MedicalXpress

Researchers create novel assay to test for epigenetic abnormalities in preimplanted mice embryos

September 27 2013

Scientists from A*STAR's Institute of Medical Biology (IMB) and Institute of Molecular and Cell Biology (IMCB) have created a novel assay to probe the DNA methylation stateof multiple genomic loci in single cells. This work on epigenetics was reported in the influential scientific journal, *Science* on 6 September 2013.

An embryo's normal development requires certain epigenetic changes to take place during early development; one type of epigenetic change is called 'DNA methylation'. This is a crucial process for an embryo's early development because it selectively 'switches off' certain genes – helping its cells grow into different cell types.

Errors in this epigenetic process, such as 'switching off' the wrong genes, are known causes of early developmental diseases and cell death . Two of which are Beckwith-Wiedemann and Silver-Russell syndromes. Both syndromes are extreme examples of epigenetic diseases - Beckwith-Wiedemann syndrome causes rapid overgrowth in infants while Silver-Russell syndrome causes slow growth resulting in delayed development and learning disabilities in children.

An important first-step to address the debilitating effects of epigenetic diseases is to find a way to identify embryos with 'troubled' methylation states. The single cell methylation assay developed by the researchers from IMB and IMCB can be used to safely extract one cell for testing in

an embryo fertilised in vitro. Previous similar assays required large numbers of cells for testing, which would destroy the embryo. The benefit of extracting one cell per assay is that the remaining cells of the embryo can be left to mature normally.

Unique microfluidic technique secret to discovery

Working hand-in-hand, scientists from IMB and IMCB were able to use a special technique using a microfluidic device to perform the assay with the small amounts of DNA present in a single cell. Microfluidics is the process of handling minute volumes of liquid. The Microfluidics Systems Biology Lab at IMCB includes an interdisciplinary team of engineers and biologists. According to Dr. William F. Burkholder, who co-directs the lab said, "It is having engineers and biologists working together and learning from each other that facilitates the development of cutting-edge tools for biomedical research."

Potential screening and treatment

The scientists also made another important discovery – they were able to return normal epigenetic functions back to a preimplanted embryo suffering from improper epigenetic development. Researchers used a technique called 'pronuclear transfer' that takes the genome from a defective embryo and inserts it into a healthy embryo. Even though this technique had been performed successfully before, this is the first time scientists have shown an embryo with defective maternal epigenetic regulation can be rescued using the technique.

The success of pronuclear transfer and the single cell assay raises the possibility that therapeutic treatments in the field of Assisted Reproductive Technology (ART) can be developed to correct maternally-inherited epigenetic disease syndromes. The lead researcher on this

study, Dr. Daniel M. Messerschmidt said, "It becomes increasingly evident that epigenetic defects which predominantly develop at the very early stages of pregnancy cause infertility, abortion or complex syndromes. Studies like ours, in which new powerful methods are developed to uncover the detailed molecular principles involved, create the basis for future clinical research, and eventually, clinical applications".

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