

A*Star, Max Planck make stem cell breakthrough

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Singapore: Scientists at A*STAR's Genome Institute of Singapore (GIS) and the Max Planck Institute for Molecular Genetics (MPIMG) in Berlin (Germany) have discovered a molecular network in human embryonic stem cells (hESCs) that integrates cell communication signals to keep the cell in its stem cell state.

Scientists at the GIS and MPIMG studied which genetic information is activated in the cell, and thereby discovered a network for molecular communication in hESCs. They mapped the kinase interactions across the entire genome, and discovered that ERK2, a protein that belongs to the ERK signaling family, targets important sites such as non-coding genes and histones, cell cycle, metabolism and also stem cell-specific genes.

The ERK signaling pathway involves an additional protein, ELK1 which interacts with ERK2 to activate the genetic information. Interestingly, the team also discovered that ELK1 has a second, totally opposite function. At genomic sites which are not targeted by ERK signaling, ELK1 silences genetic information, thereby keeping the cell in its undifferentiated state. The authors propose a model that integrates this bi-directional control to keep the cell in the stem cell state.

First author Dr Jonathan GÅrke from Stem Cell and Developmental Biology at the GIS said, "The ERK signaling pathway has been known for many years, but this is the first time we are able to see the full spectrum of the response in the genome of stem cells. We have found many biological processes that are associated with this signaling pathway, but we also found new and unexpected patterns such as this dual mode of ELK1. It will be interesting to see how this communication network changes in other cells, tissues, or in disease."

"A remarkable feature of this study is, how the information was extracted by computational means from the experimental data," said Prof Martin Vingron from MPIMG and co-author of this study.

Prof Ng Huck Hui added, "This is an important study because it describes the cell's signaling networks and its integration into the general regulatory network. Understanding the biology of embryonic stem cells is a first step to understanding the capabilities and caveats of stem cells in future medical applications."

