Researchers discover key molecule for stem cell pluripotency

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Researchers of the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch have discovered what enables embryonic stem cells to differentiate into diverse cell types and thus to be pluripotent. This pluripotency depends on a specific molecule – E-cadherin – hitherto primarily known for its role in mediating cell-cell adhesion as a kind of "intracellular glue". If E-cadherin is absent, the stem cells lose their pluripotency. The molecule also plays a crucial role in the reprogramming of somatic cells (body cells) into pluripotent stem cells.

Dr. Daniel Besser, Prof. Walter Birchmeier and Torben Redmer from the MDC, a member of the Helmholtz Association, used mouse embryonic fibroblasts (MEFs) in their stem cell experiments. In a first step they showed that the pluripotency of these stem cells is directly associated with the cell-adhesion molecule E-cadherin. If E-cadherin is absent, the stem cells lose their pluripotency.

In a second step the researchers investigated what happens when somatic cells that normally neither have E-cadherin nor are pluripotent are reprogrammed into a pluripotent stem cell state. In this reprogramming technique, somatic cells are converted into induced pluripotent stem cells (iPSCs). This new technique may help researchers avoid the controversies that come with the use of human embryos to produce human embryonic stem cells for research purposes.

The MDC researchers found that in contrast to the original cells, the new pluripotent cells derived from mouse connective tissue contained E-

cadherin. "Thus, we have double proof that E-cadherin is directly associated with stem-cell pluripotency. E-Cadherin is necessary for maintaining pluripotent stem cells and also for inducing the pluripotent state in the reprogramming of somatic cells," Dr. Besser said. "If E-cadherin is absent, somatic cells cannot be reprogrammed into viable pluripotent cells." In addition, E-Cadherin can replace OCT 4, one of the signaling molecules until now considered indispensable for reprogramming.

Next, the MDC researchers want to find out to what extent E-cadherin also regulates human embryonic stem cells. "Understanding the molecular relationships is essential for using human somatic cells to develop stem cell therapy for diseases such as heart attack, Alzheimer's or Parkinson's disease or diabetes," Dr. Besser said.

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