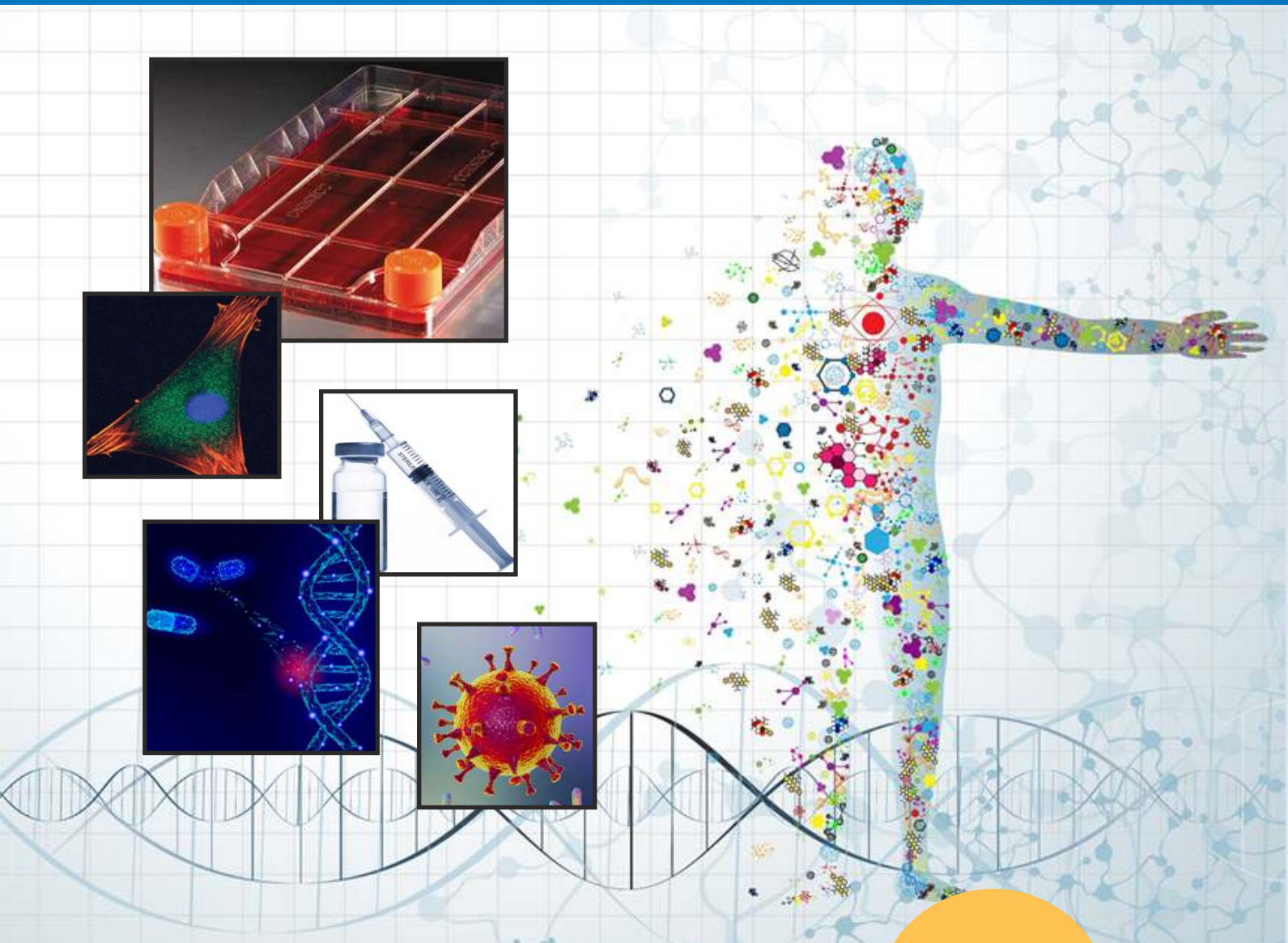


Biotheracues

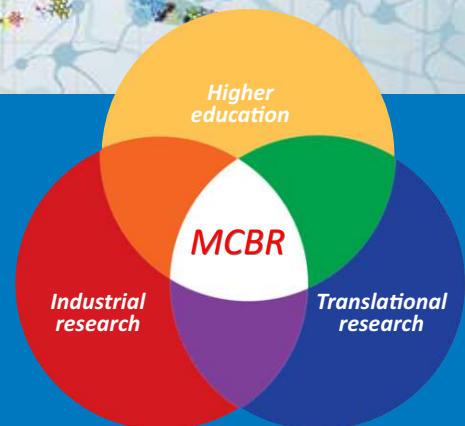
Vol: 1

Jan-March, 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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Message from the Chief Editor

I am delighted to introduce to you the inaugural issue of Biotheracues; it was certainly overdue since the inception of the Manipal Centre for Biotherapeutics Research (MCBR). It not only brings out the activities and events that have taken place in MCBR in the last quarter of 2021 till the end of March 2022, but also throws the spotlight on the various activities and achievements of our students and faculty members during this period. I would like to take this opportunity to inform you that admission to the first batch of M.Sc. in Biotherapeutics (by research) has started for the 2022-23 academic year. To date, this is the only such master-degree program available in Asia.



Dr Souvik Dey

This center has made steady progress in terms of building infrastructure for doing quality translational research work in the last six months. Concurrently with the inauguration of the Annexe building in February, MCBR also started its first industrial tie-up, with Suma Genomics, a start-up born in academia, fast expanding its footprint in the clinical arena of rare-disease diagnosis. We already have five enrolled students doing their doctoral research work at MCBR. The faculties and Ph.D. scholars of this centre have successfully hosted multiple webinars in this small frame of time. MCBR faculties also have participated in National and International level conferences by delivering invited talks and oral presentations to showcase their research work. They have also made active collaboration with other departments and colleges in MAHE. However, they are not only doing research and writing papers but also having their share of fun from time to time: they have rejoiced during birthdays with cakes and chocolates; we have celebrated National Science Day with entertaining and competitive quiz contests and cheered after winning the awards!

