Cell Stem Cell

CellPress

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.

(Re)engineering Cell Fate

Katie Galloway
MIT Chemical Engineering

In 2019, I opened my lab at MIT to develop synthetic biology tools to engineer cell fate. While prokaryotic and single-cell eukaryotic organisms have dominated the field of synthetic biology, the advent of improved vectors and genetic editing tools is unleashing the potential of synthetic biology to reshape how we study development and treat disease.

My lab constructs synthetic gene circuits as model chromatin systems to understand the biophysical basis of gene regulation and the resulting impact of feedback on transcriptional networks. Elucidating the principles of mammalian circuit design offers the opportunity to engineer cellular behaviors, identify cell types, and track diseased states. Further, understanding how cell types differentially process classes of synthetic circuits will improve our ability to predict the response of native transcriptional networks.

In conjunction with our circuit work, we are interested in defining the molecular rules of cell fate transitions. With novel reporter circuits, we are identifying rare events in reprogramming and illuminating the molecular mechanisms that drive rapid and robust cell-fate transitions. With these insights, my lab constructs regulatory circuits that interface with native networks, optimize cellular reprogramming, and track cell fate transitions. Ultimately, we aim to develop the next generation of integrated genomic circuits capable of tasks such as tissue regeneration and surveillance of pathological states.

Fighting Lung Diseases

Ying Xi
ShanghaiTech University

After a 5-year postdoc training at UCSF and 3 years of industrial experience at Genentech Inc., I established my own lab in Shanghai last year. As a new lung biology lab, we are interested in lung regeneration and pulmonary diseases. In particular, we are focusing on how the lung epithelium responds to injury and disease and how to promote alveolar repair and regeneration to fight diseases involving alveoli destruction, including severe, acute lung injury due to influenza or SARS-CoV-2 infection and chronic fibrotic diseases like idiopathic pulmonary fibrosis—all of which currently lack curative treatments.

The adult lung is a largely quiescent tissue, but it can respond robustly to injury to replace damaged or lost cells. Recent advances have identified regional epithelial stem/progenitor cell populations that mediate adult lung homeostasis and regeneration and have uncovered aberrant epithelial repair in severe injury and disease.

Our lab employs organoid culture, animal models of lung injury, lineage tracing, and single-cell transcriptome analysis to characterize the behavior of these stem/progenitor cells and the signaling pathways and environmental influences that govern their proliferation and differentiation in disease. Our ultimate goal is to develop molecular and cellular therapies for human lung diseases.

The Germline and the Frontline

Harry Leitch
MRC London Institute of Medical Sciences

My lab studies mammalian germline development, with a particular interest in the regulation of pluripotency. So far we have mainly focused on fundamental discovery science; we combine *in vivo* work with *in vitro* approaches using pluripotent stem cells, in both mice and, increasingly, humans. Although my passion is basic research, I trained as an M.D./Ph.D. and I remain clinically active. My initial clinical training was in pediatrics/neonatology and now I specialize in Clinical Genetics. This has led to the development of more translational projects in the lab, which focus on modeling the severest forms of infertility and studying the origin of pediatric germ cell tumors. The impact of COVID-19 has been profound. Our research institute has closed and we are all working from home. This is especially tough for wet lab scientists, who do lots of mouse work. However, we have kept up our usual meeting schedule and are trying to find new ways to interact and use this time productively. I have also returned to work in the neonatal intensive care unit, plugging gaps left by sick doctors or those who have to shield or self-isolate. My team has been very accommodating, allowing us to stay in touch now that my clinical workload has increased dramatically. While it is a privilege to make a clinical contribution, I miss the lab, my team, and my research friends and colleagues. I look forward to the day I'm no longer needed on the frontline and can get back to studying the germline.

Carrying On the Conversation

Anastasia N. Tikhonova
NYU School of Medicine

Every biological function of the body is driven by highly coordinated cellular responses. My graduate training in immunology exposed me to the nuances and importance of microenvironmental context in cellular dialog—a principle I now apply to studying hematopoiesis. Through cell-cell interactions and secretion of soluble factors, the bone marrow niche hosts hematopoietic stem cells (HSCs) and facilitates blood and immune lineage development. The focus of my research program is to discern the mechanisms that underlie dysregulated HSC-niche crosstalk and target those interactions to halt aberrant hematopoiesis.

Following postdoctoral training in NYC, I was excited to move to Toronto and start my faculty appointment at Princess Margaret Cancer Centre. As COVID-19 sent shockwaves through the world, my move was deferred. When society resumes operation, I will build my lab in a scientific culture informed by the urgency of the current pandemic. The crisis underscored a dire need for evidence-based policymaking, giving the research community a renewed voice. Worldwide, groups working on the virus began sharing unpublished data, reagents, and ideas to facilitate rapid discoveries. Can we continue to foster a community that quickly and openly shares data and information? Will scientists carry on the conversation and emphasize the importance of research support to the general public? These lingering questions leave me with a sense of hope: "We can and we will!"

Lineages in Time and Space

Guangdun Peng
Guangzhou Institutes of Biomedicine and Health

My lab is interested in how stem cell fates are specified and determined in time and space. We are in our second year studying developmental cell lineages, but I never expected at the start of this year how profoundly our lives would change. As a junior PI, I am lucky to have a very energetic team working with me. We had been pushing very hard to make progress on some competitive projects and some lab members even volunteered to keep working during the Chinese New Year holiday, and we were shocked by the systematic shutdown happening throughout the country. I first thought it might be another big flu or, at most, a short period of containment similar to SARS 17 years ago. We reduced research activity as much as possible, but quickly ran out of stock reagents and progress has been severely affected. I am thankful for my lab members who stand strongly with me, and together we will overcome this difficult situation. Some of my colleagues are devoting themselves to fighting COVID-19 and working around the clock, which is very inspiring. Even in these difficult times we are adapting and moving forward, and isolation does not restrict us. We have started virtual seminars, and a large research community around the country has been thriving via web meetings and online discussions. The supply chain will gradually return with the coming of summer, and meanwhile I am using this time and space to thoroughly examine my research plans for a lifelong career.

An Intro to the Sumigray Lab

Kaelyn Sumigray
Yale School of Medicine

The mammalian intestine is arranged in a continuous ribbon of crypts and villi. Crypts are cup-like invaginations that house the stem cells and form in mice during the first 10 days after birth. My lab is studying the mechanisms that drive crypt formation. Our underlying hypothesis is that crypt architecture is an essential niche component. Several roles for the mammalian intestinal crypt have been proposed, but they have not been directly tested. For example, the crypt structure has been proposed to protect stem cells from environmental insults and/or soluble molecules in the intestinal lumen. By understanding *how* the crypt forms, we are poised to disrupt its formation to address such roles in stem cell and intestinal biology.

As cell and developmental biologists, we are addressing fundamental stem cell biology questions from a morphogenic perspective. This unique approach has allowed us to identify novel steps that are important in intestinal development that we hope to expand to other areas, including cancer biology. One of the questions we are currently studying is the extrinsic regulation of crypt morphogenesis: who are the players and how do they instruct epithelial cells? We are also trying to understand how intestinal epithelial cells interact with their extracellular matrix and the importance of maintaining clonality within crypts and villi. My goal is to transform our understanding of stem cell niches by defining the roles provided by their physical architecture.