Genetic Engineering & Biotechnology News

Cell Conversion Shortcuts Mapped with Predictive System

Mogrify, a predictive computational system for direct reprogramming between human cell types, has been validated in two new human cell conversions. This image shows a rendering of the cellular reprogramming landscape from real data. [Cherrie Kong]

In the cell-fate conversion landscape, the road less traveled is transdifferentiation, even though it is the straighter path between one cell type and another. The more circuitous route, up to pluripotency and then down again, is better trod, in part because the pluripotency-inducing conversion factors—Oct3/Oct4, Sox2, c-Myc, and Klf4—are so well known.

In contrast, conversion factors that would open up cell-conversion shortcuts tend to be off the beaten path. Only a few have been identified, mostly because finding them entails exhaustive trial-and-error testing. But if these factors could be found systematically, that might make all the difference to regenerative medicine.

In the hope of blazing new cellular reprogramming trails, an international team led by researchers at the University of Bristol has introduced Mogrify, a computer system that combines gene expression data with regulatory network information to predict the reprogramming factors necessary to induce cell conversion. The team described Mogrify in the journal Nature Genetics, in an article entitled, “A predictive computational framework for direct reprogramming between human cell types.”

“We have applied Mogrify to 173 human cell types and 134 tissues, defining an atlas of cellular reprogramming,” wrote the authors. “Mogrify correctly predicts the transcription factors used in known transdifferentiations. Furthermore, we validated two new transdifferentiations predicted by Mogrify.”

According to study leader Julian Gough, Ph.D., professor of bioinformatics at the University of Bristol, the tests on two new human cell conversions succeeded straightaway. “The speed with which this was achieved,” said Dr. Gough, “suggests Mogrify will enable the creation of a great number of human cell types in the lab.”

He continues: “The ability to produce numerous types of human cells will lead directly to tissue therapies of all kinds, to treat conditions from arthritis to macular degeneration, to heart disease. The fuller understanding, at the molecular level of cell production leading on from this, may allow us to grow whole organs from somebody's own cells.”

To achieve this result, Dr. Gough worked with then-Ph.D. student Dr. Owen Rackham (who now works at Duke-NUS Medical School in Singapore) for five years to develop a computational algorithm to predict the cellular factors for cell conversions. The algorithm was conceived from data collected as a part of the FANTOM international consortium (based at RIKEN, Japan) of which Dr. Gough is a longtime member. The algorithm has been made available online for other researchers and scientists, so that the field may advance rapidly.

“This represents a significant breakthrough in regenerative medicine,” Dr. Gough adds. “[It] paves the way for life-changing medical advances within a few years from now, and the possibility in the longer term of improving the quality of longer lives, as well as making them longer.”

Interview originally posted in GEN, Jan 2016