We envision MCBR becoming the cherished higher-education research centre in the field of biotherapeutics and the go-to research hub for industries to collaborate in the coming months and years. I sincerely hope this center will soon be buzzing with more student-faculty interactions and lead to bio-thera-cues in time to come.

Message from the Coordinator

On 15th October 2021, MAHE established 'Manipal Centre for Biotherapeutics Research (MCBR)' on marking another milestone in MAHE's pursuit towards promoting high-quality education and research. With the support of various funding agencies, collaboration of pharma and biopharma companies, MCBR envisions to carry out translational biological research leading to newer processes, affordable novel products and services to uplift the quality of life of common people. MCBR offers doctoral and postdoctoral programs, in addition to MSc (by Research) in Biotherapeutics to create skilled human resources required for the pharma and biopharma industries and research centres.



Dr Raviraja N S

Biotherapeutics Research is a rapidly developing area of science that continues to gain importance in the top ranking universities of developed countries. Biotherapeutics products include recombinant proteins and hormones, monoclonal antibodies (mAbs), cytokines, growth factors, gene therapy products, vaccines, cell-based products, gene-silencing/editing therapies, tissue-engineered products, and stem cell therapies. Biological drugs are one of the rapidly growing market segments that accounts for almost one-half of recent new drug approvals. Although biologics produced in developed countries provide hope for many unmet medical needs, their high costs pose an entry barrier to the developing markets. At MCBR, we envision developing safe, efficacious and affordable products in collaboration with industry partners.

I consider it my privilege to be the founder Coordinator of MCBR. I am proud to state that all the initial faculty at MCBR are foreign-trained in their respective research areas. I hope MCBR will emerge as one of the eminent centres of biotherapeutics research in this part of the globe.

