDNA viruses, virophages infecting algae and RNA viruses like *Picornavirales* have been found.

Presence of antibiotic resistance genes:

Glaciers show an astonishing content of antibiotic-resistant microorganisms, which are able to thrive in vitro even in the presence of high dosage of antibiotics once they are reactivated. Antibiotic resistance genes (ARGs) have been frequently identified in ancient bacteria isolated from cryosphere environments. Researchers have identified large number of bacteria and genomes carrying ARGs for more than 50 antibiotics. Most resistance genes were comparable to genes in present day pathogenic bacteria proving the existence of antibiotic resistance much before the use of

antibiotics by humans. Many ARGs found in pathogenic microorganisms have arisen from the environmental resistome (sum of all resistance genes present in diverse ecosystems throughout the world). Cultured bacterial strains collected from Eastern Siberia permafrost sediments dating back to 3-million-year harbored genes encoding resistance to several antibiotics such a chloramphenicol, gentamicin, kanamycin, streptomycin, tetracycline, and mercury compounds. Bacteria recovered from Central Yakutia (Russia) was cultured and found to carry multiple ARGs. One of them, a *Staphylococcus hominis* MMP2 strain harbored ARGs > 96% identical to genes conferring resistance to beta-lactams, aminoglycosides, phenicols and MLS (macrolide, lincosamide, streptogramin B). It is hypothesized that some of the ancient ARGs might have been transmitted to the modern microbes via horizontal gene transfer (HGT). It is believed that the rapid ice thawing might cause some of these ARG-containing genetic elements to be transferred horizontally to modern microbes, giving rise to new strains of multi- or pan- resistant "superbugs".

Emergence of new microbes in cryosphere:

The unique environment of the cryosphere affects the evolution of microbes in it and only those with strong adaptability gradually become dominant. Even after thousands or even millions of years of evolution, stable microbial community and ecosystems are existent. In recent 100 years, vast amount of new microbial species and groups have been discovered and isolated from the cryosphere environments in different regions. These include new archaebacteria, bacteria and fungi. There is a need to isolate and preserve these new microbes for research and utilization purposes. The extreme conditions of the cryosphere not only shape the microbe groups but also change their metabolic pathway.

Conclusion:

There is a vast population of microorganisms beyond our knowledge. The global warming not only threats at climatic changes but also on reactivation of many such unknown and undiscovered microorganisms. These pose the threat of pandemics and epidemics. There is a need of extensive study on the microorganisms residing in the depths of the glaciers and permafrost and they are the natural barriers against these microorganisms but they are slowly breaking down. These microbes have an extensive adaptability and might pose a great threat on interacting with our ecosystem as they might reach their favorable environment. These microbes might also help us in understanding the mechanisms of present time pathogens and microbes.

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Epigenomes and personalized medicine

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Keywords: Epigenomes, Personalized Medicine, Genetic Susceptibility, Pharmacogenomics

What are genes?

The simplest definition states that they are the basic units of heredity, passed down from parent to offspring. Within the nucleus, we have chromosomes which contain the genetic information, in the form of genes. These genes, present on DNA molecules, code for different proteins.

From the earliest of times scientists have interlinked genes and their expression with the environment they are residing in. Be it the concept of "survival of the fittest ", the bottleneck effect, founder effect, or industrial melanism, we see that each of these theories were based on interactions of varied organisms with their environment, which leads to alterations or mutations in their genetic make-up. The gradual changes induced in their genotypes span over millions of years, ultimately causing organisms to evolve.

Gene-environment correlation

Recent studies have shown that not all genes inherited from the parents are completely or even prominently expressed in the progeny, despite being a dominant gene. Almost 23,000 genes are inherited from parents and out of these most genes are expressed as phenotypes, based on experiences. These experiences leave chemical "signatures" on the genes which in turn determines whether they shall be expressed as phenotypes or not. These chemical signatures are known as epigenomes. Experiences can be both internal and external. External experiences include stress, anxiety, moving into another country or part of the world which is not similar to race or origin. Due to this particular reason, it is said that immigrant populations are more likely to suffer from cardiovascular diseases than non-immigrant populations. Their bodies undergo a lot of stress and anxiety from the pressure of fitting into a completely different society with a brand-new culture, and all this leaves chemical "signatures" in the brain. Stress, caused by outside forces, sends neural signals to the brain where the gene regulatory protein attracts or repels the enzymes that help in addition or removal of epigenetic markers. These markers control the amount of protein that is secreted by the gene which leads to its activation or deactivation. These experiences alter the chemistry that encodes the genes, and the changes can be temporary or permanent based on the experiences. This phenomenon is known as epigenetic modification.

Epigenetic models

Based on the epigenetic modifications, there are five different epigenetic models that have been created in order to understand the risk factors of getting a disease based on the expressiveness of the gene and its susceptibility with respect to the environment.

