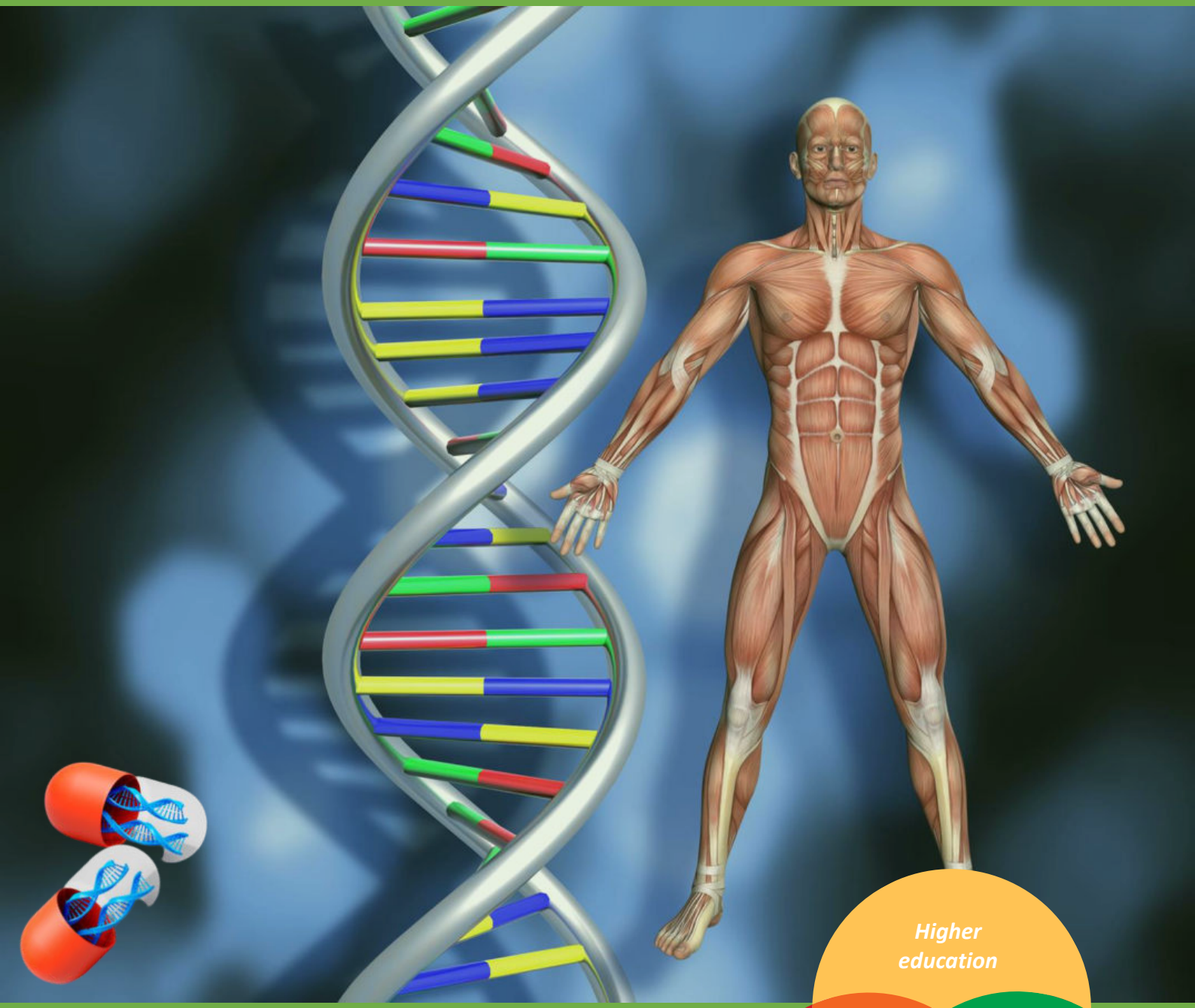
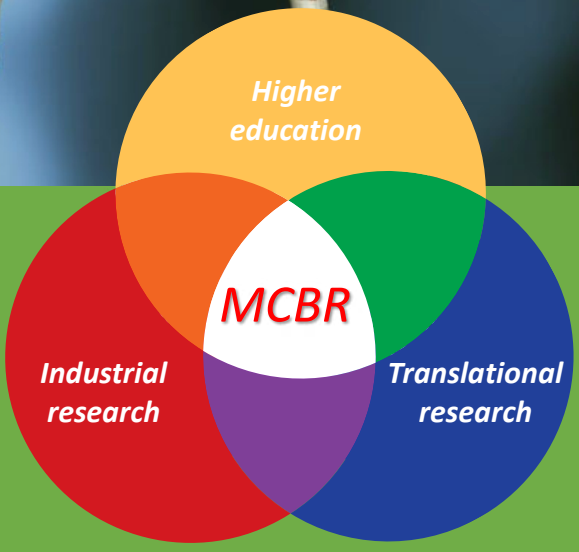
Vol: 10 April - June 2024

