IL-7: Bringing New Youth to the T Cell Pool

When we are young, our immune system's pool of T cells is generated and kept fresh through the action of the thymus, a small organ located at the base of the neck. As we age, the thymus shrinks and becomes less active, and the job of maintaining our T cell repertoire gradually shifts away from the thymus to other lymphoid organs.

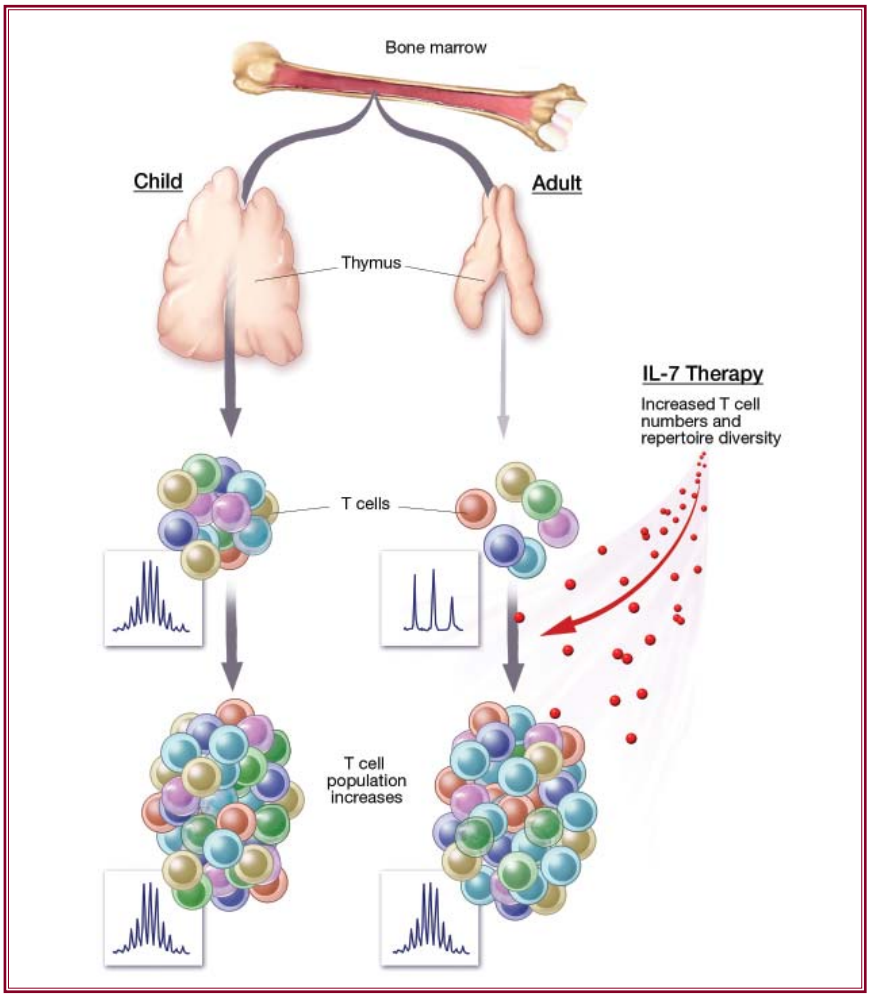
This shift in maintenance responsibility can be a cause for concern for cancer patients, particularly ones over the age of 45 or 50. Chemotherapy can deplete patients' T cells, leaving them vulnerable to infection for some time after completing treatment. The T cell pool of younger patients often comes back within months, mostly through increased activity of the thymus. However, the immune system of older patients, in whom the thymus is relatively inactive, struggles to restock its store of naïve T cells, reducing these patients' ability to adapt to new pathogens or to rely on their T cells to continue fighting their cancer.

In the June 23, 2008, online issue of the *Journal of Experimental Medicine*, a team of researchers led by Claude Sportès, M.D., Staff Clinician; Ron Gress, M.D., Chief of CCR's Experimental Transplantation and Immunology Branch; and Crystal Mackall, M.D., Chief of CCR's Pediatric Oncology Branch, reported on a study of the cytokine interleukin-7 (IL-7) as a means of reconstituting patients' T cell repertoires. Past studies have shown that IL-7 is required for maintaining an adequate T cell pool and that in animal models the cytokine can help restore a depleted repertoire of these essential immune cells.

Given these past data, Sportès, Gress, Mackall, and their collaborators reasoned that IL-7 might be able to rejuvenate immune function in cancer patients. After two weeks of treatment with the cytokine, the researchers found that the patients' numbers of helper ($CD4^+$) and cytotoxic ($CD8^+$) T cells rose dramatically (for $CD8^+$ cells, the numbers increased over 400 percent) and stayed high for up to six weeks after the IL-7 treatment stopped. In addition, the new cells were overwhelmingly of a naïve phenotype, even in older patients. Thus, the treatment seemed to return some of the patients' immune system components to a younger state.

These findings could have significant clinical relevance in immune reconstitution and rejuvenation following a variety of insults on the immune system. Apart from helping rejuvenate cancer patients' immunity, IL-7 treatment could help improve the health of other immunocompromised patients such as those with HIV/AIDS or those in the normal aging population, or it could be used to boost the effectiveness of vaccines or forms of immunotherapy both inside and outside the field of cancer treatment.

Read more about the efforts of Drs. Sportès, Gress, and Mackall on their respective CCR Web sites at http://ccr.cancer.gov/staff/staff.asp?profileid=5907, http://ccr.cancer.gov/staff/staff.asp?profileid=5821, and http://ccr.cancer.gov/staff/staff.asp?profileid=5595.



(*Image: NIH Medical Arts*)

As the activity of the thymus decreases with age, the number and the diversity of immune system T cells decrease; chemotherapy can further deplete the T cell repertoire. Treatment with the cytokine IL-7 has been shown to reconstitute the T cell pool, rejuvenating immune function in cancer patients.