CellPress

Cell Stem Cell

Voices

Introductions to the Community: Early-Career Researchers in the Time of COVID-19

COVID-19 has unfortunately halted lab work, conferences, and in-person networking, which is especially detrimental to researchers just starting their labs. Through social media and our reviewer networks, we met some early-career stem cell investigators impacted by the closures. Here, they introduce themselves and their research to our readers.

Context Is Everything

Marta Shahbazi
MRC Laboratory of Molecular Biology (LMB)

"Genes alone are powerless," my university teacher proclaimed! The sequencing of the human genome had just been completed, and he wanted to emphasize the critical role of cell and tissue environment in animating, even determining, the function of genes. Context, it turns out, animates our daily lives too. Just weeks after opening my own group at the LMB the institute closed. My environmental context changed abruptly, and with it my interactions and functions.

I am at heart a curious scientist, but this parenthesis in my life has changed the way I express this. I enjoy time with my 6-month-old daughter, and I spend more time reading, thinking, and planning. The intense focus of completing experiments has been replaced by more diffuse contemplation. Although the transition has not been easy, I am lucky. My husband, despite being a key worker, rushes back home every day so I can delve into science. The LMB has been reassuring, pausing clocks that underpin training and tenure as we readjust to a new normal.

How will this temporary change in context impact me? Hard to predict, but as I now return to the lab, I want to answer the same question for pluripotent stem cells. These cells form an epithelial tissue early in mammalian embryogenesis. How does this change in context feed back to modulate gene function, pluripotency loss, and differentiation? What environmental changes underlie reacquisition of pluripotency during reprogramming? The answers will lie in how "powerless genes" are empowered by context.

Human Disease Models and Therapeutics

Samira Musah
Duke University

I am a stem cell biologist and bioengineer. In 2019, I opened my research lab at Duke University, with a joint appointment in the Departments of Biomedical Engineering and Medicine (in the Division of Nephrology). In addition to being a Duke MEDx Investigator, I am an Affiliated Faculty of Duke's Regeneration Next initiative.

My lab's research focuses on developing methods to direct differentiation of human pluripotent stem cells and to reprogram cells with specificity and efficiency. We extend these methods to engineer functional models of human organs. We aim to understand the roles of molecular and biophysical cues in organ development, and to harness these organ developmental processes to uncover disease mechanisms and develop new therapeutics.

More than 14% of the United States population suffers from kidney disease, which lacks targeted therapies. My lab seeks to advance the treatment of kidney disease through three core research areas: (i) using patient-derived stem cells to study kidney development and disease mechanisms; (ii) engineering functional human kidney models for use in drug discovery; and (iii) engaging in direct reprogramming of cells to autonomously sense and trigger regenerative pathways for injury repair.

The impacts of the COVID-19 pandemic have been overwhelming; our lab shut down for months, limiting our ability to train new personnel and acquire preliminary data for grant applications. We hope to soon return to the lab at full capacity, safely and responsibly.

Embryonic Tale of Tumorigenesis

Ankur Sharma
Genome Institute of Singapore

My upcoming laboratory at Harry Perkins Institute of Medical Research and Curtin University focuses on the triquetra of early development, regeneration, and cancer. We are interested in understanding the developmental origin of cancer by uncovering the similarities between embryogenesis and tumor development. In close association with our clinical collaborators, we also study how tumors co-evolve with their microenvironment, especially in the context of tumor initiation and drug resistance. To address these questions, we combine single-cell genomics, spatial transcriptomics, and machine learning approaches. We are expanding our collaborations to integrate experimental, computational, and clinical knowledge to exhume the "seeds" of cancer development.

In the pre-COVID era, I was set to start my lab in mid-2020; however, the current pandemic has deferred my move for a few more months. Surely, COVID has forced us into quiescence, but just like a cell, we have continued to communicate with our ecosystem, building new collaborations and a stronger team to combat cancer. I am extremely grateful to the leadership and collogues at The Perkins and Curtin who are working with me to make things easier; I couldn't have asked for a better niche. The recent crisis has highlighted the need for affordable and borderless science for the collective benefit of society. Therefore, we are eagerly looking forward to the "new beginnings" and our resilience to fight cancer is stronger than ever.

