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**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.

**Unraveling the Mechanisms of Female Infertility**

My lab studies meiosis, a specialized form of cell division that generates fertilizable eggs. We are particularly interested in cooperative actions of the actin and microtubule cytoskeletons that prevent egg aneuploidy, a leading cause of human infertility. Advanced microscopy enables us to visualize dynamic actin-microtubule interactions in space and time in these large cells. Together with recently innovated powerful protein disruption assays, this approach is helping us to uncover secrets of one of the earliest stages of every human life.

When the UK went into COVID-19 lockdown in March 2020, we were in the process of finalizing experiments for my lab’s first research paper—we had made an exciting discovery that oocytes (progenitors of eggs) can use their nucleus to regulate F-actin networks in the cytoplasm. Because we use mice for our research, it took us considerably longer to resume experiments after lockdown. We were resilient nonetheless and quickly formed links with a local slaughterhouse from which we freely sourced pig, cow, and sheep ovaries. We have now begun to establish these as a model to study cytoskeletal ensembles in mammalian oocytes.

The pandemic has put my young lab’s organizational and support structures to the test, and I would say we are emerging from it stronger than ever. We have since published our recent discovery as a preprint and are doing revision experiments to publish it in a research journal. Having just gone into yet another national lockdown, perhaps we now know how to handle these research stop-and-starts with far better resilience.

**Delivering Insights into Regeneration**

The loss of terminally differentiated cells responsible for organ function underlies the therapeutic intractability and lifelong morbidity of numerous diseases including diabetes, heart attack, stroke, and neurodegeneration. The organs in which these diseases occur lack stem cell populations to replace the lost cells and any remaining functional cells have permanently exited the cell cycle as part of their differentiation process. Undoubtedly, a means of making these differentiated cells proliferate would provide desperately needed cures for countless diseases. Although cellular differentiation and proliferative capacity are typically mutually exclusive, the liver, and the hepatocytes responsible for its function, exists as a remarkable and informative exception. The liver has the unique ability to completely regenerate itself after injury. Moreover, this regeneration occurs not via a stem cell population but rather by proliferation of the differentiated hepatocytes. It is wholly unclear why hepatocytes can proliferate and the liver can regenerate but other differentiated cell types and organs cannot. Our lab is building tools for *in vivo* functional genomics so that we can dissect these processes directly in the mouse with the rigor and tractability traditionally restricted to cell culture systems. With these methods, we will uncover molecular explanations for the differential regenerative abilities of organs and aspire to one day confer regenerative capacity to non-regenerative tissues in the setting of disease.

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**Binyam Mogessie**  
University of Bristol

**Kristin Knouse**  
Whitehead Institute for Biomedical Research
Chromatin Structure and HSC Fate

I am a physician scientist with a clinical focus on myeloid malignancies, and I am starting a laboratory program investigating how mutations in the cohesin complex and other chromatin modifiers contribute to hematopoietic transformation. Our lab aims to assess how DNA topological control regulates transcriptional output in various malignant contexts using high-order chromat fiber assays that we have optimized for low primary cell input. In the long term, we hope to systematically dissect the dynamic short- and long-range DNA-DNA interactions and the molecular events that influence HSC fate decisions.

I am a survivor of acute lymphocytic leukemia and often hear the phrase, “everything happens for a reason.” This never sat well with me. I decided to become a physician scientist not because I was fated to do so, but rather because I wanted to take my cancer narrative, the darkest time in my life, and give it new meaning. COVID-19 has been a dark time in all of our lives. I took over the MSKCC inpatient leukemia service in late March 2020, at the peak of the virus in NYC. I moved out of my home in hopes of protecting my young daughter and newly pregnant wife; I was also on the job market giving Zoom chalk talks on my daughter’s easel and trying not to take hiring freezes personally. Thanks to the efforts of many, my new home in the Columbia Stem Cell Initiative cleared the hiring freeze and the Viny lab is now booting up. I am humbled by the resilience of the entire scientific community. It is our work in the service of others that gives meaning to this dark time and hopefully brings new light.

Unraveling Complexities of Brain Growth

When COVID-19 struck, I was submitting our work on ZIKA virus to Cell Stem Cell. I thought the lab would be back to normal when we received feedback on it. Months after submission, we were still on hold and addressing reviewers’ comments was a big challenge. My institute provided me a letter for commuting in an empty city, supporting the urgent need for studying other viruses to prevent future outbreaks due to accelerating climate change. My co-workers and I were in a race to finish experiments. Collaborators were more than helpful, sharing supplies and giving access to facilities. Just as challenging was combining remote working and homeschooling my children. Regular online meetings with other mother PIs and the team provided key social support and kept our science going. The bright side? I had time to refine ideas for future projects, and the paper is now published!

In 2020, I started my career as a young PI. My goal is to elucidate the molecular and cellular mechanisms underlying the evolutionary human brain expansion. I seek to understand the human brain abnormality known as microcephaly by studying the roles of centrosomes and primary cilia in cell division and tissue growth. I use human organoid and animal models to study these mechanisms in the most dynamic system we can get our hands on: the embryonic neural tube. I am fueled by enthusiasm for my new career. I believe that we need to embrace a “new normal” with the support of funders and scientific journals, and that policy changes are needed to address pressures in academia that this pandemic has further revealed.

Long-Term Maintenance of Brain Health

Most neural cells are generated during development and have to maintain their function and cellular identity over decades—but how? From my early fascination with dynamic regulation of brain development, I have become more curious about mechanisms that preserve long-term robustness of the brain. By focusing on cell-type-specific nuclear architecture and epigenetic regulation, I aim to understand biological links between long-term maintenance of brain function and age-related brain dysfunction.

Thanks to support from the ERC and my new institute, my family and I moved from sunny San Diego to historical Dresden in March 2019. Working in different scientific cultures in Japan, the US, and Germany is quite an experience, and I have been fortunate to work with supportive colleagues to adapt to my new environments. After hectic times setting up the lab, the pandemic hit just as our new projects were about to launch. The situation since has been tough, and issues such as childcare, isolation at home, and other life events affected all of us in the lab. However, my family also welcomed our
second son, and our team has been pushing new projects forward. Beyond encouraging them as a PI, I was encouraged by them, and realized unforeseen aspects of being a PI with appreciation. Although adapting to these changes has not been easy, I believe the unexpected lessons we have learned during the pandemic will lead us to success in our projects and we will identify how healthy brains are maintained throughout challenges in life.