REPORT

Report on participation of the ICMR International Fellow (ICMR-IF) in Training/Research abroad.

1. Name and designation of ICMR- IF :

   Priya Srinivas, Scientist G and Dean, Academic Affairs

2. Address :

   Rajiv Gandhi Centre for Biotechnology, Thycaudu P O, Thiruvananthapuram-695014, Kerala, India

3. Frontline area of research in which training/research was carried out :

   Microfluidic organs-on-chip organoid cultures and detecting changes in cellular function by secreted cancer biomarkers and its paracrine actions using microfluidic systems.

4. Name & address of Professor and host institute :

   Professor. Alexander Revzin, Professor of Biomedical Engineering, College of Medicine, Mayo Clinic, Rochester, Minnesota, USA.

5. Duration of fellowship with exact date :3 months; 27/3/2023 to 27/6/2023

6. Highlights of work conducted :

   i) Technique/expertise acquired :

- Design and fabrication of the microfluidic device
  - Photomask design using AutoCAD
  - Fabrication protocols for developing of photoresist
- Microfluidic device fabrication with Polydimethylsiloxane (PDMS), a silicone elastomer
  - Pouring and degassing the PDMS
  - Peeling and cutting out microfluidic chips
  - Bonding a microfluidic device to a glass substrate by plasma bonding
  - Microfluidic Device testing protocols
- *Ex vivo* organoid culture of cancer tissue with micro fluidic system
- Microfluidic Cancer-on-Chip platform for coculture studies with cancer cells and macrophages for paracrine activity studies
- Microfluidic device making with more cost-effective fabrication using polymethylmethacrylate (PMMA), an acrylic-based thermoplastic exhibiting

good mechanical stability, chemical resistivity, and high transparency with glass-like optical clarity.

ii) Research results, including any papers, prepared/submitted for publication:

- Co-cultures using both microfluidic and standard approaches to explore paracrine interactions of β-human chorionic gonadotropin (β-hCG) stimulation of BRCA1-defective cancer cells. Results of the experiments are attached as Annexure-1.
- The study will be continued in India and the results will be included along with the manuscript that "β-hCG expression in breast Cancers".
- Conference Presentation: Invited Speaker: *"Pregnancy hormone can modulate cancer progression in BRCA1 defective cancers"*. presented a joint event between the International Ovarian Cancer Research Consortium and International Society of Precision Cancer Medicine, June 12-13 at, Oklahoma, USA.

iii) Proposed utilization of the experience in India:

Immediate plans:

- I had initiated the analysis of co-culture of Cancer cells with the macrophages using microfluidic systems in comparison to standard cell cultures. This will be continued in India for testing paracrine activities of various secreted biomarkers on BRCA1 defective cancers with the microfluidic silica wafers that are provided by Professor Alexander Revzin.

Long-term plans:

- During my fellowship program at Mayo Clinic, I have submitted a project to ICMR entitled "*Analysis of tumor characteristics and therapeutic strategies for β-hCG positive Breast Cancer Patients from Kerala using microfluidic organ-on-a-chip culture device*". This is to test effects of hCG and other signals originating from BRCA1 defective cancers on stromal or immune cells residing in the tumor microenvironment using microfluidic systems and to identify therapeutics using organ-on-chip cultures. Professor Revzin has kindly agreed to support this project in providing technical advice related to designing devices and will also fabricate wafers that can be sent to my lab at Rajiv Gandhi Centre for Biotechnology.
- The possibilities of sending PhD students from my laboratory to Professor Revzin's laboratory at Mayo Clinic for performing a part of their study, involving more complex microfluidic studies like non-invasive detection of biomarkers will be explored.
- Also, while my visit to Mayo Clinic, I had discussions for initiating collaborations with Professor Kannan Nagarajan, Assistant Professor of Laboratory Medicine

and Pathology, Division of Experimental Pathology and Laboratory Medicine, Department of Laboratory Medicine and Pathology and Department of Cancer Biology, Mayo Clinic, Rochester, MN, for performing analysis on breast cancers with BRCA1 mutations for βhCG expression.

Priya Srinivas
01/07/2023

Signature of ICMR-IF
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