

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.



Jihan Osborne
University of Texas, Southwestern Medical Center

Embryology: The Blueprint for Understanding Aggressive Tumor Biology

The central cause of cancer-related mortality is metastasis. The increase in the metastatic potential of certain solid tumors has been linked to the overexpression of embryonic and lineage-specific developmental programs that regulate cell fate during organogenesis. Therefore, how this cancer cell plasticity is achieved and how to successfully target these cells are fundamental questions. My training as both a cancer biologist and a developmental biologist gives me a unique perspective in answering these two tough questions. My lab will focus on understanding how genes that regulate proper organogenesis become aberrantly used to enhance chemoresistance and metastatic potential.

I have been at the UT Southwestern campus since early January 2021. Sitting in my office (socially distancing with the door closed) while trying to hire staff for my lab, organizing data to write grants, and thinking of the most critical experiments that can be done, I cannot help but ask myself what I have learned in 2020. At the end of 2019, no one could have imagined what 2020 had in store. Like the rest of the world, I lived in an endless cycle of mixed emotions ranging from anxiety to fear, depression to anger, with intermittent periods of hope. Hope, my grandmother used to say, is comfort for fools. Yet it was hope that kept me going—and applying for this position when everyone said this was going to be a bad year to apply for academic jobs. This year I learned that dreaming of equality, peace, justice, and the tangible expectation that one's dream will be reality is not foolish.



Evgenia Salta
Netherlands Institute for Neuroscience

New Cells in Old Brains

After a very exciting and scientifically useful rollercoaster with dogmas getting overturned again and again over the past 20 years, recent reports have unequivocally demonstrated that adult-born neurons are generated in human hippocampus throughout adulthood. This process of adult hippocampal neurogenesis is compromised in the brain of Alzheimer's patients and, intriguingly, the levels of neurogenesis in the Alzheimer's hippocampus correlate with the ante-mortem cognitive status of the affected individuals. My lab studies how adult hippocampal neurogenesis impacts, and is impacted by, Alzheimer's disease pathology and whether it can be recruited to "rejuvenate" the degenerating brain and prevent or counteract memory loss.

Just before the pandemic hit, I was in the process of recruiting my new team, making practical arrangements for my new lab, and finalizing a strenuous manuscript revision. And then COVID-19 happened. Was it more difficult than normal to remotely set up a new life, a new lab, and a new team in a different country? Probably. Will the pandemic have a greater impact on starting PIs than on already established ones? Possibly. Could things be worse than what they have been? Definitely. I am privileged to be granted the opportunity to do what I love and to receive tremendous support from previous and new mentors, colleagues, and collaborators. I am fortunate to be surrounded by a team of caring individuals and devoted scientists. The pandemic has taken its toll on our students and mentees more than on us. This is a good time to be grateful and supportive.





Huili Hu
Shandong University

Adult Stem Cells: Cell Fate and Tissue Repair

During my early scientific career, I was fascinated by the ability of organoid technology and manipulation to recapitulate tissue. My passion for applying stem/progenitor cells in regenerative medicine, which began during my postdoc at the Hubrecht Institute, continues in the present. My lab at Shandong University, established in 2019, seeks to understand adult cell fate decisions in homeostasis, regeneration, and disease, focusing on liver, the gastrointestinal tract, and organ crosstalk. We are developing organoids (including hepatocyte and tumor organoids), mouse models, and multi-omics approaches to study cell plasticity. We are creating new approaches to explore mechanisms of dedifferentiation, transdifferentiation, and functional reconstruction within injured tissue, with an eye toward interdisciplinary collaboration to link experimental approaches with translational medicine.

Our group was recruited and formed in a supportive environment. Everything was going well during my transition into an independent PI. Later, COVID-19 provided unanticipated challenges. However, thanks to my friends, colleagues, and young enthusiastic lab members early during the pandemic, we managed to mostly minimize its effects on lab research. I am grateful for our good administration and for family support. The lab has almost returned to pre-COVID-19 activity, except for the requirement for remote communication and online conferences. This return has filled our days with more cooperation, understanding, and appreciation.



