Boosting immune responses against leukaemia

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(Medical Xpress)—In the first of its kind, a translational study undertaken at the Malaghan Institute of Medical Research has revealed that boosting the activity of a rare type of immune cell could be an effective way to vaccinate patients with chronic lymphocytic leukaemia (CLL) against their own cancer.

CLL is the most common blood cancer in New Zealand. The prevalence of CLL increases with age, reaching 1 in 400 in individuals over 70 years old. Although many people with CLL never need treatment, a significant number of patients are diagnosed at a young age or have aggressive disease, exhausting conventional therapies.

Haematologist Dr Robert Weinkove says that bone marrow transplantation is the only curative treatment for CLL and involves replacing the immune system of patients with that of a matched donor.

"Part of the reason that bone marrow transplants work is that the new (donor) immune system recognises the leukaemia cells as foreign and destroys them," says Dr Weinkove. "This is a good demonstration of how immune therapies can successfully cure established cancers in humans."

Bone marrow transplants are not without their problems however. Not all patients find a donor; patients are prone to infections for months or even years afterwards; and the treatment itself can be so toxic that it is not suitable for many patients.

"To identify more targeted, low risk immune therapies, we focused on a rare type of immune cell called invariant natural killer T (iNKT) cells," says Dr Weinkove.

Previous research at the Malaghan Institute and overseas has shown that iNKT cells can be activated by a compound called α-galactosylceramide (α-GalCer), which was first found in a Japanese marine sponge. This leads to significantly enhanced tumour-specific immune responses.

While iNKT cells are promising targets for immunotherapies, in many cancer patients iNKT cell numbers are either reduced, or the cells do not work properly. Since iNKT cells had never been characterised in patients with CLL before, Dr Weinkove launched a collaborative study between the Wellington Hospital Blood and Cancer Centre and the Malaghan Institute, to determine the number, phenotype and function of iNKT cells in people with this form of leukaemia.

Between 2008 and 2011, Dr Weinkove collected blood samples from 40 patients with CLL and from 30 healthy volunteers of a similar age, from the greater Wellington region. He then undertook a series of laboratory tests to compare the number and function of the iNKT cells from these individuals.

This study, which has recently been published in the open-access, international scientific journal *Haematologica*, constitutes the first comprehensive investigation of iNKT cell numbers and function in patients with CLL.

"We found that we could detect and isolate iNKT cells from individuals with CLL, and that these cells were able to respond to α-GalCer," says Dr Weinkove. "This is important because it suggests that iNKT cells remain functional in these patients, and that targeting them with treatments like α-GalCer might be a way of enhancing their ability to drive anti-cancer immune responses."

Having shown such great promise in the laboratory, the next step will be to see if these results can be replicated in patients.

"Designing and running safe clinical trials is a major undertaking, but we are exploring a number of ideas, including the possibility of giving α-GalCer to patients with blood cancers to boost their immune responses," says Dr Weinkove.

This work complements the dendritic cell cancer vaccination programme at the Malaghan Institute.

More information: Weinkove R, Brooks CR, Carter JM, Hermans IF, Ronchese F (2012) Functional invariant natural killer T cell and CD1d axis in chronic lymphocytic leukemia: implications for immunotherapy. *Haematologica*, doi: 10.3324/haematol.2012.072835

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