Missing immune response may prove a vital link for new leukaemia treatments

Posted on Thursday 19th September 2013

Patients suffering from leukaemia could have their immune system engineered to fight the disease, after scientists at the University of Birmingham discovered that they lacked an immune response to a certain class of proteins and this response could be restored through stem cell transplants.

The discovery may even eventually lead to a vaccination against leukaemia for at risk groups who are found to be lacking the necessary immune response.

Cell growth and survival are controlled by complex signalling pathways, but in cancer cells these signals have gone awry. The signals are transmitted using protein modifications, such as adding a phosphate group. This modification is retained when the proteins are broken up into fragments, called peptides, and presented on the cell surface for inspection by immune cells (T cells). This results in the presentation of phosphopeptides by leukaemic cells, enabling them to be recognised as abnormal by the immune system.

The Birmingham researchers identified 95 phosphopeptides from leukaemia samples, taken directly from patients.

They went on to show that healthy people exhibited an unexpected immune response, with T-cells that recognised these phosphopeptides, and that this response was lacking in patients with leukaemia.

When leukaemia sufferers were given a stem cell transplant, there was a dramatic recovery of this response and T-cells recognising phosphopeptides-were able to kill leukaemia cells in the lab.

The researchers concluded that phosphopeptides may therefore be the target of cancer immune surveillance in humans – giving rise to the possibility of new treatments, which include engineering T-cells outside of the body to equip them with the immune response needed to fight the leukaemia, before putting them back into the patient.

The discovery also gives rise to the possibility of screening people to see if they have the immune response – those who do not may be at risk of developing leukaemia, and a vaccination could even be developed to protect these people with the necessary immune response.

Dr Mark Cobbold, from the School of Immunity and Infection at the University of Birmingham, said: “This is the first study to identify phosphorylated tumour antigens that are present on patient tumour samples and also the first study to look at immune responses to this new group of antigens in humans.

“We were surprised to see that healthy individuals had immunity to these antigens. It could be that just as our immune system fights off infections on a daily basis, it is also fighting cells that develop mutations that could lead to cancer.

“As we enter old age these responses could wane and this would explain why, just as older people get more serious infections due to impaired immunity, older people are also at greater risk from cancer.

“These findings need to be confirmed by other research groups, but could lead to new treatment options for patients with leukaemia or other cancers or preventative vaccination for at-risk groups.”

Professor Chris Bunce, Research Director at Leukaemia & Lymphoma Resarch, said: “Stem cell transplants can offer leukaemia patients the chance of a complete cure but they are not always successful and can have severe side-effects. By pinpointing key antigens, some of which are found only on the surface of leukaemia cells, this research could lead to new ways of modifying patients’ own immune systems to attack only leukaemia cells or even stop them from developing in the first place.”

The research MHC Class I-Associated Phosphopeptides Are the Targets of Memory-like Immunity in Leukemia is published online in Science Translational Medicine today (18 September). The work was funded by Leukaemia & Lymphoma Research and the Kay Kendal Leukaemia Fund.

Notes to editors

Dr Mark Cobbold is available forinterview. Contact **Kara Bradley (mailto:k.j.bradley@bham.ac.uk)** , University of Birmingham press office, 0121414 5134 or 07789 921163 for more information.

© University of Birmingham 2015