Inauguration of Manipal Centre for Biotherapeutics Research

15th October 2021



The inauguration of the Manipal Centre for Biotherapeutics Research (MCBR), MAHE took place on 15th October 2021 by Mr. Anurag Bagaria, Chairman and CEO of Kemwell Biopharma, Bengaluru. He said “I am very happy to see that MAHE has taken the lead in the country to establish a dedicated centre for carrying out Biotherapeutics Research, a science that continues to gain momentum in the universities of the developed countries. I am confident that this centre will emerge as one of the eminent



centres in this part of the globe.” The Master of Ceremony was Dr. Sachin Kadam, praised MAHE for establishing a centre dedicated wholly to Biotherapeutics research. He expressed confidence in the institute and the vision of academic-industry collaborations in developing more products in this research area.



Dr Ranjan R Pai, Chairman of MEMG, Bengaluru was the *guest of honour*. In his speech, he stressed the need for the pharma companies to have more collaborative ventures with academic institutions to manage time and money more efficiently, and ultimately help in the country's development. The webpage of MCBR was launched by the Chief Guest Mrs. Vasanti R Pai. Dr. HS Ballal, Pro-Chancellor of MAHE shared the vision of MAHE in the field of Biotherapeutics. Lt. Gen. (Dr) MD Venkatesh, Vice-Chancellor of MAHE gave a brief overview of biotherapeutics and the aims of MCBR. Dr. Raviraja N S, Director of Corporate Relations and Coordinator of MCBR outlined



the aims of MCBR, the infrastructure and the need for academia and industries to work together in collaboration for mutual growth.

Dr Vasan Sambandamurthy, CEO of the *DBT Wellcome Trust India Alliance*, discussed the necessity of collaboration between industry and academics in biotherapeutics research. Dr. Mukesh Kumar, Vice President and Head of Clinical Research and Development at *Cipla Limited*, discussed the importance of academia-industry collaboration to consistently discover sustainable approaches to overcoming contemporary healthcare concerns. Mr. Manohar BN, Managing Director and Chief Executive Officer, *Stempeutics Research Pvt. Ltd.*, discussed the industry's present issues and the need for cost-effective new solutions. Dr. Sairam Atluri, co-founder of RCRI in Hyderabad, and Dr. Roberto Salvi, Lab Head at *Curio Biotech* in Switzerland, are in advanced stages of collaboration negotiations with MCBR and have offered their best wishes to the company. Dr. Manjunath S Muttigi, Assistant Professor, MCBR, closed the inauguration with a vote of thanks.

Activities at MCBR

Research progress

Publications:

1. **Raghavendra Upadhy***, Leelavathi N. Madhu*, Shama Rao and Ashok K. Shetty. Proficiency of Extracellular Vesicles from hiPSC - derived Neural Stem Cells in Modulating Proinflammatory Human Microglia: Role Pentraxin-3 and miRNA-21-5p. (In Press) *Frontiers in Molecular Neuroscience*.(IF: 5.63) (# shared contribution).
2. Namdev Dhas, Mónica C. García Ritu Kudarha, Abhijeet Pandey, Ajinkya Nitin Nikam, Divya Gopalan, Gasper Fernandes, Soji Soman, Sanjay Kulkarni, **Raviraja N Seetharam***, Ruchi Tiwari, Sarika Wairkar, Chandrakantsing Pardeshi and Srinivas Mutalik. Advancements in cell membrane camouflaged nanoparticles: A bioinspired platform for cancer therapy. *Journal of Controlled Release*, Volume 346, June 2022, Pages 71-97. <https://doi.org/10.1016/j.jconrel.2022.04.019>
3. SahithiAttaluri*, **Raghavendra Upadhy***, Leelavathi N. Madhu, Dinesh Upadhy, Maheedhar Kodali, Bing Shuai, Ashok K. Shetty. Cognitive and Mood Dysfunction in an Animal Model of Chronic Gulf War Illness is Linked with Altered Leukotriene Signaling in the Brain and Elevated Systemic Inflammation. (In Press) *Frontiers in Immunology*. (IF:6.29). (* shared contribution).
4. Soumyadeep Mukherjee, Arpita Kar, Paramita Paul, **Souvik Dey**, Avik Biswas and Subhasis Barik. In Silico Integration of Transcriptome and Interactome Predicts an ETP-ALL-Specific Transcriptional Footprint that Decodes its Developmental Propensity. (In Press) *Frontiers in Cell and Developmental Biology*. (IF: 6.68).
5. **Sachin Kadam**, Tareeka Sonawane, Aakanksha Patil, Abhishek Tomar (Jan - March 2022) "The best COVID-19 Vaccine: Understanding the conundrum behind comparing vaccines". *JKIMSU*, Vol. 11, (No. 1): Page 1- 13. ISSN 2231-4261.

