Vigyan Patrika

Biopatrika

Lab Grown Mini-embryos For Toxicity Screening

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Work done in the lab of Dr. Rajarshi Pal at Eyestem Research, Centre for Cellular and Molecular Platforms (C-CAMP) and the University of Trans-Disciplinary Health Sciences (TDU) and Technology, Bengaluru.

Vijay completed his Masters in Microbiology from Andhra University, Visakhapatnam. He then completed his Ph.D. from AMET University, Chennai. The focus of his doctoral thesis was characterization of Mesenchymal stem cells derived from different tissue sources and their suitability in therapy. Earlier, he started his career as an Embryologist in Satya IVF clinic where he gained expertise in IVF & micromanipulation techniques. He further gained valuable experience on isolation, culturing, and differentiating human embryonic stem cells at Reliance Life Sciences, Mumbai. At Lonza, Hyderabad he was involved in developing 3D cornea and Tissue engineered skin for Drug toxicity and penetration studies. From 2015 to 2017, he worked with OvaScience, Abu Dhabi on cutting-edge treatments for Infertility. Currently, at Eyestem, he is handling the project on creating a biobank for patient-specific iPSC and other cell lines.

How would you explain your research outcomes to the non-scientific community?

Every year, 100's of novel drugs are approved by USFDA (United States Food and Drug Administration) or other regulatory agencies worldwide. Did you ever wonder that any drug (medicine) we take may have side-effects (toxicity) on our body? Establishing the safety of these drugs especially during pregnancy is extremely important. But how do we test them ethically without using a human embryo or fetus and what are the different embryonic or fetal tissues that might potentially be affected?

To address these questions, we generated mini embryo-like structures in a dish (called Embryoid Bodies - EB) that replicate the characteristics of a developing fetus in a mother's womb using Human induced pluripotent stem cells (hiPSCs). Theoretically, hiPSCs are engineered equivalents of Human embryonic stem cells which can give rise to any organ in the body. These EBs, mimicking gastrulation stage embryos, are easy to scale up for high throughput screening of drugs and pharmaceutical compounds. Such a biologically relevant in vitro model also reduces the usage of animals for drug screening and disease research. Employing this robust platform, we showed for the first time that established drugs like Folic acid, and Dexamethasone could cause Embryotoxicity in humans at certain concentrations.

How do these findings contribute to your research area?

Our team focuses on developing novel, scalable and affordable solutions using Pluripotent stem cells encompassing Cell therapy, Disease modelling and Drug screening. The current findings regarding the toxicity of known drugs perfectly corroborates with our broad area of interest. We will continue to break boundaries and create such unique platform technologies that will be helpful for the drug development process.

What was the exciting moment during your research?

I started my career as a Clinical Embryologist. When I looked at a fertilized human egg under the microscope for the first time, it took my breath away. Then, I witnessed the metamorphosis of the same embryo into a newborn after 36-40 weeks in gestation, and that moment cannot be expressed in words. After a long duration, I went through a similar experience when I successfully derived human iPSC lines from children suffering from Inherited Retinal dystrophies in my current lab using Episomal (non-viral, non-integrating) method. Adding to this excitement is the fulfillment when several Highly reputed Research labs around the world approached to collaborate on these patient-specific iPSC lines.

What do you hope to do next?

In the lab of Dr. Rajarshi Pal, apart from drug screening and toxicological testing, we have a strong cell therapy program for treating complex and incurable retinal disorders. I personally wish to bolster my lab's translational goals and contribute through my expertise and experience involving embryology and hiPSC research. To be precise, I want to create retinal organoids from the patient-specific hiPSC lines to understand the disease pathology at molecular level, and examine their phenotype after gene (mutation) correction.

Where do you seek scientific inspiration?

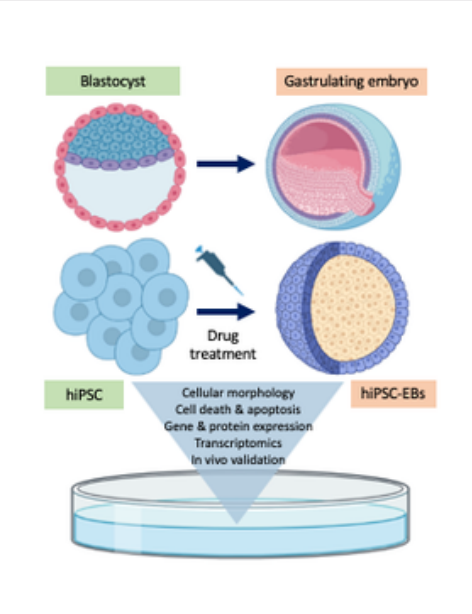
I constantly get inspired from the joy and enthusiasm that comes from day-to-day experimental observations. I am very excited to see that these stem cells are like blank slates and they do respond to the biochemical signals that I provide them. In fact, they reciprocate to the external cues by displaying change in their morphology, numbers and other features. Needless to say that my mentors and also the great scientists across the globe keep inspiring me to work even harder in order to achieve my goals.

How do you intend to help Indian science improve?

I feel that Indian science is going through a tremendous growth phase and of course we would like to actively contribute to that. We are a part of an extraordinary startup ecosystem at C-CAMP where deep science ideas and innovations are encouraged and nurtured to develop novel solutions for real life problems. I am confident that the collaboration between industry and academia is one of the best approaches to foster meaningful scientific research and that is the approach we have adopted.

Reference

Konala VBR, Nandakumar S, Surendran H, Datar S, Bhonde R, Pal R. Neuronal and cardiac toxicity of pharmacological compounds identified through transcriptomic analysis of human pluripotent stem cell-derived embryoid bodies. Toxicol Appl Pharmacol. 2021 Dec 15;433:115792. doi: 10.1016/j.taap.2021.



Collation of early embryonic development and iPSC differentiation indicates the comparable stages. This model allows us to recreate both pre- and post-implantation development in a dish. Drug-treated iPSC and EBs were screened for teratogenic effects using multiple readouts. (Created in BioRender.com)