8 Feb 20

MEMORANDUM OF UNDERSTANDING

Mr. Hari Singh

Between

ICMR CENTRE FOR INNVOATION AND BIO-DESIGN (CIBIOD), PGIMER, CHANDIGARH

AND

MEHR CHAND MAHAJAN DAV COLLEGE FOR WOMEN, CHANDIGARH

This Memorandum of Understanding is made on 8th Feb 2020

BETWEEN the ICMR CENTRE FOR INNVOATION AND BIO-DESIGN (CIBIOD), PGIMER, CHANDIGARH, hereinafter referred to as CIBioD, which expression shall mean and include its successor-in office and assigns and represented by its representatives.

AND

The Mehr Chand Mahajan DAV College for Women, Chandigarh is the executive body of the DAV Trust and Management Society, which, subject to the overall control of the society, conducts the day to day affairs of the society. It controls the administration and finances of its around 800 institutions. It being a nerve centre, formulates the policies, plans and procedures to shape the destiny of the DAV network.

At the DAV-CMC, it is a constant endeavour to modernize the system facilitating congenial working environment. Regular meetings of Office Bearers bring about meaningful decisions taken by consensus emanating from objective, dispassionate and unbiased considerations. The huge organizational set up is monitored by capable, experienced and dynamic personalities.

BACKGROUND

ICMR Centre of Innovation and Bio Design (CIBioD) aims to promote innovation inmedical devices and instruments by creating a conducive ecosystem with theinvolvement of multiple premier technology institutes in the region in collaboration with Post Graduate Institute of MedicalEducation and Research(PGIMER), Chandigarh with following sub-goals like innovation

centre for devising indigenous technologies, instruments and devices for affordable health care, Manpower training for researchers, clinicians and faculty working in area of medical sciences etc.

AND WHEREAS, Mehr Chand Mahajan DAV College for Women, Chandigarh

The DAV movement was founded in the sacred memory of **Maharishi Dayanand Sarswati, the founder of the Arya Samaj**, a unique figure of Indian nationalism, the harbinger of a new era. Imbued with Vedic scholarship and humanism, Swamiji was an embodiment of faith in God, purity, truth and moral courage. The great religious missionary was a forerunner in the field of women's emancipation. The D.A.V. movement, named after him is a bold attempt in the direction of amalgamating the best in Indian culture and Western scientific learning.

The movement owes its existence to the sacrifices of the men of vision and action like Mahatma Hans Raj, Lala Lajpat Rai and Pandit Guru Dutt Vidyarthi. Over the years, the D.A.V. College Trust and Managing Society has grown into the biggest Non-Government Educational Organisation in the country. The D.A.V. Managing Committee is running more than **800 educational institutions** in India and abroad

OBJECTIVES

Both CIBioD and Mehr Chand Mahajan DAV College for Women, Chandigarh are, now

- Recognizing the importance of research & development, innovation and training in the areas related to medical devices, instruments, affordable healthcare, bio-design and other allied areas, and facilitate innovation and deployment of solutions.
- Appreciating the need for integrating the reservoir of highly qualified manpower in the fields of expertise available at both places and foster relationship between academia and practitioners.
- Desiring to amalgamate their efforts by pooling their expertise and resources and to form a nucleus for promoting Research & Development and training by exploiting the unique expertise, intellectual and infrastructural capabilities of both the parties.

FINANCIAL TERMS

There is no direct financial obligation on either institution unless specifically agreed to. The financial requirement of individual institutions for joint project proposals will be separately mentioned in joint projects while submitting to funding agencies. Before start of any activity, financial terms will be decided pertaining to that particular activity in advance.

DURATION

This agreement shall come into effect on the day of the approval by both institutions with an initial duration of three years.

TERMINATION

Either institution may terminate this agreement provided that a written notice to this intent is given to the other at least three months prior to the termination.

INTELLECTUAL PROPERTY RIGHT (IPR)

Rights regarding publications, patents, royalty, ownership of software, design, product developed, etc. under the scope of this MOU, shall be decided by the two parties by mutual consent.

Intellectual Properties, which are in possession of prior to this agreement or to be acquired outside the collaborative project with Mehr Chand Mahajan DAV College for Women, Chandigarh, will remain the exclusive property of Mehr Chand Mahajan DAV College for Women, Chandigarh.

Intellectual Property/ies that may come about in the course of execution of collaborative project(s) between CIBioD and Mehr Chand Mahajan DAV College for Women, Chandigarh will be the joint property unless otherwise mentioned clearly in project proposals or project specific agreements.

CONFIDENTIALITY

a) During the Term of MOU, either party may provide to the other proprietary and confidential information that it considers essential for the conduct of any PROJECT at their sole discretion.
b) PROPRIETARY INFORMATION for the purposes of this AGREEMENT shall include all data, samples discoveries, inventions, technical information, reports, known-how and other information related to and disclosed by either party to the other in any form of written material and it shall be the duty of the receiving party to maintain its confidentiality.
c) The Mehr Chand Mahajan DAV College for Women, Chandigarh and CIBioD agree to hold PROPRIETARY INFORMATION in confidence and to project it against disclosure to the public and third parties. Accordingly, both Post graduate Government college for Girls and CIBioD shall employ protective measures fully commensurate with those used by them to protect their own trade secrets and other confidential information from disclosure to the public and to third parties, but in no event less than ordinary degree of care required by law to preserve the secrecy of information that under such law in deemed confidential. By way of example, such efforts will include the act of obtaining the execution of suitable confidentiality agreements from other parties and from other persons to whom such information is disclosed in the course of execution of the PROJECT and to retrieve the connected documents on completion of the project where given for the same.
d) The Mehr Chand Mahajan DAV College for Women, Chandigarh and CIBioD agree to use PROPRIETARY INFORMATION only for the specific project during the term of such project.
e) The Mehr Chand Mahajan DAV College for Women, Chandigarh and CIBioD agree not to copy, reproduce or otherwise reduce to writing any Part of PROPRIETARY INFORMATION except and only as may be reasonably necessary for the PROJECT.

f) INFORMATION disclosed by either party to the other in the form of result of the study/ research originating from the projects under the agreement shall be treated as confidential and should not be shared with any third party, including and country, without the expressed permission of giving party.

g) Both Mehr Chand Mahajan DAV College for Women, Chandigarh and CIBioD will be free to publish research results out of projects under this agreement that does not contain proprietary information. In case it contains proprietary information decision to publish will be on a mutual consent basis so as to unsure protection of the related intellectual property.

h) The non-disclosure clause will survive five years from the date of expiry of this MOU.

CO-ORDINATION COMMITTEE

The following will constitute the Coordination Committee to monitor and review the collaborative program (s) between the two institutions:

a)Representative of Mehr Chand Mahajan DAV College for Women, Chandigarh or his nominee(s)

b) ICMR Centre For Innovation & Bio-Design, PGIMER, Chandigarh or his nominee(s)

The Coordination Committee shall:

a) Review the progress of the identified programs (at least twice a year)

b) Consider new R&D and training proposals for the collaboration and implementation on case to case basis including IPR and financial arrangements

c) Consider the addition/deletion of areas of co-operation between the two entities during review.

d) Consider the continuance of the MoU

Any difference of opinion arising on any matters under the preview of the MoU will be referred to the Representative of Mehr Chand Mahajan DAV College for Women, Chandigarh and Representative of CIBioD for resolution through mutual consent.

Both the parties hereto set their hands and signed the agreement on the day, month and year mentioned above. It has been executed in two originals; one has been retained by CIBioD and the other by Mehr Chand Mahajan DAV College for Women, Chandigarh.

8/2/20

Representative of

Mehr Chand Mahajan DAV College for Women, Chandigarh,

Representative of

CIBioD, PGIMER, CHANDIGARH

A Golden Opportunity for Students / Researchers / Faculty

SHORT TERM ATTACHMENT PROGRAMME

Registration Begins : March 01st, 2021

Registration Ends : March 15th, 2021

Salient features of this Programme :

《 Learning about Innovation, Incubation, Prototyping, Clinical Validations & Commercialization 》

《 Peronal Interaction Programme (PIP) with experts of MedTech Industry 》

《 Flexible hours of Training in Virtual Mode 》

《 Certificate will be given after successful completion of the Attachment 》

CIBioD

Register Now

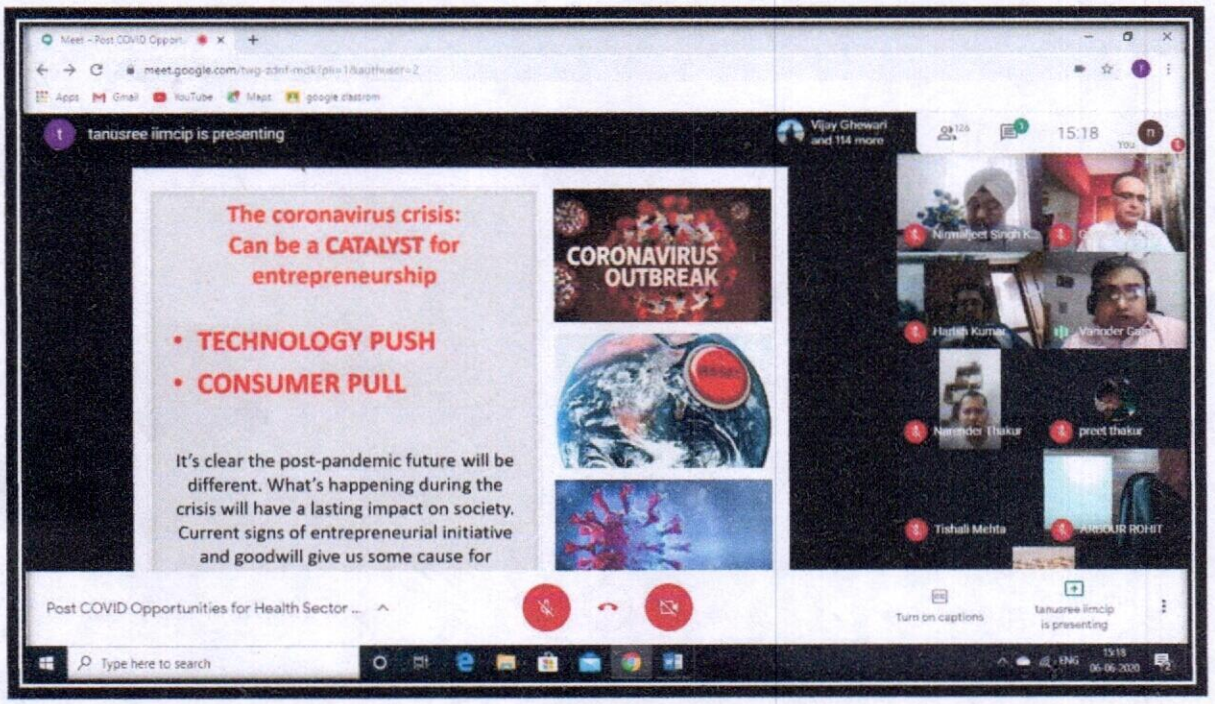
https://forms.gle/J8TFu4FEKHx2LyRi6

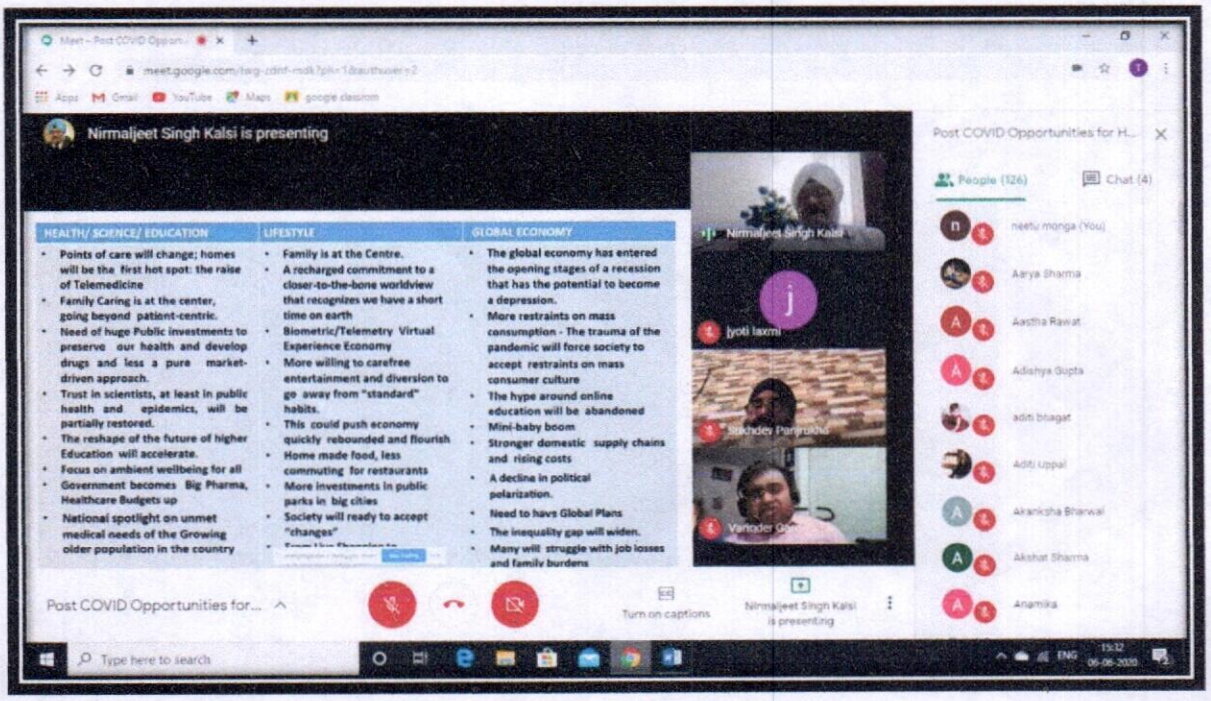
To know more about CIBioD and the Programme, visit our website

www.cibiod.in

REPORT OF THE ACTIVITIES ATTENDED BY FACULTY AND STUDENTS OF MEHR CHAND MAHAJAN DAV COLLEGE FOR WOMEN, CHANDIGARH UNDER THE AEGIS OF ICMR- CENTRE FOR INNOVATION AND BIO-DESIGN (CIBioD), PGIMER, CHANDIGARH

