The black box at the beginning of life

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Kyoto University scientists are casting light into the black box of human "germ cell" development. It is hoped that their new model may lead to findings in all stages of human development, from the creation of sperm and eggs to the process of embryo-to-adult development. Credit: Kyoto University

Life begins with an egg and a sperm: that much is clear. But how do these "germ cells" form, and how do they pass genetic traits from one generation to the next?

Researchers working at Kyoto University have created a lab-based human germ cell development model that should shed light on these basic questions. The hope is that their accomplishment may lead to a molecular-level understanding of conditions such as infertility.

The underlying mechanisms of early germ cell development in humans have remained unclear because of a lack of robust experimental methods, as well as inherent difficulties with studying human embryos. In a promising breakthrough, recently published in *Cell Stem Cell*, the research team has recreated human germ cell development in the laboratory, revealing specific key elements and events that occur at the beginning of human life.

"When I read about his work I knew I had to come back [to Japan]", said co-first author Kotaro Sasaki, referring to lead researcher Mitinori Saitou's previous work in the field. Sasaki, who had established a pathology career in the United States, returned to join Saitou's team in Kyoto. For this study, five laboratories at the university's Center for iPS Cell Research and Application (CiRA) collaborated.

To date, most such research has been restricted to mice. While this work provides useful information that is generally applicable to mammals, there has still been a lack of information specific to humans.

To that end, Saitou's team recreated the developmental process of human germ cells, which gives rise to reproductive sperm and eggs. In addition to illustrating key transcription interactions and signaling events, the scientists gained insight into how epigenetic marks—traits that are inherited without changes to the DNA sequence—are "erased" at the

beginning of germ cell development.

"We demonstrated the early events in human germ cell development," explains Sasaki. "Our work should provide a basis to gain a better understanding of how certain disorders such as infertility and growth impairment come about."

The team's model, still in its early stages, is hoped to form a foundation for continuing studies on germ cell lineage. "By further reconstituting human germ cell development in vitro, we may be able to discover the mechanisms throughout the entire developmental process from embryo to adult," says Professor Saitou.

More information: "Robust In Vitro Induction of Human Germ Cell Fate from Pluripotent Stem Cells" *Cell stem cell* 17, Published Online: July 16, 2015. dx.doi.org/10.1016/j.stem.2015.06.014

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