

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.

Rare Is Many, Rare Is Strong



Dwi U. Kemaladewi
UPMC Children's Hospital of Pittsburgh

...and rare is proud: a powerful slogan of Rare Disease Day 2020. The last day of February is devoted to raising global awareness among the general public and policy makers about rare diseases and the impact on patients' lives. In February 2019, I established the Interventional Genomics in Rare Diseases lab in Pittsburgh.

We study neuromuscular pathology and aim to develop therapeutic interventions for rare diseases, with an initial focus on LAMA2-deficient congenital muscular dystrophy (LAMA2-CMD). We use CRISPR activation to upregulate *LAMA1* to compensate for the lack of *LAMA2* in muscles and nerves. My lab performs preclinical studies to evaluate the safety and efficacy of *LAMA1* upregulation in mice and patient cells. This work may enable a mutation-independent treatment for all LAMA2-CMD patients and potentially other rare diseases.

We just celebrated our 1st anniversary when COVID-19 hit. My lab was at the sweet spot of laying the necessary groundwork before testing valuable samples. I had to cancel visits from postdoc candidates and senior scientists with whom I wanted to iron out collaborative projects. Still, I am grateful that our university, the NIH, and funding agencies are extending tenure clock, ESI status, and progress report deadlines. My lab members remain healthy and passionate about their projects. After all, this pandemic and rare diseases have a few things in common: they happen infrequently yet affect the global community and cause significant economic loss.

How Lipids Influence Stem Cells



Marlen Knobloch
University of Lausanne

My laboratory studies how metabolism regulates stem cell behavior. While we primarily focus on neural stem cells, we also investigate whether metabolic activities control different somatic stem cells in similar ways. We are specifically interested in lipid metabolism and how the buildup and breakdown of lipids, as well as their external availability, affects stem cells. For example, what role do lipid droplets play in instructing stem cell behavior? These versatile, lipid-storing organelles are essential hubs for lipid metabolism and have not yet received much attention in our field. With human brain organoids, we plan to corroborate our findings obtained from mouse studies in a human context. As mutations in lipid metabolic pathways are quite common, we are studying the impact of such disturbances on neural stem cells using patient-derived induced pluripotent stem cells.

The halt of all laboratory work within a few days due to COVID-19 was a challenge for everybody. On top of that, as a mother of two small children, the closing of the schools and nurseries posed additional challenges. Thanks to virtual meeting rooms, my team and I are keeping up by discussing projects, results, and literature. Luckily, everybody had some data to analyze, so we are making the best out of this stay-at-home time. However, as our lab fully relies on wet lab experiments, we are all eager to go back and will surely look at our privilege to conduct exciting research with different eyes.

An Intro to the Arnes Lab



Luis Arnes
University of Copenhagen

In our laboratory, we study regeneration and cellular plasticity in the pancreas. Following injury, mature pancreas cells can acquire alternative cellular states recapitulating those of embryonic pancreatic progenitors. Although a physiological process of tissue homeostasis, it renders the tissue susceptible to cancer. We seek to understand the role of transcriptional enhancers and noncoding RNAs in these cell fate changes in the embryonic and regenerating adult pancreas, bridging both developmental and cancer biology. To achieve this goal, we use a combination of mouse models and embryonic stem cells. Our studies will provide molecular drivers of cellular and pathological associated plasticity that may lead to novel treatments in regenerative therapies and pancreatic cancer.

The outbreak of SARS-CoV-2 forced the shutdown of research institutions while at peak productivity. Suddenly, only critical experiments could continue. With the pressure of the tenure track weighing heavily, I felt that every single experiment was crucial. COVID-19 is challenging current studies, but the team has gone the extra mile to safeguard essential activities. Despite the overwhelming feeling of uncertainty, we continue scientific discussions remotely, which are vital to maintaining high spirits, especially of international students. We will emerge with new ideas and innovative ways of sharing and discussing science. We are excited and prepared for a "COVID-compliant" reopening.

Cell Fate and Embryogenesis



Fan Zhou
Tsinghua University

My forthcoming lab focuses on understanding how multi-dimensional molecular architecture (e.g., gene networks coordinated with epigenetic factors) regulate cell fate decisions and transitions during mammalian/human embryogenesis. We aim to integrate single-cell *in vitro/vivo* functional identification, single-cell omics analysis, and genetic manipulation to link the genome with cumulative cellular phenotypes. Our work mainly includes the following: (1) employing/developing single-cell multi-omics analysis to uncover the molecular patterns of lineage specialization during embryonic development; (2) establishing *in vitro/vivo* models to understand the regulatory mechanism of cell fate transition during embryogenesis from the phenotypic/functional dimension; and (3) exploring the regulatory principles in embryo implantation and tumor evolution in reproductive system.

With years of training in stem cell and early embryo development, I am excited to have the opportunity to independently carry out research on cell fate and embryogenesis at Tsinghua. Understanding the principles of cell fate will not only shed light on how orderly embryo body plans emerge from a single-cell fertilized egg to build a complex and highly functional organism, but also reveal how potential regulators trigger diseases such as cancer, essentially a disordered transformation of cell fates. I am looking forward to this unfolding journey with all of my future lab members.

Transition under a Pandemic



Mingxia Gu
Cincinnati Children's Hospital

After 10 years of training at Stanford University, I am very excited to move to the next phase of my academic career: starting my independent research lab at Cincinnati Children's Hospital, one of the top pediatric programs nationwide. When I signed the offer to start in February 2020, I never thought it would be in the middle of a global pandemic. The transition has been challenging, but as a new team, we responded very quickly and developed a research plan to tackle vascular injury in COVID-19.

Our group has always been passionate about exploring the role of vascular deficiency in the etiology of congenital heart and lung defects. By analyzing patient samples, we have uncovered novel disease-related cellular phenotypes and identified transcriptomic and epigenomic changes at single-cell resolution. Using patient-derived iPSCs and organoids, we model disease progression *in vitro*, with the goal of developing therapies to target fundamental pathobiology using a personalized high-throughput drug screening platform. Alleviating unpleasant and debilitating symptoms in sick children is the single most gratifying part of my job and my primary motivation for pursuing a career in pediatric stem cell research.

Yes, we are in the midst of an unprecedented time. While dealing with enormous uncertainty, we are more interconnected as a group, sharing each other's fears and faith, resilience and optimism, and enjoying little cheerful moments every day. Together we will find a path forward.

Inflammation Shaping Tissues



Jose Ordovás-Montañés
Boston Children's Hospital

Barrier tissues such as the intestine, airway, and skin have remarkable regeneration capacity due to specialized stem cells that rapidly give rise to epithelial cells, together with the support of underlying stromal and immune cells. However, in chronic diseases sustained by inflammatory cytokines, this regenerative system becomes dysregulated with significant deviations from healthy tissues. Our lab opened in November of 2019 and studies how inflammation-induced changes to these stem cells may be at the root of chronic diseases. Using technologies such as scRNA-seq and organoids, we try to answer the following questions: which cellular compartments harbor memories of inflammation in tissue, and how might we develop effective mechanisms by which to promote or erase them? In short, where and how are health and disease stored in tissues? By systematically mapping cells, we are generating comprehensive tissue atlases and beginning to understand which cells may drive and sustain disease states. It is through answering these questions that we aim to do our part in improving the health and wellbeing of people living with these diseases. COVID-19 has temporarily put a hold on our wet lab work, but we are still contributing from our homes: strengthening our computational skills and holding journal clubs, lab meetings, and social hours over video. We are doing our best as a collective to ensure that we are not only remaining dedicated to our science but to each other in these times.