Biotheracues

Quarterly Newsletter of Manipal Centre for Biotherapeutics Research





MANIPAL
ACADEMY of HIGHER EDUCATION
(Institution of Eminence Deemed to be University)
INSPIRED BY LIFE

Contents

From the desk of the Coordinator (MCBR)

Dear all,

It gives me immense pleasure to release 10th volume of MCBR quarterly Newsletter "Biotheracues". It has been two and a half years since MCBR was established as a Research Centre Under MAHE to carry out translational research in the domain of Biotherapeutics. Currently, we have research groups working on Cell & Cell-free therapeutics, Gene & Protein therapeutics, Molecular Signal Transduction, Biomaterials & 3D bioprinting, Brain Aging & Neurotherapeutics and Nano-formulation & Nanomedicine. We have envisioned expanding to the areas of Vaccinology and CAR-T therapy in the upcoming quarter.

We are extremely pleased to announce that the first batch students of MSc (by Research) in Biotherapeutics have graduated and became our esteemed alumni. The partner industries where they have carried out three semesters research internship have praised this unique master's program in India and appreciated the quality of students, which is a testament to the program's success. As they enter the real-world opportunities and challenges, MCBR wishes them all the success. We also would like to place on record the extraordinary support extended by the MAHE leadership in making this centre one of the prominent research centres in India focusing on Biotherapeutics Research.

Dr. Raviraja N. S.

Message from the Chief Editor

Dear friends and well-wishers of MCBR,

I am delighted to share with you the tenth edition of Biotheracues. The past quarter has been marked by significant achievements and memorable events at MCBR. We dedicated ourselves to advancing research through the successful organization of two workshops, active participation in Research Day, engaging invited talks, and contributing to Manipal Quest hosted by Manipal Academy of Higher Education (MAHE). One of the memorable moments of this quarter was bidding farewell to the first MSc batch of 13 outstanding students. They excelled not only in their academics but also in their research internships within industries. I am proud to announce that two students achieved the highest CGPA, securing the first rank. Congratulations to all of them! We extend our best wishes for their future endeavors. Amidst our academic pursuits, we also found time for moments of joy through farewell gatherings, birthday celebrations, and a delightful potluck lunch at MCBR.

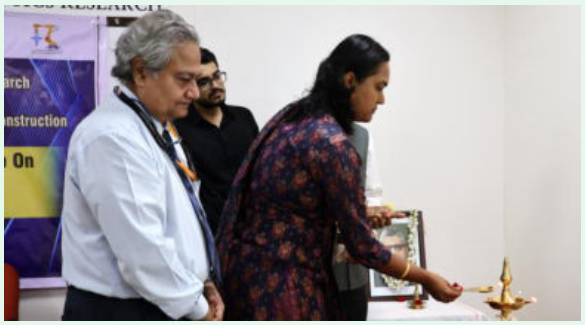
As we conclude this quarter on a high note, I am thrilled to share fantastic news: Dr. Raviraja N. S., our esteemed Coordinator, will assume the role of Chief Operating Officer (COO) at MAHE starting from 1st July 2024. Heartiest congratulations to him on this well-deserved appointment! Looking ahead, let us draw motivation from Dr. Raviraja's success and strive for excellence in our respective roles. Your continued support and valuable feedback are crucial in shaping the future editions of Biotheracues. So, please feel free to share your suggestions and recommendations to enhance our newsletter for everyone's benefit. Thank you.

Dr. Abhayraj S. Joshi

Patent Drafting Workshop at Manipal Centre for Biotherapeutics Research, MAHE, Manipal

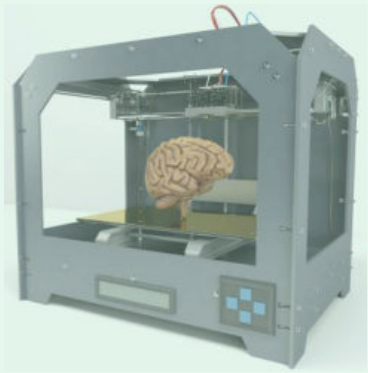
Manipal Centre for Biotherapeutics Research (MCBR, MAHE) and **Directorate of Research** jointly held a one-day workshop on ***"Patent Drafting"*** on 8th May 2024 at MCBR. Dr. Kirthanashri S. V. – Associate Professor and Co-Coordinator (MCBR) welcomed the guests. Dr. S. Varadhrajan – guest of honor for the workshop and Coordinator of IPTTO, MAHE gave overview of the workshop. Dr. Pullela Phani Kumar – Associate Dean of RV University, Bengaluru and the Chief Guest of the workshop addressed the audience with his insights. Dr. Raviraja N. S. – Professor and Coordinator of MCBR delivered presidential address. Mr. Pranav Bhat – Attorney, Astraea Innovative Solutions was also among the guests of honors.