Brett Shook
George Washington University School of Medicine
and Health Sciences

Communication Is Key

After injury, proper cellular communication is essential for repair and restoration of tissue function. Cells at the injured location must actively recruit immune cells that initially clear pathogens and debris, then orchestrate stem and progenitor cell-mediated repair. When tissue-resident cells do not properly communicate with immune cells, the resulting delayed or excessive immune cell infiltration impairs healing and leads to tissue dysfunction. My lab uses skin as a model to uncover cellular interactions necessary for rapid, robust infiltration of immune cells after damage. Specifically, we investigate how local keratinocytes, fibroblasts, and adipocytes are activated after injury to recruit myeloid cells and define how a breakdown in cellular activation and communication contributes to impaired healing.

Like damaged tissue, this pandemic pushed my group outside of homeostatic set-points. Before the pandemic hit, I was proud of how my group initially grew and the exciting data being generated. Suddenly, things came to a screeching halt. When COVID-19 restrictions were implemented, I quickly lost my entire research team and hiring was placed on hold. As restrictions eased, my group slowly recovered and began settling into the “new norm.” Now my lab relies on multiple modes of communication to have productive interactions, both in person and virtually. We still face challenges associated with current restrictions; however, like our response to injury, we work hard to ensure our communication is rapid, efficient, and clear so that we can maintain function and productivity.



Yun Li
University of Toronto

Uniqueness and Vulnerability of the Human Brain

I think one of the most fascinating things about the human brain is how it is different from that of other animals, and how this uniqueness may contribute to our vulnerability to brain diseases. Using pluripotent stem cell-derived neural cells and brain organoids, my group aims to study human brain development in normal and disease conditions. In particular, we focus on pathways that control cellular growth for their roles in regulating brain development, evolution, and disease. Since starting in 2018, I was fortunate to attract a group of talented trainees that want to use our *in vitro* models to answer these fundamental questions. With the support of excellent collaborators, we are exploring how abnormal cellular growth leads to autism, epilepsy, and degeneration. The current situation further highlights the translational value of our stem cells and organoid models in studying human diseases. Working with the lab of my long-time collaborator Julien Muffat, we are also recon-

structuring immune-competent neural cultures to study the impact of viruses on the brain.

The pandemic hit us right in the middle of many long-term experiments, jeopardizing our momentum. However, I am incredibly inspired to see how resilient my lab members have been. We adapt to changes in the way we work, pushing forward on all fronts, and the lab has emerged stronger. I am very optimistic about the future of my lab, the team we are building, and the exciting science that we are producing and look forward to sharing soon.



Nagarajan (Raj) Kannan
Mayo Clinic College of Medicine and Science

Mayo Clinic Stem Cell and Cancer Biology Laboratory

My lab leverages stem cell science to investigate clonal and lineage compositions of “normal” human epithelial tissues and identify cellular risk states and linked molecular programs that control the genesis of premalignant clones. At Mayo, we established the first comprehensive “living” tissue organoid biobanks for breast and fallopian tubes from healthy individuals and cancer patients. Amidst the pandemic, we also launched a bold Regenerative Medicine initiative to develop the first autologous salivary transplant biobank to treat radiotherapy-induced xerostomia and improve quality of life in cancer survivors. Our major emphasis is to develop *in vitro* and *in vivo* assays to track clonal regenerative activities. We have created NGS pipelines for cellular DNA barcoding-based clonal tracking and to investigate normal and malignant stem cells.

I suggested that the International Society for Stem Cell Research conduct a survey to identify adverse impacts of the pandemic on ECRs, and we discussed the findings in a Commentary published in the June 2020 issue of *Stem Cell Reports*. I had the opportunity to co-lead a study on COVID-19 published in the December 2020 issue of *Cell Death & Discovery* where we described COVID-engine, a blood-based systems biology approach to study host response to coronaviruses. COVID-19 is a true testament to the Sanskrit wisdom *Vasudeiva Kutumbakam* (the world is one family) and has reinforced the joy and importance of pursuing a team approach in order to maintain sanity and ensure scientific progress for a shared future.