Hosting of webinars

- ▶ **Webinar on “Stem Cell Therapy for Diabetes-Myth or Reality” on 15th November 2021:** Ms. Shweta Verma was the Master of Ceremony and hosted the webinar. The webinar was inaugurated by Dr. PLNG Rao, Pro-Vice-Chancellor, Health Sciences, MAHE. Dr. (Lt. Col.) Pawan Kumar Gupta was the invited speaker. He has served the Armed Forces for 24 years and has a vast experience in Pathology, Haematology, Transfusion medicine and Stem Cells. He spoke about the current trends in stem cell therapy for diabetes, and the future prospects in the same field. The webinar was concluded by a question and answer session by faculties and research scholars. The final vote of thanks was given by Dr. Sachin Kadam, Associate Professor, MCBR.
- ▶ **Webinar and panel discussion on 3D Bioprinting on 2nd March 2022 with invited speakers from Next Big Innovation Labs (NBIL):** Ms. Shivangi Paliwal was the Master of Ceremony and hosted the webinar. Speakers were Mr. Piyush Padmanabhan, Co-CEO and Co-Founder, NBIL and Mrs. Pooja Venkatesh, Head of Biotechnology, IP and Regulatory effect, NBIL. The webinar was concluded by a panel discussion about the future prospects of 3D Bioprinting and a vote of thanks by Dr. Manjunatha SM, Assistant Professor, MCBR.

Faculty Corner

- ▶ Prof. Raviraja NS chaired a session in BIOTEM-2021, an annual SBAOI and STERMI conference in December 2021.
- ▶ Dr. Souvik Dey participated in the International Virtual Workshop 'Bioelectronic Medicine', jointly organized by IIT (BHU) Varanasi and IISc

Bangalore and co-hosted by Henry Royce Institute, University of Manchester, UK on December 16, 2021.

- ▶ Prof. Raviraja NS was a Distinguished Resource Person & Speaker at the National Seminar organized by Brainware University and IAPST on Dec 21, on “BIOMEDICAL RESEARCH UPDATES”.
- ▶ Dr. Souvik Dey delivered an invited talk, in person at the 38th Meeting of SRBCE cum National Conference on Reproduction and Endocrinology held between 28th-30th December 2021 on the topic entitled Relationship of GSK3 α and calcineurin in the regulation of male fertility.
- ▶ Dr Sachin Kadam, Associate Professor, MCBR, delivered a talk at the "International Conference on Reproductive Healthcare and 32nd Annual Meeting" organised by the Indian Society for the Study of Reproduction and Fertility (ISSRF) on 12th Feb 2022. The title of the talk was: Effect of Platelet Rich Plasma factor in female reproductive health and menstruation.
- ▶ Dr Souvik Dey made an oral presentation at the 32nd Annual Meeting of the ISSRF cum International Conference on Reproductive Healthcare held between 11-13th February 2022 on the topic entitled PKAC α 2, PP1 γ 2, PPP3R2/CC & GSK3 α forms a quad to regulate male fertility in mammals.
- ▶ Dr Souvik Dey successfully completed a two-month certificate course on Bioinformatics conducted by MSLS, MAHE in February-March, 2022.