4 Days Hands-on Workshop on 3D Bioprinting at Manipal Centre for Biotherapeutics Research, MAHE, Manipal



Manipal Centre for Biotherapeutics Research (MCBR, MAHE) along with **Kore Additive Manufacturing and Medical Reconstruction (Kore AMMR)** jointly conducted a 4 days hands-on workshop on 3D bioprinting. The workshop was inaugurated by Pro vice chancellor (Health Sciences) – Dr. Sharath K. Rao. Dr. Raviraja N. S., Professor and Coordinator of MCBR gave the welcome speech and Dr. Kirthanashri S. V. briefly outlined the workshop activities. Mr. Chaitanya Doshi – CEO of Kore AMMR addressed the attendees and gave excellent information about 3D bioprinting. Dr. Abhayraj Joshi gave vote of thanks and inauguration ceremony was followed by high tea.

4 Days Hands-on Workshop on 3D Bioprinting at Manipal Centre for Biotherapeutics Research, MAHE, Manipal



In the 3D Bioprinting workshop jointly conducted by MCBR and Kore AMMR, on the first day, Dr. Kirthanashri S. V. (Associate Professor, MCBR) and Dr. Manash Paul (Associate Professor, MSLS) gave lectures in the morning session. The afternoon session was dedicated to hands on training of the advanced 3D Bioprinting software such as OpenScad and AutoDesk.

On the second day, in the morning session, Dr. Shibu C. – Cofounder and Director of Matrix-Heal Pvt. Ltd., Hyderabad delivered an excellent talk on “Opportunities in 3D Bioprinting” which was followed by hands on training of printing software such as Cura and Mendel. In the afternoon session, attendees of workshop got opportunity to work on 3D bioprinter situated at MCBR lab.

4 Days Hands-on Workshop on 3D Bioprinting at Manipal Centre for Biotherapeutics Research, MAHE, Manipal

On third day, Dr. S. Varadharajan – Coordinator of IPTTO, MAHE delivered his talk on "Regulatory Affairs and Patenting Issues in 3D Bioprinting" which was followed by hands on training on 3D bioprinter and characterization of 3D bioprinted scaffolds.

On the final day, Mr. Chaitanya Doshi – CEO of Kore AMMR delivered talk on "Microfluidics and 3D Bioprinting" and then attendees got hands on training on microfluidics system. In the afternoon session Valedictory function was conducted followed by high tea. Overall workshop was a great success and we received very positive feedback from all the participants.

Farewell

Farewell to 1st M. Sc. Batch

On 8th June 2024, we bade farewell to our very first M. Sc. batch by organizing a small farewell ceremony and lunch. From this batch, all students perform exceptionally good, and we also received very nice remarks from several industries where they were doing their internship project. Most notably, two students from the first batch, Ms. Madhavi Hegde and Ms. Divya Mallya secured first rank with the highest CGPA (9.85/10.00).

During the farewell ceremony, Dr. Raviraja N.S. (Coordinator, MCBR) delivered a nice and motivational speech and guided graduating M. Sc. Students for the future. All faculty members expressed their views and wished well to the departing batch. The ceremony also included excellent dance performances by Ms. Bhavya (Second M. Sc. batch 2023-2025), Mr. Rounak, and Mr. Praneeth (Ph. D.. Scholars) followed by lunch.

Activities at MCBR

Adjunct Faculty Recruitment

Dr. Srinivasan Vijayaraghavan – Professor at Department of Biological Sciences of Kent State University, Kent, Ohio, USA has been appointed as an adjunct faculty from 1st April 2024. Dr. Vijayaraghavan holds around 40 years of research and teaching experience and his core areas of research include Molecular Biology, Reproductive Biology, Biochemistry, Eukaryotic Cell Biology, and Bioenergetics. MCBR wholeheartedly welcomes Dr. Vijayaraghavan and looks forward to getting benefitted from his rich experience.

Research Progress

Publications:

- Adarsh Gopinathan, Runali Sankhe, Ekta Rathi, Triveni Kodi, Raghavendra Upadhya, K. Sreedhara Ranganath Pai, and Anoop Kishore. An *in-silico* drug repurposing approach to identify HDAC1 inhibitors against glioblastoma. **JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS**, 2024.