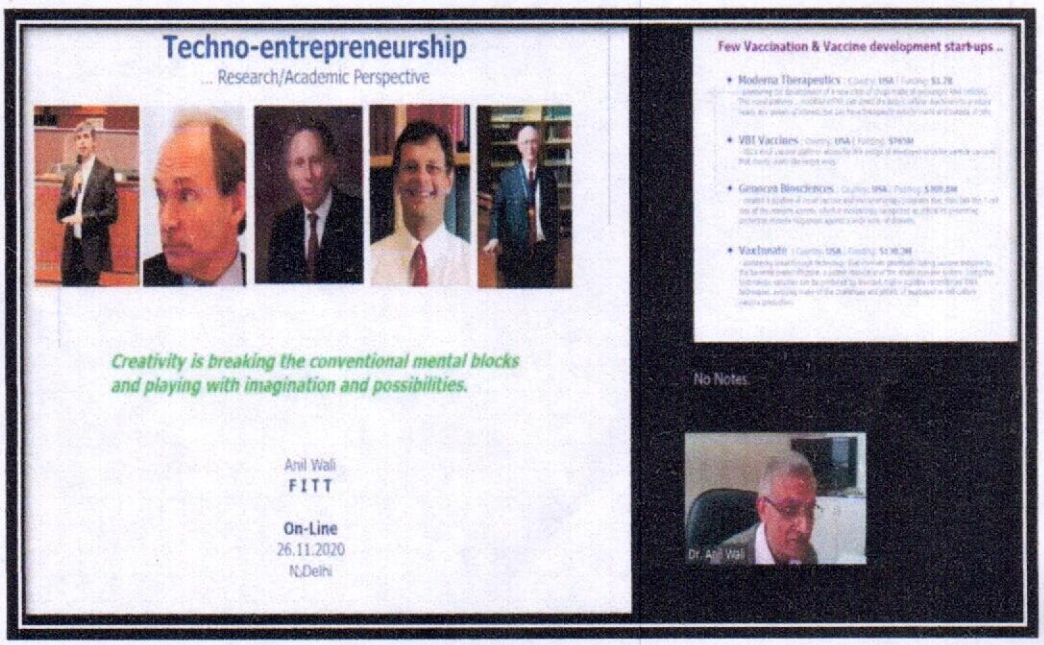
- Three faculty members and 64 students of B.Sc. Medical and B.Sc. MFT attended an informative discussion session on **"Post Covid opportunities for Health Sector start-ups"** by Dr.Nirmaljeet Singh Kalsi, IAS (Retd.), Former additional Chief Secretary, Punjab and Dr.Varinder Garg, MBBS, MD (Radiology), Principal Investigator CIBioD, PGIMER on 06.06.2020.

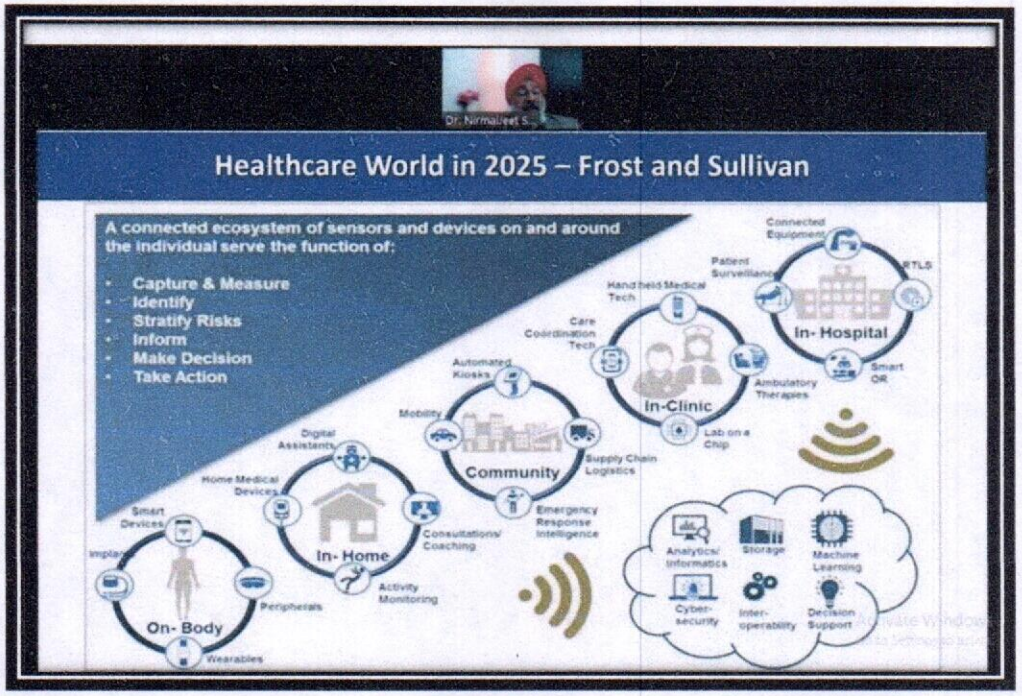


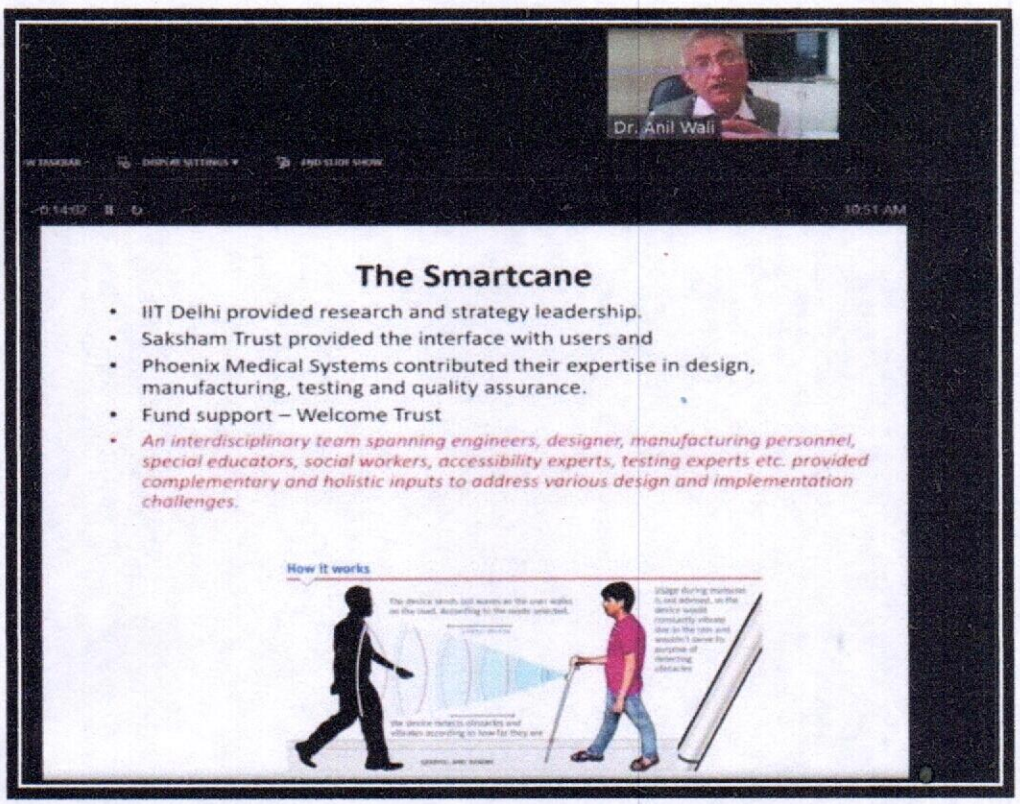


- Rashi Jain, MeghanaGoel, Aarya Sharma of B.Sc. Medical &Cheshta Kamboj, Ramandeep Kaur, Mehakleen Kaur of B.Sc. (Microbial & Food Technology) got selected for an Attachment Program of ICMR- Center for Innovation & Bio-design (CIBioD), PGIMER, Chandigarh held in June & July 2020. The program was a multidisciplinary initiative designed to incubate, prototype and commercialize novel ideas in Health care.

- Five faculty members and 18 students attended a 2 days Virtual International Summit on "Atmanirbhar Bharat: India as Manufacturing Hub for Global Health"hosted byICMR-Centre for Innovation and Bio-Design (CIBioD), PGIMER, Chandigarh in collaboration with India-EU ICT standardisation project on November 26-27, 2020. This international summit aimed to bring all the stakeholders on common platform for generating awareness about innovation and entrepreneurship in Medical devices and Telehealth.




Dr. Nirmaljeet S...
Healthcare World in 2025 – Frost and Sullivan
A connected ecosystem of sensors and devices on and around the individual serve the function of:
Capture & Measure
Identify
Stratify Risks
Inform
Make Decision
Take Action
Connected Equipment
Patient Surveillance
RTLS
Hand held Medical Tech
Care Coordination Tech
In- Hospital
Smart OR
Ambulatory Therapies
In-Clinic
Lab on a Chip
Automated Kiosks
Mobility
Digital Assistants
Community
Supply Chain Logistics
Home Medical Devices
Emergency Response Intelligence
Smart Devices
Consultations/ Coaching
In- Home
Activity Monitoring
Peripherals
On- Body
Wearables
Analytics/ Informatics
Storage
Machine Learning
Cyber-security
Inter-operability
Decision Support


Dr. Anil Wali
10:51 AM
The Smartcane
IIT Delhi provided research and strategy leadership.
Saksham Trust provided the interface with users and
Phoenix Medical Systems contributed their expertise in design, manufacturing, testing and quality assurance.
Fund support – Welcome Trust
An interdisciplinary team spanning engineers, designer, manufacturing personnel, special educators, social workers, accessibility experts, testing experts etc. provided complementary and holistic inputs to address various design and implementation challenges.
How it works

Dr. Varinder Garg
MD (Radiology)
Principal Investigator

Date: April 24, 2020

Inviting Applications for Short Term Attachments at Center for Innovation & BioDesign (CIBioD) at PGIMER, Chandigarh

Headquartered at Asia's premier clinical research institute, **PGIMER, Chandigarh**, **the Center for Innovation & BioDesign (CIBioD)** is an initiative of Indian Council of Medical Research aimed at promoting research, innovation and entrepreneurship in Indian Healthcare System. The ICMR-CIBioD is first Healthcare Innovation Hub and Start up Incubator established by ICMR at a premium medical research institute and hospital of global repute in India with a structured Incubation/ Acceleration/ Fellowship Program for Innovators and Researchers in field of Medicine, Pharma, Biomedical Devices, Engineering, Software and Instruments from across the country.

It is a golden opportunity for the young and bright Science/ Engineering/ Management/ Medicine students, who want to learn and get involved with cutting edge health related technologies, currently pursuing their degree/ diploma programmes or who have passed out in the last couple of years to **APPLY FOR SHORT TERM ATTACHMENTS at ICMR-CIBioD, Advanced Cardiac Centre, PGIMER, Chandigarh (UT)** (www.cibiod.in).

Interested persons should register themselves for the short-term attachment via e-mail. Some **salient features** of the attachment are:

- Learning about **Innovation, Incubation, Prototyping and Commercialization** of Novel Ideas in Affordable and Scalable Health Care.
- Primary areas of learning will be in the **usage of knowledge of technology and social science** in medical profession for the benefit of the overall society.
- Students will get a chance to work on the live projects in groups comprising of **Faculty, Research Scholars, Entrepreneurs and expert from Industry**.
- Some students based on the performance may also get the exposure to work in the best research labs of the country.
- **A Certificate and Letter of Recommendation** will be given to each student at the end of successful completion of the Attachment.
- Based on the performance, some of the selected students will be considered for **scholarship of Rs. 5000/- per month.**

Duration of Attachment:

- Full time (duration for 3 months/ 6 months/ 12 months or Any other duration)
- Part-Time (duration for 3 months/ 6 months/ 12 months)
- Work at home/ Assignment based option is also available.

Submit your biodata along with a write-up (Maximum 1500 words) on any of the following topics at www.cibiod.in on 'Short Term Attachment' Link

- Novel Ideas in Health Care: Affordability and Scalability using one or more of the following technologies
  - Innovation in Basic Sciences
  - Internet of Medical Things (IoMT)
  - Machine Learning (ML)
  - Artificial Intelligence (AI)

- Chat Bots
- Cloud and Virtualization in Medical Services
- Ethics and Social Values
- Blockchain
- Data Science/ Big Data
- Augmented Reality/ Virtual Reality (AR/VR)
- GIS/ GPS/ LBS
- Robotics and Automation
- Human Computer Interface
- Enterprise and Business Technology
- Cyber/ Information/ Data Security

Thanking you & Warm regards

Dr. Varinder Garg
MD, (Radiology)
PCMS-I
OSD to Union Health Minister
PGIMER, Chandigarh - India

Prof. (Dr.) Surinder S. Rana
MD, DM (Gastroenterology)
Co-Principal Investigator
PGIMER, Chandigarh

Prof. Harish Kumar
Professor Computer Science & Engineering
Co-Principal Investigator
UIET, Panjab University, Chandigarh

CIBioD

Center for Innovation and Bio-Design

Certificate

OF ATTACHMENT

PRESENTED TO

Chesta Kamboj

Congratulations!