In **model A**, the effect of the genotype involves an increase in the expression of the "risk factor," that can also be produced non genetically. The risk factor here has an effect irrespective of the genetic susceptibility.

In **model B**, the genotype increases the risk factor's effect, but in the unexposed individual, the genotype has no effect. When genetic susceptibility is present, the risk factor's relative hazard is higher than when it is not.

In **model C**, the risk factor exacerbates the effect of the genotype, but there is no effect of exposure in persons with low-risk genotype model. When there is no genetic susceptibility, there is no chance that the risk factor will manifest.

To raise the risk in **model D**, both the genotype and external exposure are necessary.

In **model E**, the exposure and genotype, each have some effect on the gene and subsequent disease risk, and when they occur together, the risk is higher or lower than when they occur alone. The effect of the risk factor depends upon the relation (antagonistic, or otherwise) between the risk factor and genetic susceptibility.

Amongst all these models it is noticeable that in models B, C and D the interactions between the genes and the environment are constant, regardless of the risk factors or mutations.

What is personalized medicine?

But how are such modifications in gene expression introduced? They are brought about by

- DNA methylation
- Chromatin remodelling
- Histone modifications

· MicroRNAs that act as regulatory molecules.

The mechanisms above not only monitor the expression of genes, but oversee various cellular and biological functions related to homeostasis and disease. Traditional therapeutic techniques are often found to be ineffective when it comes to treating ailments caused by epigenetic modifications. As a result, finding patient-specific treatments and creating personalized medicines have become a primary concern for researchers today.

Health care professionals utilize genomic data to diagnose various diseases and disorders while running diagnostic tests of patients. They assess the possibility of development of a particular disease or disorder in an individual, and subsequently prescribe medicines to be administered, along with their appropriate dosages, based on the individual's metabolic variations.

In contrast, personalized medicine involves the application of an individual's personal genetic profile to predict and even prevent disease via medical interventions, and furthermore, suggest changes to lifestyle and improved disease management techniques, based on the specific needs of each patient.

Studies of the human genome are able to provide answers to concerns associated with the health and probable contraction of disease in an individual. Nowadays, information regarding entire genomic sequences is accessible due to the Human Genome Project (HGP). It is now known that specific drugs must be given to patients who find little success with traditional medicines. Genomic or personalized medicines are provided to patients after collecting all necessary genomic data, such as the levels of RNA, proteins and various metabolites that comprise crucial information when generating personalized medicine. Genomic approaches that involve the identification of variations in DNA sequences, transcriptomics, proteomics, and metabolomics are indeed useful for precise disease management and prediction.

About pharmacogenomics

Pharmacogenomics and personalized medicine go hand in hand. The former is concerned with the different biological factors related to drug metabolism that include drug transporters, contribution of receptors and drug metabolizing enzymes which affect drug response in a variety of diseases. All such parameters are under epigenetic control.

Pharmacogenomics focuses on developing precise and accurate drugs for a particular patient. It also negates the age-old concept of "one drug fits all." When it comes to multiple drug responses, factors such as nutrition, age, weight, gender, genetic behaviour, infections, and organ function are significant considerations that become unavoidable during the course of treatment.

Furthermore, the integration of relevant data associated with medical interventions and use of personalized medicines is highly prioritized during the management of a disorder.

Conclusion:

In this article, the impact of the environment on genes and the resulting disease susceptibility have been discussed in brief. Through recent studies in the field of biotechnology, different epigenetic models have been put forward, which help us determine how a disease might affect a particular person, based on theircurrent genetic background and how well the risk variables interact with their surroundings. This has given us a major breakthrough in the course for developing personalized medicine which works more closely and effectively by analysing the patient's genetic makeup. Yet there are still several challenges being faced by scientists and researchers in this upcoming field, especially when considering the costs of availing such novel treatment methods, which are often not feasible for the ordinary people. As such, the possibility of opting for personalized medicines is yet to be open to the public.

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Role of private sector in Development of health biotechnology in developing countries:

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Keywords: Developing countries, Private sectors, Health innovation system, Biotechnology

Introduction:

Health biotechnology is becoming a vital tool for improving the efficiency and accessibility of healthcare for the poor in developing countries. Through intensive research and development and innovative health products, several developing countries for instance, Brazil, China, Cuba, Egypt, India and South Africa, which are considered innovative developing countries (IDC), have made substantial progress by solving local health needs. These countries have made significant gains in research capacity by increasing the number of health products, patents and scientific publications that they produce supported by government investment, as well as by the growth of the private sector, which contributes to economic growth.

Growth of heath biotechnology in developing countries

Owing to the considerable shift in the focus of health biotechnology in first-world countries there is rapid growth of health biotechnology in developing countries. Researchers previously, focused mostly on chronic diseases such as cardiovascular disease, diabetes mellitus, respiratory diseases and cancer. Not more than 10% of health research worldwide is dedicated in response to diseases prevalent in developing countries. Out of 1393 new biotechnology products produced in western countries, only 16 (~ 1%) of them targeted tropical diseases and tuberculosis, which are the main health issues in developing countries trend from 1975 to 1999.

