

## Japanese scientists discover anti-cancer property in diabetes drug

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Scientists at the Okayama University in Japan have announced that their studies have revealed how a diabetes drug helps towards the rejection of tumours by supporting immune cells. In a press release, the scientists have claimed that a 30-40% decrease in the risk of cancer has been observed in patients using the drug metformin to treat diabetes 2.

This characteristic is in striking contrast with insulin-based diabetes treatments, which are linked to increases in cancer, however the mechanism behind metformin's anticancer effects has so far not been well understood. Now Heiichiro Udono and colleagues at Okayama University and Kawasaki University in Japan explained the anticancer responses in a report investigating the drug's effects on the immune system's T cells.

The researchers tested the effects of dissolving metformin in the drinking water of mice injected with leukaemia cells and confirmed complete rejection of the tumours. When the mice were subsequently re-injected with twice the amount of cancer cells, no tumours formed suggesting an immunologic memory response. Renal and skin cancers also responded to the treatment and low doses similar to diabetes prescription concentrations were still effective for tumour rejection. Further experiments with mice lacking certain cell types showed that the influence of metformin on CD8+ T cells in particular was responsible for the anticancer effects.

During chronic diseases including cancer, CD8+ T cells undergo a process called 'immune exhaustion', where after repeated antigen (Ag) stimulation the cells can no longer secrete chemicals crucial for the immune system to function. 'Apoptosis' or

cell death of these exhausted T cells ensues. The researchers incubated isolated T cells and found that CD8+ T cells from metformin-treated mice still produced immune response chemicals.

Further comparisons revealed specific memory characteristics and protein producing abilities in the T cells of metformin treated mice. "These findings provide novel insights into anticancer immunity," conclude the researchers in a report of their results. Further work is needed to study the effects on different types of tumours and to clarify the specific cellular and molecular mechanisms involved.

Metformin is antihyperglycemic, and so counters insulin resistance. Early use has been shown to increase survival in patients either suffering from obesity-involved type 2 diabetes or cardiovascular disease or both.

The observed anticancer effects triggered further epidemiological studies that confirmed a 30-40% reduction in cancer risk for patients treated with metformin. It was further shown to reduce cancer in a breast cancer mouse model and to increase life expectancy. However while the mechanism seemed to stem from destruction of cancer initiating cells, until now the mechanism was unclear.