Researchers create egg and sperm precursors using human embryonic stem cells

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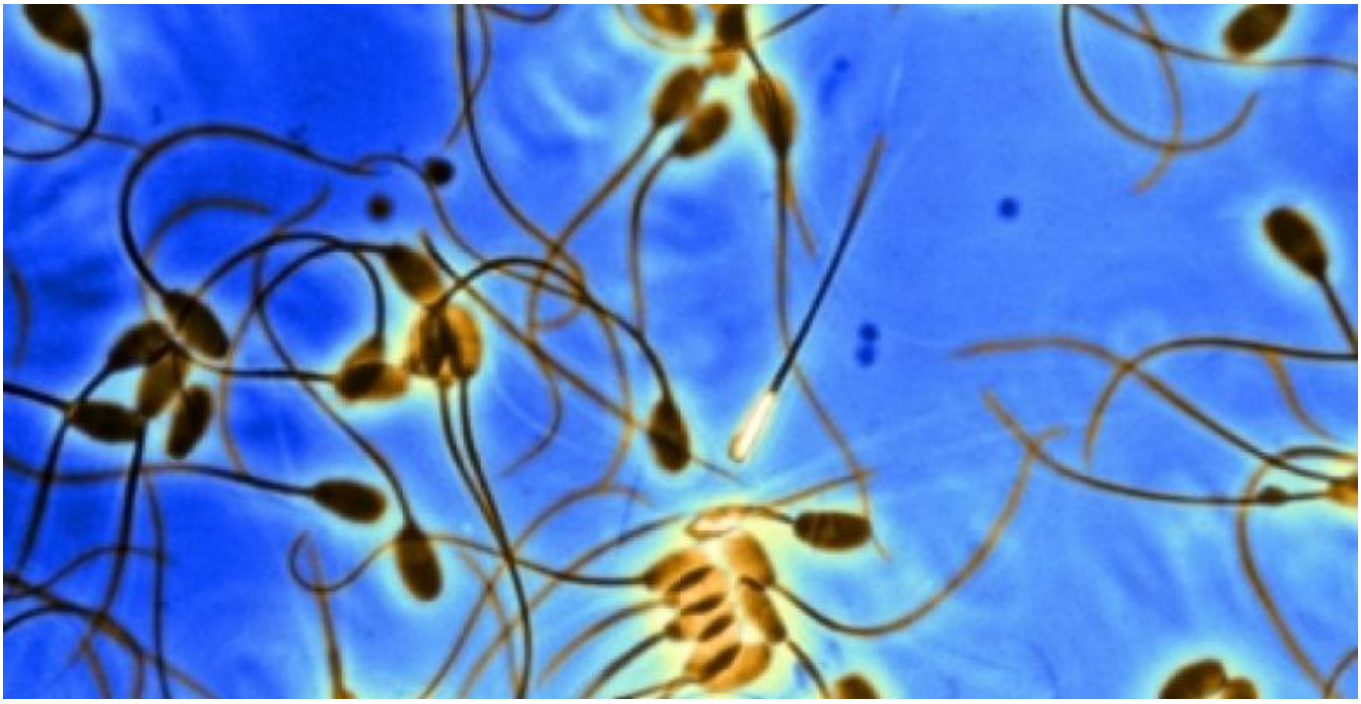

Lead researcher Prof. Azim Surani, of the Gurdon Institute at the University of Cambridge, and his team say their findings may not only have implications for fertility treatment, but they could also open the door to new treatments for age-related diseases.

In addition, the research highlights significant differences in embryo development between humans and rodents, according to the team, meaning results of studies using mice and rats may not directly apply to humans.

The researchers publish their findings in the journal *Cell*.

Primordial germ cells (PGCs) - cells that become sperm and egg - are created during the early development of mammals. When a mammal reproduces, PGCs pass on genetic data to offspring.

Prof. Surani and his team explain that as a sperm fertilizes an egg, the egg forms a blastocyst - a group of cells created in the early stages of an embryo. Some cells in the blastocyst form the inner cell mass, which becomes the fetus. Other cells in the blastocyst form the outer cell wall, which becomes the placenta.

Researchers discovered that a gene called SOX17 plays an important role in transforming human stem cells into PGCs. The green cells in this image of an embryoid are SOX17 positive.*Image credit: Walfred Tang, University of Cambridge*

According to the researchers, cells in the inner cell mass change into stem cells, which are able to become any cell type in the body. Some of these cells turn into PGCs.

"The creation of PGCs is one of the earliest events during early mammalian development," says first study author Dr. Naoko Irie, also of the Gurdon Institute at the University of Cambridge. "It's a stage we've managed to recreate using stem cells from mice and rats, but until now few researchers have done this systematically using human stem cells."

SOX17 crucial for changing human stem cells into PGCs

In their study, Prof. Surani and his team discovered that a gene called SOX17 plays an important role in a process called "specification" - transforming human stem cells into PGCs. Past research has found that SOX17 is involved in changing human stem cells into endodermal cells, but the gene has never before been linked to PGC specification.

The mouse equivalent of the SOX17 gene, however, is not involved in PGC specification. The team says this finding indicates major differences between the embryonic development of mice and humans.

"It has highlighted important differences between embryo development in humans and rodents that may mean findings in mice and rats may not be directly extrapolated to humans," says Dr. Irie.

The researchers found they were also able to create PGCs using reprogrammed adult cells, including skin cells. They say this process may open the door to research on patient-specific cells, which may increase understanding of infertility, the human germline and germ cell tumors.

Findings may increase knowledge of inherited epigenetic mutations

In addition, the team says their findings may increase knowledge of how environmental factors that may affect gene activity - such as smoking or diet - can be inherited.

The researchers explain that environmental factors can affect genes via methylation - a process in which molecules bind to DNA and increase or reduce gene activity. Methylation patterns can be passed on to offspring.

In this study, the team identified a process that eliminates such methylation patterns during PGC specification. They note, however, that traces of methylation patterns may still be passed down to offspring.

Commenting on this finding, Prof. Surani says:

> "Germ cells are 'immortal' in the sense that they provide an enduring link between all generations, carrying genetic information from one generation to the next.
>
> The comprehensive erasure of epigenetic information ensures that most, if not all,

> epigenetic mutations are erased, which promotes 'rejuvenation' of the lineage and allows it to give rise to endless generations. These mechanisms are of wider interest toward understanding age-related diseases, which in part might be due to cumulative epigenetic mutations."

Earlier this year, *Medical News Today* reported on a study by researchers from the Wellcome Trust Sanger Institute in the UK revealing an important "sperm meets egg" protein discovery.

The research followed a 2005 study in which scientists from Japan found a protein on sperm's surface - called Izumo - that recognizes the egg to form an embryo. The Sanger Institute team found the protein on the egg - called Juno - that the sperm recognizes.