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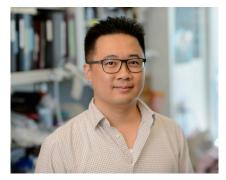
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# **Voices**

# 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.



Cincinnati Children's Hospital Medical Center

# An Unexpected Delay

It was early March and after 6 months of renovation, my tissue culture room was finally complete. As stem cell biologists we know we will spend hours in this room and have to get it right. I had a research assistant, cells ready to be cultured, and my own ideas to test when our institute shutdown the very next day. Reality had set in, and I felt that I had all of this momentum but nowhere to go. I tried to channel that energy into anything productive, but the next few months felt unfulfilling. I had worries about balancing working from home and virtual learning for the kids, the fear of a second shutdown if I started experiments, and wondering if grant reviewers would understand if I had no preliminary data. Thankfully, our institute provided both well-being and research support during this time, and it has helped me feel optimistic and that we are not alone. As we restart lab operations, I am excited to think about my scientific goals again.

Our lab aims to uncover cell-type-specific contributions to neurological disease, especially from a glial perspective. Glial cells are fascinating. These are the most abundant cell types in the brain and have numerous roles in development and maintaining homeostasis. They have been implicated in multiple diseases for which there are few answers. With the ability to generate subsets of these cells more rapidly from pluripotent stem cells, we are currently working with clinicians and engineers to develop meaningful platforms to integrate patient data toward understanding the role glia play in neurodevelopmental disorders.



Noelia Urbán IMBA - Institute of Molecular Biotechnology of the Austrian Academy of Sciences

### How to Wake Up a Stem Cell?

Adult neural stem cells (ANSCs) persist in specific locations of the brain of most mammals where they produce neurons that integrate into existing neuronal networks to modulate brain function. ANSCs are inactive—or guiescent—until receiving the right activation stimuli. They also have a limited ability to self-renew, meaning that their activation is tightly coupled with exhaustion. Stem cell numbers rapidly decline with age, halting neurogenesis and causing symptoms characteristic of neural disorders such as dementia and depression. Although adult neurogenesis can be modulated by exercise, diet, or stress, the specific signals by which those stimuli regulate ANSCs or the molecular pathways they activate are largely unknown. We use transgenic mice and in vitro tools to elucidate how systemic stimuli influence the transition of ANSCs between quiescence and activation, with the ultimate goal of devising strategies to prevent stem cell exhaustion during aging.

The pandemic hit us right when our very long experiments were starting to kick off and coincided with several changes in the group. Contrary to what I feared, we actually came closer together as a team, which makes me extremely proud of the people I have the pleasure to work with. My personal experience of the COVID-19 crisis is mixed with that of becoming a working parent and I am finding it hard to tell their influences apart. Despite the many challenges ahead, I look forward to navigating the era of the "new normal," where scientific collaborations and science communication are more important than ever





Alice Soragni University of California, Los Angeles



Kyogo Kawaguchi RIKEN Cluster for Pioneering Research



Joel W Blanchard Icahn School of Medicine at Mt. Sinai

#### **Patient-Derived Organoids for Personalized Medicine**

My laboratory, established just a little over 3.5 years ago at the University of California, Los Angeles, focuses on developing organoid models of disease to investigate cancer onset, progression, and response to therapy. Patient-derived organoids can be easily developed from a variety of normal tissues and tumors; they are invaluable models to investigate the biology of healthy and diseased organs. We are particularly interested in using patient-derived organoids to investigate tumor evolution and heterogeneity in rare cancers. While some rare cancers are well characterized, the majority remains understudied, with some having no approved first line therapy and little information on drug sensitivities. We are working to implement our personalized organoid screening platform to identify actionable information for rare cancers.

This was supposed to be our most productive year yet; I was looking forward to travel more than ever before. All came to an abrupt stop in light of the COVID-19 pandemic. The 3 months we spent at home during the first shutdown have been incredibly challenging, as we juggled novel professional and personal obstacles. We are now back in the lab at reduced capacity; we have found ways to become differentially productive and resume our work on rare tumors. Nonetheless, the consequences of the pandemic will be long-lived, with a catastrophic impact on many early-career researchers, women, and parents. I hope that the challenges of the past few months will inspire better, more just, and equitable ways to practice science and support vulnerable researchers moving forward.