- Abhijna Ballal R., Shivakumar Reddy K., Divya Chandran, Sumukha Hegde, Raghavendra Upadhya, Praveen Kumar SE, Smita Shenoy, Vasudha Devi, & Dinesh Upadhya. *Cell-specific extracellular vesicle-encapsulated exogenous GABA controls seizures in epilepsy*. **STEM CELL RESEARCH & THERAPY**, 2024.

- Shifana Ali, Ahmed Ziyad, K. Sreedhara Ranganath Pai, Anju Muraleedharan, Adhithya Gopan, Raghavendra Upadhya, Raviraja N Seetharam, and Kalaivani Manokaran. *Influence of Ascorbic Acid on Di-(2-Ethylhexyl) Phthalate-induced Ovarian Gene Alterations in Pubertal Female Wistar Rats*. **JOURNAL OF PHARMACOLOGY AND PHARMACOTHERAPEUTICS**, 2024.

Invited talk:

- **Dr. Shibu Chameettachal**, Co-founder and director, Matrix-heal Pvt. Ltd., Hyderabad, India delivered a talk on 23rd April 2024 on the topic **"Transforming Biomedical Research into Viable Solutions"** had an excellent discussion with MCBR faculty, research staff, and M. Sc. students.

Research Day at Manipal – A day dedicated for improving Collaborative Research

Manipal Academy of Higher Education (MAHE) arranged a research day with the theme of "*Enrich"* and *"Collaborate"* at Dr. TMA Pai Hall for all campuses of MAHE. The faculty and research scholars from all the institutes united to showcase their laboratory infrastructures, core research areas, and research outputs. MCBR also participated actively at the *Enrich* and *Collaborate* booths. The presentations and posters were prepared by Dr. Abhayraj Joshi and Dr. Abhishek Kumar Singh for *Enrich* and *Collaborate* booths, respectively. The booths were manned for entire event by all MCBR faculties and all research scholars. Everybody had invigorating, exciting, and motivational experience from this research-oriented initiative of MAHE. In the evening, Lt. Gen. Dr. M. D. Venkatesh visited each booth and at MCBR booth, he praised MCBR's leadership and entire progress.

Manipal Academy of Higher Education (MAHE) also arranged *"LIFEATHON"* event – Final Round presentation on 8th June 2024 at Dr. TMA Pai Hall. From MCBR, Dr. Raghavendra Upadhya and his students (Mr. Ramnarayan Bhat and Ms. Abigail) as well as Dr. Kirthanashri S. V. and her students (Ms. Amrutha Hebbar) participated in this event. Lt. Gen. Dr. M. D. Venkatesh visited their booth Lifeathon event and lauded their research ideas and work.

MANIPAL QUEST 1.0 AT MANIPAL

On 9th June 2024, Manipal Academy of Higher Education (MAHE) arranged an Inter-health Sciences Postgraduate Research Conference – *"Manipal Quest 1.0*". Three Ph. D. research scholars from MCBR – Ms. Varsha, Mr. Anirudh, and Mr. Praneeth presented their posters. Faculty members attended this conference and Dr. Abhishek Kumar Singh also worked as judge for one of the poster sessions of the conference.

Posters from MCBR:

1. Ms. Varsha – Bioengineered decellularized nerve conduits for nerve tissue regeneration
2. Mr. Anirudh – Advancements in Leydig cell isolation techniques
3. Mr. Praneeth – Navigating through GSK3 inhibitor challenges: Strategies for triumph

ARTICLE UNDER FOCUS

JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS
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An *in silico* drug repurposing approach to identify HDAC1 inhibitors against glioblastoma

Adarsh Gopinathan[a], Runali Sankhe[a], Ekta Rathi[b], Triveni Kodi[a], Raghavendra Upadhya[c], K. Sreedhara Ranganath Pai[a] and Anoop Kishore[a]