Inauguration of Annexe Building

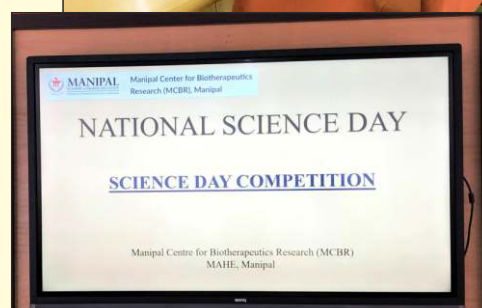


On 1st February 2022, MAHE Vice-Chancellor Lt Gen (Dr) M D Venkatesh and MAHE Pro Vice-Chancellor (Health Sciences) Dr M Venkatraya Prabhu inaugurated the MCBR Annexe building. Numerous University leaders attended the inauguration ceremony, including Capt. Belliappa, Col. Prakash Chandra, Dr. Shrihari Upadhyaya, Vittaldas Bhat, and Jai Vittal. MAHE Vice-Chancellor extended his best wishes for potential industry-academia collaborations. He wished Suma Genomics Pvt. Ltd. a prosperous relationship and welcomed them to the first level of the annexe

building. Suma Genomics is the brainchild of Dr Girisha Katta, professor and head of the Department of Medical Genetics at KMC, Manipal. The start-up was incubated and graduated from Manipal Universal Business Technology Incubator (MUTBI). Dr Raviraja NS discussed the strategic collaboration between Suma Genomics and MCBR and the resulting papers and patents of high quality.

National Science Day celebration

We celebrated the National Science Day on 28th February through multiple quiz contests organized by our Ph.D. students and competed by our faculties and technical staff. Both individual and group events were held. We thank Jahnvi, Shweta and Shivangi for organizing such an entertaining quiz contest.



Notable visitors

Manipal Centre for Biotherapeutics Research had visits from many eminent professors and scientists. Each visit provided an overview of the MCBR's infrastructure, ongoing activities, and research priorities. The visits also involved interactions with faculties and research scholars and potential research collaborations. Some of the visitors are enlisted here:



Dr Anita Aggarwal, Scientist F, Department of Science and Technology, Govt of India (*picture 1*) and Dr. T Lazar Mathew, Senior Advisor, MCHP and DAMP, MAHE (*picture 1*)



MEMG Chairman Dr. Ranjan R Pai and MAHE Vice-Chancellor Lt Gen (Dr) MD Venkatesh (*picture 2*)



Professor Bikramjit Basu, a *Bhatnagar* Awardee from Materials Research Centre Indian Institute of Science, Bengaluru (*picture 3*)



Dr Muralidhara Padigaru, Vice President -R&D, Omniactive Health Technologies Limited



Dr Uday Kumar K,
Vice President, Stempeutics
Research, Bengaluru



Dr. Laxminarayana Kurady Bairy, Dean,
RAKCOMS and Chief Academic Officer,
RAK Medical and Health Sciences
University, UAE



Mr R Sundararajan (Chairman),
Mr Saikat Ray (CEO), Mr
Vijayaraghavan (Scientific
Director) from Velbiom
Probiotics, Bengaluru



Ms Pooja Venkatesh & Mr Piyush Padmanabhan, Co-CEOs -Next Big Innovation Lab, Bengaluru.

Industry tie-up

Suma Genomics, a faculty-entrepreneurship of Dr Girisha Katta, started its operation at MCBR on February 01, 2022. It provides testing services for rare disorders, cancers and precision medicine, and conducts cutting-edge research in genomic technology. Suma Genomics staff will serve as guest teachers at MCBR, while M. Sc. (by research) in Biotherapeutics students from MCBR will complete internship projects at Suma Genomics.

