Understanding human totipotency and development

Dr. Miguel A. Esteban
Research Scientist at 3DC STAR Lab, BGI CELL
Shenzhen, China

Abstract

Totipotency refers to the remarkable capacity of a single cell—the fertilized zygote—to give rise to an entire organism, encompassing both embryonic and extraembryonic tissues. Understanding the molecular and cellular mechanisms that underlie mammalian totipotency and early development has been a central scientific pursuit since the time of Aristotle. Over the centuries, studies in a variety of model organisms have provided invaluable insights into how life begins from a single cell. However, it has become increasingly clear that significant developmental differences exist even among closely related species, including primates. These distinctions highlight the importance of studying human development directly.

Yet, research using human embryos is constrained by fundamental practical, ethical, and legal considerations. As a result, our understanding of the earliest stages of human life has remained limited. Excitingly, recent advances in the generation of human totipotent stem cells and the creation of stem cell–derived embryo models now offer unprecedented opportunities to explore the principles of human development *in vitro*. These systems enable us to model early embryogenesis, study lineage specification, and investigate cross-species developmental compatibility under controlled laboratory conditions.

In this talk, I will discuss our recent progress in defining human totipotent cell states, establishing interspecies chimeras, and developing embryo-like structures derived from stem cells. Together, these studies aim to illuminate the molecular logic of human totipotency and open new avenues for understanding both normal development and disease.