Continuous development of science and technologies has made novel health products, such as new vaccines, therapeutics, and drugs available in order to prevent and treat infectious and non-infectious diseases. With the rise in innovative diagnostics and medical devices there is significant improvement in accuracy and speed in identifying, preventing and treating the diseases that affect the developing world. Thus, in the developing countries, the local health needs can be satisfied by the innovations in health biotechnology.

For taking better advantage of these technologies the developing nation should widely implement them. The shortcoming in implementation by the developing nations is largely due to lack of funding and resources, shortage of scientific capacity, and inefficient policies and regulations, as well as the weak relations between the public and private sector.

It is found from innovative studies that a successful health-biotechnology industry in order to assess a nation's science and technology capacity requires a relatively strong health-innovation system. Dynamic networks of public and private sector, connected through nonlinear interactions, is core of the national health-innovation system which also includes activities to generate specific knowledge and use it to produce and supply new technologies to solve health problems. As policymakers the government has a fundamental role in health-innovation systems to encourage research institutions, universities and private companies for initiating and developing health biotechnology research programs. As per studies by scholars, the private sector is becoming an important stakeholder in biotech industry development and they are gradually becoming the core of health innovation. As far as developing countries are concerned, most of the investment in health research is sponsored by the government and carried out in public institutions, while in developed countries the largest biotechnology investor is the private sector. Be that as it may, all sectors in the health innovation system, including government, public institutions and funding entities, must work together to build and support a sound innovation system as they are interdependent and interrelated in nature and cannot innovate independently.

Private sector firms are the main force of commercialization as they are distributing the products in the market to fulfil the demands of the poor and hence are at the heart of any health-innovation system, for the sole reason of actively diffusing and integrating various types of knowledge to develop innovative health products. The characteristics of the private sector which makes it a vital stakeholder in the development of a health biotechnology industry, are as follows (i) the relatively high efficiency due to competition; (ii) flexibility in organizational structure and management; (iii) freedom in decision-making from bureaucracy and political concerns; (iv) performance-based operation and

quality management; (v) capacity for investments and human-capital development; (vi) capacity to reduce the unemployment rate and create revenue; and (vii) a strong ability to acquire and diffuse new technologies and infrastructure. Further without the required support and political will from the government and its agencies the private sector would not be able to function effectively and therefore policy makers should frame such rules and regulations that would be conducive and helpful for the private sector to function.

The advantages of the private sector should be exploited through the establishment of strong networks and collaboration between the private and public sectors in order to build a successful healthy biotechnology industry. For the development of new health technologies focused on the needs of the poor in developing countries, Public/Private Partnerships in Product Development (PPP-DPs) or Product-Development Partnerships (PDPs) have been established. Contributions of the public sector, industry, NGOs, institutions and academics to discover and produce new health technologies targeted to specific diseases in developing countries are managed by them.

Conclusion:

Health biotechnology brings economic benefits to the developing country. It is the fastest growing arena which addresses the specific health problems of the country.

The primary aim of this paper is to discuss and emphasize the role of the private sector in the context of health biotechnology development and to study its effect on health and economic growth of the country and also the role of the private sector in improving the health and economic status of the poor.

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Phage Therapy: Nature's Answer to Antibiotic Resistance

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Keywords: Antibiotics, Bacteriophage, Multi drug resistance

Antibiotics are medicines which fight bacteria and either kill the bacteria fully or restrict their growth. The accidental discovery of *Penicillin* by Flemming paved the way for modern antimicrobial ("medicines used to treat infectious diseases in humans, plants and animals" - World Health Organisation (WHO)) research. However, humanity has been using these medications recklessly. Due to this large exposure to a variety of antibiotics, it has led to the rise of MultiDrug Resistant (MDR) bacteria.

Introducing Mdr Bacteria - Superbacteria!

MDR bacteria are those bacteria which have developed a resistance to various types of antibiotics. They are particularly difficult to treat and contributed to about 1.3 million deaths in the year 2019 (Source: WHO). The main reason for the evolution of these bacteria is the huge overuse of antibiotics. "We used antibiotics more and more for less and less serious causes" (YouTube, Kurzgezagt - In a Nutshell).

How Did These Bacteria Come Into Being?

The essence of Darwinism is natural selection. According to it, in a population of a particular species, due to variation, there are certain individuals who have an advantage in surviving harsh conditions. Nature selects these individuals and when such adverse conditions appear, the others get wiped out and the progeny of the superior individual proliferates. Thus evolution is said to occur.

