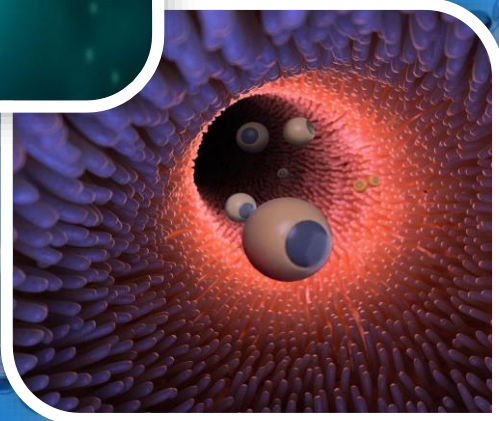


Biotherapeutics

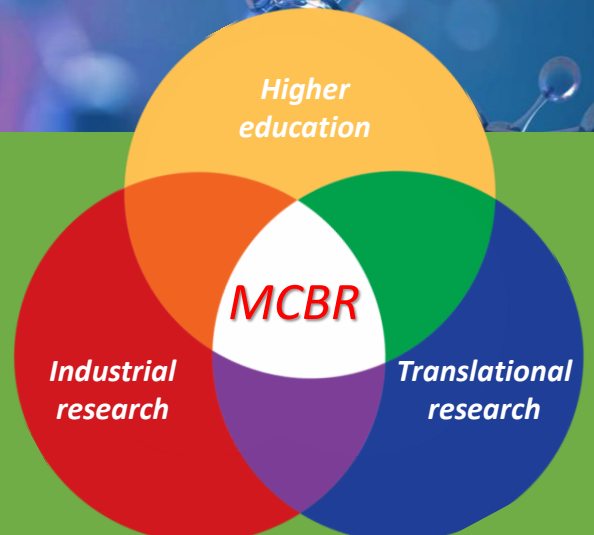
Vol: 2

April-June, 2022

Quarterly Newsletter of Manipal Centre for Biotherapeutics Research, MAHE



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



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Contents

Message from the Chief Editor

*Release event of the first issue
of Biotheracues*

Activities at MCBR

*Research progress
Hosting of webinar
Open House event
Notable visitors*

Blogs

Global research update

*Interactive events
Participation in social works*

*Fun moments:
Birthday celebrations at MCBR*

Message from the Chief Editor



Dear friends and well-wishers of MCBR,

I am happy to present the April-June, 2022 Issue of our newsletter to you.

The current issue of *Biotheracues* will give you a glimpse of the research activities and the academic exchanges that took place during this period. You will also get to know about the *open house* event conducted by MCBR, which received considerable appreciation.

Finally, we are all set and geared up to welcome our first batch of MSc students in August.

Your feedback and suggestions are welcome to make the next newsletter issue more interactive.

Warm regards.

Dr Souvik Dey

Release event of the first issue of *Biotheracues*

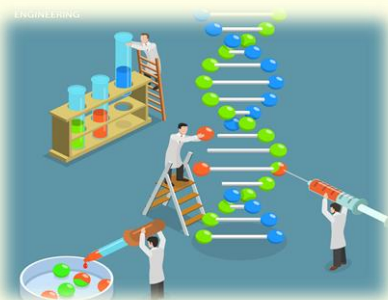
The maiden issue of *Biotheracues* was released by the Hon'ble Vice-Chancellor, MAHE, Lt. Gen. (Dr.) M. D. Venkatesh, on May 12, 2022. The faculty members of MCBR, including Prof. Raviraja N.S. and all the PhD scholars and staff were present at this newsletter launch occasion. The event took place in the fourth-floor Board Room of the MAHE administrative building. It was a memorable day for all the members of MCBR family.



Research Progress

With the joining of two more Dr. TMA Pai PhD Scholars in the last quarter, the total research scholar number is now five at MCBR. At the same time, two more faculties have been selected and are expected to join this centre within the next couple of months.

All our faculties are currently involved in research activities. They have submitted multiple collaborative projects with senior faculties from other departments of MAHE in the last three months. Some collaborative research work with MCOPS has already started.



