Novel microscale epigenomics technology: Possible to study the epigenome of rare cell populations and biopsy samples

February 11 2013

Scientists at A*STAR's Genome Institute of Singapore (GIS) have successfully developed a method to map the epigenome using 100 times fewer cells than was previously possible. The discovery, published in the journal *Developmental Cell*, means that it is now possible to study the epigenome of parts of the body with rare cell populations such as germ cells (which differentiate into the egg or sperm), and clinical biopsy samples (to advance the study, diagnosis and prevention of cancer).

This is an extremely important advancement since the proper regulation of the epigenome is essential for normal growth and health, while any abnormality in the regulation could be the cause of diseases such as cancers.

The genome, which refers to the complete set of DNA (deoxyribonucleic acid) in a cell, is identical in every cell of an individual's body. Chemical markers (also known as epigenetic markers) target the genome and influence which genes get turned on or off. It is the turning on or off of the genes that gives rise to the existence of different cells in the body, even though the genomes are identical. The epigenome refers to the record of these chemical changes that occur to the DNA.

Chromatin immunoprecipitation coupled to high-throughput sequencing (ChIP-Seq) is a commonly used method to study the epigenome of cells.

In ChIP-Seq, DNA fragments that are associated with specific epigenetic marks are baited out, sequenced and mapped to a reference genome. However, the conventional method typically requires large quantities of cells, which makes it difficult to study rare cell populations of the body or in precious clinical biopsy samples.

This limitation prompted the GIS scientists to miniaturize the ChIP method such that it is now possible to map the epigenome using much fewer cells (1,000 to 100,000 cells). The conventional method required one million to 10 million cells.

The scientists further applied this technology on a small number of mouse germ cells, which are the embryonic precursors of the sperm and egg, and uncovered many interesting epigenomic features that provide insight into the biology of the germ cells.

GIS Executive Director Prof Ng Huck Hui said, "Epigenomics is an exciting frontier for human biology research. While the sequence of human genome tells us the code for life, it doesn't tell us how this code is utilized. The mystique of the epigenome lies in the multiple forms it takes and the remarkable information that it harbours. At the Genome Institute of Singapore, we are investing efforts to develop new microscale technologies to analyse the epigenomes of human cells and tissues."

"The new ChIP-seq protocol allows us to map the epigenomes of very small populations of cells that are not accessible by conventional methods," said GIS Principal Investigator Dr Shyam Prabhakar. "It's akin to having a more powerful microscope that provides a more fine-grained view of critical biological processes. We are very excited about using this new technique to peer into the inner workings of tiny groups of cells that have a massive impact on human health. For example, tumours in cancer patients are known to be heterogeneous at the fine

scale - some sub-regions are relatively benign, while others are lethal. The new protocol will help us characterize this fine-scale variation, and hopefully lead to more precise treatments for cancer and a host of other diseases."

More information: Ng, J. et al. In vivo epigenomic profiling of germ cells reveals germ cell molecular signatures, *Developmental Cell*, Feb. 11, 2013.

Provided by Agency for Science, Technology and Research (A*STAR), Singapore