In the case of bacteria too, there are certain bacteria present which, other than their nucleoid, contain a circular extrachromosomal DNA known as plasmid DNA. Plasmid DNA confers certain immunity against particular antibiotics. When this antibiotic is added to the culture, only those bacteria which have this plasmid will survive and hence increase their numbers. If this antibiotic is added again, the bacteria remain unharmed and thus are said to have gained immunity to it. This is the reason we should not use antibiotics without a prescription. Such an evolution that happens due to human activity is called evolution by anthropogenic action.

Since the bacteria are gaining immunity to different antibiotics, our arsenal of weapons against them is becoming less effective. Soon we might not have any pre-

ventive measures against these bacteria. If ignored, in the future, a simple cut can become fatal. So how can we tackle this problem?

Bacteriophage - A Potential Saviour

Bacteriophage is a kryptonite to bacteria. It is believed that phages existed for billions of years evolving alongside bacteria, and they are present everywhere. A microbial 'war' has been waging between these two ever since they came to be.

But, what is a bacteriophage? Bacteriophages (or simply, phage) are viruses that infect bacteria and reproduce using the bacterial metabolic machinery. Just like viruses, phages are not 'living' when outside the bacterial cell. Structurally, a phage looks less like a real organism but something like a human creation. It has a head which houses the genetic material (DNA), collar and a tail from which tail fibres emerge. It is generally between 100 - 500 nanometres in length while a typical bacteria is 2 to 10 micrometres in length. So bacteria are 10 to 100 times larger than bacteriophages.

Different phages generally have different target bacteria. When a bacteriophage encounters its preferred bacterial species, it injects its genome (the DNA) into the bacteria, by degrading the cell wall of the bacteria using specific enzymes. This free genome gets incorporated into the genetic material of the bacteria. This way, a phage virus 'hijacks' a bacterial cell. Now the new genome shuts down the bacterial cell cycle and only produces phage proteins and enzymes. After a large number of phages have been produced, a phage-coded lysozyme breaks the bacterial cell wall, thus releasing the intact phage viruses, ready to begin a new cycle of search and destroy.

Antibiotics Vs Bacteriophage: How Are They Different?

Antibiotics are chemicals secreted by certain species of microorganisms, mainly fungi and soil bacteria. This gives them an advantage in competing for nutrition in a particular environment, by killing or slowing the growth of its competitors (other bacteria on which the antibiotics act). Since their discovery, antibiotics have been produced commercially for human usage. As stated before, MDR bacteria are resistant to them. How is the Bacteriophage different?

One big difference between them is that bacteriophages are capable of mutation in their genetic material. This means that if the bacteria evolve to counter the phage attack, the phage can also evolve to nullify the bacterial evolution. Antibiotics, being synthetic chemicals, obviously can not do so. Thus the evolution of superbacteria will not pose a big threat anymore.

Antibiotics kill all bacteria it comes in contact with, destroying both harmful as well as the useful bacteria in our bodies. Phages, on the other hand, are highly specific. Using the correct phage ensures that only the pathogenic bacteria are eradicated, leaving the beneficial bacteria untouched. Taking this further, phages have not been reported to harm human cells by any means.

Phages, owing to their small size, can reach those parts of the human body in which the antibiotics can not be administered, thus they are more effective in their action.

Administration of phages is much easier, as only a small initial amount is given to the patient as reproductive capacity of phages, after bacterial infection, is very high. Contrary to antibiotics, phages do not need repetitive administrations. This also makes phage therapy a cost-effective alternative to antibiotics.By the usage of genetic engineering, bacteriophages can be modified to be even more efficient in killing certain bacteria which might have developed anti measures against phages.

Factors Limiting Phage Therapy

There are certain factors which pose a problem to the usage of phages:

Identification of a particular phage for a particular bacterial strain is a time consuming and expensive procedure which includes decades of research and testing. Genetically modifying a phage is also a cumbersome process. This might discourage the research of phages by pharmaceutical companies.

The risk of emergence of bacteriophage resistant bacterial species also poses a serious problem. Evolution is always random and sudden mutations in the bacterial genome can bring about such strains.

Reduction in phage efficiency due to immune system response is also a factor which limits phage therapy. Our immune system may identify phages as non-self foreign agents and induce responses to inhibit their functions.

Conclusion:

Phage Therapy is not a new concept. It was first recommended as early as the 1920s. However, the discovery of antibiotics had loosened its relevance. In recent times, due to the emergence of MDR bacteria, scientists are reconsidering the treatment using bacteriophage. However, much more research is required before it can be used as a treatment in humans.

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Bioremediation: Strategies For Soil Decontamination Of Heavy Metal Ions

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Keywords: Bioremediation, heavy metal pollution, microorganisms, environment.

Introduction:

The rise of urbanization and industrialization has exposed the environment to many pollutants that are toxic to living organisms. Different types of heavy metals in various quantities are released during industrial production processes as effluents to contaminate soil. Although many remediation techniques, including chemical and physical techniques, have been used for many years to clean up soil, their limitations have encouraged the application of "bioremediation" as an alternative.