Publications:

1. B Vona, DA Schwartzbaum, AA Rodriguez, SS Lewis, MB Toosi, **P Radhakrishnan**, N Bozan, R Akin, M Doosti, R Manju, D Duman, CJ Si neni, S Nampoothiri, EG Karimiani, H Houlden G Bademci, M Tekin, **KM Girisha**, R Maroofian, S Douzgou. (2022). Biallelic KITLG variants lead to a distinct spectrum of hypomelanosis and sensorineural hearing loss. *European Academy of Dermatology & Venereology*. (Q1_IF: 6.166).
<https://doi.org/10.1111/jdv.18207>
2. Namdev Dhas, Monica ´ C. Garca, Ritu Kudarha, Abhijeet Pandey, Ajinkya Nitin Nikam, Divya Gopalan, Gasper Fernandes, Soji Soman, Sanjay Kulkarni, **Raviraja N. Seetharam**, Ruchi Tiwari, Sarika Wairkarf, Chandrakantsing Pardeshi, Srinivas Mutalik. (2022). Advancements in cell membrane camouflaged nanoparticles: A bioinspired platform for cancer therapy. *Journal of Controlled Release*. (Q1_IF:9.776).
doi: 10.1016/j.jconrel.2022.04.019.



Hosting of webinar

We successfully organized an Invited Talk entitled, “*Drug Targeting by Nanoformulations*”, by **Prof. Biswajit Mukherjee, Department of Pharmaceutical Technology, Jadavpur University, Kolkata** in collaboration with *Manipal School of Pharmaceutical Sciences (MCOPS)* on 25th June using a virtual platform. Prof. Mukherjee, an ex-DAAD Research Fellow, Germany has been involved in the application of nanoformulation in optimizing modern drug delivery systems for more than two decades.

Prof. Srinivas Mutalik co-moderated the event. Chief guests for this webinar were Prof. C. Mallikarjuna Rao, Principal, MCOPS, MAHE and Prof. Raviraja N.S., Coordinator, MCBR, MAHE. Faculties and research scholars from MCBR and MCOPS attended this event. The presentation by Prof. Mukherjee was followed by a Q & A session.



Open House event

We conducted an OPEN HOUSE event for MCBR on 28th June 2022. Other faculties, doctoral research scholars and technical staff of MCBR actively participated in organizing this event. 62 visitors, including prospective MSc students, their parents, faculties and research scholars from other departments, schools, and centres attended this event. Research and academic facilities in MCBR were showcased and queries related to our MSc curriculum and research collaboration opportunities were answered.



Manipal Centre for Biotherapeutics Research (MCBR)

Get to Know Your future alma mater & collaborators

OPEN HOUSE

A free, fun and interactive day for everyone!

TUESDAY, JUNE 28
10 AM - 1 PM

AT MCBR
MCBR BUILDING, BEHIND 10th BLOCK MIT HOSTEL, MANIPAL 576104.

Parents, Prospective Students & Potential Collaborators are invited to explore our centre and find all information about it.

FACILITY TOUR
ACADEMIC DISPLAY
RESEARCH OVERVIEW

<https://manipal.edu/mcbr-manipal.html>
MORE INFO: (0820) 2928504 OR mcbr.mah@manipal.edu

Research scholars from MCOPS was given a tour of our research facility by one of our faculties.



Research scholars and faculty from other departments of MAHE can be seen with Dr. Manjunatha SM, Asst. Professor, MCBR in front of MCBR clean room.



Research scholars and faculties from MCOPS can be seen with Dr. Raghavendra Upadhy, Asst. Professor, MCBR inside MCBR main research laboratory.

Prospective MSc students along with their parents are having refreshments in the MCBR courtyard after visiting our academic and research facilities. They also met Prof. Raviraja NS, and satisfied their queries about the MSc curriculum.



DBT-Ramalingaswami Fellows from KMC visited MCBR during this event. From left corner: Dr. Rama Rao Damerla, Dept. of Medical Genetics, KMC; Dr. Souvik Dey, MCBR; Dr. Somasish Ghosh Dastidar and Dr. Pavan Agrawal, Centre for Molecular Neuroscience, KMC.

Notable visitors

Many notable industrialists, scientists and administrators visited MCBR during last three months. Some of them can be seen with our faculties and research scholars in the following pictures:

Mr. Ashok Chandak, Director, Chandak Laboratories Private. Limited, Hyderabad visited MCBR in the early part of April.



Dr. Manutosh Acharya, Vice President, OmniActive Health Technologies, Mumbai made a visit to MCBR in April.

Dr. Ashok Shetty, Associate Director and Professor, Institute of Regenerative Medicine, Texas A&M University visited us also in April.





Dr. Rajendra Upadhy, Assistant Research Professor, Duke University Research Center, Durham, USA made a visit to MCBR in June.



Dr. Anup Naha, Associate Professor, MCOPS & Chief Coordinator, Volunteer Services Organization (VSO), MAHE visited us recently and presented the great vision and ongoing activities of VSO and encouraged our students to get enrolled in this social endeavor.

