Adult mice generated from induced pluripotent stem cells.

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Public Summary:
Recent landmark experiments have shown that transient overexpression of a small number of transcription factors can reprogram differentiated cells into induced pluripotent stem (iPS) cells that resemble embryonic stem (ES) cells. These iPS cells hold great promise for medicine because they have the potential to generate patient-specific cell types for cell replacement therapy and produce in vitro models of disease, without requiring embryonic tissues or oocytes. Although current iPS cell lines resemble ES cells, they have not passed the most stringent test of pluripotency by generating full-term or adult mice in tetraploid complementation assays, raising questions as to whether they are sufficiently potent to generate all of the cell types in an organism. Whether this difference between iPS and ES cells reflects intrinsic limitations of direct reprogramming is not known. Here we report fertile adult mice derived entirely from iPS cells that we generated by inducible genetic reprogramming of mouse embryonic fibroblasts. Producing adult mice derived entirely from a reprogrammed fibroblast shows that all features of a differentiated cell can be restored to an embryonic level of pluripotency without exposure to unknown ooplasmic factors.

Scientific Abstract:
Recent landmark experiments have shown that transient overexpression of a small number of transcription factors can reprogram differentiated cells into induced pluripotent stem (iPS) cells that resemble embryonic stem (ES) cells. These iPS cells hold great promise for medicine because they have the potential to generate patient-specific cell types for cell replacement therapy and produce in vitro models of disease, without requiring embryonic tissues or oocytes. Although current iPS cell lines resemble ES cells, they have not passed the most stringent test of pluripotency by generating full-term or adult mice in tetraploid complementation assays, raising questions as to whether they are sufficiently potent to generate all of the cell types in an organism. Whether this difference between iPS and ES cells reflects intrinsic limitations of direct reprogramming is not known. Here we report fertile adult mice derived entirely from iPS cells that we generated by inducible genetic reprogramming of mouse embryonic fibroblasts. Producing adult mice derived entirely from a reprogrammed fibroblast shows that all features of a differentiated cell can be restored to an embryonic level of pluripotency without exposure to unknown ooplasmic factors. Comparing these fully pluripotent iPS cell lines to less developmentally potent lines may reveal molecular markers of different pluripotent states. Furthermore, mice derived entirely from iPS cells will provide a new resource to assess the functional and genomic stability of cells and tissues derived from iPS cells, which is important to validate their utility in cell replacement therapy and research applications.