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Though treatment and diagnosis have advanced significantly, brain tumors continue to be a major public health concern worldwide. Eighty percent of brain cancers are caused by glioblastoma (GBM). After receiving a glioblastoma diagnosis, a patient's average survival time is around 15 months. The function of peptidase enzymes, particularly the neutral endopeptidase Neprilysin (NEP), in controlling tumor growth has recently come into focus. Reduced expression of NEP protein is linked to the development of various malignancies, and there is a positive correlation between neprilysin expression and a number of tumors, including GBM. Histone deacetylase (HDAC) enzymes, particularly HDAC1, are a major cause of the downregulation of NEP protein. Furthermore, research has shown that downregulating NEP gene expression is caused by elevated HDAC1 levels. Therefore, increasing NEP levels may be a desirable goal for HDAC1 inhibition, which may be a useful therapeutic strategy for GBM. In this work, HDAC1 inhibitors from the ZINC15 database are identified using Schrodinger Maestro, a computational drug repurposing tool. By means of molecular docking, 1379 FDA-approved medications were selected from the ZINC15 database. The top 10 compounds were chosen based on docking score and ligand-protein interaction, and these were subsequently used in molecular dynamics (MD) simulations and binding energy calculations. Amo0ng them, the three most potent medications from the MD simulations—Panobinostat, Tasimelteon, and Melphalan—were examined for cytotoxicity and HDAC1 protein levels in C6 and U87 MG-glioblastoma cells. Of these medications, Panobinostat demonstrated a strong cytotoxic effect as well as a significant decrease in HDAC1 protein levels.

AlphaFold 3: Unfolding the Mysteries of Protein Structure

Mr. H.S. Anirudh Srinivas, *Dr. TMA Pai Scholar, MCBR, MAHE*

In the emerging field of molecular science, computational biology serves as a groundbreaking discipline that combines the power of computational techniques with biological research. This innovative field is transforming how we understand, predict and manipulate biological systems. One of the most remarkable achievements is AlphaFold, an AI driven solution developed by Google DeepMind that has revolutionized protein structure determination by transforming complex data into valuable insights and visualization.

Traditionally, determining protein structures relied on techniques such as nuclear magnetic resonance (NMR) spectroscopy and X-ray crystallography. These methods though foundational are time-consuming, labor-intensive, and expensive hindering their widespread application as well as its reach to every nook and corner of society. AlphaFold offers a revolutionary alternative. It utilizes deep learning to analyze vast datasets of protein sequences and known structures. By training on this data, AlphaFold can identify complex relationships between a protein's amino acid sequence and its 3D structure. This allows AlphaFold to predict protein structures with remarkable accuracy in a fraction of the time required by traditional methods.

One of the key advancements is AlphaFold 3's ability to predict the joint structures of complex assemblies, including nucleic acids, proteins, ions, small molecules and even modified residues. Whereas previous tools often just focused on individual molecules. AlphaFold predicts interaction between protein and ligand outperforming state-of-the-art docking tools. This advancement in protein structure estimation has the potential to significantly accelerate research across diverse fields, from drug discovery to materials science and new therapeutics.

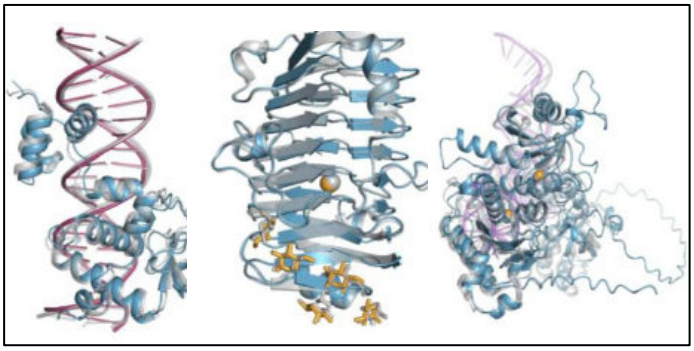


Fig.1: A.7R6R - DNA binding protein: AlphaFold 3's prediction for a molecular complex featuring a protein (blue) bound to a double helix of DNA (pink) is a near-perfect match to the true molecular structure discovered through painstaking experiments (grey). **B.** 7BBV - Enzyme: AlphaFold 3's prediction for a molecular complex featuring an enzyme protein (blue), an ion (yellow sphere) and simple sugars (yellow), along with the true structure (grey). This enzyme is found in a soil-borne fungus (Verticillium dahliae) that damages a wide range of plants. Insights into how this enzyme interacts with plant cells could help researchers develop healthier, more resilient crops. **C.** 8AW3 - RNA modifying protein: AlphaFold 3's prediction for a molecular complex featuring a protein (blue), a strand of RNA (purple), and two ions (yellow) closely matches the true structure (grey). This complex is involved with the creation of other proteins — a cellular process fundamental to life and health.

Biotherapeutic Applications:

Accurate protein structure prediction is crucial for understanding biomolecular interactions, which is essential for drug development. AlphaFold 3 facilitates the rational design of therapeutics by providing detailed structural insights, enhancing drug targeting precision and faster development by reducing the trial-and-error nature of drug development allowing. Including many new potential avenues like reengineering Proteins, antibody discovery and novel biotherapeutics.

