PSA vaccine for prostate cancer

A promising therapeutic vaccine for prostate cancer, which targets prostate-specific-antigen (PSA)-producing cells, is being tested in phase Ib trials by researchers at the University of Illinois, Chicago, USA.

PSA, a kallikrein-like protein, has long been used as a marker of prostate cancer. It is produced naturally by the prostate gland in small amounts, but production is increased in men with prostate cancer through over-production by malignant cells. By directing the immune response towards cells that produce large amounts of PSA, tumour cells could be targeted.

Speaking at the Experimental Biology 2002 meeting in New Orleans (LA, USA; April 2002), David Peace explained that his laboratory had identified a nine-amino-acid homologue of PSA. The compound binds to the most common human leukocyte antigen HLA-A2 and elicits a specific cytotoxic T-lymphocyte response. "Vaccination with this peptide epitope causes subsets of lymphocytes to become highly specific killers that selectively destroy PSA-producing tumour cells," says Peace. "Our recent findings suggest this also occurs with lymphocytes from patients with advanced tumours, whose immune systems may be functionally compromised." The group is also developing PSA peptide vaccines for other HLA phenotypes.

The phase Ib trials include patients who have already undergone surgery or radiation therapy but are at high risk of recurrence (PSA concentration >10 ng/mL, rising blood PSA, or a Gleason score of 7), and in others with D1 or D2 disease in remission. The vaccine is administered once every 21 days for 9 weeks, either subcutaneously with an adjuvant or intravenously after loading onto dendritic cells.

Vaccines against PSA have been tried before but with limited success because they either incurred the risk of autoimmune reactions or failed to stimulate production of killer T cells. By using only a small epitope of PSA, the chances of cross-reactivity with other kallikreins that have similarities to PSA is reduced. "We expect this [epitope] to translate into a vaccine with very few side-effects," says Peace. "The cytolytic T lymphocytes generated exhibit a distinct cytokine profile which may also have important clinical implications," adds co-investigator Supriya Perambakam.

Onco-immunologist Eduardo Reyes (Alcalá University, Spain) told TLO: "This looks like an exciting development, especially for treating advanced disease, for which we currently have limited options."

Adrian Burton

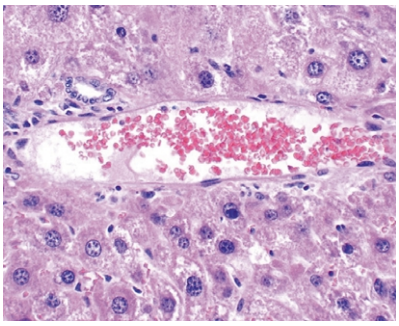
Photodynamic purging may stop graft rejections

Photodynamic elimination of immunoreactive T lymphocytes from bone-marrow grafts can prevent GVHD (graft-versus-host disease) in mice while sparing the graft's anti-leukaemia ability, a new study shows (*Blood* 2002; **99:** 3083–88).

Lead investigator Nelson Chao (Duke University Medical Center, NC, USA) explains: "The graft-versus-leukaemia [GVL] effect remains which means that the T cells that cause GVHD were removed, but the [photodynamic elimination] process allowed the other important cells to survive."

"Separating GVL from GVHD is a major goal of bone-marrow transplantation," says James Ferrara (University of Michigan, MI, USA). "The approach seems promising because it specifically deletes host-specific T cells, leaving other T cells, which might mediate GVL or enhance immune reconstitution, intact." He adds: "It would certainly seem promising for translational research in a new clinical trial."

The researchers primed spleen cells from C57BL/6 mice with BALB/c spleen cells in a mixed lymphocyte culture. To selectively eliminate immunoreactive T lymphocytes, the primed cells were treated with a photodynamic cell-purging process.



Courtesy of Benny Chen

The effect of photodynamic cell purging.

The cells were then transplanted into a mouse host. The investigators found that selective T-cell depletion prevented GVHD while preserving the GVL effect and other immune responses.

This study supports findings of another recently published study (early online publication, *Blood*, DOI 10.1182/blood-2001-12-0353) done by Denis Roy and colleagues (Maisonneuve-Rosemont Hospital Research Center, QC, Canada). Using human cells, they showed that photodynamic treatment with TH9402 specifically eliminates anti-host reactivity from allogeneic grafts, but preserves donor T-cell response against non-host antigens in the context of allogeneic MHC-mismatched transplantation.

The study also suggested that the selectivity of TH9402 photodynamic therapy for activated T lymphocytes could be exploited to selectively eliminate alloreactive T-cell clones that develop after solid-organ transplants and autoreactive clones that cause diseases such as lupus erythematosus, rheumatoid arthritis, and systemic sclerosis.

"The study [by Chao and colleagues] demonstrates that the photodynamic approach also works in an in vivo model," says Roy, whose team has designed a clinical trial to test this strategy. "We are very confident that it will work in humans," he adds.

Khabir Ahmad