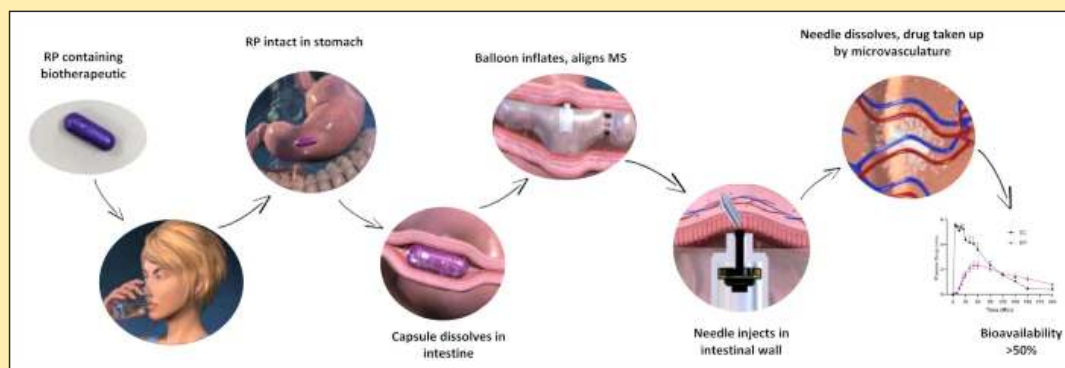


Blogs

Robotic Pills as an Alternative to Painful Injections for Biotherapeutics Drug Delivery

by *Shweta Verma, Dr. TMA Pai PhD Scholar*

Biotherapeutics are active substances isolated from a biological source and show high efficiency. The administration of these biological drugs is dominated by injections. Despite numerous attempts, their oral delivery is unsuccessful either due to degradation in the digestive environment due to proteases and enzymes or poor absorption in the intestine. Also delivering drugs with protease inhibitors and enhanced permeation enhancer reduces bioavailability by less than 1%. Thus, convenient oral delivery of biotherapeutic drugs is a goal for patients for better therapeutic outcomes. In order to overcome the limitation of the current therapy, a robotic pill for drug



delivery has been designed that is versatile and orally ingestible using materials classified as food grade, food additive or GRAS by FDA. This pill proposed to replace painful injectable medications for chronic diseases. A team in Rani Therapeutics designed RP made from ingestible polymers to safely inject drug to small intestine. Drugs with protein nature are not able to pass through stomach if taken orally as they get degraded by the acidic nature of stomach. The idea of robotic pills was to invent pills as effective as injected drugs that can withstand stomach acids and enzymes and deliver drug at the target site without causing pain to the patient.

RPs can protect the pill from degradation in gastrointestinal tract and gets self-injected in the intestine as safe and pain-free injection. RP is a mechanical swallowable device enclosed in capsule shell composed of methylcellulose. It is enteric coated to prevent degradation in acidic environment of stomach. The pH-sensitive enteric-coating was used in order to protect the RP from dissolution. The sterile biotherapeutic drug is loaded precisely in hollow dissolvable needle made of polyethylene glycol within a microsyringe that is attached to folded balloon that inflate autonomously.

Upon clinical studies of RP in healthy humans showed reliable drug delivery up to 25 to 80% with rate of success related to balloon size directly. In either study fasting and fed condition didn't showed any effect on deployment of drug through RP. These studies showed safety, versatile performance and oral drug delivery in healthy volunteers. The safety and reliability of robotic pills is yet to be determined by long term studies with repeated administration in patients with chronic diseases. Studies showed that there was no discomfort or pain on administration, deployment or drug delivery through needle and all the remains from device were safely excreted. Further studies in the larger patient population with repeated administration and with different biotherapeutics drugs can confirm the reliability of robotic pills. And this platform can offer an alternative drug delivery platform for many patients with chronic disease and frequent administration of painful parenteral injections.

Reference and Image courtesy:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8677648/?report=classic>

Digital Therapeutics

by Shivangi Paliwal, Dr. TMA Pai PhD Scholar

Digital therapeutics, according to the Digital Therapeutics Alliance are the products that work on the basis of evidence & provide interventions guided by high-quality software programs to patients in order to prevent, manage or treat a medical disease or disorder. Digital therapeutics are designed to provide ease to patients so that they can have greater control over their care, along with providing clinical outcomes. Through the use of this, clinicians can collect, synthesize & analyze patient data for better outcomes & lesser medical interventions.

the aid of communication with an external sensor. The impact of digital therapeutics in improving the outcomes with minimized medical intervention is found to have statistical significance on health-related behavior. Currently, there is an ongoing development of these digital therapeutics for evaluating the efficacy of treatment on metastatic breast cancer. The digital therapeutics will monitor the patient's symptoms & vital signs & will alert the physician based on calculations & experts' suggestions about the efficacy of treatment.