Dr. Vadiraja Bhat,
Country Biopharma
Business Development
Manager, Agilent
Technologies, USA made a
visit to MCBR in June.



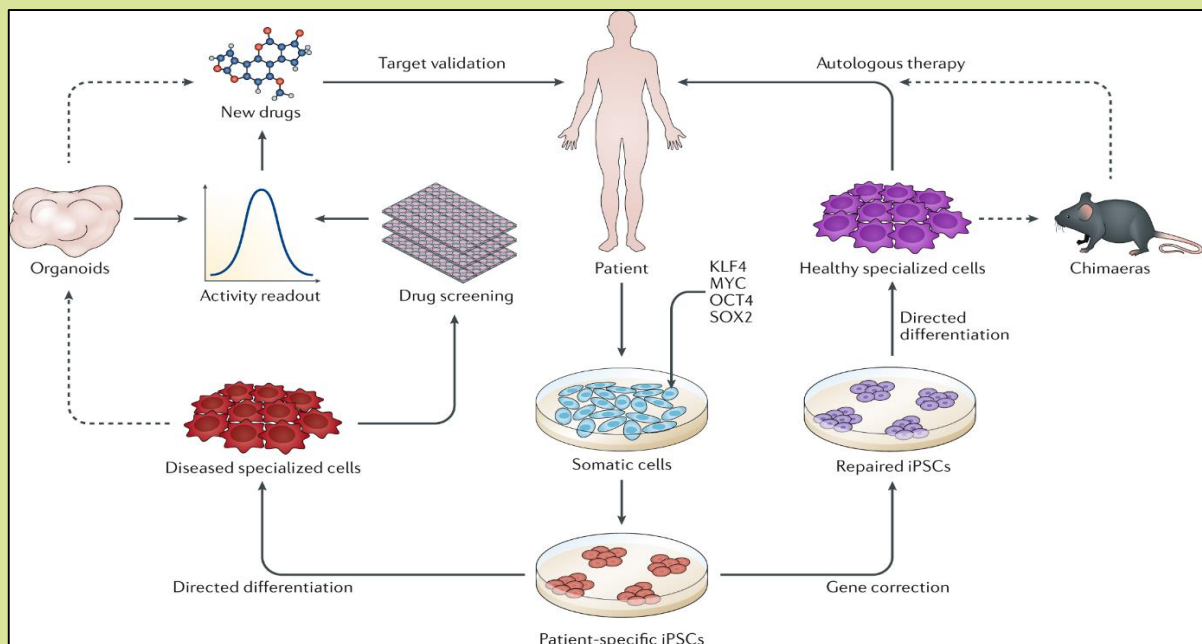


Blogs

iPSC technology: Cellular Reprogramming for vast biomedical applications

by *Jahnavy M Joshi, DST-INSPIRE Fellow*

In 2006, Dr. Yamanaka and Dr. Takahashi gave a ground-breaking study that reprogrammed mouse fibroblasts into pluripotent stem cells, for which they were awarded a Nobel prize in 2012. Since then, these reprogrammed stem cells called induced Pluripotent Stem Cells (iPSCs), are being explored. The original study screened 24 candidate genes that played a pivotal role during embryogenesis, and 4 factors were found to be crucial for a somatic cell to turn into a stem cell. This technology enabled a researcher to obtain a stem cell from any somatic source only by adding four transcription factors, called Yamanaka Factors- Oct3/4, Sox2, Klf4, c-Myc by the retroviral method. The iPSCs generated in the laboratory by this technology could differentiate into almost any type of cell according to the media it was cultured in. This has opened new avenues in disease modeling, drug screening and regenerative medicine.



The similar properties of iPSCs to Embryonic Stem Cells (ESCs) allow bypassing the ethical concerns regarding ESCs. It opens alternatives for applications in personalized medicine as iPSCs are the inexhaustible source and can be maintained in lab conditions. iPSC models are being used to study the stem cell properties, drug screening, and epigenetics during development and the differentiated iPSCs are being used to create various disease models which are generally hard to obtain. However, years of research on iPSCs have not yet yielded clinical applications because of the various challenges of this technology. The reprogramming process requires a lot of manual work and process errors are unavoidable.

