

Efficient generation of human iPSCs by a synthetic self-replicative RNA.

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Public Summary:

Induced pluripotent stem cells provide a new source of replacement of disease or injured tissue and as a resource to study what treatments may be beneficial for individual patients. The generation of stem cells using non-embryonic tissue and without introducing genetic mutations is a major goal for bridging stem cells from lab to the clinic. Here we developed a new approach to generate stem cells using an RNA-based method. This method efficiently generates new stem cells without introduction of genetic mutations and overcomes a major obstacle in the stem cell field.

Scientific Abstract:

The generation of human induced pluripotent stem cells (iPSCs) holds great promise for the development of regenerative medicine therapies to treat a wide range of human diseases. However, the generation of iPSCs in the absence of integrative DNA vectors remains problematic. Here, we report a simple, highly reproducible RNA-based iPSC generation approach that utilizes a single, synthetic self-replicating VEE-RF RNA replicon that expresses four reprogramming factors (OCT4, KLF4, and SOX2, with c-MYC or GLIS1) at consistent high levels prior to regulated RNA degradation. A single VEE-RF RNA transfection into newborn or adult human fibroblasts resulted in efficient generation of iPSCs with all the hallmarks of stem cells, including cell surface markers, global gene expression profiles, and in vivo pluripotency, to differentiate into all three germ layers. The VEE-RF RNA-based approach has broad applicability for the generation of iPSCs for ultimate use in human stem cell therapies in regenerative medicine.

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