MONASH University

MONASH INNOVATION

MOGRIFY™: DIRECT REPROGRAMMING BETWEEN ALL HUMAN CELL TYPES

A new algorithm identifies the minimal transcription factor (TF) combinations required to reprogram one somatic human cell type directly into another, without the need to first reprogram cells to a primitive or pluripotent (iPS) cell fate. Novel TF subsets validated *in vitro* for cell conversions.

- **Capacity to reprogram human somatic cells directly in to any desired cell type *in vitro***
- **Avoids reprogramming of somatic cells via more primitive or pluripotent (i.e. iPS) cells**
- **Cell reprogramming can occur through transient expression of TF's to establish fate and avoid genetic modification of resultant cells**
- **Direct creation of any therapeutic and/or experimentally relevant cell populations**

THE CHALLENGE

Transcription factor mediated cell reprogramming is usually achieved by the overexpression of a specific set of key TFs in a given cell type. Previous discoveries have relied on exhaustive testing of sets of transcription factors known to play a role in the desired cell type - an approach that is both inefficient and unscaleable. With roughly 2000 different TFs and approximately 400 unique cell types in humans, the space of possible sets is very large and impractical to explore using current approaches.

There is a clear need for a computational framework to guide experimentation. Attempts to produce algorithms predicting specific cell-to-cell conversions have been implemented but are computationally intractable or require vast amounts of data for the large number possible cell types. No novel cell conversions have resulted from TF predictions from these methods and there is no existing resource which provides a directory of TF predictions.

ARMI
AUSTRALIAN REGENERATIVE MEDICINE INSTITUTE

THE TECHNOLOGY

An international research collaboration including researchers from the Australian Institute of Regenerative Medicine at Monash University, has developed and tested a novel network-based method (MOGRIFY™) to provide transcription factors that induce the conversion of one specific cell type to another.

The algorithm's validation comes from predicting known reprogramming factors previously used for several published cell conversions. Monash researchers have validated MOGRIFY by testing new predictions where human fibroblast and keratinocytes have been directly reprogrammed into target cell types.

MOGRIFY presents a radical change in the paradigm shift for cell reprogramming. The MOGRIFY algorithm accesses the FANTOM5 consortium database of human gene expression profiles and acts as a TF 'Atlas' for the identification of cell specific combinations. The team has applied MOGRIFY to 518 different human cell types from the FANTOM5 datasets.

MOGRIFY has predicted known reprogramming TFs for previously published conversions and the team has experimentally validated somatic cell reprogramming using novel TF combinations in vitro.

Intellectual Property: Provisional application 2015905349 on methods and novel TF subsets for cell conversion.

THE OPPORTUNITY

Monash University, on behalf of its research collaborators, seeks partners to further develop the algorithm and protocols based on predicted TFs for the generation of specific cell types, for commercial use.

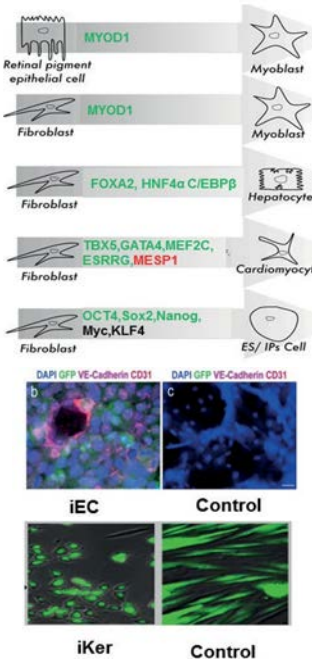

Figure 1: (A) MOGRIFY predicts TFs used in previously published transdifferentiation. Green: predicted by MOGRIFY. Red: not predicted. Black: Not predicted and shown not to be essential.
(B) Transdifferentiation of HEKa into endothelial cells: IF of a transdifferentiation culture showing the presence of Ve-Cadherin and CD31 positive cells. Control: HEKa cells exposed to same media.
(C) Fibroblast to Keratinocytes (iKer) conversion: Fibroblasts were infected with the MOGRIFY's predicted TFs. After TFs expression, morphological changes became clear with fibroblasts adopting a clear cobble stone keratinocytes appearance.

Reference

Rackham et al. (2016) A predictive computational framework for direct reprogramming between human cell types. Nature Genetics 48, 331-335.

KEY CONTACT

Dr Kathy Nielsen
Senior Commercialisation Manager
Monash Innovation
T: + 61 3 9905 5918
E: katherine.nielsen@monash.edu

CRICOS provider: Monash University 00008C
Produced by Monash Innovation: June 16