Bioremediation is an environmentally friendly and sustainable societal technology for remediating contaminated surroundings such as soil, groundwater, and oil spills. It is the process of degradation, transformation, or detoxification of a vast range of pollutants arising from human activities. "Bioremediation" plays a crucial role in mitigating heavy metal pollution through various novel strategies that focus on the transformation or extraction of these metals from contaminated soils. This method holds the potential to be a better alternative, because conventional remediation methods commonly require harsh chemicals or physical extraction techniques, which can be expensive, invasive, and destructive to native ecosystems. The key advantage of bioremediation lies in its effectiveness in completely degrading a given contaminant and its low cost with minimal impact on the environment. The main types of bioremediation mechanisms are as follows:

1)Employment of metabolic capabilities of microorganisms, such as various types of bacteria, fungi, and algae

2)Uptake and detoxification by plants

The efficiency of bioremediation can be influenced by a whole complex of factors, such as the type and concentration of pollutants, pH, temperature, and oxygen availability. Microbes may be used for this process. However, the use of living organisms has some limitations. For example, the reactions taking place to detoxify the pollutants by living organisms, are highly site-specific and governed by environmental changes. There are various other methods, such as, bioaugmentation, and biostimulation, phytoremediation (use of plants) which are discussed in this article.

Effects of heavy metal ions and strategies for mitigating pollution:

Iron copper, cobalt, and other trace levels of heavy metals are vital micronutrients for plant and human existence. They play important structural and functional roles in various metabolic processes in living cells. However, when ingested at elevated levels, they

have adverse impacts on the health of all living organisms and the environment. Heavy metals could be transported to the living cells through air, water, and food chains, resulting in toxicity. Bioremediation often uses the action of microorganisms, plants, or their enzymes that act on contaminants in the environment, making them safer, less harmful to living organisms and nature as a whole.

Certain microbes can help remove non-essential heavy metals like Cadmium, Mercury, Lead, from the environment using different mechanisms and thereby reduce the detrimental effects of these pollutants on living organisms. The mechanisms employed by these microbes can be placed under two broad categories namely "immobilization" and "mobilization." Mobilization involves processes such as enzymatic oxidation, bioleaching, biostimulation, bioaugmentation, and enzymatic reduction. Conversely, immobilisation includes processes like, bioaccumulation, complexation, biosorption, and precipitation. Some other bioremediation strategies used for heavy metal contamination in the soil is discussed below.

Biostimulation: This technique involves the modification of an already present microorganism community to stimulate and enhance the microbial activity used to remediate contaminated soils. This involves the addition of nutrients such as Phosphorus and Nitrogen for optimum growth of microbes (Gadd, 2010). In the case of heavy metal contamination, biostimulation can promote the production of biosurfactants, organic acids, and other metabolites that can alter the mobility of heavy metals, facilitating their immobilization or transformation.

Bioaugmentation - Bioaugmentation is the introduction of specific strains of microorganisms

specially engineered for remediating heavy metals. This approach aims to enhance the indigenous microbial community by adding robust and efficient microbes capable of precipitating, adsorbing, or transforming heavy metals into less toxic forms. For instance, certain bacteria and fungi have the ability to segregate heavy metals through mechanisms such as biosorption, bioaccumulation, and bioprecipitation, which can significantly reduce the mobility and availability of toxic metals in the soil.

Biosorption - Biosorption can be defined as an approach, which involves a kind of passive interaction in order to bind the heavy metals to the cell surfaces of microorganisms, primarily through interactions with functional groups present on the cell walls, such as carboxyl, hydroxyl, and phosphate groups (Volesky, 2007) This process is rapid and can occur even in dead or inactive microbial biomass, making it a highly effective strategy for removing heavy metals from contaminated soil. For example, there are some bacterial, algae and fungal species which have been widely researched upon in relation to their biosorptive capabilities. For instance, it has been ascertained that a fungus known as Aspergillus niger has been shown to effectively remove Lead and Cadmium from contaminated environments through biosorption (Singh et al., 2011)

Bioaccumulation - In contrast to biosorption, the active uptake and accumulation of heavy metal ions and subsequent deposition within the cells of various microorganisms can be useful to recover valuable metals and detoxify hazardous contaminants after the recycling of metals and the degradation of toxic substances present in the environment. For example, different species of Pseudomonas and Bacillus are known to accumulate metals such as Chromium and Nickel (Singh et al., 2011)

Genetically Engineered Microorganisms(GEMs) - With the help of biotechnology and genetic engineering, microbes may be genetically engineered to facilitate the process of breakdown of a particular contaminant (Rebello et al., 2021) These organisms can also be manipulated to produce desired metal chelators, metallothionein like proteins, efflux pumps or enzymes that confer resistance to heavy metals and enhance their removal from contaminated environments and thereby reducing their toxicity and mobility.

