STEM CELLS

Nanog: the gift of choice

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Nanog
<http://ca.expasy.org/uniprot/Q7TN85>

Although mouse embryonic stem (ES) cells were first isolated 25 years ago, many important questions about these remarkable cells remain unanswered. For instance, it's well known that ES cells can 'donate' pluripotency to somatic cells after ES–somatic cell fusion; however, the identity of the ES cell-derived factors that reset the epigenome of the somatic cell are unknown. Austin Smith and colleagues now reveal that the transcription factor **Nanog** is crucial for this reprogramming process.

Nanog is a homeodomain protein that is expressed in early embryos

and that maintains pluripotency in ES cells. But does Nanog also have a role in the transfer of pluripotency?

To answer this question, Smith and co-workers first showed that overexpression of Nanog markedly increased the yield of pluripotent hybrid colonies formed by fusion of ES cells with neural stem (NS) cells. In the presence of high levels of Nanog, conversion of ES–NS cell hybrids to ES cell colonies was as efficient as that of ES–ES cell fusions.

In a second series of experiments, the authors showed that high levels of Nanog increased the amount of hybrid colonies formed by fusion of ES cells with more differentiated cells, such as thymocytes or fibroblasts. In both cases, however, fewer colonies were produced compared with the ES–NS cell fusions. Smith and colleagues suggest that these lower hybrid yields could reflect fundamental differences in the epi-

genome of cells at different developmental stages. Chromatin modifiers might be relatively inactive in ES cells, giving rise to an epigenome that responds readily to transcriptional regulators, endowing the cell with diverse developmental options. As cells differentiate, the addition of repressive chromatin modifications might render the epigenome less malleable, progressively restricting lineage options and ease of reprogramming.

Finally, transfection of NS cells with a Nanog transgene had no effect on the NS cell phenotype, indicating that Nanog cooperates with other as-yet-unknown ES cell factors to orchestrate pluripotency.

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ORIGINAL RESEARCH PAPER Silva, J., Chambers, I., Pollard, S. & Smith, A. Nanog promotes transfer of pluripotency after cell fusion. *Nature* **441**, 997–1001 (2006)