Insights into the development of sperm and egg cell precursors in the embryo

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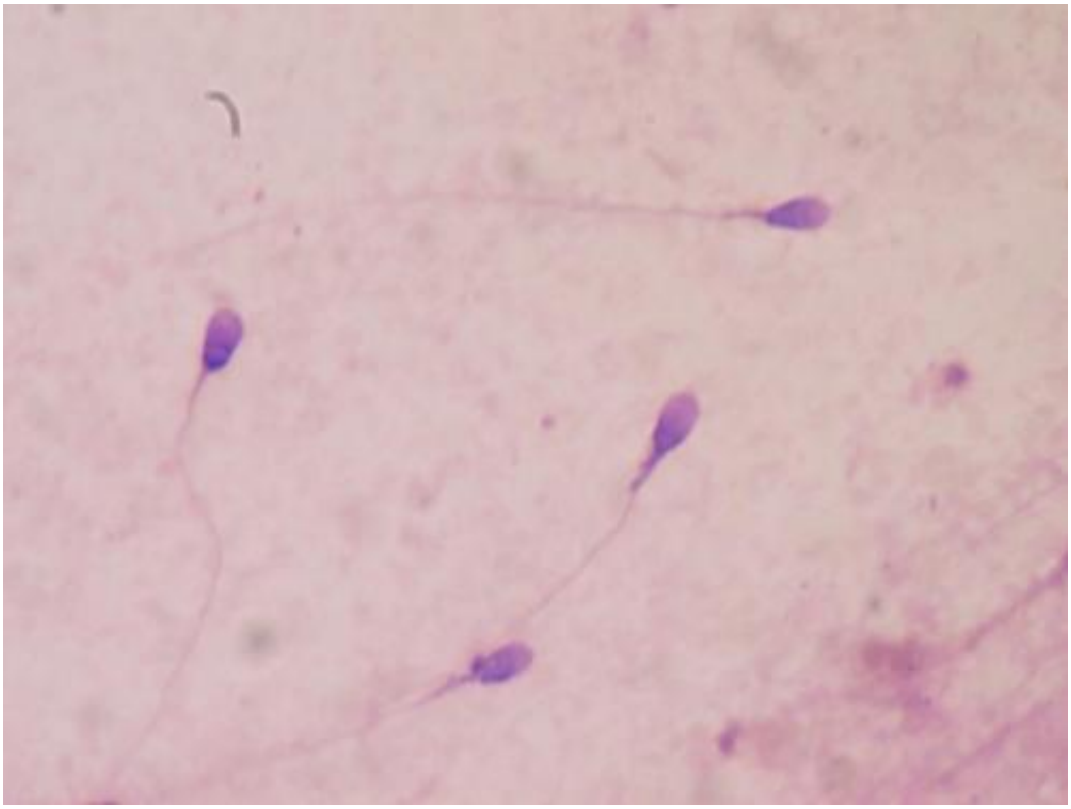

Human sperm stained for semen quality testing in the clinical laboratory. Credit: Bobjgalindo/Wikipedia

Researchers at the Babraham Institute have investigated the early stages of the development of cells called primordial germ cells and developed strategies to generate 'lookalike' cells in the lab. The generation of human 'lookalike' primordial germ cells is of importance for future

fertility studies and the analysis of potential transgenerational epigenetic inheritance in humans.

A bit like someone looking into a mirror reflected in another mirror, as one new life is developing as an embryo, the capacity to produce the next generation of life is already being established in that embryo. Research carried out between the groups of Wolf Reik and Peter Rugg-Gunn in the Epigenetics research programme at the Babraham Institute have investigated the early stages of the development of cells called primordial germ cells and developed strategies to generate these cells in the lab. Primordial germ cells give rise to sperm or egg cells and, in humans, are already present in embryos at the second week of development.

As reported in the latest issue of *Developmental Cell*, the researchers developed a method to generate primordial germ cell 'lookalike' cells to look in detail at what was happening at the epigenetic level, comparing what happens in cells from mice and humans. Epigenetics refers to reversible modifications to DNA that don't affect the DNA sequence but alter how genes are read. The specific pattern of epigenetic marks in a cell type specifies identity and this epigenetic control is vital to what makes our cells different, for example a skin cell from a liver cell, when they all contain the same genetic instructions.

The development of primordial germ cells is characterised by widespread epigenetic remodelling. These cells need to 'forget' their own programmed instructions and create a blank slate for the blueprint of either a sperm or egg cell to be laid down.

Creating and analysing accurate 'lookalike' primordial germ cells opened the window on characterising the early stages of specification of these cells and the regulation of developmental timings. This insight has been previously limited by the difficulty of obtaining these cells from

embryos. The generation of human 'lookalike' primordial germ cells is also of importance for future fertility studies and analysis of potential transgenerational epigenetic inheritance in humans.

As explained by lead researcher, Dr Ferdinand von Meyenn, postdoctoral researcher in the Epigenetics research programme at the Babraham Institute and first author on the paper: "Our method establishes a reliable system that can be used to explore the early stages of epigenetic reprogramming in primordial germ cell-like cells and how this is regulated in the generation of reproductive cells. This method also provides an experimental system for future fertility studies in humans. Our side by side analysis uncovers the dynamics of epigenetic programming occurring in germ cell development at single base resolution in human and mouse cells."

Professor Wolf Reik, Head of the Epigenetics research programme, said: "Charting the different developmental timings in the early reprogramming events observed in the human and mouse-derived cells gives the first mechanistic insight into how these events are regulated which is tremendously exciting. The next steps are to capture what happens in the later stages of primordial germ cell development and the related epigenetic events. In particular, this new method will allow us to answer questions regarding transgenerational epigenetic inheritance in humans."

More information: Ferdinand von Meyenn et al. Comparative Principles of DNA Methylation Reprogramming during Human and Mouse In Vitro Primordial Germ Cell Specification, *Developmental Cell* (2016). DOI: 10.1016/j.devcel.2016.09.015

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