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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.

Judith Agudo
DFCI, Harvard Medical School

**Stem cells hide, we should not**
During my training as an immunologist, I developed a secret love for stem cells. While studying type 1 diabetes, I had a naïve question: are stem cells spared during autoimmunity? If not, regeneration could be compromised once immunological tolerance was restored. Thus, I sought to study whether tissue stem cells can evade cellular immunity. I discovered that most tissue stem cells are susceptible to immune attack, but some have an outstanding ability to cloak themselves from immune cells. My lab investigates the mechanisms controlling immune privilege in such stem cells and, as an extension, in cancer stem cells. We aim to use this knowledge to protect cells that are susceptible to immune recognition and, conversely, to identify how to effectively eliminate cancer stem cells by immunotherapy.

When the pandemic started, everything got disrupted: the lab was closed, and I was stuck at home with my two little children. I was stressed about my trainees, my future, and my family in Spain. Then, another junior PI, who is also a mother of three children, reached out to me about my well-being and success. We started joint lab meetings and had honest conversations about our struggles. I felt seen and understood, and that made a whole world of difference. I learned a lesson and I no longer cloak like my beloved immune-privileged stem cells. I have joined committees for the advancement of women in science and for diversity, equity, and inclusion. COVID has taught me to speak up for myself, but also to work for those that may not have a voice.

Chia-Wei Cheng
CSCI/Columbia University

**From nutrition facts to stem cell fate**
Adaptation to dietary changes profoundly influenced human evolution and continues to impact our modern lives. Tissue-resident adult stem and progenitor cells adjust their activity in response to their nutritional environment to maintain tissue homeostasis. Such adaptation relies on systemic mediators of inter-organ crosstalk to coordinate whole-body metabolism with the intracellular machinery that converts nutritional signals into transcriptional control of cell fate determination. My lab focuses on the interface of nutritional and transcriptional regulatory networks. We study how adult stem and progenitor cells perceive nutritional states and fine-tune their lineage decisions during tissue regeneration and disease development. Our goal is to translate nutrition facts into stem cell fate in the hopes of inspiring new therapeutic strategies.

To this end, we use genetic mouse models, organoid systems, and transplantation experiments to identify and characterize the endocrinical and metabolic cell-fate determinants in the contexts of tissue homeostasis and adaptation to diet.

The damages caused by the COVID-19 pandemic are fact, not fate. I think the unexpected challenges in the past year are exceptional opportunities to explore new possibilities. Despite this ongoing uncertainty, the Cheng Lab at the Columbia Stem Cell Initiative (CSCI) started in the spring of 2021. With the guidance from leaders and the support from peers, we are excited to grow within our nourished niche and join the process of regeneration.
**Starving LSCs**

Acute myeloid leukemia (AML) is a devastating disease initiated and maintained by leukemia stem cells (LSCs). To improve outcomes of AML patients, therapies designed to better eradicate LSCs are urgently needed. The goal of my lab is to develop new therapeutic strategies to target LSCs by identifying, characterizing, and targeting LSC-specific metabolic properties in AML patient samples.

I immigrated to Canada in the spring of 2020 to start my lab at the Princess Margaret Cancer Centre. After a rushed drive with my husband and two dogs, we crossed the US-Canada border to find ourselves in a new city that would be shut down for months. Starting my faculty position during lockdown meant I had to hire and train lab members without meeting them face to face. While hardly ideal circumstances, this situation has forced my lab to quickly hone our communication skills and work together, which I believe will make us stronger in the long run. I have learned how self-motivated, resourceful, and talented my lab members are and it is exciting to see them starting to discover novel insights into LSC metabolism. This would not be possible without the support of my new colleagues. One thing I am particularly grateful for is to be going through this experience with another junior faculty member, Dr. Anastasia Tikhonova. Facing challenges together makes them feel more manageable and the process of overcoming them fun. I am hopeful for a bright future and will be forever thankful for the support I have been given by my team and colleagues.

