

## Reprogramming ML II fibroblasts to iPSCs

For reprogramming ML II fibroblasts into iPSCs, the Epi5™ Episomal iPSC Reprogramming Kit (Cat. A15960, Invitrogen, ThermoFisher Scientific) was used, which is a non-integrative approach based on episomal vectors. The manufacturer's protocol for feeder-free conditions was followed, with minor modifications. Briefly:

1. At day -3, MLII fibroblasts were seeded in fibroblast medium at  $3 \times 10^4$  cells per well of a 6-well plate coated with vitronectin (Catalog A14700, Gibco, ThermoFisher Scientific) diluted 1:100 in DPBS.
2. At day -1, the spent medium was replaced
3. At day 0, the ML II fibroblasts, at passage 6, were transfected with the Epi5™ vectors using Lipofectamine 3000 (Invitrogen, ThermoFisher Scientific) and incubated for 24 hours
4. At day 1, medium was changed to N2B27 supplemented with bFGF (added freshly prior to use)
5. The spent medium was replaced every other day, up to day 15 post-transfection
6. At day 15, medium was changed to Essential 8™ Flex Medium (Gibco, ThermoFisher Scientific)
7. The spent medium was replaced every other day and the plates observed for the emergence of cell clumps indicative of iPSC colonies. At day 25 post-transfection, the first cell clump indicative of transformed cells was observed and a second cell clump at day 30.
8. At days 28 and 32, the first and second iPSC colonies were respectively picked and each was transferred to one well of a 12-well plate coated with vitronectin for expansion.