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Cancer-specific killer T cells created from iPS cells

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Japanese researchers create cancer-specific killer T cells from induced pluripotent stem cells

Singapore: Researchers from the RIKEN Research Centre for Allergy and Immunology in Japan have succeeded, for the first time, in creating cancer-specific immune system cells, called killer T lymphocytes, from induced pluripotent stem cells (iPS cells). To create these killer cells, the team first had to reprogram T lymphocytes specialized in killing a certain type of cancer into iPS cells. The iPS cells then generated fully active, cancer-specific T lymphocytes. These lymphocytes regenerated from iPS cells could potentially serve as cancer therapy in the future.

Previous research has shown that killer T lymphocytes produced in the lab using conventional methods are inefficient in killing cancer cells mainly because they have a very short life-span, which limits their use as treatment for cancer. To overcome these problems, the Japanese researchers led by Dr Hiroshi Kawamoto and presenting their results in the journal *Cell Stem Cell* online, reprogrammed mature human killer T lymphocytes into iPS cells and investigated how these cells differentiate.

The team induced killer T lymphocytes specific for a certain type of skin cancer to reprogram into iPS cells by exposing the lymphocytes to the 'Yamanaka factors'. The 'Yamanaka factors' are a group of compounds, named after Nobel prize winner Dr Shinya Yamanaka, that induce cells to revert back to a non-specialized, pluripotent stage. The iPS cells obtained were then grown in the lab and induced to differentiate into killer T lymphocytes again. This new batch of T lymphocytes was shown to be specific for the same type of skin cancer as the original lymphocytes: they maintained the genetic reorganization enabling them to express the cancer-specific receptor on their surface. The new T lymphocytes were also shown to be active and to produce the anti-tumor compound interferon Î³.

"We have succeeded in the expansion of antigen-specific T cells by making iPS cells and differentiating them back into functional T cells. The next step will be to test whether these T cells can selectively kill tumor cells but not other cells in the

body. If they do, these cells might be directly injected to patients for therapy. This could be realized in the not-so-distant future," explains Dr Kawamoto.