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Defining the Leukemia Niche

Jeevisha Bajaj
University of Rochester Medical Center

As a graduate student working with oncologists in India, I was struck by the number of patients presenting with late-stage cancers. While diseases like CML are managed well in developed countries, rapid progression to drug-resistant acute stage is the sad reality elsewhere. To identify novel therapeutic approaches to target leukemia, I was drawn toward the microenvironment of disease-propagating cancer stem cells. After my work at UCSD on adhesive interactions of leukemia with its niche, I was elated to start my own lab at Rochester in late 2019. My lab's goal is to determine molecular mechanisms of cancer stem cell interactions with their microenvironment during disease progression. We address this in mouse models and primary patient samples using tools such as CRISPR and *in vivo* imaging.

In the busy and exciting phase of setting up my lab, we were suddenly struck by the pandemic. As a young investigator, it was disorienting to abruptly cease all work and idle. With reopening, I was delighted to start again, although the hiring freeze and travel restrictions impacted our pace. A COVID scare in our group soon after was unnerving, but we moved on. The experience has served as a powerful reminder of how science is a cooperative activity, and how much we rely on our colleagues.

In these uncertain times, support and encouragement from senior colleagues at URMC has been a great comfort. The pandemic will pass and I am confident we will soon create a flourishing lab environment.

Chromatin Plasticity

Giacomo Donati
University of Turin

After a postdoc at CR-UK Cambridge Institute and at King's College London (UK) in a vibrant multi-disciplinary lab, I moved back to Italy where I established my laboratory (http://www.donatilab.org) at the Molecular Biotechnology Center in Turin. There I built a fantastic international team of motivated scientists in a stimulating academic environment.

As a geneticist with cellular and molecular biology backgrounds, I am interested in how cells quickly respond to stimuli and easily adapt to these changes to restore homeostasis, and skin represents a great model to answer fundamental biological questions of this phenomenon. Like many epithelia, skin is renewed periodically and repaired upon injury throughout life by multiple pools of adult stem cells. During wound healing many cell lineages at various differentiation states act to restore skin integrity through acquisition of cell plasticity. In our lab, we integrate state-of-the-art cellular and molecular biology techniques, such as lineage tracing, functional genetic screenings, *in vivo* single-cell omics, and computational methods to identify the network of epigenetic and transcriptional regulators controlling cell plasticity during tissue repair. Importantly, since cancer and wound healing share many features at the molecular and cellular level, including several inflammatory events, our findings hold great potential to identify new therapeutic targets for cancer treatment.

Deciphering Aging Mechanisms

Weiqi Zhang
Beijing Institute of Genomics, CAS

Aging triggers functional decline, a root cause of devastating human disorders that impact individuals, families, and society. My lab is searching for mechanisms underlying age-related decline and teasing apart the molecules involved, with an emphasis on epigenetic regulation. Given the complicated but clear relationships between regeneration and aging, our group is also committed to delaying aging-related functional decline by promoting regeneration.

Though the COVID-19 pandemic interrupted the pace of our work, being surrounded by supportive collaborators, colleagues, and students has been tremendously helpful. Indeed, frequent, comprehensive discussions have continued both online and offline, and our efforts have been redirected toward data mining and integration. For example, in collaboration with data experts, we built a database called Aging Atlas, which compiles large gene expression and regulation datasets from high-throughput omics technologies. This will serve as a valuable resource for the aging field. This epidemic is also surfacing new questions for the aging field as elderly people are more vulnerable to COVID-19. We have thus initiated efforts to uncover links between advanced age and COVID-19 severity. By studying why humans age, and how to delay aging, I believe treatments for human chronic diseases and infectious diseases, such as COVID-19, can be rationally developed.