induced by an experimental tumour vaccine alone.

Geert Kersten, CEO of CEL-SCI, said: 'The fact that we were able to see protection without disease antigen in several diseases opens up the possibility that derG could become an inexpensive general immune regulatory drug that protects people from a large number of diseases.' Zimmerman added, 'We did not receive any reports of any adverse side effects [in the animals], such as weight loss or gain, diarrhoea, constipation, coat loss or discoloration, or evidence of neurological effects from any of the three study sites.'

Further treatments

Potential future indications for derG could be protection against other infectious diseases and a treatment for influenza, hepatitis B and C, and allergies. It could also have the potential to enhance protective immunity following vaccination and could eliminate the necessity of booster shots.

Zimmerman added that the next steps are: (1) to optimize for dose; (2) to evaluate in other strains and species for preventive and therapeutic efficacy with appropriate disease models; and (3) large scale ADME/tox studies. He envisaged the peptide going into clinical trials within two to three years.

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Tailoring vaccines to individual lymphomas

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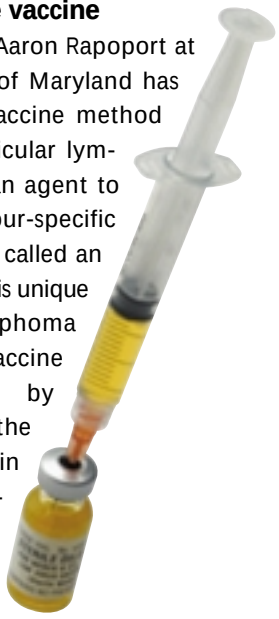
A custom-made vaccine has been developed to combat non-Hodgkin's lymphoma (NHL) that uses a patient's own tumour cells. Researchers at the University of Maryland Greenebaum Cancer Center (Baltimore, MD, USA) are testing the vaccine as part of a Phase III multi-centre study at 25 institutions across North America. The vaccine is particularly targeted at follicular lymphoma, a common and low-grade form of NHL.

Lymphomas: types and treatments

Non-Hodgkin's lymphoma is a term that encompasses a wide variety of diseases. Lymphomas are cancers of the lymphatic system, which filters the blood and protects the body from illness. As the cancer grows, the body accumulates large numbers of non-functioning lymphocytes, which can block and compromise the lymphatic system and rapidly metastasize to other organs. There are two general types of lymphoma: Hodgkin's (named after Thomas Hodgkin, who was the first to recognize this form in 1832) and non-Hodgkin's lymphoma. NHL is much more heterologous, less predictable and can attack more types of lymphatic tissue than Hodgkin's lymphoma can (for a background to the disease see http://www.patientcenters.com/lymphoma/).

One particularly common but lower-risk type of NHL is follicular lymphoma. This disease afflicts mainly middle-aged and elderly people and can readily spread to different parts of the lymphatic system. Most cases are the result of overexpression of the BCL-2 gene, which produces a protein that blocks apoptosis. Current therapies for the disease depend on the extent of the cancer's progress. If the lymphoma is caught early, it can be treated with localized radiotherapy. Treatment is often deferred, however, until symptoms appear. When the disease is more advanced, chemotherapy or whole-body radiation might be necessary. Generally, low-grade follicular cancers are easily treated, but are prone to recur.

A tailor-made vaccine



A team led by Aaron Rapoport at the University of Maryland has developed a vaccine method to combat follicular lymphoma using an agent to target a tumour-specific surface protein called an idiotype, which is unique to every lymphoma patient. The vaccine is developed by conjugating the idiotype protein to an immunogenic carrier protein, keyhole limpet

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haemocyanin, which is potently capable of eliciting an immune response. Once injected, the vaccine prompts the immune system to attack only cells that carry the idiotype, that is, the cancer cells. 'Without this, the body's immune system is somewhat blind to the lymphoma. Lymphomas and other types of cancers use mechanisms to evade the body's immune system', said Rapoport. The work builds on earlier studies by Ronald Levy at Stamford University [1].

In early clinical trials, about two-thirds of patients showed positive immunological responses to the vaccine [2]. But the time and expense necessary to create each personalized immunotherapy limited its development. Genitope Corporation (Redwood City, CA, USA) has overcome this limitation through its proprietary high-throughput gene expression technology. A Phase III clinical trial is now under way and hopes to attract 480 patients across the USA. These patients must be over 18, not pregnant or lactating, have been diagnosed with follicular cancer and should not have previously received chemotherapy.

Patients enrolled in the study have a small biopsy taken from their tumour, either from a lymph node or bone marrow. The tissue is sent to Genitope (the sponsors of this research), where the tumour-specific genetic material is isolated, expressed and purified into a vaccine-like immunotherapy. Meanwhile, patients receive eight rounds of chemotherapy with the drugs cytoxan, vincristine and prednisone. They must experience at least 50% reduction in tumour burden to remain in the study.

After a 26-week rest period following chemotherapy (allowing the immune system to recover), two-thirds of patients subcutaneously receive the specifically tailored vaccine, along with a proven immune system stimulant – granulocyte-macrophage colony-stimulating factor – that acts as an adjuvant [3]. The remaining third receive injections comprising only the carrier protein and the stimulant, which could also beneficially activate the immune system. The patients receive a series of seven vaccinations over six months, followed by periodic scans to check on the progress of the disease. 'I believe this technology offers the potential for better treatment results than we have previously seen', concluded Rapoport. This is the first demonstration that a personalized immunotherapy, when used as the initial treatment for patients with follicular NHL, can induce tumour-specific immune responses.

The research complements similar trials that are currently taking place around the world. Freda Stevenson of Southampton University (Southampton, UK) was one of the pioneers of this approach, generating immunity to lymphoma in animals [4]. 'The Rapoport trial is a Phase III study, so it will be interesting to see what happens', she commented. 'However, it remains a difficult and tedious vaccine preparation.'

A spokesperson from Genitope Corporation maintains that the manufacturing and technological enhancements used to develop the vaccines in the Phase III study are expected to overcome previous limitations, which have inhibited commercial viability of these treatments in the past. The company hopes to complete the study by early next year.

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