

Fig S1. Representative images showing immunostaining of differentiated EPS cells by EB assay. EB was immunostained by anti-FOXA2, anti- β -III TUBULIN, anti-GATA3, anti-EOMES and anti-CDX2 antibodies.

Fig S2. The generation of *IL6* knock-in EPS cells. Diagrams of the generation human *IL6* gene knock-in EPS cells. Primers for knock-in detection are indicated as pairs of arrows.

Fig S3. (A) Off-target effects of human *IL3* knock-in EPS cells. Left, T7E1 assay. Right, sequencing (20 clones per sample). **(B)** Off-target effects of human *IL6* knock-in EPS cells. Left, T7E1 assay. Right, sequencing (20 clones per sample).

Fig S4. Representative images showing immunostaining of EPS and EPS-*IL3* with lineage-specific markers. Error bar, 25 μ m.

Fig S5. ES-IL3 cells cultured in 2i condition were generated using the same gene targeting strategy with EPS-IL3 cells. Two ES-IL3 sub-lines were selected for tetraploid complementation experiments at passage 20. 46 blastocysts were injected with ES-IL3 cells and surrogate mothers were sacrificed on day E10.5. (A) Placenta obtained from tetraploid assay using ES-IL3 cells, E10.5. (B) The development of EPS-IL3 and ES-IL3 cells in tetraploid blastocysts.