You have been selected by The ***Center for Innovation and Bio-Design (CIBioD)*** *for an* ***Attachment Program.***

The Project is a Multi-Disciplinary Initiative designed to Incubate, Prototype, and Commercialize Novel Ideas in Health Care.

Gunjan Sharma
CIBioD Project Director

Star ATTACHMENT

CIBioD

Center for Innovation and Bio-Design

Incubating, Prototyping and Commercializing Novel Ideas in Health Care

OFFER LETTER

of Attachment

Presented to

Ramandeep kaur

Congratulations!

You have been selected by The Center for Innovation and Bio-Design (CIBioD) for your internship period.

CIBioD

Center for Innovation and Bio-Design

Incubating, Prototyping and Commercializing Novel Ideas in Health Care

CIBioD

Center for Innovation and Bio-Design

Certificate

OF ATTACHMENT

PRESENTED TO

Mehakleen Kaur

Congratulations!

*You have been selected by The **Center for Innovation and Bio-Design (CIBioD)** for an **Attachment Program.***

The Project is a Multi-Disciplinary Initiative designed to Incubate, Prototype, and Commercialize Novel Ideas in Health Care.

Gunjan Sharma

CIBioD Project Director

Shah ATTACHMENT

2020-21

CIBioD Linkage:

Another fruitful collaboration of the department has been its association with ICMR-Centre for Innovation and Bio-Design (CIBioD), PGIMER to strengthen the culture of Innovative thinking, idea development and quality research within the students at an early stage.

The following activities were done under this linkages in 2020-21:

1) The following students completed short term attachment courses at CIbiod.

Details :

- Ramandeep Kaur (Batch 2018-2021) [course completed on 22 Oct 2020]
- Chestha (Batch 2018-2021) [course completed on 18/12/2020]
- Mehakleen Kaur (Batch 2018-2021) [course completed on 04/11/2020]

2) There have been **04 publications out of their research work** published in E-Avishkar, a research journal of PGIMER, CHD. Details are :

a) Mehakleen Kaur : PCM Based Cooling Jacket; **1 July 2020** [https://www.cibiod.in/LearningResources.html]
b) Ramandeep Kaur : Glutamatergic Synapse: A Promising Target To Treat Major Depressive Disorder (MDD) ; **1 July 2020**
c) Chestha : Glutamatergic Synapse: A Promising Target To Treat Major Depressive Disorder (MDD) ; **1 July 2020**
d) Ramandeep Kaur : EMERGING BIOSENSORS FOR POINT OF CARE CANCER DETECTION**; 01 July 2020**

2021-22

The following student completed short term attachment courses at Cibiod.

- Noveldeep Kaur (Batch 2020-23) [course completed on 07/Dec /2021]

Research project titled "Automated Bed Pooping system in Intelligent Patient Care", in association with CiBiod [**Nov 2021 – May 2022**] at **Incubation Lab** of our college. We are happy to share that the patent application for this project has been filed and patent application number received (202311029243)

To Whomsoever it may concern

Date: 22/10/2020

Ref no : CIBioD/20/208

Name: Ramandeep kaur

This is to certify that she has participated in an Online Student Attachment Programme.

She has attended the Online Sessions and Report Writing training.

We wish her luck for future Endeavours.

Project Manager

Gunjan

CIBioD

To Whomsoever it may concern

Date: 22/10/2020

Ref no : CIBioD/20/208

Name: Ramandeep kaur

This is to certify that she has participated in an Online Student Attachment Programme.

She has attended the Online Sessions and Report Writing training.

We wish her luck for future Endeavours.

Project Manager

Gunjan

CIBioD

CIBioD

Center for Innovation and Bio-Design, PGIMER, Chandigarh, India

Certificate of Recognition

Date: 19/01/2021

Ref no: CIBioD/20/299

This is to certify that **Ms. Ramandeep Kaur** has contributed as a Volunteer during Online/Virtual International Summit ATMANIRBHAR BHARAT: India as a Manufacturing Hub for Global Health on November 26-27, 2020. I wish her luck for his/her future endeavors.

वीरेन्द्र गर्ग

Dr. Varinder Garg,
Principal Investigator,
ICMR CIBioD,
PGIMER, Chandigarh

www.cibiod.in

CIBioD

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Innovation in Medtech & Telehealth for Making Healthcare Affordable

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PCM Based Cooling Jacket

Varinder Garg[1], Harish Kumar[2], Surinder Rana[3], Bikramjeet Singh Kalsi[4], Mehak Sood[5], Siddhant Mukherjee[6], Mehakleen Kaur[7]

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[3] M.D., D.M Gastroenterology, Professor, Department of Gastroenterology, PGIMER, Sector 12, Chandigarh, 160012. Email: rana.surindersingh@pgimer.edu.in
[4] B. Tech., Computer Science, UIET Panjab University, Chandigarh 160014.
[5] M.Sc. Chemistry, Department of Chemistry, Post Graduate Government College for Girls, Sector-11, Chandigarh.
[6] B.Tech., M.Tech., Biomedical Instrumentation, Department of Instrumentation and Control, College of Engineering Pune (COEP), Shivajinagar, Pune
[7] B.Sc Microbial & Food Technology, Department of Food Science, Mehr Chand Mahajan DAV College for Women, Chandigarh (Affiliated to Panjab University).

ABSTRACT

To diminish a healthcare worker's thermal discomfort in a moderately hot environment, a new microclimate cooling jacket was designed. This cooling jacket was intended to be worn under the personal protective equipment (PPE). These encapsulated phase change materials (PCMs) in the form of macrocapsules were used. The cooling effect is based on the latent heat absorption of phase change material; a highly-productive means of thermal storage. Two kinds of macrocapsules were selected: n-Eicosane (melting point 35 °C) and Octadecane (melting point 28 °C).

MacroPCMs were inserted into small knitted sacks, which were then adhered to the inner surface of the jacket i.e. near the skin. Air gaps between the macroPCM particles facilitate both heat and moisture transport through the jacket. The goal of PCM is to create reusable energy to maintain body temperature, as well as to optimize the performance of protective wear such as jackets. When the wearer's body temperature increases or decreases, the PCMs applied to the fabric will change state helping to regulate the wearer's body temperature by providing warmth or cooling. Maintaining a stable body temperature can improve working conditions and provides comfort.

Key Words: Phase Changing Materials, PPE, macrocapsules, MacroPCM.

PCM BASED COOLING JACKET

INTRODUCTION

Phase Change Materials (PCMs) have been suggested as latent energy storage materials. This theory derives from the use of chemical bonds to store and release heat. The thermal energy transfer occurs when a material changes from a solid to a liquid, or from a liquid to a solid. This is called a change in state, or "phase." PCM, proven to possess thermal-regulating characteristics, is proposed for applications in clothing materials in conditions that require workers to face extreme temperatures. PCM also is believed to conserve energy and maintain certain temperatures, so PCMs have been chosen for latent energy storage materials.

Cooling jacket fall into two categories: liquid- or air-cooled jackets and phase change material jackets. Liquid- or air-cooled jackets provide efficient cooling, but the worker is restricted in movement due to auxiliary equipment required to circulate the fluid. PCM jackets consist of a torso garment containing pockets surrounding the chest cavity that holds the PCM packs. Body heat carried to the surface of the skin by the circulatory system is absorbed by the PCM packs. A garment loaded with packs is completely unattached to any external devices, making it much more portable than liquid- or air-cooled garments. Cooling Jacket is required to diminish thermal discomfort in a moderately hot environment, designed especially for doctors and healthcare workers working 10-12 hours in PPE, continuous use of PPE cause discomfort and fatigue. Cooling jackets reduce body temperature and protect from heat stress and heat-related injuries, Ice packs on the other hand are difficult to carry and may even cause numbness in particular part of the body and cannot be used for long hours.

Fig 1: Discomfort of the doctor while wearing normal PPE kits

SOLUTION

PCM based Cooling Jacket has features like Lightweight and durable, cools in just 15-20 minutes, lighter than water vests, lasts longer than water-based vests, no wear and tear problem, provide cooling sensation for about 6 hours, no risk of ice burns or condensation, reusable; activate in freezer or simply cool water, non-toxic and environment friendly and doesn’t require any separate, expensive equipment or electricity for charging.

Fig 2: Prototype design

The cooling jacket was intended to be worn under a chemical protective garment. As coolants, encapsulated phase change materials in the form of macrocapsules were used.

The cooling effect is based on the latent heat absorption of phase change material; a highly-productive means of thermal storage. MacroPCMs were inserted into small knitted sacks, which were then adhered to the inner surface of the vest i.e. near the skin. Air gaps between the macroPCM particles facilitate both heat and moisture transport through the jacket.

Fig 3: Parts of Cooling vest

Parts of Cooling vest

1) T-shirt
2) Cooling Jacket
3) PPE

METHOD OF PREPARATION

The first step involved dissolving three-isocyanate (Toluene- 2,4,6-triyltriisocyanate) in double amount of ethyl acetate in the homogenizer. Then n-eicosane or octadecane was added and the solution was stirred until it is completely dissolved. Next, PVA aqueous solution (5% weight) is added to the solution.

Once all chemicals were added, the solution is mixed in the homogenizer for ten minutes at a temperature of 40°C to create a completely homogeneous solution. Stirring is continued until polymerization occurred and the ethyl acetate is completely volatile. Macroencapsulated phase change materials (PCMs) are successfully prepared by in-situ polymerisation and interfacial condensation.

An interlock material can be made of a 35% cotton/65% polyester blend. The interlock material had two layers and between these layers was a coated PCM fabric.
All the layers were surrounded by PANEX, a woven carbon fabric, which formed an outer shell. This combination of layers would provide protection and cooling to the between the jacket.

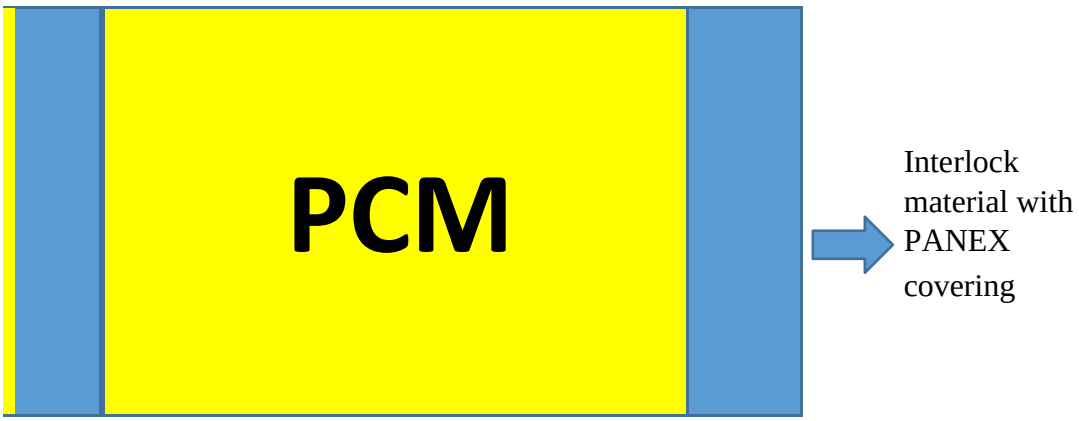

Fig 4: Pictorial representation of PCM with PANEX Covering

PROTOTYPE DESIGN

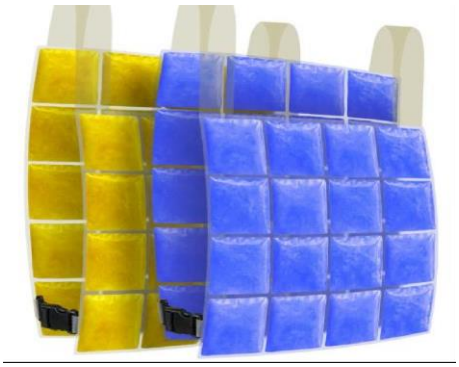

Fig 5: Representation of our design for our prototype

PCM BASED COOLING JACKET

COST

1. Toluene-2,4,6-triyltriisocyanate = 6000/100g
2. Ethyl acetate = 65/kg
3. N-Eicosane = 18000/kg
4. Octadecane = 17000/kg
5. Polyvinyl Alcohol (PVA) = 165/lt

Cost of 1 Jacket:

Toluene-2,4,6-triyltriisocyanate = 600 (10g)	Ethyl acetate = 1.3 (20g)
N-Eicosane	= 1800 (100g)
Octadecane	= 1700 (100g)
Polyvinyl Alcohol (PVA)	= 8.25 (50 ml)
TOTAL	= 2509.55 FOR 1 Jacket

If we compare the price of this vest with the reusable PPE kit developed by the Gujrat-based company named Sure Safety which says it charges about Rs 25 lakh to Rs 30 lakh including piping with one-time installation and decontamination chamber for a set of 10 PPE kits and additional kits being charged from Rs 10,000 to Rs 15,000, our prototype is way cheaper, non-toxic, easy-to-develop, safe, doesn't require extra equipment and maintenance and easily cleaned via soap water. Our prototype can stand out from the rest of the products currently in use as it is much safer than these products, especially in the time of COVID-19. [1]

APPLICATIONS OF COOLING JACKET

This jacket is useful for Doctors and healthcare workers working using current PPE kits, Military men working in harsh climate, Athletes while exercising, Fire Fighters, Workers working in industries at elevated temp and can be used in hospitals as chilling therapy

REFERENCES

[1] COVID-19: Gujarat-based company develops reusable PPE kit.Nandini Oza. Published in April 21, 2020. Link: https://www.theweek.in/news/sci-tech/2020/04/21/covid-19- gujarat-based-company-develops-reusable-ppe-kit.html

PCM BASED COOLING JACKET

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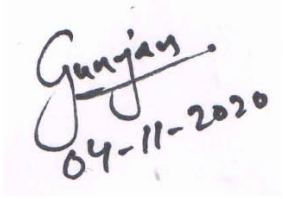

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Emerging Biosensors for Point of Care Cancer Detection

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ABSTRACT

Cancer is a group of diseases characterized by the six hallmarks namely, self-reliance for growth signals, unresponsiveness to anti-growth signals, evasion of programmed cell death or apoptosis, sustained angiogenesis, infinite replication potential and tissue invasion and metastasis (Hanahan & Weinberg, 2000). The original set has been extended to include two more hallmarks viz. altered energy metabolism pathways and escaping immune-targeted destruction (Hanahan & Weinberg, 2011). Cancer is one of the leading causes for mortality worldwide, with approx. 9.6 million deaths reported globally in 2018 (Bray et al., 2018; Ferlay et al., 2018). The number of deaths has doubled from 1990 to 2016 in India (Dhillon et al., 2018). Its prevalence has been estimated at 18.1 million new cases globally per year in 2018 with 1.15 million new cases per year in India (Ferlay et al., 2019). This number is expected to double by 2030 (Smith & Mallath, 2019). Moreover, cancer treatment puts an enormous financial burden on the patient. The Out of Pocket (OOP) Expenditure can range anywhere from $7500 to $25000 per month for patients with multiple prescribed cancer therapies (Carrera, Kantarjian, & Blinder, 2018). Furthermore, five-year cancer survival rate ranges from as high as 98% in prostate cancer to as low as 9% for pancreatic cancer (Siegel, Miller, & Jemal, 2020).