References:

1. Abramson, J., Adler, J., Dunger, J., Evans, R., Green, T., Pritzel, A., Ronneberger, O., Willmore, L., Ballard, A. J., Bambrick, J., Bodenstein, S. W., Evans, D. A., Hung, C. C., O'Neill, M., Reiman, D., Tunyasuvunakool, K., Wu, Z., Žemgulytė, A., Arvaniti, E., Beattie, C., … Jumper, J. M. (2024). Accurate structure prediction of biomolecular interactions with AlphaFold 3. *Nature*, *630*(8016), 493–500.
2. Jumper, J., Evans, R., Pritzel, A., Green, T., Figurnov, M., Ronneberger, O., Tunyasuvunakool, K., Bates, R., Žídek, A., Potapenko, A., Bridgland, A., Meyer, C., Kohl, S. A. A., Ballard, A. J., Cowie, A., Romera-Paredes, B., Nikolov, S., Jain, R., Adler, J., Back, T., … Hassabis, D. (2021). Highly accurate protein structure prediction with AlphaFold. *Nature*, *596*(7873), 583–589.
3. Mosalaganti, S., Obarska-Kosinska, A., Siggel, M., Taniguchi, R., Turoňová, B., Zimmerli, C. E., Buczak, K., Schmidt, F. H., Margiotta, E., Mackmull, M. T., Hagen, W. J. H., Hummer, G., Kosinski, J., & Beck, M. (2022). AI-based structure prediction empowers integrative structural analysis of human nuclear pores. *Science (New York, N.Y.)*, *376*(6598), eabm9506.
4. https://blog.google/technology/ai/google-deepmind-isomorphic-alphafold-3-ai-model/#alphafold-server

Organ-on-a-Chip: Pioneering advancements in healthcare

Ms. Prachi Agarwal, *Dr. TMA Pai Scholar, MCBR, MAHE*

Over the years, scientists have been working on bringing in the better technology and improvement in healthcare sector. The difficulties observed highlights the urgent need for creating a system with low failure rates that is usually faced while using the animal models. It is the urgent requirement to develop an alternative method that closely mimics the human physiology that is critical for improving the efficiency and reliability of the treatment and in drug development. Organ-on-chip (OoC) is a promising technology that reconstructs human organ functions on a microscale combining biology with microtechnology in order to replicate key aspects of human physiology. Microfluidics plays a crucial role in OoC development by creating the intricate structures of the chips and enabling precise control over fluid dynamics within the system. OoC contain networks of fine microchannels that can guide and manipulate the tiny volumes of fluids. The term "organ" refers to the minute tissues grown within these chips that can simulate one or more tissue-specific functions. These systems can be effectively worked out to mimic the human physiology and the disease, making them a valuable tool for advanced *in vitro* experimentation and creating an environment that closely approximates *in vivo* conditions, both biochemically and substantially. It offers enhanced control over the microenvironment to sustain tissue life and observe behaviour of cells and tissues. These technological advancements have led to OoCs that can provide multi-parametric readouts of organ functions, offering insights into integrated human and animal biology. OoC technology serves as a bridge in the spectrum of model biological systems, offering a higher level of physiological relevance compared to 2D and 3D cell cultures while being more accessible for direct investigation than whole organisms. This technology has grown rapidly, driven by the need for human-like testing systems in pharmaceutical, cosmetic, food, and chemical industries as alternatives to animal testing. Significant advances in tissue engineering and microfabrication have propelled OoC development, enabling the creation of complex 3D co-culture systems that replicate organ-specific functions. Innovations in cell manipulation, integration of primary cells, and the use of induced pluripotent stem cells (iPSCs) for personalized models have further enhanced the capabilities of OoCs.

There is an active work going on in the field of OoC creating a market size of around $100 million in the year 2020 and is projected to reach over $1 billion by 2030. The market is driven by the increasing demand for drug testing, personalized medicine, and organ replacement.

