In the news

ARMED T CELLS ATTACK CANCER

A study published in *Science* has provided the first direct evidence that genetic modification of a patient's own T cells can be used to fight tumours. This treatment has led to tumour regression in two men dying of advanced skin cancer (*ScienceXpress*, 31 August 2006).

The trial, based at the National Cancer Institute (Bethesda, Maryland) and headed by Steven Rosenberg, involved 17 patients with advanced metastatic melanoma that had proved unresponsive to standard therapies. In two patients, "The tumors went away, and both of the patients are now completely disease-free over a year and a half later", said Rosenberg (*nytimes.com*, 1 September 2006).

Previous attempts at cancer immunotherapy have relied on the transfer of tumour-infiltrating lymphocytes following *ex vivo* expansion, but these cells are often difficult to isolate and identify. So Rosenberg and colleagues isolated T cells from the blood of the 17 patients and infected them with retroviral vectors encoding T-cell receptors that specifically recognize melanoma-associated antigens. This modification was designed to increase the cancer-detecting abilities of the T cells when infused back into the patients. The study reports that the genetically engineered T cells persisted in 15 patients, making up at least 10% of circulating T cells 2 months after treatment (*ScienceXpress*, 31 August 2006).

This approach is one of only a few published successes in the field of gene therapy, a troubled field that has been hindered by safety concerns, including the development of leukaemia in patients with severe immunodeficiency who were participating in a gene-therapy trial in France in 2002. However, cancer expert Thomas Gajewski, at the University of Chicago (Illinois), told *New Scientist* that the risk of such a complication in the melanoma trial is slim "because [the treatment] involves inserting genes into mature immune cells, which are less likely to multiply uncontrollably than the stem cells that were genetically altered in the French trial." (*NewScientist.com*, 31 August 2006). Nevertheless, experts in gene therapy expressed cautious optimism. Michel Sadelain, of the Memorial Sloan-Kettering Cancer Center (New York), said, "This certainly is a significant technical advance that is going to fuel more interest … [but] The response here is rather disappointing." (*nytimes.com*, 1 September 2006); 15 patients failed to respond to the treatment.

The researchers suspect that the low response rate was because the expression and the function of the T-cell-receptor transgenes were not optimal; "they say they have improved their technique in the months since the trial was done" (*news@nature.com*, 28 August 2006).

Now, Rosenberg plans to test the approach against other forms of cancer; "We have now expressed other lymphocyte receptors that recognise breast, lung, and other cancers" (*Telegraph.co.uk*, 1 September 2006). At present, he is awaiting approval to use cells that express these receptors in new trials in patients with other types of cancer (*Reuters.com*, 31 August 2006).

Lucy Bird, Associate Editor, Nature Reviews Immunology