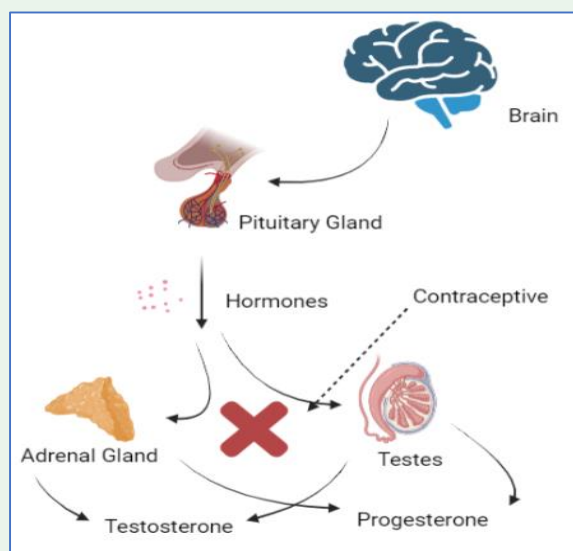
In addition, the components, media, infrastructure, and specialization required are expensive and not every lab can afford them. A major drawback associated with the iPSCs is the incorporation of c-Myc which is an oncogene. To avoid this, a team of researchers has substituted c-Myc with Cyclin D1 which makes iPSCs safer for use in humans without the fear of the effects of the oncogenic gene. Undoubtedly, iPSC technology opens new avenues in research and shows promising future applications.

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1. Alvarez-Palomo, A. B., Requena-Osete, J., Delgado-Morales, R., Moreno-Manzano, V., Grau-Bove, C., Tejera, A. M., Otero, M. J., Barrot, C., Santos-Barriopedro, I., Vaquero, A., Mezquita-Pla, J., Moran, S., Naya, C. H., Garcia-Martínez, I., Pérez, F. V., Blasco, M. A., Esteller, M., & Edel, M. J. (2021). A synthetic mRNA cell reprogramming method using CYCLIN D1 promotes DNA repair, generating improved genetically stable human induced pluripotent stem cells. *Stem cells (Dayton, Ohio)*, 39(7), 866–881. <https://doi.org/10.1002/stem.3358>
2. Takahashi, K., & Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell*, 126(4), 663–676. <https://doi.org/10.1016/j.cell.2006.07.024>

Contraception – mutual obligation

by Shivangi Paliwal, Dr TMA Pai PhD Scholar



Ladies have numerous choices for birth control, extending from oral pills to transdermal patches to intrauterine devices, and eventually as a result, they bear most of the burden of anticipating pregnancy. But men's birth control alternatives — and, thus, obligations — seem before long be growing. As of now, men have two successful choices for birth control: male condoms and vasectomy. However, one is susceptible to failure whereas other is nearly irreversible. So, it is required for men to have an efficient, reversible but long-lasting birth control measures, almost like the birth control pill for women. Current reports suggest a non-hormonal male contraceptive option that successfully anticipates pregnancy in mice, without any evident side effects.

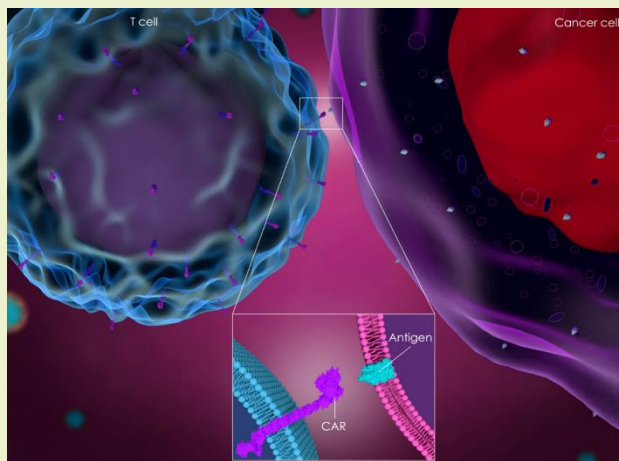
To evaluate the safety and tolerability of effective contraception in male subjects, researchers tested the synthetic orally active anabolic androgen steroid, 11 β -methyl-19 nortestosterone 17 β -dodecyl carbonate. The result suggests that the levels of the two hormones required for sperm production have dropped significantly, and additionally can be reversed by terminating treatment. Male spermatogenesis is affected as synthetic analog of testosterone mimics the combined effects of androgen and progesterone. The overall effects of low testosterone were minimal because the analog mimicked systemic hormone, but were insufficient to support sperm production in the testes.

Current advances in contraceptives for men aim to develop two oral medications, 11- β , MNTDC and dimethandrolone undecanoate, in order to make rapid progress in this area. Reported side effects include acne, fatigue, and headache in about 66% of subjects. Safety studies also revealed the idea of men of today's generation that they are not determined to stop taking pills, regardless of side effects, and want to have an equal share for the contraceptive responsibilities with women.