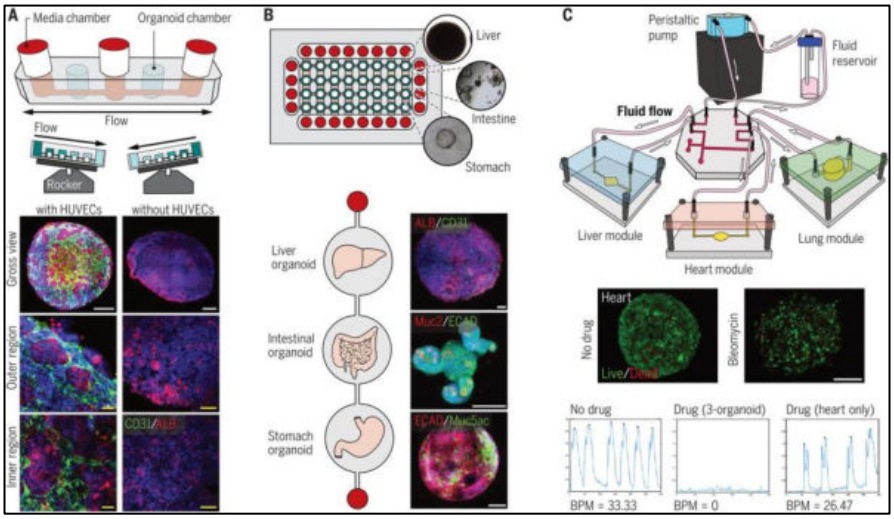


Fig. 1: Modelling tissue–tissue and organ–organ interactions in organoids-on-a-chip

Reference:

1. Nahak, B. K., Mishra, A., Preetam, S., & Tiwari, A. (2022). Advances in organ-on-a-chip materials and devices. *ACS applied biomaterials*, *5*(8), 3576-3607.
2. Beißner, N., Lorenz, T., & Reichl, S. (2016). Organ on chip. *Microsystems for pharmatechnology: manipulation of fluids, particles, droplets, and cells*, 299-339.
3. Yesil-Celiktas, O., Hassan, S., Miri, A. K., Maharjan, S., Al-kharboosh, R., Quiñones-Hinojosa, A., & Zhang, Y. S. (2018). Mimicking human pathophysiology in organ-on-chip devices. *Advanced Biosystems*, *2*(10), 1800109.
4. Leung, C. M., De Haan, P., Ronaldson-Bouchard, K., Kim, G. A., Ko, J., Rho, H. S., ... & Toh, Y. C. (2022). A guide to the organ-on-a-chip. *Nature Reviews Methods Primers*, *2*(1), 33.
5. Leung, C. M., De Haan, P., Ronaldson-Bouchard, K., Kim, G. A., Ko, J., Rho, H. S., ... & Toh, Y. C. (2022). A guide to the organ-on-a-chip. *Nature Reviews Methods Primers*, *2*(1), 33.
6. Organ-on-Chip Market Size, Share, Competitive Landscape and Trend Analysis Report by Type : Global Opportunity Analysis and Industry Forecast, 2020-2030

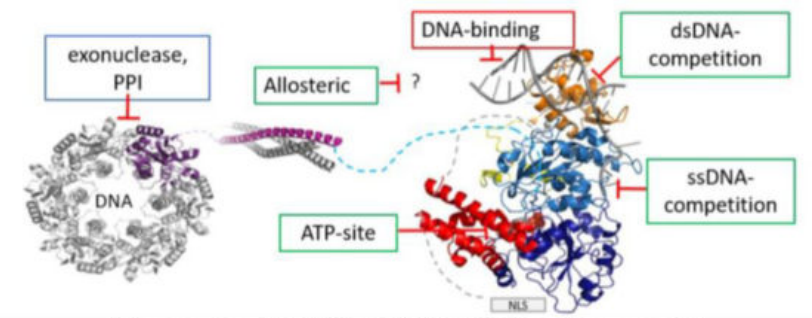
WRN helicases: Targeting an Achilles heel of cancer

Dr. Raghavendra Upadhya, Assistant Professor, MCBR

WRN helicases, members of the RecQ helicase family encompassing RECQL1, RECQL4, RECQL5, and BLM, are encoded by the WRN gene and are essential in maintaining genomic stability. WRN helicases play key regulatory roles throughout the replication process, including unwinding of DNA double helix preventing replication fork collapse, maturation of Okazaki fragments, and polymerization of DNA strands during replication. They are also involved in resolving complex DNA structures such as forks, flaps, bubbles, displacement loops (D-loops), G-quadruplexes, and holiday junctions during DNA replication and repair. Additionally, they also regulated by telomeric maintenance preventing telomere dysfunction. A mutated WRN gene causes a rare autosomal recessive WRN syndrome characterized by premature aging and increased risk of cancer (1–4). The importance of WRN helicase in maintaining genomic stability makes them a potential synthetic lethal target in cancer therapy. The privation of miss match repair (MMR) by various aberrations occurs in 10 - 30% of cancer types leading to microsatellite instability (MSI) phenotype. Large-scale functional genomic screening projects have identified that such cancer cells exhibiting MSI phenotype and deficiencies in homologous recombinant (HRR) pathways are vulnerable to WRN inhibition. WRN inhibition in such cells leads to synthetic lethality due to the simultaneous impairment of two essential pathways (5,6). The discovery of synthetic lethality resulting from WRN inhibition in MSI cancer cells has spurred the development of multiple inhibitors aimed at selectively targeting these cancer cells for potential therapeutic advantages. However, the development of selective, specific, and efficient inhibitors for WNR helicase is challenging due to high susceptibility for artifacts through protein interference (7). The ATP-dependent helicase domain of the multifunctional WRN enzyme is the most targeted domain by the inhibitors developed. HRO-761 is one such example of one of the promising candidates that have been identified as potential WRN inhibitors. The pharmacological inhibition caused by HRO761 recapitulated the phenotype observed by WRN genetic suppression via DNA damage and reduction of tumor in a p53-independent manner. Many of such inhibitors (MSC617145, NSC19630, VVD133214 etc.) are in development phase. Some have shown promise in preclinical studies, while others are primarily used as research tools to understand the role of WRN helicase in genomic stability and cancer.

