Scientists discover stage at which an embryonic cell is fated to become a stem cell

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Cambridge scientists have discovered the stage at which some of the cells of a fertilised mammalian egg are fated to develop into stem cells and why this occurs. The findings of the study, which overturn the long-held belief that cells are the same until the fourth cleavage (division) of the embryo, are reported in today's edition of *Nature*.

After fertilisation, the cells of the embryo at first undergo equal, symmetrical divisions and unequal, asymmetrical ones that direct smaller daughter cells towards the inside of the embryo. These become the inner cell mass of stem cells. Previously, it was believed that the mammalian embryo starts its development with identical cells and only as these inside and outside cells form do differences between cells first emerge.

However, research led by Professor Magdelena Zernicka-Goetz, University of Cambridge, has revealed evidence to suggest that differences between the embryonic cells are already apparent at the 4-cell-stage, before the cells become partitioned between the inside or outside of the embryo. And those differences depend on the orientation and order of the very first cleavage divisions of the embryo.

Professor Zernicka-Goetz said, "Our findings were surprising since they showed that cells of the mammalian embryo first start to differ from each other much earlier in development than previously supposed but also they give us a real clue on how to manipulate embryonic cells so that they will develop with the properties of the natural stem cells of the embryo."

The study also found cell fate and transcription activity is determined by the level of a methylated form of histone H3, one of the basic proteins around which DNA is packaged and which when modified in this way affects gene expression. They found that the higher the levels of this modified form of histone H3, the more predisposed the mammalian embryonic cells were to develop the qualities of inner embryonic cells, a population that have stem-cell-like properties. Thus, their results show that manipulating epigenetic information in this protein in early mouse embryos can influence cell fate determination

Source: University of Cambridge