References:

1. <https://www.livescience.com/65078-male-birth-control-pill-tested-safety.html>
2. *Virtual Mentor*. 2012;14(2):146-151. doi: 10.1001/virtualmentor.2012.14.2.msoc1-1202.

CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers''



CAR-T cell therapy: 3D renders of Interaction of CAR-T cells with a cancer cell (Source: The Doctors Weighs In)

Historically, the procedures like surgery, radiotherapy, and chemotherapy have been the foundation for many years for treating various types of cancer. In contrast to this, the last decade saw the emergence of a new promising cancer treatment called, Chimeric Antigen Receptor (CAR) T-cell therapy, a type of immunotherapy that basically trains and strengthens the patient's own white blood cells to fight back and kill tumors, for treating advanced hematological malignancies. Thanks to the dedicated research which utilized 60 years of knowledge and a deep understanding of genetic engineering and antibody therapy which resulted in therapeutic efficacy with response rates of up to 90% in patients with relapsed/refractory B-cell acute lymphoblastic leukemia and up to 60% of patients with B-cell non-Hodgkin's lymphoma. Following this, since 2017, as many as six CAR-T cell therapies have been approved by the US FDA thus generating a lot of excitement among clinicians and researchers worldwide in eradicating the advanced liquid tumor.

However, despite these successes, CAR-T cell therapy has come under severe criticism in terms of cost with the recently approved therapy running between 5-10 Cr. Nevertheless, the CAR-T cells have got the tag of "living drugs" which helps to orchestrate the immune system and directly kill the cancer cells with higher success. Although CAR-T cell therapy has become a standard treatment in western countries, its adoption in India has not yet taken place at a full scale owing to its cost and the manufacturing complexity of CAR-T cells. Recently, to promote and support the development of CAR-T cell therapy, BIRAC and DBT have taken several initiatives and schemes with an overall aim to bring down the cost to 20 lakhs so that millions of patients can afford the cost. The year 2021 has been historical for India as The Tata Memorial Hospital and IIT Mumbai teamed up together to introduce the first CAR-T cell therapy at the Bone Marrow Transplant unit at ACTREC, Tata Memorial Centre in Mumbai with a manufacturing facility located in Bioscience and Bioengineering department of IIT Mumbai. This therapy is being carried out under the supervision of Dr. Gaurav Narula, TMC, and Dr. Rahul Purwar, IIT Mumbai. Apart from these initiatives, many private companies have jumped into the foray. Recently, companies like Dr. Reddy's with its partner Shenzhen Pregene Biopharma and Dr. Kiran Mazumdar Shaw through her start-up, Immuneel have taken the initiative to bring affordable CAR-T therapy to India. Domestically, though there has been exciting news around the corner with many initiatives with lots of collaborative effort both from public and private entities, several major hurdles still exist which must be addressed moving forward to fulfil the promises the therapy offers.

Interactive events

An interactive evening for the faculties, research scholars and staff was organized by the Cultural Program Committee, MCBR in the early weeks of June. Everyone participated and enjoyed *Dumb Charades* in that event. It was followed by consuming delicious *Pav Bhaji* and *Aam panna* (unripe mango juice), all prepared by our PhD students.



Participation in social works



Dr. Raviraja N S is currently the Director, International Services of Rotary Club Manipal Town (RCMT) and Zonal Coordinator of Skin and Tissue Donation, Zone IV, Rotary District 3182. MAHE and RCMT felicitated AKS Rtn Dr. Vasanth Prabhu (USA) for his contribution towards establishing the skin bank at Kasturba Hospital, Manipal.

Ms. Mrunmayi Gadre, one of our Dr. TMA Pai PhD Scholars, was very happy to be a part of this VSO event. She said, “this being my first I was very excited and also nervous to see how they really work. The event I went to was BEACH ADOPTION on 26th June 2022, Sunday”.

There were around 26 participants along with 4 helping hands and 5 Government personnel. They were taken to the beach stretch between Malpe and Padukare by the university bus. The waste was segregated into several categories mainly being, plastic, glass, clothes and thermocol waste. “We spent 2 hours at the beach cleaning the shore, due to the high tides all the waste was pushed between the rocks, hence we all struggled to reach the waste but successfully collected 20 bags of waste”, she added.

Fun moments: Birthday celebrations at MCBR

MCBR celebrated the birthdays of one of our faculties and staff with cakes and claps!



20th May - Dr. Souvik Dey

26th May – Mr. Abhishek Kulal

Send your feedback and suggestions to mabr.mahe@manipal.edu



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