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**Epigenomics in cells, tissues, and beyond**

I’m fascinated by how epigenomic modifications determine not only cell fate, but also an array of subcellular and even tissue-level processes. For instance, epigenomic modifications influence regional mutation rates, but also more globally determine the tissue’s inflammatory state by controlling the expression of endogenous retroviruses. Increasingly, epigenomic deregulation is implicated in cancer initiation, in particular in pediatric cancers. In my lab we are addressing some intriguing yet unresolved questions: what are the epigenomic changes that turn a healthy cell into a cancerous one? Why is the developing body particularly vulnerable to epigenomically driven malignant transformation? Can the identification of the cells-of-origin of developmental cancers unlock novel treatment opportunities?

I was ready to hit the ground running when I returned to the lab in March 2020 after maternity leave, with 4 months to complete a publication before the planned opening of my lab at IRSJD. That same month, the WHO declared a global pandemic, and life as we knew it came to a standstill. Yet, thanks to the scheduling creativity, collegiality, and kindness of the people around me, my plans were postponed only by a few months. The COVID-19 pandemic has been challenging, but it has also fostered solidarity, mutual understanding, and cooperation. Countless Zoom hours have consolidated old collaborations and forged new ones. My lab emerges from this experience with the firm belief that it is the consideration and appreciation of the people around us that ultimately make us more resilient.

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**Sharpening the scientific axe**

When COVID hit hard and my postdoc lab was forced to shut down, I was lucky enough to have already signed my dream job offer. But, with a skyrocketing number of cases delaying necessary lab renovations, my starting date was inevitably pushed back. One day, I was skimming through some books on management when I came upon this famous quote, and I realized the practice of scientific research fit perfectly with this lesson about preparedness.

“Sharpening the axe” can mean something different to different people. To me, as a junior group leader in the times of COVID, it mostly meant honing in and polishing my scientific vision. The slow-down presented a great opportunity to take some time off from the bench to just think about science. What were the implications of my recent work and how did it relate to other findings in the field? How could it help address big, longstanding questions in stem cell and developmental biology? This sharpening has...
more than paid off, leading to exciting new questions, collaborations, and ground-breaking ideas.

Now as the group leader of the Quantitative Stem Cell Dynamics lab at IRB Barcelona, I will be taking on the challenge of understanding how functional patterns emerge and evolve in regenerating and developing tissues, and how they drive disease variability, which is central to the success of personalized medicine. Overall, the lesson I learned is this: take time off, talk to collaborators, and think of the bigger picture. I know I’m not waiting until the next pandemic.

**Regeneration at your fingertips**

Why do mammals fail to regenerate their limbs while some vertebrates, such as salamanders, have this capacity? Remarkably, mice and humans are still able to regenerate the tips of their fingers or toes, demonstrating that mammals are capable of multi-tissue regeneration. Using the mouse digit tip as a model system, my research focuses on understanding the molecular and cellular processes that promote complex tissue regeneration in lieu of fibrotic wound healing. After 5 years of postdoctoral training at the Hospital for Sick Children in Canada, I was thrilled to receive an offer to establish my own laboratory at the Wellcome-MRC Cambridge Stem Cell Institute. Only days after flying back to Canada following the interview, the COVID-19 pandemic shocked the nation and the lockdowns began. This ultimately delayed the next chapter of my life by 9 months. Although the pandemic has brought with it many challenges, I am overwhelmed by the support that I have received from both my past and present institute. Colleagues have gone out of their way to offer advice and provide support and with video conferencing becoming the “new normal.” I have had the opportunity to engage with many great scientific minds that I would not have imagined possible prior to the crisis. The pandemic has taught me that resilience, flexibility, and collaboration are fundamental traits for every young scientist and as I open the doors to my shiny new laboratory, I am hopeful and excited to begin the scientific journey ahead.