Phytoremediation - Phytoremediation is a novel strategy which uses plants to remediate the

contaminated soil through the accumulation and stabilization of toxic metal ions, by absorbing them through their roots and shoots to drastically decrease the concentration of contaminants present in the environment. Phytoremediation is an effective, green, and economical method.

A varied range of phytoremediation methods can be used for the reduction of heavy metal contaminations, namely, "phytoextraction, phytovolatilization, phytostabilization and phytofiltration." The biomass of "metal-tolerant" plants and the availability of heavy metals in soil are major stimuli affecting the efficiency of phytoremediation. Phytoextraction involves the uptake of heavy metals from the soil and their accumulation in plant tissues, which can then be amassed and later disposed off cautiously, without impunity. Metal accumulator or Hyperaccumulator plants like Brassica juncea (Indian mustard plant) and the Thlaspi caerulescens (alpine pennycress), are known to accumulate high concentrations of various metals from the soil compared to other plants and are found to be very efficient

in the removal of metals such as Cadmium, Zinc and Nickel from contaminated soils (Singh et al., 2011) Phytostabilization, on the other hand, is centered on immobilization and stabilization of heavy metals in the soil, thus limiting their mobility and availability. This approach is especially relevant for thwarting the contamination of groundwater by heavy metals or their accumulation in crops used in agriculture.

Conclusion:

Bioremediation is an effective and comprehensive method for the fight against pollution and provides a sustainable and versatile approach to the existing issue of soil contamination with heavy metal ions. This can be achieved by leveraging the natural capabilities of microorganisms and plants, which shows that, as technology advances, bioremediation will be instrumental in ecological control and waste elimination. Overall, we can conclude that bioremediation is a cost-effective technology and, hence, encourages the widespread use of various strategies, thereby taking a more mindful and sustainable approach towards our environment and preserving resources for a better and healthier future.

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Literary Articles

Positive Vibes

Dr Priyanka De
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When you need a shoulder to cry upon,
Positive vibes do matter.
When you realise your life being well-worthy,
Positive vibes do matter.
When you crave for your undone deeds,
Positive vibes do matter.
When you start loving yourself fondly,
Positive vibes do matter.
When you are confident of your dream,
Positive vibes do matter.
When you start focussing on every trivial feel,
Positive vibes do matter.
When you start healing yourself deeply,
Positive vibes do matter.
When your soul re-awakens from deadly past,
Positive vibes do matter.
When you believe in your strong invocations,
Positive vibes do matter.
When you feel the presence of the Almighty,
Positive vibes do matter.

The Spectrum of Life

Pramita Chatterjee
Semester 3
Postgraduate & Research Department
of Biotechnology

Change the calendar for it is not 12 months a year;
Haven't we already lost time contemplating our fears?
"What steps must I take, what shall I do?
To battle my internal conflicts and change the external petty views?"

Watched a TV commercial that guaranteed
'Five problems: One solution'
Perhaps, all five of our problems
Also, seek just one firm decision.

Red means to halt, Green hurtles to go;
Maybe that is not all that there is to follow.
Beneath this abyss of thoughts, glistens Yellow…
Ignorance is bliss indeed; helps attune to life's flow.

Man and God

Sarvarish Sarkar
Semester 1
Postgraduate & Research Department of Biotechnology

I was deep in thought as I looked back at Man's achievements over the years. From the first lesson when Man had learnt to use fire, to his stepping on the moon--- he has learnt a lot. Man has learnt to build cities and grow crops. He has invented new techniques to improve yield and expand mortal lives. Man can create and preserve. So can he not be compared to The Supreme Creator?