Digital therapeutics are utilized for a variety of conditions. It makes use of cognitive-behavioural therapy to motivate patients to modify their lifestyles. This method has been included for the management & prevention of a variety of lifestyle-related diseases such as type II diabetes, obesity, substance abuse, hypertension, anxiety, depression, insomnia & other kinds of diseases like Alzheimer's disease, dementia, etc. The major focus of digital therapeutics is on diabetes & obesity prevention & management. The methodology employed for digital therapeutics involves sending notifications & reminders to the patients to make lifestyle changes. The lifestyle-related modifications have the potential of risk minimization for obesity or diabetes. It also involves a method that deals with the administration of an ingestible radio tag to efficiently monitor the efficacy of the medicine with

Although, there is a stringent regulatory system for approval of digital biotherapeutics as it has an application of the scientific approach for analyzing the patient data for better outcomes.

Digital therapeutics are designed to solve the highest areas of unmet needs of patients using a dynamic combination of precision medicines & an entire range of digital tools operated by AI & longitudinal health data & scientific evidence.

Reference and Image courtesy:

<https://www.astrazeneca.com/what-science-can-do/topics/clinical-innovation/digital-therapeutics-augmenting-patient-health-outcomes.html>

Global research update

Dual Stem Cell Transplantation completely cures HIV infected woman



The International Maternal Pediatric Adolescent AIDS Clinical Trial Network or IMPAACT's P1107 reported the first instance of HIV cure in a woman living with HIV who underwent a dual stem cell transplant (umbilical cord blood and half-matched bone marrow) for the treatment of acute myelogenous leukemia. At the 29th Conference on Retroviruses and Opportunistic Infections, the researchers from IMPAACT P1107 presented the case study in oral abstract form (CROI 2022). As a result, she has been HIV-free for 14 months and has not needed to resume ART at 37 months after donation as part of this study. In addition, in 2017, she was diagnosed with leukemia and had dual stem cell therapy, which resulted in her complete remission.

For the therapy of cancer, hematological disease, or another underlying disease, researchers in this observational study used cord blood stem cells mutated in the CCR5 gene. CCR5 co-receptors are missing from these T cells as a result of this genetic mutation. It is hypothesized that chemotherapy and a stem cell transplant using CCR5-mutated stem cells can modify the immune system in such a way that it becomes genetically resistant to HIV infection in individuals with cancer or other disorders. CCR5-mutated umbilical cord cells and adult stem cells were used in this example, which is particularly challenging for people of African or mixed heritage to achieve.

Only two cases of HIV remission or cure following stem cell transplantation have been documented prior to this investigation. The Berlin patient was the first to come

forward in 2009. In this case, the patient had acute myelogenous leukemia. There is a second example that has just come to light, known as the "London patient," in which an HIV-infected man who received a bone marrow stem cell transplant has been HIV-free for more than 30 months. Another woman's HIV remission implies that people with HIV who also need stem cell transplantation for another ailment can benefit from a dual transplant method.

In this example, stem cell transplantation has been proven to be a viable method of curing HIV, but it is important to stress that this is an intrusive and risky medical treatment that cannot currently be scaled up to treat the millions of HIV-infected persons in the globe. A stem cell donor for a patient with a CCR5 mutation, which occurs in less than one percent of people, is extremely difficult to come by.

Reference and Image courtesy:

<https://www.who.int/news/item/24-03-2022-first-case-of-hiv-cure-in-a-woman-after-stem-cell-transplantation-reported-at-croi-2022>

Fun moments: Birthday celebrations at MCBR

MCBR celebrated the birthdays of research scholars, technical staff and faculties by sharing a cake (or two!) and best wishes!!



- 1st November – Ms. Shivangi Paliwal
- 28th January – Dr. Manjunatha SM
- 3rd March – Mr. Prasad
- 4th March – Prof. Raviraja NS
- 23rd March – Dr. Raghavendra



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