Fig. S1

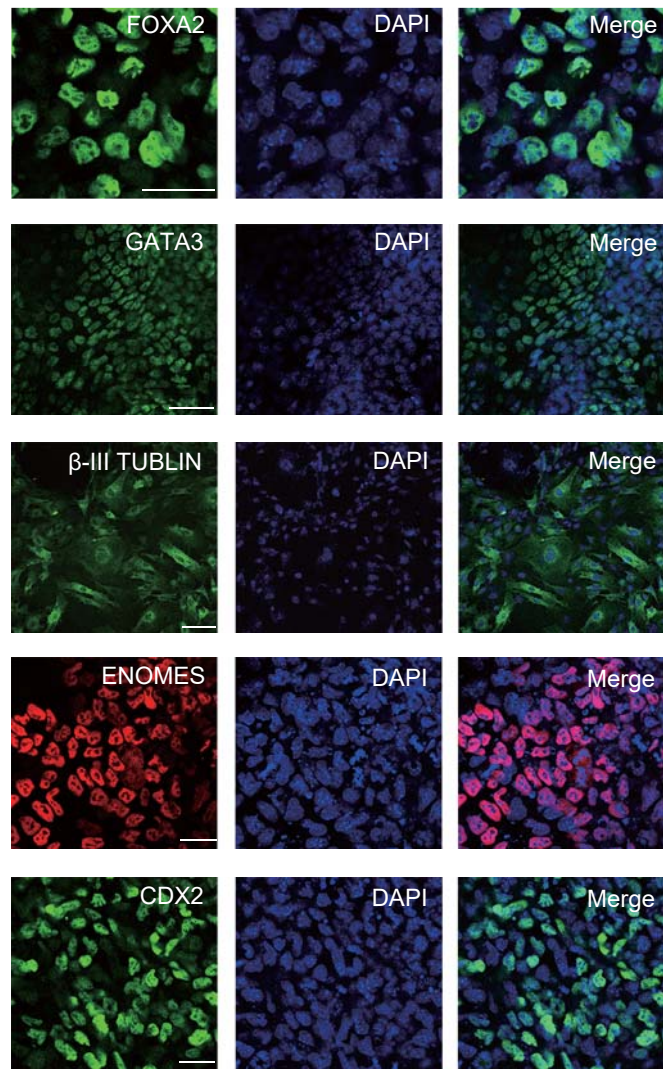


Fig. S2

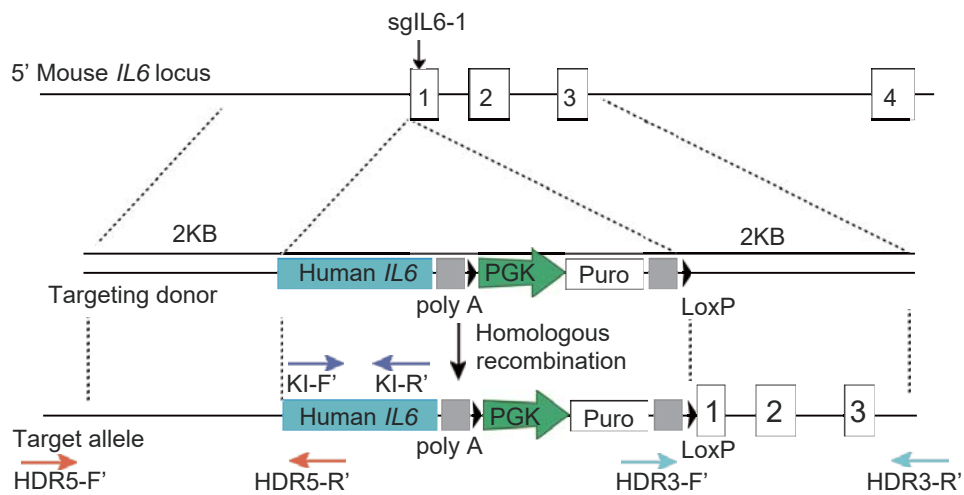


Fig. S4

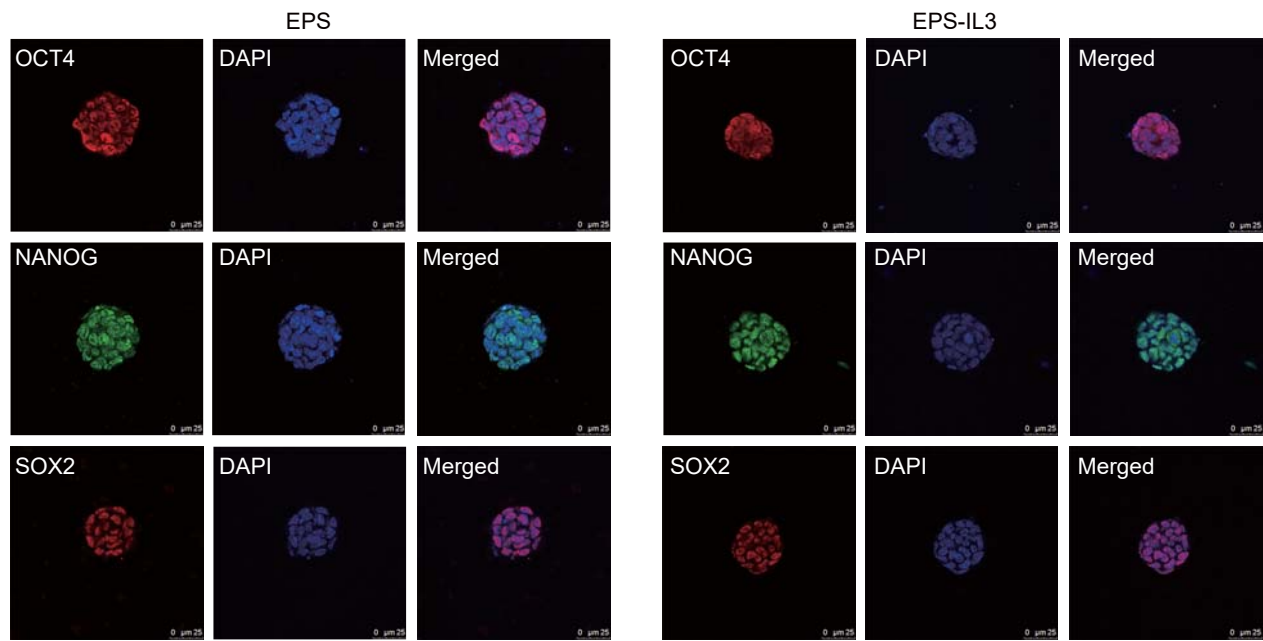


Fig. S5