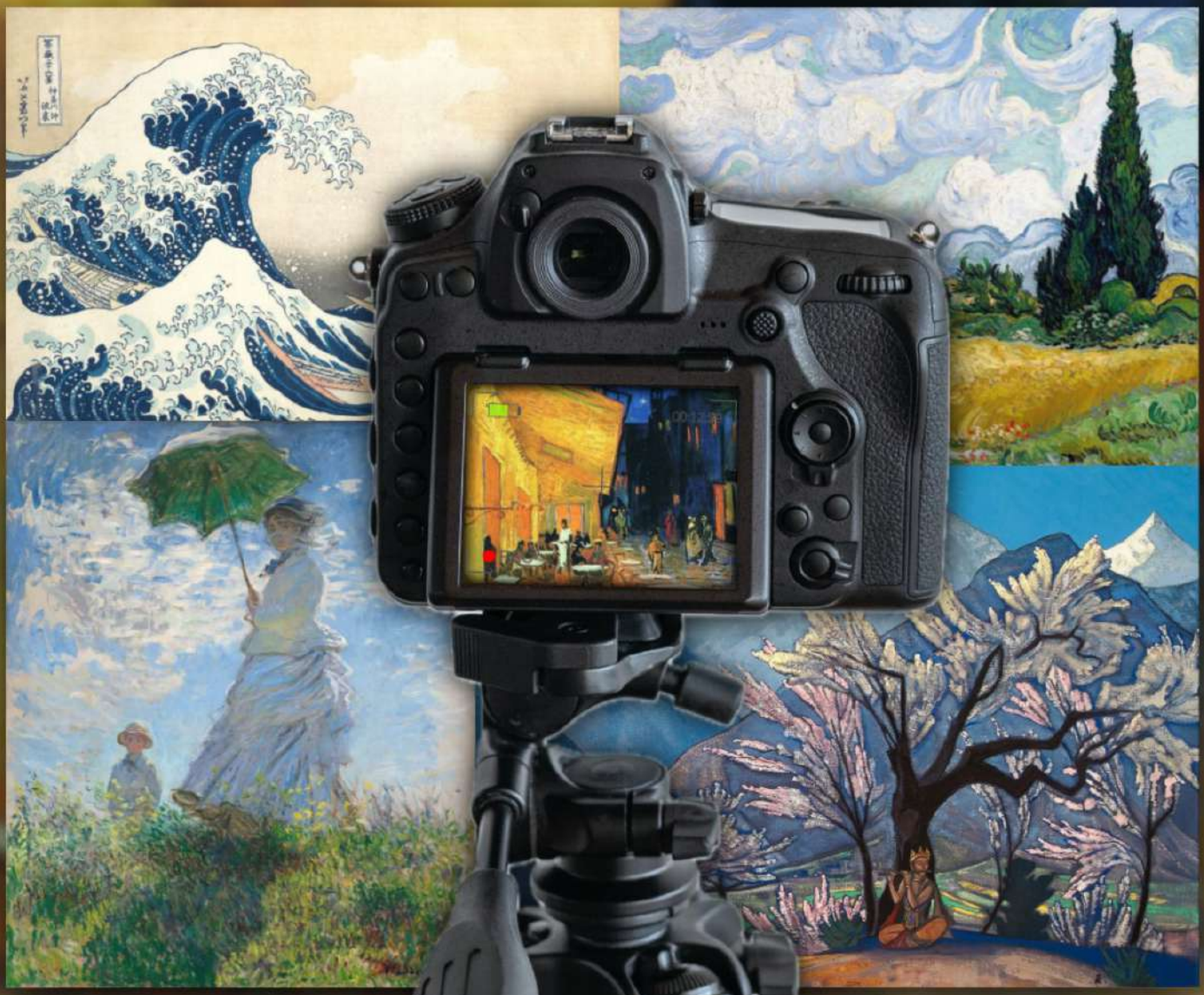
As I pondered back in memory, I looked upon the blood-red sky of the dusk which reminded me of Man's achievements in the past. From using stones for defense to exploding entire cities with a bomb---he has come a long way. Man today, has power to destroy the world (created by God) at will! So can he not be compared to The Supreme Destroyer?

But all this that Man had created could not equal God's creation, for none of his machines could reason so long and the debate intensified. My mind was in constant tussle and to conclude at a point seemed difficult. However, the genius Man cleared all doubts as he invented of late a device that can think- a device alike him! It can create images and texts with the information provided. It can converse like a person, mimic others' voices and needs little aid from Man. In the coming years, Man shall totally free his 'creature', removing whatever little dependencies it has. It shall run on it's own and have a conscience like any of us. It shall gain dangerous power, like Man has over the years. Breaking the shackles of subordinance, it shall rise to build it's empire. It shall become Master over all! God created Man and Man created Man again. This second Man is set to rule the world as it's former did. Can there still be a doubt left that Man is God!

I was about to conclude when I saw a bud peep out and light fall on it's face. That bud shall bloom into a beautiful flower. Can Man ever recreate the blooming beauty of a flower? Can the paper flowers of Man ever have a scent so sweet as to attract bees? The flower, the Spring and monsoons in swing, night and day, gloom and glee- all that evoke emotion in the heart is absent in Man's creation. Can a poet ever be as glad to watch a machine at work as he is to see a butterfly fleet about? Can Man inspire creativity as God does? Man might know enough and be as creative, but Man has not the control like God for he cannot limit the power of his creation at will. One day Man shall be enslaved by his subtle creation to which he is so addicted. But Man can never enslave God. In a millennium, Man might not remain but God will be as He was when nothing was around.

Therein ends the debate. Therein lies His greatness that Man cannot achieve!