Keywords: Pancreatic Cancer, Metastasis, Apoptosis.

EMERGING BIOSENSORS FOR POINT OF CARE CANCER DETECTION

Biosensors for Point of Care Testing

Researchers nowadays, are keenly interested in detection of cancer at the very early stage using biosensors because of their high efficiency, sensitivity, accuracy and specificity. In the new era of genomic oncology, genetic biomarkers are becoming the core of cancer biomarkers; that can be identified by the specially designed biosensors.

1.1 Breast Cancer

Breast cancer is very common cancer among women, implicating 2.1 million women each year and also causes greatest number of cancers related deaths. Breast cancer is second most common cancer among all. According to WHO, in 2018 it is estimated 15% of the women died of breast cancer than of all cancer related deaths, that's approximately 627000 in number. Some important biomarkers responsible for breast cancer are BRAC1, BRAC2, CA15-3, CA125, CA27.29, CEA, NY-BR-1, ING-1, HER2 (Human epidermal growth factor receptor), ER (estrogen receptor) / PR (progesterone receptor).

In breast cancer patients, CA15-3 is an important biomarker. Clinically CA15-3 is most often used to monitor patient in cases of advanced breast cancer. It has been seen that the concentrations of CA15-3 increase by 10% in stage1 cancer, 20% in stage 2, 40% in stage 3, 75% in stage 4 of breast cancer. The relationship between CA15-3 levels and breast cancer has shown that the individuals with the values of <30U/mL, before the treatment onset had significantly higher survival times than individuals who had higher levels. For the determination of biomarkers in the breast cancer with high sensitivity and diagnostic accuracy, the biosensors with nanomaterial and their specific characteristics such as metal oxide, metal nanoparticles, nanospheres and integrated nanostructures, such as graphene or reduced graphene oxide, composed of metal oxide and multiwalled carbon nanotubes were provided.

1.1.1 The Detection of Breast Cancer Biomarkers with Microfluidic Immuno–Biochip

The early detection of Epidermal growth factor receptor 2 (EGFr2 or ErbB2) protein with label- free microfluidic immunosensor which is with femtomolar sensitivity. This sensor applies exclusively structured immune-electrode which is made up of porous hierarchical graphene foam modified with electrospun carbon-doped titanium dioxide nanofibers(nTiO2) which is working as an electrochemical electrode.

Because of the brilliant biocompatibility, the applications which are ideal for the electrochemical sensor are high reaction kinetics, anatase nTiO2 and good stability for proteins. The 3D and the porous features of graphene foam allow nTiO2 to penetrate and attach to the surface of graphene foam by physical adsorption. The graphene foams combine with the functional nTiO2 which yields in large surface area, high charge transfer resistance, and porous access to sensing surface by the analyte, which results in new possibilities for the development of electrochemical immunosensors. The antibody of ErbB2 on the graphene foam – nTiO2 composite gets covalently immobilized by the enabling of EDC-NHS chemistry. To get an immunosensor's design, the working electrode was designed to hang above the gold counter electrode in a microfluidic channel. The immunosensor went through electrochemical impedance spectroscopy and differential pulse voltammetry to quantify breast cancer biomarkers. The high sensitivities of the two methods are 0.585μA μ/M cm/2 and 43.7kΩ μ/M cm/2 in which wide concentration range of target ErbB2 antigen from 1×10 ¯15 M to 0.1×10¯6 M and from 1×10¯13 M to 0.1×10¯6 M respectively. Usage of the anti ErbB2, results in high specificity, even in the presence of ErbB3 and ErbB4. Many applications will be derived from the integration of graphene foam – nTiO2 composite into microfluidic devices, in the field of electrochemical detection of chemical and biological species.

1.1.2 Early Diagnosis by DNA Biosensors Based on AuNPs

For early detection breast cancer biomarkers by electrochemical detection of HER2, two different DNA modified gold nanoparticles and graphene oxide loaded on glassy carbon electrodes were prepared. In this electrochemical DNA biosensor, a "sandwich type" detection strategy was employed and its response was measured by Amperometric detection. For the sensitive detection of the breast cancer biomarker ErbB2 and the control marker CD24, the electrochemical signal enhancement was achieved via gold nanoparticles and graphene oxide system. The modified graphene oxide was described by using Fourier transform infrared spectroscopy, transmission electron microscopy, Raman spectroscopy, scanning electron microscope, UV-visible spectroscopy and energy-dispersive X-ray spectroscopy. Some important steps involved in modification of glassy carbon electrode with gold nanoparticles, graphene oxide and DNA probes, target and reporter probe were electrochemically characterised using electrochemical impedance spectroscopy and cyclic voltammetry.

The detection limits of 0.16nM and 0.23nM were obtained with sensitivity 378nA/nM and 219nA/nM for ErbB2 and CD24 respectively by using Amperometric detection of a horse radish peroxide label.

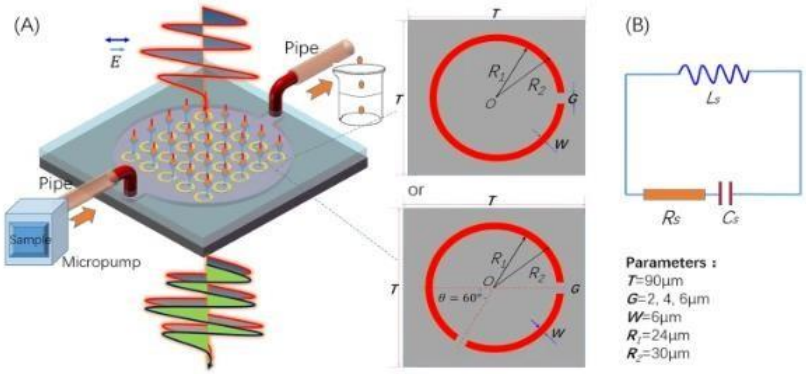
1.2 Liver Cancer

Liver cancer is considered to be the fourth most lethal cancer globally, and hepatocellular carcinoma (HCC) accounts for 75–85% of liver cancer cases. The most approachable HCC biomarkers are (1) the AFP, its isoform lens culinaris agglutinin-reactive fraction of alpha- fetoprotein (AFP-L3); and (2) des-γ-carboxy prothrombin (DCP). However, there are many other molecules that might be taken into account, including glypican 3 (GPC3), glutamine synthase (GS), heat shock protein 70 (HSP70), cytokeratin 19 (CK19), Golgi protein 73 (GP73), midkine, osteopontin (OPN), squamous cell carcinoma antigen (SCCA), Annexin A2, fibroblast growth factor 3/4 (FGF3/4), micro-RNAs (miRNAs), Long non-coding RNAs (lncRNAs), circulating tumor cells (CTCs), cell-free DNA (cfDNA), and other biomarkers.

Recently, specially designed metamaterials in the Terahertz range are being widely used as biosensors for liver cancer detection. It works on the principle of resonating frequencies, where the frequency range of Terahertz Wave (0.1THz to 10 THz) matches with the vibrational frequency of biomolecules released from biomarkers. The intensity of peak gives the estimation of the concentration of the biomarkers in the body. This technique provides the promising results, moreover, it a label-free, non-contact and non-destructive inspection technique on the specific biomolecules. To obtain the sharp peaks, the metamaterials can be designed as asymmetric structures, which can cause fano resonance; provided the structure can resonate and eliminating the substrate effect. Because of the limitation of the THz sensors to work on dry or semi-hydrated sample due to strong water absorption at THz range, Microfluidic chips are integrated with biosensors providing advantages such as low cost, less sample requirement, higher accuracy and rapid testing. The metamaterials are designed with antibody specific to antigen of biomarker in the aqueous phase.

Designing of Metamaterial Biosensor Microfluidic Chip: The metal-split-ring resonators(MSSRs) and poly-(dimethylsiloxane) microchannel form the basic structure of biosensor. The dimethylsiloxane (PDMS) form the microfluidics layer over the metamaterial to prevent the loss of THz wave transmission.

The THz wave which is electrically polarised is launched on the THz chip in integration of microfluidics chip, where the electric field parallel to MSSRs excites the inductive-capacitive resonance, which induced the current in the nearby MSSRs. This leads to electric energy and magnetic energy transfer between the inductance and capacitance. The chip detects the strong electrical field generated among the dielectric gap and provides us the signal. The metamaterial was fabricated on highly resistive silicon substrate. The designing involves 4-6 µm width(W) of split ring, inner radius and outer radius of range 24-26 µm and 28-30µm respectively. The size of gap can be changed from 2µm to 6µm based on the accuracy requirement.



(**A**) The sketch of THz metamaterials biosensor chip integrated with microfluidics; (**B**) Equivalent circuit with {RLC}s for the SRRs.

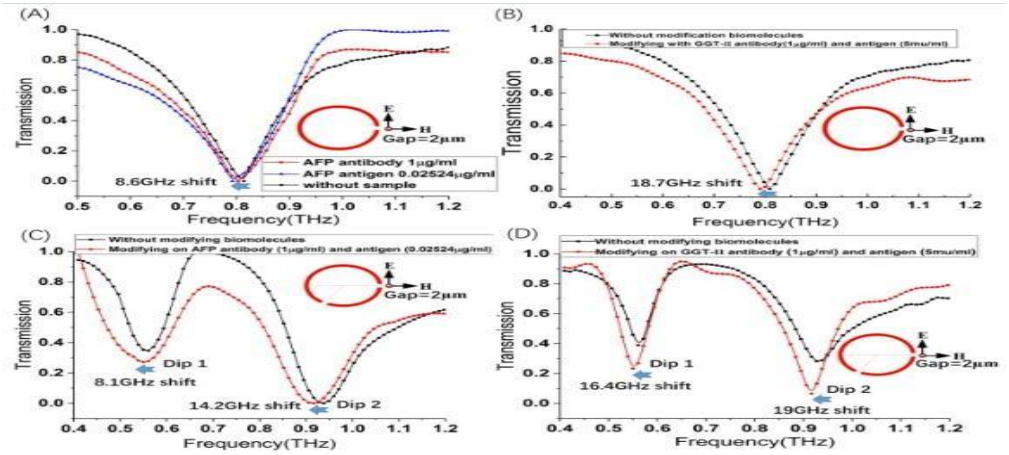
RESULTS

Liver cancer antibody Alpha fetoprotein (AFP) (1 µg/mL solution in PBS buffer) were coupled to the surface of the SRRs through chemical reaction between amidogen beside the alkaline aminophenol (Arg and Lys) of IgG and the active carboxyl; and maintaining 16 hours at 4 °C. AFP antigen or Glutamine transferase isozymes II (GGT-II) antigen with different concentrations was injected into the chamber to incubate for more than 40 min. The reflection spectra or transmission spectra were recorded through THz-TDS setup during different time. The MSSRs biosensors integrated with microfluidics is based on THz spectral dip frequency shifts, which can be changed with refractive index. A figure of merit (FOM) obtained by dividing the sensitivity by the resonance frequency line width is widelyused to characterize SRRs sensing capabilities. FOM is described as:

FOM=S/FWHM

where, FWHM repents full width at half maximum.

Larger the value of FOM, precise will be the results. The results of AFP and GGT II at 2 µm are shown in the graph since we know, lower the gap, higher will be precision. The testing results of the two AFP and GGT II show in agreement with the experimental results. However, the accuracy can be enchanced using advanced Metamaterials operating on fano resonances.



The typical tested results of liver cancer biomarker. (**A**) The results for AFP of SRRs with a 2 µm gap; (**B**) The results for GGT-II liver cancer marker testing of SRRS with a 2 µm gap; (**C**) The results for AFP of SRRs with 2 gaps (2 µm); (**D**) The results for GGT-II liver cancer marker testing of SRRS with 2 gaps (2 µm).

1.1 Lung Cancer

Lung cancer is the leading cause of cancer-related deaths, with mortality being closely associated with smoking habits (Barta, Powell, & Wisnivesky, 2019). The common symptoms include coughing up blood, weight loss, fever, fatigue and anorexia among others. The main problem associated with LC is its misdiagnosis as tuberculosis in countries where TB is prevalent. This is due to the fact that both diseases share common symptoms (Prabhakar, Shende, & Augustine, 2018). However, it can be distinguished on the basis of patient's medical history and whether the person smokes or not as TB can occur in non-smokers. Moreover, TB

Yet another biosensor which prove effective are the microcantilever sensors for liver cancer detection. In microcantilever, a cavity was designed in the free end of the cantilever for local body immobilization. This local immobilization approach reduces the adsorption induced variation of Stiffness constant, k in comparison to the whole surface adsorption.

