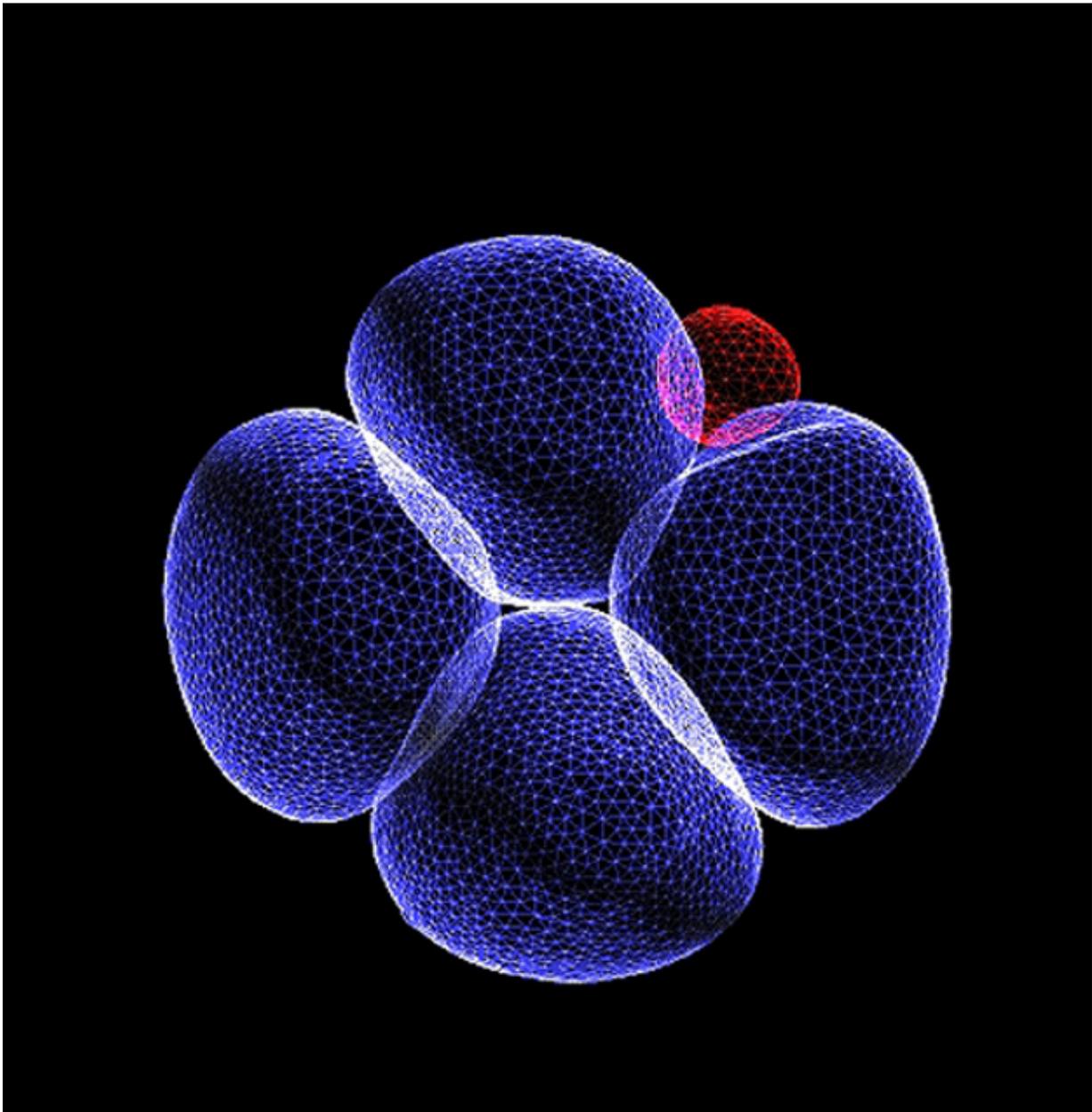


Embryo development: Some cells are more equal than others even at four-cell stage

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A four-cell stage embryo. Credit: Zernicka-Goetz Lab, University of Cambridge

Genetic 'signatures' of early-stage embryos confirm that our development begins to take shape as early as the second day after conception, when we are a mere four cells in size, according to new research led by the University of Cambridge and EMBL-EBI. Although they seem to be identical, the cells of the two day-old embryo are already beginning to display subtle differences.

Once an egg has been fertilised by a sperm, it divides several times, becoming a large free-floating ball of stem [cells](#). At first, these stem cells are 'totipotent', the state at which a stem cell can divide and grow and produce everything—every single cell of the whole body and the placenta, to attach the embryo to the mother's womb. The [stem cells](#) then change to a 'pluripotent' state, in which their [development](#) is restricted to generating the cells of the whole body, but not the placenta. However, the point during development at which cells begin to show a preference for becoming a specific cell type is unclear.

Now, in a study published in the journal *Cell*, scientists at the University of Cambridge and the European Bioinformatics Institute (EMBL-EBI) suggests that as early as the four-cell embryo stage, the cells are indeed different.

The researchers used the latest sequencing technologies to model embryo development in mice, looking at the activity of individual genes at a single cell level. They showed that some genes in each of the four cells behaved differently. The activity of one gene in particular, Sox21, differed the most between cells; this gene forms part of the 'pluripotency network'. The team found when this gene's activity was reduced, the

activity of a master regulator that directs cells to develop into the placenta increased.

"We know that life starts when a sperm fertilises an egg, but we're interested in when the important decisions that determine our future development occur," says Professor Magdalena Zernicka-Goetz from the Department of Physiology, Development and Neuroscience at the University of Cambridge. "We now know that even as early as the four-stage embryo - just two days after fertilisation - the embryo is being guided in a particular direction and its cells are no longer identical."

Dr John Marioni of EMBL-EBI, the Wellcome Trust Sanger Institute and the Cancer Research UK Cambridge Institute, adds: "We can make use of powerful sequencing tools to deepen our understanding of the molecular mechanisms that drive development in [individual cells](#). Because of these high-resolution techniques, we are now able to see the genetic and epigenetic signatures that indicate the direction in which early embryonic cells will tend to travel."

More information: Heterogeneity in Oct4 and Sox2 Targets Biases Cell Fate in Four-Cell Mouse Embryos. *Cell*; 24 March 2016. [DOI: 10.1016/j.cell.2016.01.047](https://doi.org/10.1016/j.cell.2016.01.047)

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