References:

1. Singh DK, Ahn B, Bohr VA. Roles of RECQ helicases in recombination-based DNA repair, genomic stability and aging. Biogerontology. 2009 Jun;10(3):235–52.
2. Yu CE, Oshima J, Fu YH, Wijsman EM, Hisama F, Alisch R, et al. Positional cloning of the Werner's syndrome gene. Science. 1996 Apr 12;272(5259):258–62.
3. Yokote K, Chanprasert S, Lee L, Eirich K, Takemoto M, Watanabe A, et al. WRN Mutation Update: Mutation Spectrum, Patient Registries, and Translational Prospects. Hum Mutat. 2017 Jan;38(1):7–15.
4. Mendoza O, Bourdoncle A, Boulé JB, Brosh RM, Mergny JL. G-quadruplexes and helicases. Nucleic Acids Res. 2016 Mar 18;44(5):1989–2006.
5. Ferretti S, Hamon J, de Kanter R, Scheufler C, Andraos-Rey R, Barbe S, et al. Discovery of WRN inhibitor HRO761 with synthetic lethality in MSI cancers. Nature. 2024 May;629(8011):443–9.
6. Morales-Juarez DA, Jackson SP. Clinical prospects of WRN inhibition as a treatment for MSI tumours. NPJ Precis Oncol. 2022 Nov 15;6(1):85.
7. Heuser A, Abdul Rahman W, Bechter E, Blank J, Buhr S, Erdmann D, et al. Challenges for the Discovery of Non-Covalent WRN Helicase Inhibitors. ChemMedChem. 2024 Apr 16;19(8):e202300613.



How to inhibit WRN helicase?

NOTABLE VISITORS

Dr. Anand Bhogu, Assistant Vice President (Business Development) and **Dr. Praveen Kumar Shetty**, Assistant Vice President (Clinical Development) at **BioPlus Life Sciences** visited MCBR on 4th April 2024 and keenly observed the research infrastructure of MCBR. They praised the MCBR for its vision and mission.

Delegates from Stempeutics Research (India) and Medinet Inc. (Japan): **Dr. Kunihiko Suzuki** (Advisor to Medinet), **Dr. Shoji Ikeda** (Corporate Officer & Division Director, Regenerative Medicine, Medinet), **Dr. Madhusudan Peshwa** (Advisor to Stempeutics Research), and **Dr. Suresh Kannan** (Scientist, Stempeutics Research) visited MCBR on 3rd May 2024 and louded our efforts towards biotherapeutics research.

Ms. Veronica Vale and **Australian Dental Council** visited MCBR on 15th May 2024 and had tour of lab facilities. They praised MCBR's state-of-the-art research infrastructure.

Dr. Sundar Swaminathan (Associate Faculty, Department of Bioengineering), from Indian Institute of Science (IISc), Bangalore, visited MCBR on 21st May 2024 and had interaction with all research scholars and faculty members.

FUN MOMENTS

We celebrated birthdays of Dr. Abhayraj Joshi (17th May) and Dr. Souvik Dey (20th May) with a delicious cake, claps, and laughs.

On 26th June, we celebrated Dr. Ramya's birthday. On the same day, we also bade farewell to Mr. Liston who will be joining as a Ph. D. scholar at Brown University (USA) soon.

We celebrated success of Mr. Avinash and Mr. Prithish, our non-teaching staff of MCBR in Carrom Tournament held by Manipal Academy of Higher Education (MAHE). They secured

FUN MOMENTS

We also had potluck lunch on 29th June 2024 and tasted around 27 dishes made by our faculty members, non-teaching staff, and Ph.D. scholars and researchers. Dr. Vadiraj Bhat (Agilent) also visited us and participated in potluck lunch.

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MANIPAL
ACADEMY of HIGHER EDUCATION
(Institution of Eminence Deemed to be University)

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