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A novel cantilever array-based bio-sensor was batch-fabricated with IC compatible MEMS technology for precise liver cancer biomarker detection, that is piezoelectrically driven into vibration and those vibrations can be detected by Wheatstone bridge. The resonance frequency depends on two factors- stiffness constant,k and mass, m.

BIOMARKER DETECTION: For the detection of Biomarkers various concentrations of antigens were taken into account. The figure depicts the measured frequency shift of locally immobilized anti-AFP levers to the various concentrations of antigen AFP, and a linear regression was obtained with a relative uncertainty less than 5%.

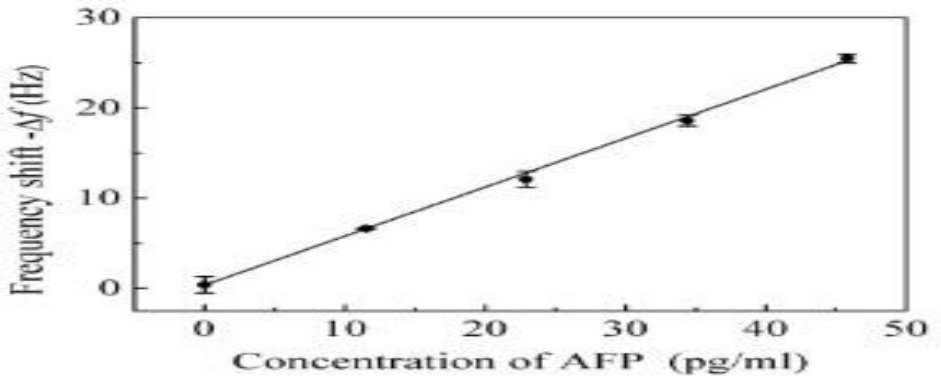

Figure 2: The relative resonance frequency shift versus AFP antigen concentration of 0-50 pg/ml.

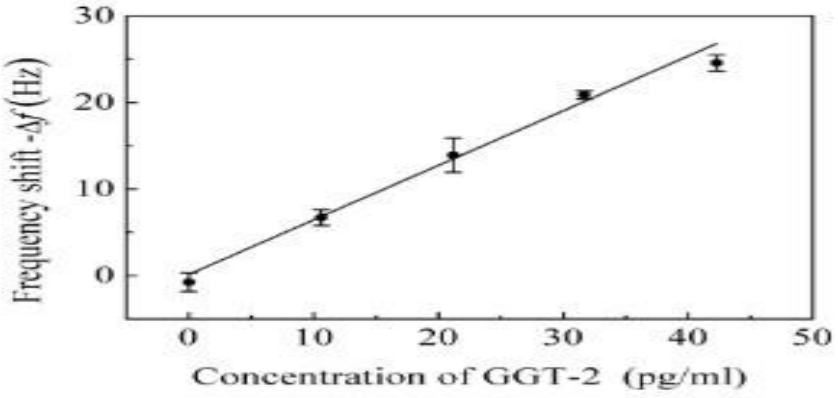

Figure 3: The relative resonance frequency shift versus GGT-2 antigen concentration of 0-50 pg/ml.

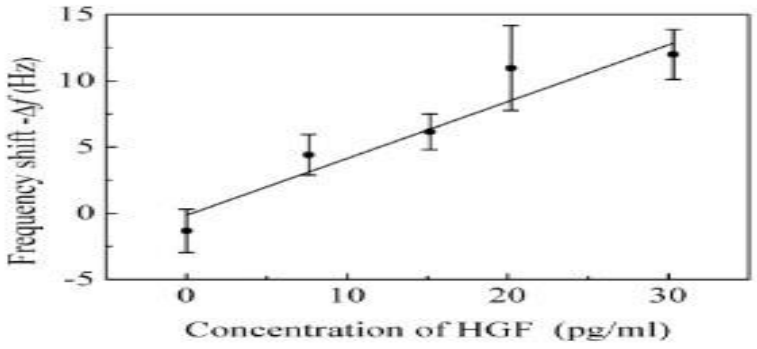

Figure 4: The relative resonance frequency shift versus HGF antigen concentration of 0 30 pg/ml.

Eliminating the effect of k can help detecting the various liver cancer biomarkers more efficiently.

can act as starting point for LC (Prabhakar et al., 2018). Lung cancer can be further classified into LCT, SCLC and NSCLC based on histology (Roointan et al., 2019).

Biomarkers and biosensors can be employed for early diagnosis of lung cancer due to their fast response time and high sensitivity. The biomarkers can be broadly classified into genetics and epigenetics biomarkers and protein-based biomarkers. Some of the common biomarkers utilized are CEA or Carcinoembryonic Antigen, NSE or Neuron-specific enolase, CYFRA21- 1, VEGF, Annexin-II and miRNAs like miR-205, miR-210, miR-708 (Roointan et al., 2019).

1.1.1 Modified Surface Plasmon Resonance based Biosensors

SPR based biosensors have received a lot of interest lately due to their high sensitivity, non- invasiveness and real time results analysis. A label-free, optical SPR works on the principle of detection of changes in refractive index when analyte molecules bind to the immobilized biorecognition element on the surface of biosensor chip (Piliarik, Vaisocherová, & Homola, 2009). These biosensors are cost-effective, portable, and easy-to-use with high specificity and accuracy. Moreover, their specificity and sensitivity can be greatly enhanced by making slight modifications.

Chiu and Yang constructed a novel SPR biosensor using carboxyl-MoS_2 nanocomposite film (instead of using just MoS_2) for detection of LC biomarker CYFRA 21-1. This modification resulted in a fifteen-fold enhancement in the binding affinity K_a and more than two-fold enhancement in SPR angle shift. The LOD of this biosensor (=0.05 pg/mL) was found to be 10^4 times more sensitive than traditional ELISA (=0.60 ng/mL) (Chiu & Yang, 2020).

Miti et al. developed a miRNA biosensor based on localized SPR. This biosensor used HCR or Hybridization Chain reaction for amplification. It works on the principle that two DNA hairpins, in the presence of target sequence, will initiate assembly. This can then be successfully detected using SPR. This biosensor was successful in detecting LC biosensor miRNA-17 and the overall procedure was completed within an hour (Miti et al., 2020). SPR based biosensors hold a lot of potential to be widely adopted as POC diagnostic devices for detection of various types of cancer biomarkers.

1.2 Prostate Cancer

Prostate cancer is the second most common cancer among men. Generally, the tumour formed is latent i.e. it does not mature and affects the patient's life. Thus, it is very important to identify whether the tumour is latent or not as early identification can help save lives. Despite the

limited specificity and high rate of overdiagnosis, Prostate Specific Antigen (PSA) is the most commonly used biomarker for the detection of prostate cancer. To counter this issue new prostate cancer antigen have been proposed. These biomarkers have higher accuracy of PSA in the management of early Prostate Cancer Antigen. Some of the commercially available Prostate cancer antigens are: PCA3 score, four-kallikrein panel and Prostate Health Index. There are also new emerging biomarkers such as PSA glycoforms, microRNAs, TMPRSS2: ERG fusion gene, androgen receptor variants, circulating tumour cells, and PTEN gene. These biomarkers can change the early management of Prostate cancer. Using these biomarkers biosensors can be designed. These biosensors help in diagnosis of cancer.

1.2.1 Bioconjugation Single use biosensor

Detection of Prostate cancer is done most commonly with the help of PSA despite its high rate of false positive tests. Apart from PSA, alpha-methylacyl-CoA racemase (AMACR) is also highly expressed biomarker in the Prostate cancer cells.

The novel bioconjugate single use Biosensor is capable of detecting both PSA and AMACR in undiluted human serum. The preparation of biosensor via bioconjugation mechanism does not take much time and can be prepared just prior to the test. This type of biosensor is accurate, single use and cost effective. It also requires very small quantity of test medium coupled with its short preparation time it becomes a very attractive choice for detection of biomarkers produced by prostate cancer cells.

Detection of AMACR is conventionally done with the help of ELISA, chemiluminescence immunoassay, radioimmunoassay, and fluoro-immunoassay. Even though these methods have fairly high accuracy the process is fairly laborious, expensive and time consuming. Thus the cost effective biosensor technology became more popular for detection of biomarkers in early stages of disease monitoring. The most common way to detect AMACR is using Square Wave Voltammetry to directly detect AMACR using aptamers immobilized on a polymer substrate.

Bioconjugation mechanism conjugate two or more molecules into a single molecule which contains properties of all the components. This method makes for zero-length linkage between the protein and the electrode element of the biosensor. Bioconjugation also has improved clinical applications as it shortens the preparation time and enhances the coverage of biosensor surface. The interaction between antigen and antibody is the biorecognition mechanism. Anti- PSA and Anti-AMACR were modified with N-succinimidyl S-acetylthioacetate(SATA) with the help of bioconjugation mechanism. This leads to a thiol linked anti-PSA or anti-AMACR

which directly links to the thin gold sheet electrode element of the biosensor during incubation. Preparation including the incubation takes about one day.

Thus, the use of bioconjugation in preparation and pulse voltammetry in I measurement results in a single use, cost effective and highly sensitive and selective biosensor for detection and management of early-stage prostate cancer with the help of PSA and AMACR biomarkers. This type of biosensor is proving it self to be a very effective diagnostic tool for the screening application of prostate cancer.

1.2.2 Graphene based biosensor

Graphene is playing an important role in the biosensor field with remarkable physical, optical, electrochemical and magnetic properties.

The use of graphene can significantly enhance the electrochemical signal of various electrodes because of various properties such as high electrochemical surface area, descent conductivity, high electron transfer rate, and a broad range of chemical functional groups on the surface of graphene. There are certain limitations in the use of graphene as it has irreversible self-agglomerations, non-specificity, less colloidal stability repeatability and poor reliability.

Based on graphene two types of biosensors can be made, firstly, graphene material based on GO, GQDs and rGO are assembled in the surface of the biosensor, mainly the electrode or transistor channel, to construct a novel biosensor interface with improved molecular receptors. Based the increased specific surface area and unique π–π orbital interactions on the interface excellent biosensor performance can be achieved. Secondly graphene materials can be applied as carriers for construction of novel nanocomposite. This is approach is very suitable for sensitive protein biomarker analysis because of its unique catalytic and chemical reactions and biosensor signal amplification.

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DECLARATION OF INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Glutamatergic Synapse: A Promising Target to Treat Major Depressive Disorder (MDD)

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ABSTRACT

After few decades, mono-amine hypothesis could grab the attention of millions with the captivating evidence that, prevailing changes in the areas of brain with complex networks of cognitive and emotional behaviors for long time witnessing mood and anxiety disorders. Major Depressive Disorder (MDD) encompasses a large number of psychological illness include, loss of interest, mood disturbance, loss of appetite, insomnia, feeling of fatigue and decreased concentration and standing as the major illness worldwide. Later on, a wealth of data from experimental models started exploring on the environmental factors enhancing the stress which enhances some powerful exerts and induces limbic remodeling or the reduction of synapses pivoted by “Glutamatergic Synapse”. As the majority of neurons in the brain circuits use glutamate as neurotransmitter, it should be recognized that the glutamatergic system is the primary key for the pathophysiology, potentially addressing the therapeutic action of antidepressant drugs.

GLUTAMATERGIC SYNAPSE: A PROMISING TARGET TO TREAT MAJOR DEPRESSIVE DISORDER (MDD)

A radical shift from the monoamine hypothesis to neuroplasticity hypothesis supported by glutamate signaling visualizes a considerable advancement in the technology, which drives to look into new hypothesis and therapies. Our work, displays an extensive analysis of Glutamate signaling pathway and the enthralling genes involved in it. In addition, the role of glutamate receptors and the inhibitory pathway GABA was elucidated for the convoluting cause of MDD. We propose a hypothesis to bridge the gap between the failure of existing drug therapies based on mono amine theory and the discovery of biomarker based on the glutamate signaling to bring out novel advancements in the pharmacology for the treatment of MDD.

Keywords: Mono amine hypothesis, Glutamatergic synapse, neuroplasticity, MDD, GABA,.

INTRODUCTION

Depression is an extensive chronic medical illness that can affect thoughts, mood, and physical health. It is characterized by disturbing mood, lack of endurance, anxiety, sadness, insomnia, and an inability to enjoy life. However a lot of displeased outcomes were observed by the patients diagnosed with depression. It is a common cause of death and morbidity, but the biological bases of the insufficiencies in emotional and intellectual processing remain incompletely understood. Current antidepressant therapies are effective in only some patients and act slowly**.** Stress and depression are associated with neuronal atrophy, characterized by loss of synaptic connections in key cortical and limbic brain regions implicated in depression. This is thought to occur in part via decreased expression and function of growth factors, such as brain-derived neurotrophic factor (BDNF), in the prefrontal cortex (PFC) and hippocampus [1].

Major Depressive Disorder (MDD):

Major depressive disorder (MDD) is a severe, debilitating medical illness that affects millions of individuals worldwide. This mental disorder is caused by the combination of genetic, environmental, and psychological factors. A total of 16.6% of the U.S. population and 350 million people worldwide have been victimized under this disorder which further, is a growing problem. It was originally predicted by World Health Organization (WHO), that this will be the second leading cause of disability worldwide by 2020 [2].

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Due to the worldwide impact of MDD, it is important to understand this disease in a greater extent. Recent studies have largely focused on identifying mechanisms and cellular targets that may explain the etiology of MDD and provide novel substrates for development of more effective and faster-acting therapeutic agents. The hippocampus shows a high degree of functional and structural plasticity in response to many types of stimuli including stress [3]. The hippocampus is considered as one of the main limbic structure concerned with the MDD. Brain imaging and post-mortem studies provide evidence of changes in cellular building and/or morphology within this brain region, including decrease in hippocampal volume in MDD patients, deterioration of hippocampal pyramidal neurons and decreased neuropil.