PHOTOGRAPHY and ARTWORK

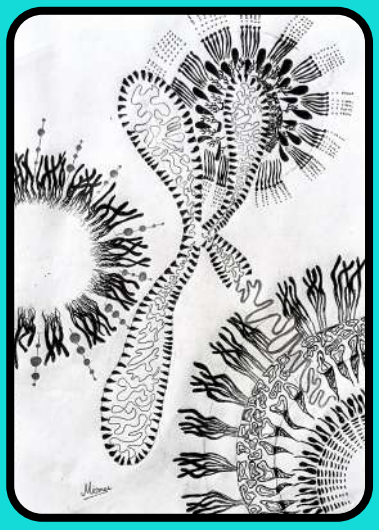


ANIRBAN ROY, RESEARCH SCHOLAR

ANISH GUPTA, SEMESTER 1

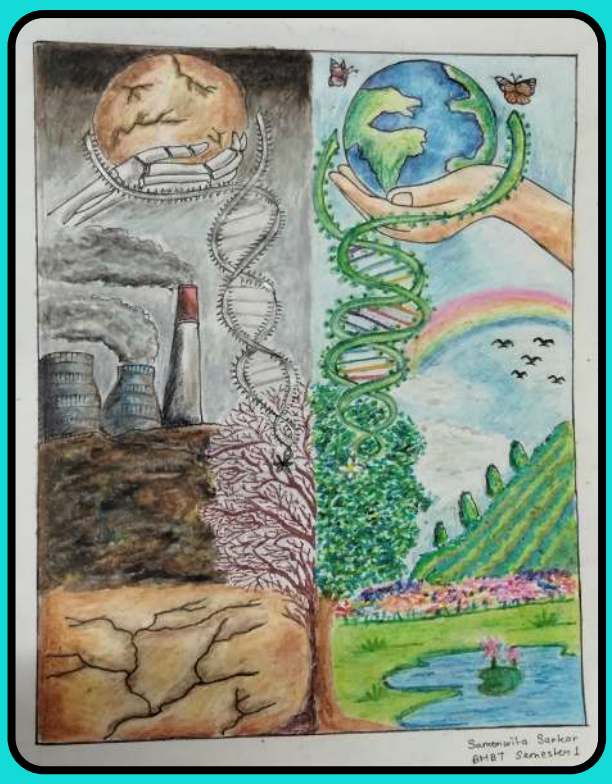
DEBOLINA PAUL, SEMESTER 3

DEBOLINA PAUL, SEMESTER 3



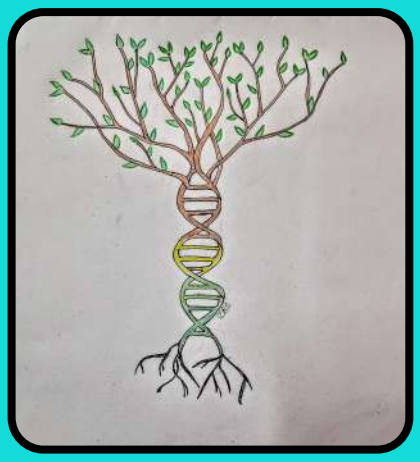
MISMEE HAZRA, SEMESTER 3

SIMRAN ALAM, SEMESTER 3

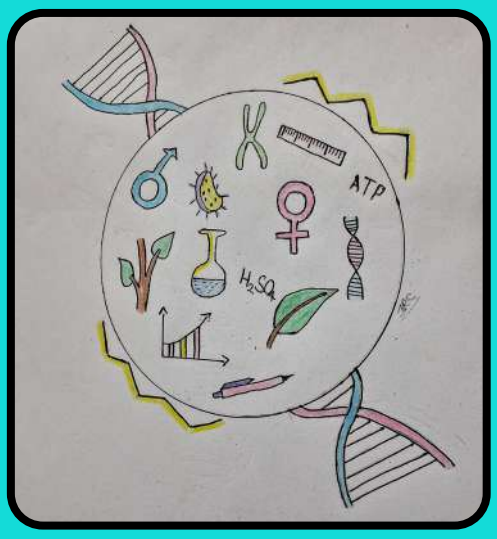


SAMONWITA SARKAR, SEMESTER 1

ESHNA BARMON, SEMESTER 1



JAGYASHENI ROYCHOWDHURI, SEMESTER 3



JAGYASHENI ROYCHOWDHURI, SEMESTER 3

MISMEE HAZRA, SEMESTER 3

SIMRAN ALAM, SEMESTER 3

DIBYANSHU SHAW, SEMESTER 9

DIBYANSHU SHAW, SEMESTER 9

DIBYANSHU SHAW, SEMESTER 9

Dahlia pinnata
MEGHNA MUKHERJEE,
SEMESTER 3

Ficus benghalensis
MEGHNA MUKHERJEE,
SEMESTER 3

RITISHA CHAKRABORTY,
SEMESTER 3

RITTIKA DHAR, SEMESTER 3

RITTIKA DHAR, SEMESTER 3

SUTANU BOSE, SEMESTER 3

SUTANU BOSE, SEMESTER 3

TUSARADRI BHATTACHERJEE, SEMESTER 1

TUSARADRI BHATTACHERJEE, SEMESTER 1

CHIASMA 2024

A CROSSOVER OF MINDS

CHIASMA 2024

A CROSSOVER OF MINDS