Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

High Efficiency Generation of Integration-free iPSCs for the Clinic

Product

Platform Technology: Combined iPSC reprogramming and gene correction

Indication

Generation of clinically & commercially viable gene-corrected cells

Value Propositions

- High efficiency
- High quality iPSCs
- Cost effective
- Rapid production

Market

- Genetic disorders
- Tissue regeneration
- Disease modelling

Intellectual Property

- PCT stage: Published
  Methods and compositions for reprogramming cells
  WO2017091547A1
  US20220403390A1

Key Documents

- High-efficiency RNA-based reprogramming of human primary fibroblasts Link
- RNA-based reprogramming of human primary fibroblasts into induced pluripotent stem cells Link

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iPSC Reprogramming Challenges

Induced pluripotent stem cells (iPSCs) are a type of pluripotent stem cell generated directly from adult cells that can propagate indefinitely to give rise to every other cell type in the body. iPSCs are a valuable tool to study human development and disease. They are also useful for drug discovery and the development of cellular transplantation therapies, especially for genetic diseases. Despite improvements in reprogramming methods, the reprogramming efficiency remains low, and the risk of mutations is high. The need for genetic correction as a separate step during GMP production increases costs.

High Quality & Integration-free iPSC

A University of Colorado research group led by Drs. Ganna Bilousova and Igor Kogut has developed an RNA-based approach to reprogram human primary cells into high quality, integration-free iPSCs. The approach uses in vitro transcribed messenger RNAs synthesized with modified nucleotides (modified mRNAs) encoding pluripotency factors (SOX2, KLF4, cMYC, LIN28A, NANOG, OCT4-MyoD fusion) and mature embryonic stem cell-specific microRNA-367/302 mimics. The resulting iPSC colonies can then be isolated and directly expanded in feeder-free conditions.

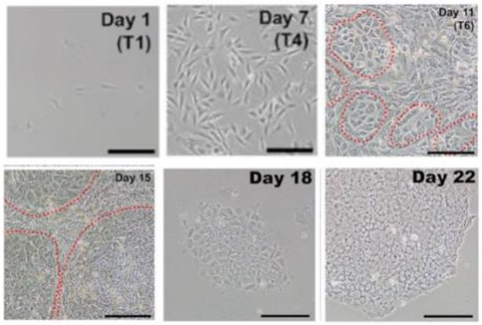

Figure 1. Representative images of cells during reprogramming. The first transfection (T1) occurs on Day1, and the cells appear very sparse at this point. Cells continue to increase in density throughout the protocol (Day7). iPSC clusters begin to appear as early as Day11 (circled in red). By Day15, iPSC colonies are large with discreet boundaries. After initial passage, iPSCs form colonies that appear loose with poorly defined borders (Day18). The cells rapidly proliferate and tightly cluster into colonies with distinct borders (Day22).

Second generation technology allows concurrent gene correction during cellular reprogramming, decreasing expected costs of production. This technology is currently in development for the treatment of Epidermolysis bullosa, a genetic skin blistering disease, and is applicable for correction of other genetic diseases.

Advantages:

- 100% success rate for iPSC generation, including difficult to reprogram, aged and senescent fibroblasts;
- Cost effective, fast, and efficient

Updated: 10/02/2023