Preclinical studies show that exposure to either acute or chronic stressor decreases adult neurogenesis in the sub granular zone of dentate gyrus (DG) and causes atrophy of dendritic structures of pyramidal neurons [4]. The ratio of occurrence of MDD in adult men and women is approximately 1:2. Medical proof supports a shielding effect of androgens against depressive disorders. Decreased level of androgen in adult men is associated with increase in dominance of depressive disorders, and improvement appears in the hypo gonadal male patients when they are subjected to androgen replacement therapy [5]. Although most glutamate-related modifications seem to be brain region-dependent and to some extent unpredictable, but there is an outcome which shows the down regulation of glial glutamate transporters in a very consistent manner. These membrane proteins are situated mainly in the astrocytes surrounding the synaptic cleft and establish a pivotal element on the regulation of glutamatergic neurotransmission. Moreover, the reports concerning with the down regulation of glutamate transporters in MDD indicate that other components of the glial compartment may be compromised as well [6].

Over the years, a number of genes have been identified which are associated with MDD. However, in many cases, the role of these genes and their relationship in the origin and development of MDD remains uncertain. Under these conditions, the systems biology focuses on the function correlation and interaction of the candidate genes in the framework of MDD which will provide useful information on discovering the molecular mechanisms in relation to the disease [7].

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Present pharmacological treatments for MDD are often insufficient for many patients, the next generation of treatments needs to be more effective, rapid acting and better tolerated than currently available medications. Proven evidences are there that shows, the glutamatergic system holds potential in developing the next generation of novel and mechanistically distinct agents for the treatment of MDD [8].

Biomarker for MDD:

A biomarker is a characteristic feature that can be extensively used for the identification or creating differences between the normal and pathogenic process. A biomarker for MDD can be used for diagnosis, forecasting causes which may be environmental or genetic, identification of those factors which are at risk on major extant, and development of the next generation treatments. Structural and diffusion-weighted magnetic resonance imaging (MRI) are the type of Neuro- imaging techniques are thought to be the biomarkers for the MDD. In structural MRI (sMRI), a comparison was made between the depressed person and a healthy individual. There are other imaging techniques like fMRI and phMRI which broadens the understanding of glutamate site of

action mechanisms, treatments and effects. These two techniques are governed by the change in the amount of blood oxygenation level–dependent (BOLD) signal. A variant of magnetic resonance techniques, named magnetic resonance spectroscopy (^{1}H MRS) is also considered to assess the functioning of brain chemistry. At low concentration Glutamate and Glutamine are also detectable by MRS. A non-invasive nuclear medicine imaging technique named Positron emission tomography (PET) is also acceptable to study the CNS functioning. Due to its slower temporal resolution and low spatial resolution (2–6 mm) it is less effective. To improve this limitation, PET can be combined with other imaging techniques and built into the same machinery, for example single photon emission computed tomography (SPECT), which provides 3-D images that can be used, among other peculiarities [9].

Some studies showed common volumetric differences in cortical gray matter regions. In a person with MDD it is frequently observed that several regions of the brain including hippocampus, basal ganglia, orbitofrontal cortex, and prefrontal cortex have smaller volumes.

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Due to increase in advancement in neurobiology here we are aiming to indicate the genetic, molecular, and neuroimaging studies that are significant for assessment and treatment selection of this disorder. In 1990s, the glutamate hypothesis of depression was proposed, when antagonists of the N-methyl- D-aspartate (NMDA) receptor (an ionotropic glutamate receptor), were reported to shows anti- depressant like behavior of action in mice. Variations in glutamatergic neurotransmission are associated with the pathophysiology of depression, and the glutamatergic system represents a treatment target for depression [10]. Therefore, we conducted a systematic review and meta- analysis to compare the levels of specific regional glutamatergic neuro metabolites in a comprehensive fashion, including the most recent studies on the topic.

GENES OF GLUTAMATE SYNAPSE ENRICHING MDD

Glutamate is the powerful excitatory neurotransmitter in the central nervous system (CNS) of mammals. Glutamate is majorly fundamental to brain bioenergetics and metabolism. Glutamate is derived from both neuronal / glial pathways and as well as Tricarboxylic acid cycle (TCA) [11]. Glutamate signalling starts with the production of glutamate in the cytoplasm of glutamatergic neurons. Thereafter, this glutamate is pumped into synaptic vesicles of the neuron terminals. Once the informative signalling pathway passes from other neurons, it leads to the stimulatory action and induces the various signalling pathways along with glutamate pathway. This increases the levels of glutamate in the synaptic cleft and later on detected by glutamate receptors. EAATs remove the further accumulation of glutamate in the regions of synaptic cleft. A set of genes (ADCY3, ADCY9, GRIK, etc.,) were identified which are involved in the glutamate signalling pathway from the inception of glutamate synthesis in the cytoplasm of neurons till the release into the synaptic cleft [12]. Their respective location was mentioned in the tabular format to elucidate the importance of each gene.

A comprehensive map was generated using a data visualisation tool to demonstrate the synapse pathway of glutamate and its interaction with genes. Genes play a major role in the regulation of pathways by regulating its function and signaling roles. Cell designer is a software based data visualization tool to bridge the gap between the raw data. It gives a detailed, comprehensive, easily consumable map.

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It is structural diagram editor to draw biological networks and gene-regulatory mechanisms. Networks are designed using graphical notation and are stored in the database using Systems Biological Markup Language (SMBL). These networks are able to link with simulation and analysis packages using Systems Biological Workbench (SBW). Using this Cell Designer, one can browse and modify existing SBML models with references to existing databases, simulate and view the dynamics through an intuitive graphical interface.

The constructive insight from various research papers were taken from using resources like, PubMed, NCBI, Google Scholar etc., to obtain a set of promising information for the further analysis of this meaningful study. The list of important genes were taken to construct the diagrammatic part of the respective study, which brought up the detailed correlations between the genes and the signaling pathway molecules. Also, this study piqued our interest to look towards the direction of the underlying ineffectiveness of inbuilt various other signaling pathways in combating with such neuro-psychiatric disorders.

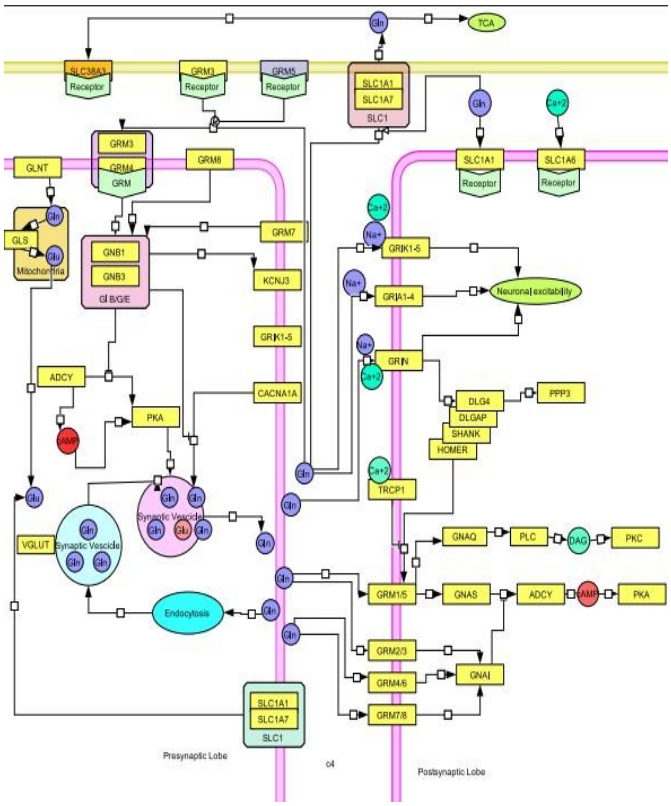

Fig 1.1 A comprehensive map of Gene interactions in Glutamate synapse

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S. No	GENESYMBOL	GENE NAME	LOCATION	EXPRESSION
1.	ADCY3	Adenylate cyclase 3	2p23.3	Ubiquitous expression in placenta and ovary
2.	ADCY9	adenylate cyclase 9	16p13.3	Ubiquitous expression in thyroid, lung
3.	ADCY6	adenylate cyclase 6	12q13.12	Ubiquitous expression in fat, heart
4.	ITPR1	inositol 1,4,5-trisphosphate receptor type 1	3p26.1	Ubiquitous expression in thyroid, brain
5.	PLD1	phospholipase D1	3q26.31	Ubiquitous expression in gall bladder, duodenum
6.	GNB1	G protein subunit beta 1	1p36.33	Ubiquitous expression in brain, small intestine
7.	GNB3	G protein subunit beta 3	12p13.31	Ubiquitous expression in ovary, heart
8.	HOMER1	homer scaffold protein 1	5q14.1	Broad expression in brain, thyroid.
9.	CACNA1A	calcium voltage-gated channel subunit alpha1 A	19p13.13	Biased expression in brain, stomach
10.	CACNA1C	calcium voltage-gated channel subunit alpha1 C	12p13.33	Broad expression in endometrium, heart
11.	CACNA1D	calcium voltage-gated channel subunit alpha1 D	3p21.1	Broad expression in adrenal gland, lung
12.	GRIA1	glutamate ionotropic receptor AMPA type subunit 1	5q33.2	Biased expression in brain and lung

13.	GRIA2	glutamate ionotropic receptor AMPA type subunit 2	4q32.1	Restricted expression towards brain
14.	GRIA4	glutamate ionotropic receptor AMPA type subunit 4	11q22.3	Biased expression in brain, adrenal gland
15.	GRIK1	glutamate ionotropic receptor kainate type subunit 1	21q21.3	Biased expression in adrenal gland, brain
16.	GRIK4	glutamate ionotropic receptor kainate type subunit 4	11q23.3	Biased expression in brain, ovary
17.	GRIN2A	glutamate ionotropic	16p13.2	Biased expression in brain, heart

Table1.1: List of Genes involved in Glutamate Signaling

RECEPTORS INVOLVED IN GLUTAMATE SIGNALLING

Then Glutamate is transported by vesicular glutamate transporters (vGLuTs) after packaged into synaptic vesicles. Being an excitatory neurotransmitter glutamate can excite nerve cells to their death by process called “excitotoixicity “. Glutamate has two broad classes of receptors: ionotropic receptor and metabotropic receptor [11]. Glutamate and its receptor play an important role in pathophysiology of major depression disorder (MDD). The detailed classification as follows:

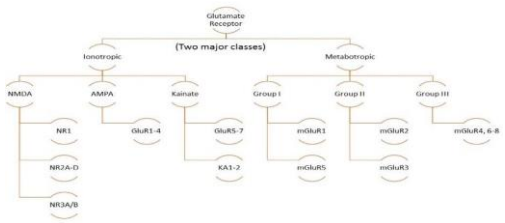

Fig 1.2: Glutamate receptors

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Two major classes of Glutamate receptor: ionotropic receptor and metabotropic receptor. Further ionotropic receptor is divided into three subclasses: 1) NMDA 2) AMPA 3) kainate. Ionotropic receptors leads to influx of ions like calcium ions and sodium ions. Metabotropic receptor is further classified into three subclasses: 1) Group I 2) Group II 3) Group III. Metabotropic receptors belongs to family of G – protein coupled receptors (GPCRs).

Release of Glutamate into synaptic cleft leads to influx of calcium ions [13].The Glutamate then binds to cognate receptors on Postsynaptic membrane. Ionotropic receptors leads to influx of calcium ions and sodium ions from extracellular space. Ionotropic receptors have three major subclasses: a) NMDA b) AMPA c) kainate. NMDA receptor have subunits: NR1, NR2A-D, NR3A/B and NMDA receptor form heterotetramic complexes and shown high calcium permeability. Activation of synaptic NMDA receptors promotes cell survival, On the other hand, overstimulation of extra synaptic NMDA receptors due to increased Glutamate induce cellular death [14].AMPA receptor has subunit : GluR1-4 and AMPA receptor forms heterotetramic complex and has low to moderate calcium permeability. Kainate have subunits: GluR5-7, KA1-2 and kainate receptor forms homotetrameric or heterotetramic complex and shown low calcium permeability. Metabotropic receptors belongs to family of G protein coupled receptor and have three subclasses: Group l, Group ll and Group III. Group I metabotropic receptor have two subunits- mGluR1, mGluR5 and Group I metabotropic receptor establish homodimeric complex and located post-synaptically. Group II metabotropic receptor have two subunits: mGluR2, mGluR3 and Group II metabotropic receptor forms homodimeric complex and located mainly pre-synaptically and Group III metabotropic receptor has subunits: mGluR4, 6-8 and Group III receptors forms homodimeric complex and located mostly pre-synaptically. Activation of NMDA receptor leads to delayed and longed excitation with the help of calcium ion influx. AMPA / kainate receptor activates due to sodium ion influx.

Pathophysiology of glutamate receptors in MDD: Alterations in Glutamate level in brain tissue, plasma, serum, Cerebrospinal fluid and alterations in activities of Glutamate receptors plays an important role in pathophysiology of various mood disorders and major depression disorder. Findings of many studies have shown the increased Glutamate level in plasma of depressed patients compared to control ones [15].

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Depressed patients have elevated Glutamate level in plasma [16]. Recent study revealed the elevation of Glutamate levels of postmortem dorsolateral

prefrontal cortex tissue in bipolar individuals [17]. Activation of extra synaptic NMDA receptors leads to cell death or cellular toxicity [18]. These studies have shown the alterations in Glutamate level and activities of Glutamate receptors linked with pathophysiology of major depression disorder.

