Cell Reports

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Q&A

Q&A with Fan Zhou

Fan Zhou spoke with *Cell Reports* about his journey in science and his recent paper in which he and his fellow authors dissected molecular dynamics along lineage progression and early mouse development.

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What is your lab focused on?

Our lab investigates peri-implantation embryogenesis—a pivotal yet understudied phase bridging blastocyst formation and gastrulation. During this transition, mammalian embryos undergo dramatic molecular reprogramming, including pluripotency exit, lineage specification, and epigenetic remodeling. Using multimodal approaches (multiomics, functional identification, and *in vitro*/*in vivo* models), we aim to decode how multidimensional regulatory networks—transcriptional, epigenetic, and functional—orchestrate lineage commitment and tissue patterning. Our work may shed light on developmental disorders, recurrent pregnancy loss, and infertility.

What kind of environment are you looking to foster?

Since founding the lab in 2020, we've prioritized cultivating a culture of mutual respect, intellectual rigor, and collaborative optimism. Beyond technical training, we emphasize the process of discovery—nurturing curiosity, resilience, and appreciation for incremental progress. We encourage trainees to view challenges as opportunities to refine both experiments and scientific judgment.

What is the take home message of your new *Cell Reports* paper?

Early mammalian embryogenesis undergoes pre- to post-implantation transition (PPT). Clinical data indicate that approximately 30% of couples suffer from early pregnancy loss due to implantation failure. During PPT, the embryo undergoes a series of cellular and molecular regulatory processes, such as pluripotency exit, lineage-specific transcription dynamics, and establishment of global repressive epigenetic programs. Notably, in recent years, we and others have reported drastic reprogramming of DNA methylation and epigenetic modifications during mammalian (including humans) peri-implantation embryogenesis. In this study, we focus on DNA methylome-transcriptome dynamics during PPT, revealing species-conserved lineage-specific DNA methylation, segregated DNA methylation dynamics in visceral endoderm subtypes, asynchronous DNA methylation of parental transposons, and non-canonical DNA methylation-transcription coupling across species. These discoveries highlight PPT as a window into epigenetic-developmental crosstalk. Crucially, they raise mechanistic questions. How do DNA methylation dynamics instruct embryogenesis? Are these patterns stage or lineage restricted? Addressing these requires innovative tools—locus-specific epigenome editing, advanced embryo models, and cross-species validation, etc.—which we are actively pursuing and trying to understand.

What major knowledge gaps remain in understanding PPT?

PPT remains a black box. Fundamental questions persist. What drives pluripotency transition and X inactivation? How do maternal-embryonic interfaces coordinate morphogenesis? What regulates cellular potency dynamics? Answering these demands disruptive technologies—single-cell multiomics, *in vivo* perturbation platforms, efficient *in vitro* embryo or cell line models, and other disruptive new technologies—paired with collaboration among global peer scientists.

What drives your interest in science?

Growing up in southern China, I was influenced by my father—a farmer and amateur musician—who instilled in me an early fascination with music and creativity. Though I initially aspired to become a musician or thoracic surgeon, serendipitous opportunities during my academic journey redirected me toward basic research. My interest crystallized upon discovering the hematopoietic stem cell system: its functional elegance and therapeutic potential in curing blood malignancies captivated me. This led to a profound curiosity about the embryonic origins of hematopoiesis. As a postdoctoral fellow, I became enthralled by early embryogenesis—a paradigm for studying cell fate determination. The spatiotemporal precision underlying lineage specialization and tissue coordination remains one of biology's grand mysteries, compelling me to develop innovative approaches to decode these processes.

While chance played a role in my trajectory, my path ultimately reflects an active pursuit, driven by curiosity about nature's principles and a conviction that fundamental discoveries can transform medicine. I am grateful for mentors, colleagues, and students who have shaped this journey. Most importantly, my team and I remain energized by the uncharted territories ahead.

What advice would you give your younger self?

Pursue your aspirations boldly. Embrace uncertainty, prioritize experiential growth over outcomes, and trust that detours often lead to meaningful destinations.

What surprised you about being a scientist?

Science embodies intellectual freedom. Since my graduate studies, I've been awed by how rigorously interrogating nature through experimentation and reasoning can progressively unveil fundamental truths. Few professions offer such profound satisfaction of curiosity; it is truly humanity's most exhilarating endeavor.

What life motto guides your mentorship?

"Pursue passion with rigor, embrace process over product, and let outcomes follow naturally." Identify questions that ignite your curiosity, engage them wholeheartedly, and remain open to serendipitous insights. Growth lies not in avoiding failure but in learning from it.

DECLARATION OF INTERESTS

The author declares no competing interests.

https://doi.org/10.1016/j.celrep.2025.115989