

Improving immunity against multiple myeloma

For patients with a type of bone marrow cancer called multiple myeloma, an autologous stem cell transplant can significantly increase survival time. This procedure involves collecting bone marrow stem cells from a patient, storing the cells, and then reinjecting them after chemotherapy. To measure how effective the transplant is, physicians look at the number of lymphocytes that are present in the patient two weeks after the transplant, a marker that is closely correlated with overall survival. In most patients, however, the cancer eventually returns.

It's not clear which types of lymphocytes are most effective in fighting off the cancer—knowledge that might contribute to improving survival. In an attempt to find out, Kenneth Meehan, M.D., a professor of medicine at Geisel and the director of the bone marrow transplant program at DHMC, led a phase II clinical trial that manipulated the stem cells removed from patients to increase the number of a certain type of immune cell to see if that would improve the killing of cancer cells.



Kenneth Meehan, the director of DHMC's bone marrow transplant program, led a clinical trial to test a treatment that manipulates immune cells to improve their effectiveness against cancer.

Based on research led by Charles Sentman, Ph.D., a Geisel professor of microbiology and immunology, Meehan suspected that T cells with a certain marker (NKG2D⁺CD3⁺CD8⁺ T cells) would be more effective than other lymphocytes in combating myeloma. Sentman had identified the marker that makes the T cells more effective in research with mice. Meehan and his colleagues manipulated the stored cells taken from the patients to increase the number of these T cells. They then reinjected the cells back into the patients, along with a standard immune-boosting molecule called interleukin-2.

The results were “striking,” Meehan says. All patients tolerated the therapy well, and compared to patients who received a standard transplant without immune therapy, those in the trial had a marked increase in the overall number of lymphocytes, more than double those who received standard treatment. There were too few patients in the trial to address the effect on longer-term survival, but Meehan says the results were encouraging.

In an unusual step, Meehan used the patients' own cancer cells to test the effectiveness of the T cells. When the stem cells were removed from the patients at diagnosis, half were set aside and saved. Meehan took some of the patients' blood post-transplant and mixed it with these original cancerous myeloma cells. “We saw a marked increase in killing effectiveness for patients who were in the trial compared to control,” Meehan says.

The next step, says Meehan, is to conduct a multicenter trial very similar to the one they just completed, but with many more patients in order to better determine just how much the altered T cells improve survival. So far, the numbers look good, but Meehan's team is eager to continue its work. “This is really an example of bench to bedside, back to bench and to bedside again,” says Meehan.

Lauren Ware

CLEANLINESS IS NEXT TO HEALTHINESS

Despite evidence that consistent hand hygiene can reduce the rate of health-care-associated infections, hospitals across the country have struggled to get providers to wash their hands consistently. In recent years, DHMC undertook a large-scale effort to improve hand hygiene and reduce health-care-associated infections. Over the course of the project, the compliance rate increased from 41% to 91%. Over the same period, the rate of health-care-associated infections dropped from 4.8 to 3.3 per 1,000 inpatient days. The authors of a study on the effort noted that there is still room for improvement, especially among physicians, but, they added, “our study adds to the evidence that sustained and significant improvement in [hand hygiene] is achievable.”

PAINFUL SPENDING INCREASES

A team of Geisel researchers recently examined changes in spending on back treatments and determined which types of treatment are responsible for much of the \$90 billion spent every year on lower back pain. From 1999 to 2008, the average expenditure (adjusted for inflation) for a patient with a back problem rose 95%, from \$487 to \$950, most of which was accounted for by spending on medical specialists. “There are important decisions on the horizon regarding the U.S. health-care system,” the authors noted in *Spine*. “Our findings imply that medical care, specifically specialty care, rather than primary care, chiropractic care, or physical therapy, is responsible for rising ambulatory care costs for spine conditions.”