Currently available medications based on monoamine hypothesis alleviate symptoms of depression but many patients do not fully respond and many take several weeks and many trials to achieve response, and monoamine hypothesis have limited understanding of pathophysiology of depression. Alterations of Glutamate level in brain tissue, plasma, serum and cerebrospinal fluid and alterations in activities of Glutamate receptors in depressed patients acts as biomarker of depression and provides complete understanding of pathophysiology of major depression disorder.

POTENT INHIBITOR OF GLUTAMATE SYNAPSE – GABA

GABA: Gamma immune butyric acid is the most prevalent inhibitory neural transmitter in central nervous system of human body. GABA is generated from glutamine, a vital amino acid in the brain. There is a promising evidence that the inhibitory GABA and excitatory glutamate system are necessary for sufficient response to stress [19]. The Hypothalamus, pituitary and adrenal axis activity is modulated by GABAergic and glutamatergic brain circuits. In case of anxiety, overactive fear circuits are centered on the amygdala (fear center). GABA neurons gets connected to amygdala, which is called synapse. The brain has an elaborate structure designed to isolate and protect it against invading toxins, chemicals and potentially harmful substances. This mechanism of self-protection is called the blood-brain barrier [20]. GABA is inhibitory, when GABA is released and binds to the post synaptic receptors, it inhibits the amygdala and slows down the hyperactivity of amygdala and reduce anxiety. According to studies, GABA shortage may be embraced in mood disorders like depression and by increasing the synapse that uses GABA as its neurotransmitter, neurotransmission may use an antidepressant effect and a mood stabilizing effect [19,20].

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Pathway

GABA gets associated with the amygdala and communicates via the synapse. In GABA neuron, there are GABA neurotransmitters in the vesicles. These vesicles release their contents into the synapse and binds to the receptors which opens up an ion channel and lets chloride ion to enter into it. This inhibits the neurotransmission post synaptically and therefore reduces hyperactivity of amygdala. GABA is reabsorbed and recycled by Gamma ray uptake pump such as serotonin uptake pump [21]. There are also some oral supplements when you take it, they block the reuptake of GABA and thereby increases the GABA concentration in the synaptic pathway and therefore more binding and opening which increases the inhibition and decrease in anxiety [22]. GABA on a concluding note acts as a balancing tool of brain's synaptic system.

For restoring the equilibrium after shrewd or acute stress, GABAergic and glutamatergic neurotransmission is crucial [23]. The synaptic receptors are saturated by GABA once it gets released from the synaptic vesicle and it activates them within 1 millisecond. In stress situations, the GABA levels in the plasma and CSF is increased. The GABA receptor functioning gets affected by the stressors. GABA level directly influences the severity of depression [24]. The timings of synaptic inhibition is controlled by $GABA_A$ receptor subunits. There is low level of GABA receptor subunits in the suicidal MDD brains. MDD, being a biochemically heterogenous illness in which CRH, 5-HT and GABA act together to influence depressive disorders. GABA processes may be therapeutically affected by SSRI treatments. The association pathway of GABA and Glutamate in the complex brain circuits are explained below:

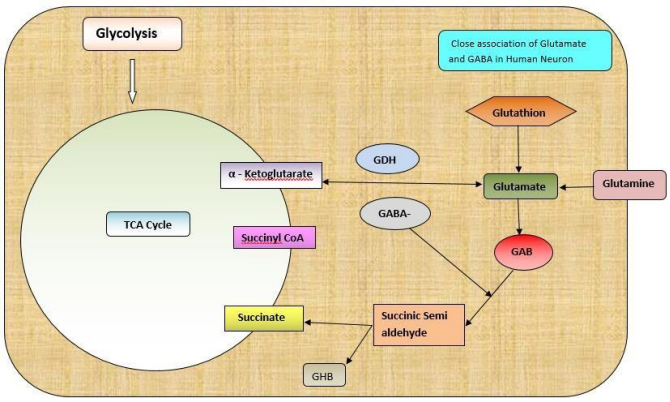

Fig1.3: Close associations of GABA and Glutamate in Neurons of Human

GLUTAMATERGIC SYNAPSE: A PROMISING TARGET TO TREAT MAJOR DEPRESSIVE DISORDER (MDD)

DRUG THERAPY

For the treatment of major depressive disorders, monoaminergic-targeted drugs have prompted great advances in the development. Most of the patients do not respond to the drugs properly as they have delayed clinical effect [25]. In the research of the neurobiology of depression, Ketamine played the role of introductory agent. The Ketamine brought the new wave of studies regarding the development of new and more effective antidepressant drugs and comprehension of the neurobiology of the depression. The different targets of glutamatergic system and neurobiological pathways are confirmed by Ketamine. The ketamine produces a remarkable rapid onset antidepressant effect hours or days in contrast to the delayed onset of current antidepressant drugs is confirmed by abundant clinical data. For the treatment of depressive illness, the discovery of ketamine's rapid onset antidepressant effect is a game changer [26].

Ketamine: -

Ketamine is N-Methyl-D-Aspartate receptor and is known to rapidly reduce suicidal ideation (SI) and depressive symptoms in patients with major depressive disorder. It exerts antidepressant effects and enhances descending inhibiting serotoninergic pathways. It is a racemic mixture comprising of (S)-Ketamine or (esketamine) and (R)-Ketamine or (arketamine). (S)-Ketamine has higher affinity for N-Methyl-D-Aspartate than (R)-Ketamine, so Esketamine was developed as an antidepressant. It was approved by Food and drug administration on 5th March 2019 [27].

Structure: -

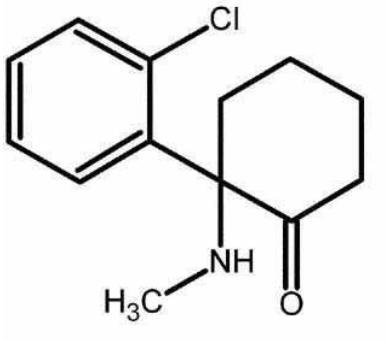

Fig1.4: Structure of Ketamine ($C_{13}H_{16}ClNO$**)**

GLUTAMATERGIC SYNAPSE: A PROMISING TARGET TO TREAT MAJOR DEPRESSIVE DISORDER (MDD)

Pharmacodynamics

Ketamine rapidly reduces the depression and suicidal thoughts within 1 day and up to 1 week significantly on clinician administration. Numerous routes of administration has been investigated. For the ease of use and high accessibility, the oral ketamine is being administered. Intravenous

(IV) has rapid antidepressant effects but poor accessibility of route IV [28]. Intravenous routes are most commonly employed but the safety and efficacy have been described by the other routes of administration i.e. oral, intranasal, subcutaneous, sublingual and intramuscular routes. Ketamine is mostly administered in the dose of 0.5 mg/kg. Some patients who respond to the low doses may require 0.1 mg/kg dose. The safety and the efficacy of ketamine dose have been demonstrated in the sessions ranging between 2 to 100 minutes but it is conventionally administered across 40 minutes [29]

Mechanism of action

Ketamine as an antidepressant includes synaptic or GluN2B- selective extra – synaptic N-Methyl- D-Aspartate receptor (NMDAR) inhibition, inhibition of NMDAR – dependent burst firing of lateral habenula neurons, inhibition of NMDARs localized on GABAergic interneurons and the role of α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid receptor. Ketamine's downstream mechanisms regulates the synaptic plasticity, including brain derived neurotrophic factor (BDNF), mechanistic target of rapamycin (mTOR), glycogen synthase kinase-3 (GSK-3) and eukaryotic elongation factor 2(eEF2). The ketamine's (R)-ketamine enantiomer and hydroxynorketamine (HNK) metabolites, (2R,6R)-HNK does not involve the mechanisms of direct inhibition of the NMDAR. The ketamine's action may act in the complementary manner to exert acute changes in synaptic plasticity, leading to the strengthening of excitatory synapses, which are necessary for antidepressant behavioral actions [30].

Absorption and role of elimination

The absorption of ketamine is very rapid and the bioavailability is 93%. Only 17% of administered drug is absorbed after the first pass of the metabolism. It presents the distribution half life of 1.95 minutes. The levels of the Cmax reach at the peak of 0.75mcg/ml in plasma and 0.2 mcg/ml in the cerebrospinal fluid.

Pharmacokinetic studies have resulted in 85-95% of the administered dose in the urine is recovered in the form of metabolites. The other routes of elimination of ketamine are bile and faeces. The resultant recovery is distributed by 91% of the administered dose in urine and 3% in the faeces, when the drug is administered intravenously.

Being a chronic condition that affects 5.1% of men and 8.1% of women during their life time, 121 million people around the world currently suffer from major depressive disorder. Over a third of the patients suffering from major depressive disorder fail to respond to two or more antidepressant treatments [31]. There are lot many drugs related to major depressive disorder like Fluoxetine, Citalopram, Sertraline, Ketamine, Dextromethorphan but all of these are not related to glutamatergic pathway except Ketamine. For the treatment of MDD, the glutamatergic system has emerged as a novel pathway with the focus on producing both rapid and sustained antidepressant effects. Dextromethorphan is considered as noncompetitive N-Methyl-D-Aspartate receptor antagonist that have antidepressant like effects. The rapid and sustained antidepressant like effects have not been evaluated [32]. The research is going on to the development of easy to administer drug given to NMDAR antagonists without the risk of brain toxicity and which is related to glutamatergic system.

CONCLUDING REMARKS

MDD is a severe psychiatric illness that affects the lives and functioning of millions of people worldwide. Compelling evidence suggests that, cellular resilience and neuroplasticity take part in the expression of affective illness [33]. This provides a credible role for implicating glutamatergic system dysregulation in the pathophysiology of MDD. The reviewed data here explains that, MDD is associated with abnormal functioning of the glutamatergic synapse and it’s signaling. A continued collaboration between preclinical studies and clinical study can fetch good results to omit the extent of these abnormalities.

A decent clinical study added with brain imaging report analysis targeting glutamatergic synapse of reasonable sampling sizes paves way to lead this review to promising research finding. The role of ketamine, targeting glutamate pathway in the treatment of MDD leads to the new revolution in the pharmacodynamics and the mode of action of the drugs.

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GLUTAMATERGIC SYNAPSE: A PROMISING TARGET TO TREAT MAJOR DEPRESSIVE DISORDER (MDD)

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To Whomsoever it may concern

Date: 28/12/2020

Ref no : CIBioD/20/241

Name: Cheshta

This is to certify that she has participated in an Online Student Attachment Programme.

She has attended the Online Sessions and Report Writing training.

We wish her luck for future Endeavours.

Project Manager

Gunjan

CIBioD

CIBioD

Center for Innovation and Bio-Design

Certificate

OF ATTACHMENT

PRESENTED TO

Chesta Kamboj

Congratulations!

You have been selected by The ***Center for Innovation and Bio-Design (CIBioD)*** *for an* ***Attachment Program.***

The Project is a Multi-Disciplinary Initiative designed to Incubate, Prototype, and Commercialize Novel Ideas in Health Care.

Gunjan Sharma

CIBioD Project Director

Star ATTACHMENT

Date: December 7, 2021

Ref. no: CIBioD/21/623

TO WHOM IT MAY CONCERN

We appreciate **Ms. Noveldeep Kaur**, a student of **Mehr Chand Mahajan DAV College for Women**, for participation in **Arogaya CIBioD Short Term Attachment (STA) Programme** held during March 2021 to September 2021 in online mode. The aim of the STA is to promote and inculcate the innovation and entrepreneurship culture among the young students. Total 21 sessions have been conducted under the major themes of Innovation in Medical technologies and devices, Cyber/Data security in Healthcare, Research Design and Methodology and Intellectual Property Rights.

We wish all success in his/her future endeavors and career ahead.

वरिन्दर गर्ग

Dr. Varinder Garg
Principal Investigator
ICMR- Center for Innovation and Bio-Design (CIBioD),
PGIMER, Chandigarh

Welcome Shweta Sen Sign out

Controller General of Patents, Designs & Trade Marks

सत्यमेव जयते

INTELLECTUAL PROPERTY INDIA
PATENTS | DESIGNS | TRADE MARKS
GEOGRAPHICAL INDICATIONS

G.A.R.6
[See Rule 22(1)]
RECEIPT

Docket No 46950 **Date/Time 2023/04/22 08:21:39**

To **UserId: integrum09**
Shweta Sen

INTEGRUM IP 191/7, TOWER 7C, SBP EXTN. III, SECTOR 126, MOHALI-140307, PUNJAB, INDIA

CBR Detail:

Sr. No.	Ref. No./Application No.	App. Number	Amount Paid	C.B.R. No.	Form Name	Remarks
1	202311029243	TEMP/E-1/33320/2023-DEL	1600	18416	FORM 1	A BIODEGRADABLE AUTOMATED POOPING SYSTEM AND A PROCESS FOR THE PREPARATION THEREOF

TransactionID	Payment Mode	Challan Identification Number	Amount Paid	Head of A/C No
N-0001137485	Online Bank Transfer	2204230000816	1600.00	1475001020000001

Total Amount : ₹ 1600.00
Amount in Words: Rupees One Thousand Six Hundred Only

Received from Shweta Sen the sum of ₹ 1600.00 on account of Payment of fee for above mentioned Application/Forms.
* This is a computer generated receipt, hecnce no signature required.

