A novel method for generating naive human iPS cells with significantly higher differentiation potency

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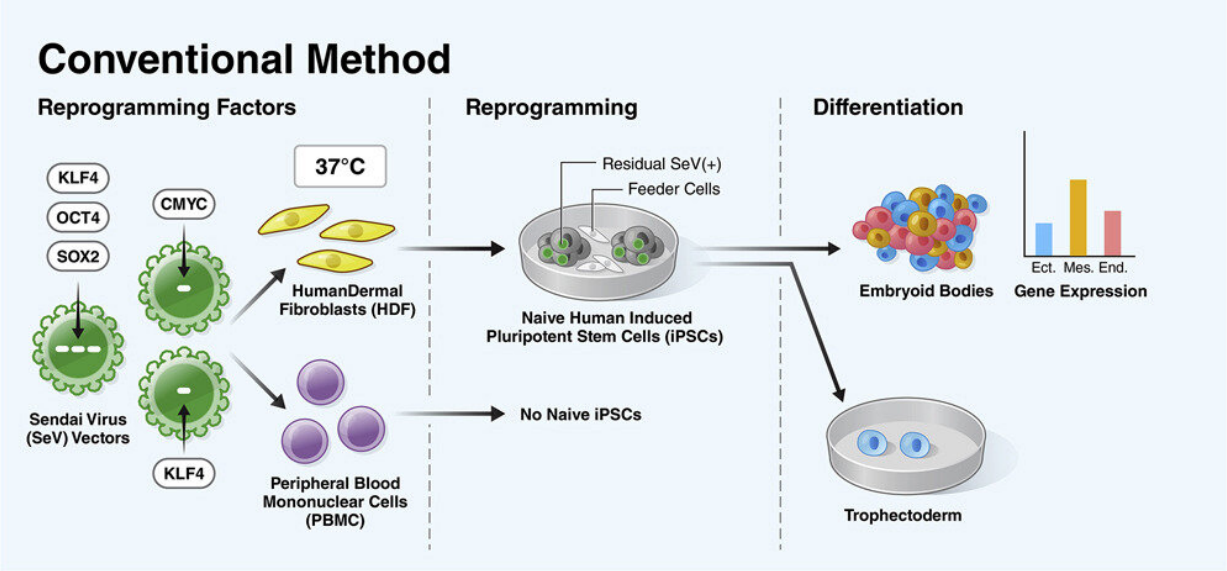

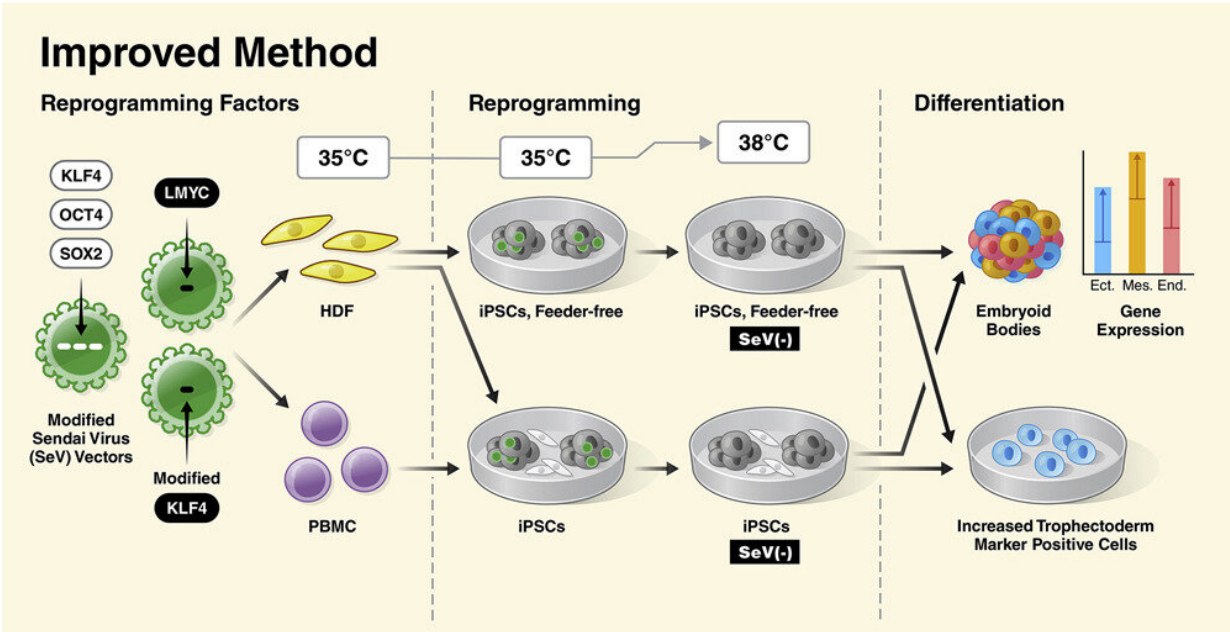

Graphical abstract. Credit: *Cell Reports Methods* (2022). DOI: 10.1016/j.crmeth.2022.100317

A joint research team led by Dr. Akira Kunitomi, a former postdoctoral fellow at CiRA (currently a researcher at the Gladstone Institute of Cardiovascular Disease), and ID Pharma Co., Ltd., has established a new method for naive iPS cell generation that uses a temperature-sensitive Sendai virus vector developed by the group to remove the vectors rapidly.

To date, only dermal fibroblasts have been successfully reprogrammed into naive iPS cells through generation methods using Sendai virus vectors and feeder cells. In a new study, the joint research group succeeded in generating naive iPS cells not only from human dermal fibroblasts but also from peripheral blood mononuclear cells by changing the combination of reprogramming genes.

The researchers subsequently created a temperature-sensitive Sendai virus vector that can be removed rapidly during the reprogramming process and established a feeder-free method to generate naive iPS cells from dermal fibroblasts using the modified Sendai virus vectors.

Furthermore, the group demonstrated that the naive iPS cells generated via the new method can better differentiate into trilineage and extra-embryonic trophectoderm than those derived by conventional methods because early removal of the Sendai virus vectors suppresses expression of exogenous genes.

Recently, naive human pluripotent stem cells have been widely used for

studies on the early human embryos by taking advantage of their high pluripotency. The new protocol created in this study is expected to contribute to the development of such research and beyond.

Since the method can be applied to the establishment of primed human iPS cells, researchers will be able to obtain cell lines free of viral vector genomes without the time-consuming clone selection process. It is also expected that the new method will facilitate the generation of autologous iPS cells from donors and further advance studies on disease modeling, drug discovery, and cell therapy.

The results of this study were published online in *Cell Reports Methods* on October 17, 2022.

More information: Akira Kunitomi et al, Improved Sendai viral system for reprogramming to naive pluripotency, *Cell Reports Methods* (2022). DOI: 10.1016/j.crmeth.2022.100317

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