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Ground-breaking study to hasten regenerative medicine development

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This discovery could lead to a faster and easier way of converting skin cells into other cell types to enhance cell-based therapies

Singapore – Scientists from A*STAR's Institute of Molecular & Cell Biology (IMCB) have discovered a key epigenetic protein H3.3 that would facilitate the engineering and conversion of skin cells to other types of cells with different functions. This cellular reprogramming could have major implications for the development of new therapies for diseases. These findings were published in leading scientific journal Nature Communications on 18 April 2018.

Epigenetics affect how genes are read by cells, and subsequently, how they produce proteins that help to carry out life functions. Epigenetic modifications, or changes in gene expression arising from the chemical variations in genes, can lead to cancer and other degenerative diseases. Environmental and lifestyle factors such as diet, pollution, stress and ageing can induce chemical changes in genes. This would cause genes to be switched off or on over time, often resulting in the switching of one cell state to another.

Together with the Mayo Clinic, the IMCB research team has discovered that it is possible to engineer cells for regenerative medicine in the laboratory using methods such as differentiation, reprogramming and transdifferentiation; all of which are tightly controlled by epigenetic regulators. They have found that H3.3 is a major epigenetic regulator, and can act as a master switch for gene expression to turn them off or on, thus reprogramming cell types in the process.

With these findings, the research team is currently re-engineering skin cells to induce pluripotent stem cells for use in clinical trials to treat retinal degeneration in patients. The skin cells can also be easily converted to blood stem cells with approximately 3 times greater efficiency. This holds great potential for treating conditions that require the transplantation of matching bone marrow, such as leukaemia. Dr Jonathan Loh, Senior Principal Investigator at A*STAR's IMCB and lead researcher for this study, said: "Our studies showed that H3.3 is a universal epigenetic switch for turning one type of cells to another. This will help accelerate the use of stem cells in cell therapy and regenerative medicine."

Dr George Daley, Dean of Harvard Medical School, said: "This study illustrates how work that deepens our understanding of

basic cell biology can lead to more effective methods of generating stem cells in the laboratory. Tweaking H3.3 levels converts skin cells to haematopoietic stem cells (HSCs) with higher efficiency. In the future, skin cell derived HSCs could potentially be a source of stem cell transplantation for debilitating medical conditions such as leukaemia or genetic blood disorders.”