#### **Work-from-Home Theory and Experiment**

Beautiful movies of cells and tissues produced in labs every day are casting a fundamental question for theoreticians: can we ever "understand" any of this? Our group in RIKEN (Kobe, Japan) studies multicellular dynamics and cell fate decisions by combining live cell imaging experiments and theoretical physics. We have so far been working on elucidating the effect of cytoskeleton chirality in the collective cell flow and developing theories related to chromatin dynamics and phase separation in cells. With help from our excellent collaborators, we are currently migrating more toward the intracellular world, with keen interest in the physical mechanism behind the robustness of cell differentiation.

Thanks to our five lab members who smoothly adapted to the new situation, the damage caused by the prolonged work-from-home period was less significant for us. It also helped that most of us had dry work on our hands, some of which has turned into exciting theory projects. Within the institute, the positive impact was the regulations on office hours and working locations getting swiftly removed, which will hopefully trigger policy reforms for RIKEN to be more inclusive for women and international members.

The online seminars and science on social media are also positive developments in this challenging period. Although the all-online scheme has a lot of benefits, it has unexpectedly led to substantial regional effects due to time and language differences. We are now seeking to maintain opportunities especially for young researchers in Japan to connect with the rest of the world.

# **Opening Windows into the Human Brain**

After 10 years of training in stem cells, neuroscience, and engineering at Harvard, Scripps, and MIT, I am excited to launch my independent career at the Icahn School of Medicine. COVID-19 has imposed many challenges and delayed the opening of my lab, but it has also afforded more time to pursue funding, recruit talent, and build collaborations. Since childhood I've been intrigued by why some people experience cognitive impairments with age and others remain cognitively normal into their nineties and beyond. When my lab opens next fall, we will investigate how genetics, diet, and traumatic injury influence susceptibility of the human brain to neurodegenerative diseases such as Alzheimer's. To achieve this, we combine engineering with stem cell biology to reconstruct human brain tissue in vitro that incorporates vasculature, myelination, and neuro-immune systems. Our tractable 3D models enable us to replay disease pathogenesis to dissect how genetic, diet, and environmental factors impact



neurodegeneration. We complement our in vitro analysis with studies on post-mortem human brain tissue and animal models. Through this interdisciplinary approach, we aim to generate pathogenic maps detailing the molecular and cellular events preceding end-stage pathology found in human brains, target and modulate these pathways as potential therapeutic strategies, and establish pioneering technology to unravel complex genetic and cellular interactions in the human brain. Our ultimate goal is to facilitate a precision medicine approach to understanding and treating neurodegenerative diseases.



Southern Medical University

#### **Epigenomics of Germline Cells**

During my Ph.D. studies in Peking University, I mainly focused on germline cycle, single-cell -omics technology (e.g., the development of the scCOOL-seq method) and data mining. In September 2019, I was thrilled to start my independent lab in Southern Medical University (Guangzhou, China). We focus on the life cycle of germline cells and will continue our research on developing/applying single-cell multi-omics technology in the germline cycle. We also aim to extend these techniques to better understand developmental disorders. Moreover, we will investigate -omics interactions (e.g., transcriptome, genetic, and epigenetic) and molecular mechanisms involved in the development and progression of disorders or diseases. We hope to identify the phase-specific regulatory elements or factors that control cell-fate transitions and investigate their functional mechanism using in vivo/in vitro models.

After busy preparation to get everything ready in my lab, COVID-19 arrived. My lab shut down shortly after we opened. None of the students could come to school to see the lab or meet lab members, which limited the training of my new team. Luckily, everyone is healthy and safe. As a young researcher, I am thankful for supportive collaborators that have provided some data to analyze as we work from home. Our students are also hardworking. Everyone reads papers about a topic at home, which we then discuss online. After a long time at home, thinking and planning, my team and I are well-prepared to come back to the lab and work together to write a new chapter in germline cells.