Print

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FORM 5
THE PATENTS ACT, 1970
(39 of 1970) &
The Patents Rules, 2003
DECLARATION AS TO INVENTORSHIP
[See section 10(6) and rule 13(6)]

1. NAME OF THE APPLICANTS:

DR. VARINDER GARG	INDIAN	Principal Investigator, Centre for Innovation and Bio-Design (CIBioD), PGIMER, Sector 12, Chandigarh-160012 India. R/O # 3334, Sector 24 D, Chandigarh, India.
DR. HARISH KUMAR	INDIAN	Co-Principal Investigator, Centre for Innovation and Bio-Design (CIBioD), PGIMER, Sector 12, Chandigarh-160012 India. R/O # E1-41, Sector- 14, Panjab University Campus, Chandigarh, India.

hereby declare that the true and first inventor(s) of the invention disclosed in the complete~~/provisional~~ specification filed in pursuance of ~~my~~ / our application numbered **…….**dated **…….**

2. INVENTORS

Aishwarya Rajaram Hiray	INDIAN	09, Shivneri, Shivteertha Colony, Abhiyanta Nagar, Nashik, Maharashtra – 422009, India.
Ramandeep Kaur	INDIAN	B-5,489 Near general bus stand, Malout road, Sri Muktsar Sahib, Punjab- 152026, India.
Manvi Singh	INDIAN	Village- Enayatpur, P.O – Katethi, Katethi, Kanpur Dehet, Uttar Pradesh- 209121, India.
Dr. Sandeep Kaur	INDIAN	Assistant Professor, Mehr Chand Mahajan DAV College for Women Sector 36, Chandigarh-160036, India.
Dr. Vandana Sharma	INDIAN	Assistant Professor, Mehr Chand Mahajan DAV College for Women, Sector 36, Chandigarh-160036, India.
Dr. Ranvir Singh	INDIAN	Department cum National Center for Human Genome Studies and Research, Pharmacy Extension Block,Sector-14, Panjab University, Chandigarh 160014, India
Shubham Rattra	INDIAN	#5162, Tdi City, Sector-116, Mohali – 140307, India
Shreerama Shiva Sai Bharadwaja	INDIAN	#11, Defence Apartment, Dhakoli, S.A.S Nagar, 140603, Punjab, India
Chaitanya	INDIAN	2133 A, Sector 42-C, Chandigarh – 160036, India

Siddhant Mukherjee	INDIAN	Beena Apartment CHS Ltd, Plot No-96, Flat No-105, Sector-14, Koparkhairane, Navi Mumbai-400709, India
Dr. Naresh Kumar	INDIAN	House No. E1/54, Panjab University Campus, Sector 14, Chandigarh 160014, India
Dr. Manish Modi	INDIAN	Professor, Department of Neurology PGIMER , Sector 12, Chandigarh -160012 India
Dr. Manoj Goyal	INDIAN	Adnl Professor, Department of Neurology PGIMER , Sector 12, Chandigarh -160012, India.

Dated this 21st day of April, 2023

3. ~~DECLARATION TO BE GIVEN WHEN THE APPLICATION IN INDIA IS FILED BY THE APPLICANT(S) IN THE CONVENTION COUNTRY:~~
~~We the applicant(s) in the convention country hereby declare that our right to apply for a patent in India is by way of assignment from the true and first inventor(s).~~
~~Dated this ___ Day of _____2011~~

4. ~~STATEMENT (to be signed by the additional inventor(s) not mentioned in the application form)~~
~~I/We assent to the invention referred to in the above declaration, being included in the complete specification filed in pursuance of the stated application. N.A.~~
~~Dated this ___ day of 2011 Signature of additional inventor(s): Name:~~

SHWETA SEN
IN/PA No-3010
(PATENT AGENT FOR APPLICANTS)

To
The Controller of Patent
The Patent Office Branch
New Delhi

FORM 1 THE PATENTS ACT 1970 (39 of 1970) and The Patents Rules, 2003 **APPLICATION FOR GRANT OF PATENT** [(See section 7,54 & 135 and sub-rule (1) of rule 20*)*		**(FOR OFFICE USE ONLY)**
	Application No:	
	Filing Date:	
	Amount of Fee Paid:	
	CBR No:	
	Signature	
1. APPLICANT'S REFERENCE / IDENTIFICATION NO. (AS ALLOTTED BY OFFICE):		

2. TYPE OF APPLICATION [Please tick(✓) at the appropriate category]					
Ordinary(✓)		Convention ( )		PCT-NP ( )	
Divisional ( )	Patent of Addition ( )	Divisional ( )	Patent of Addition ( )	Divisional ( )	Patent of Addition ( )

3A. APPLICANT~~(S)~~

Name in Full	**Nationality**	**Country of Residence**	**Address of the Applicant**
Dr. Varinder Garg	Indian	India	Principal Investigator, Centre for Innovation and Bio-Design (CIBioD), PGIMER, Chandigarh, India. R/O # 3334, Sector 24 D, Chandigarh, India.
Dr. Harish Kumar	Indian	India	Co-Principal Investigator, Centre for Innovation and Bio-Design (CIBioD), PGIMER, Chandigarh, India. R/O # E1-41, Sector- 14, Panjab University Campus, Chandigarh, India.

3B. CATEGORY OF APPLICANT [Please tick(✓) at the appropriate category]			
Natural Person (✓)	Other than Natural Person ()		
	Small Entity ( )	Startup ( )	Others ( )

4. INVENTOR(S) [Please tick(✓) at the appropriate category]		
Are all the inventor(s) same as the applicant(s) named above?	Yes ()	No (✓)
If "No", furnish the details of the inventor(s)		

Name in Full	Nationality	Country of Residence	Address of the Inventor
Aishwarya Rajaram Hiray	Indian	India	09, Shivneri, Shivteertha Colony, Abhiyanta Nagar, Nashik, Maharashtra – 422009, India.
Ramandeep Kaur	Indian	India	B-5,489 Near general bus stand, Malout road, Sri Muktsar Sahib, Punjab- 152026, India.
Manvi Singh	Indian	India	Village- Enayatpur, P.O – Katethi, Katethi, Kanpur Dehet, Uttar Pradesh- 209121, India.
Dr. Sandeep Kaur	Indian	India	Assistant Professor, Mehr Chand Mahajan DAV College for Women Sector 36, Chandigarh-160036, India.
Dr. Vandana Sharma	Indian	India	Assistant Professor, Mehr Chand Mahajan DAV College for Women, Sector 36, Chandigarh-160036, India.
Dr. Ranvir Singh	Indian	India	Department cum National Center for Human Genome Studies and Research, Pharmacy Extension Block,Sector-14, Panjab University, Chandigarh 160014, India
Shubham Rattra	Indian	India	#5162, Tdi City, Sector-116, Mohali – 140307, India
Shreerama Shiva Sai Bharadwaja	Indian	India	#11, Defence Apartment, Dhakoli, S.A.S Nagar, 140603, Punjab, India
Chaitanya	Indian	India	2133 A, Sector 42-C, Chandigarh – 160036, India
Siddhant Mukherjee	Indian	India	Beena Apartment CHS Ltd, Plot No-96, Flat No-105, Sector-14, Koparkhairane, Navi Mumbai-400709, India
Dr. Naresh Kumar	Indian	India	House No. E1/54, Panjab University Campus, Sector 14, Chandigarh 160014, India
Dr. Manish Modi	Indian	India	Professor, Department of Neurology PGIMER , Sector 12, Chandigarh -160012 India

Dr. Manoj Goyal	Indian	India	Adnl Professor, Department of Neurology PGIMER , Sector 12, Chandigarh -160012, India.

5. TITLE OF THE INVENTION- **A BIODEGRADABLE AUTOMATED POOPING SYSTEM AND A PROCESS FOR THE PREPARATION THEREOF**

6. AUTHORISED REGISTERED PATENT AGENT(S)	IN/PA No.	**3010**
	Name	**Shweta Sen**
	Mobile No.	**8283818640**
7. ADDRESS FOR SERVICE OF APPLICANT IN INDIA	Name	**Integrum IP**
	Postal Address	**191/7, SBP Extn-III, Sector-126, Mohali- 140307, Punjab, India**
	Telephone No.	
	Mobile No.	**8283818640**
	Fax No.	
	E-mail ID	**integrumip@gmail.com**

~~**8. IN CASE OF APPLICANT CLAIMING PRIORITY OF APPLICATION FIELD IN CONVENTION COUNTRY, PARTICULARS OF CONVENTION APPLICATION**~~

~~Country~~	~~Application Number~~	~~Filing Date~~	~~Name of the Applicant~~	~~Title of the invention~~	~~IPC (as classified in the convention country)~~

~~**9. IN CASE OF PCT NATIONAL PHASE APPLICATION, PARTICULARS OF INTERNATIONAL APPLICATION FILED UNDER PATENT CO-OPERATION TREATY (PCT)**~~

~~International application number~~	~~International filing date~~

~~**10. IN CASE OF DIVISIONAL APPLICATION FILED UNDER SECTION 16, PARTICULARS OF ORIGINAL (FIRST) APPLICATION**~~

~~Original (First) application No.~~	~~Date of filing of Original (First) Application~~

~~**11. IN CASE OF PATENT OF ADDITION FILED UNDER SECTION 54, PARTICULARS OF MAIN APPLICATION OR PATENT**~~

~~Main Application/Patent No.~~	~~Date of filing of Main Application~~

12. DECLARATIONS:

(i) Declaration by the Inventor (in case the applicant is an assignee: the inventor(s) may sign herein below or the applicant may upload the assignment or enclose the assignment with this patent application or send the assignment by post/electronic transmission duly authenticated within the prescribed period).

~~I~~/We, the above-named inventor(s) ~~is~~/are the true & first inventor(s) for this Invention and declare that the applicant~~(s)~~ herein is/~~are~~ my assignee or legal representative.

Dated: 21-04-2023

(Aishwarya Rajaram Hiray)
Signature

(Ramandeep Kaur)
Signature

(Manvi Singh)
Signature

(Dr. Sandeep Kaur)
Signature

(Dr. Vandana Sharma)
Signature

(Dr. Ranvir Singh)
Signature

(Shubham Rattra)
Signature

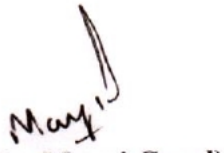
(Shreerama Shiva Sai Bharadwaja)
Signature

(Chaitanya)
Signature

(Siddanth Mukherjee)
Signature

(Dr. Naresh Kumar)
Signature

(Dr. Manish Modi)
Signature



(Dr. Manoj Goyal)
Signature

~~(ii) Declaration by the Applicant(s) in the convention country~~

~~(In case the applicant in India is different than the applicant in the convention country:~~ ~~the applicant in the convention country may sign herein below or applicant in India may upload the assignment from the applicant in the convention country or enclose the said assignment with this application for patent or send the assignment by post/electronic transmission duly authenticated within the prescribed period).~~

~~I/We, the Applicant(s) in the convention country declare that the applicant(s) herein is/are my/our assignee or legal representative.~~

~~(a) Date:~~

~~(b) Signature(s)~~

~~(c) Name(s) of the signatory~~

(iii) Declaration by the Applicant~~(s)~~

~~I~~/We, the Applicant~~(s)~~ hereby declare(s) that: -

- ~~I am~~ / We ~~are~~ in possession of the above-mentioned invention.
- The provisional~~-~~/ ~~complete~~ specification relating to the invention is filed with this application.
- ~~The invention as disclosed in the specification uses the biological material from India and the necessary permission from the competent authority shall be submitted by me/us before the grant of patent to me/us.~~
- There is no lawful ground of objection(s) to the grant of the Patent to me/us.
- I am/~~We~~ are the assignee or legal representative of true & first inventor(s).
- ~~The application or each of the applications, particulars of which are given in Paragraph 8 was the first application in convention country/countries in respect of my/our invention(s).~~
- ~~I/We claim the priority from the above mentioned application(s) filed in convention country/countries and state that no application for protection in respect of the invention had been made in a convention country before that date by me/us or by any person from which I/We derive the title.~~

- ~~My/our application in India is based on international application under Patent Cooperation Treaty (PCT) as mentioned in Paragraph 9.~~
- ~~The application is divided out of my/our application particulars of which are given in Paragraph 10 and pray that this application may be treated as deemed to have been filed on DD/MM/YYYY under section 16 of the Act.~~
- ~~The said invention is an improvement in or modification of the invention particulars of which are given in Paragraph 11~~.

13. FOLLOWING ARE THE ATTACHMENT WITH THE APPLICATION

(a) Form 2

Item	Details	Fee	Remarks
~~Complete/~~Provisional specification)	No. of pages: 9		
~~No. of Claim(s)~~	~~No. of claims:~~		
	~~No. of pages:~~		
Abstract	No. of pages: 1		
No. of Drawing(s)	No. of drawings: 04		
	No. of pages: 03		

In case of complete specification, if the applicant desires to adopt the drawings filed with his provisional specification as the drawings or part of the drawings for the complete specification are required to be mentioned here.

(b) ~~Complete specification~~/provisional specification (in connection with the international application)/as amended before the International Preliminary Examination Authority (IPEA), as applicable (2 copies).

(c) ~~Sequence listing in electronic form~~

(d) Drawings (in conformation with the international application)/as amended before the International Preliminary Examination Authority (IPEA), as applicable (2 copies).

(e) ~~Priority document(s) or a request to retrieve the priority document(s) from DAS (Digital Access Service) if the applicant had already requested the office of first filing to make the priority document(s) available to DAS.~~

(f) ~~Translation of priority document/Specification/International Search Report/International Preliminary Report on Patentability.~~

(g) Statement and undertaking on Form 3

(h) Declaration of inventor ship on Form 5

(i) Power of Authority

(j) …….

Total fee Rs. 1600 /- (Rs. One thousand six hundred only) via online payment method.

Dated: 21-04-2023

I/~~We~~ declare that to the best of my/~~our~~ knowledge, information and belief the fact and matters stated herein are correct and I/~~We~~ request that a patent may be granted to me/~~us~~ for the said invention.

Dated: **21-04-2023**

Shweta Sen
IN/ PA No.3010
(Patent Agent for Applicants)

To
The controller of patents
The patent office, at New
Delhi