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What the thymus can do on its own:
Scientists from the German Cancer Research Center prove a dogma of immunology wrong

Special white blood cells called T lymphocytes ('T' stands for thymus derived) originate, like all other blood cells, from progenitor cells in the bone marrow. The cells then mature in the thymus gland, an organ of the immune system located in the upper chest, to become active immune cells. Conventional wisdom has held that the thymus is unable to produce T cells without constant supply from the bone marrow. Scientists from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg have now managed to prove this dogma wrong by showing that the thymus is obviously capable of producing mature T cells for several months without any supply from the bone marrow. The group has now reported their results in the *Journal of Experimental Medicine*.

The thymus gland is an organ about the size of a fist that lies behind the breastbone. It is a central part of the immune system and it is the place where T lymphocytes develop into active cells of the immune system. Only cells that are able to discriminate between self and non-self are allowed to leave the thymus so that they can eliminate infected or cancerous cells while tolerating the body's self tissues.

"Normally, immature T progenitor cells migrate into the thymus where they mature," says Hans-Reimer Rodewald, head of the Division of Cellular Immunology at DKFZ. "Now we wanted to find out what happens if the thymus is not supplied with new progenitors." To this end, Vera Martins, Hans-Reimer Rodewald and their colleagues studied genetically modified mice that do not have any lymphocyte progenitor cells in the bone marrow. Into these animals, the investigators transplanted thymus glands from normal mice. They expected the donor thymus to deliver its own mature cells into the recipient animal's blood for a period of about four weeks. After that period, the thymus gland would have used up all of its own T cells and would degenerate.

"The estimated period of four weeks is based on the observation that in a thymus gland transplantation between two normal animals, the donor thymus exports its own T cells into the recipient's blood for no more than four weeks. After that, the recipient's own T cell progenitors will migrate from the bone marrow into the donor thymus and mature there," Rodewald explains.

Surprisingly, however, the donor thymus in this experiment continued to produce its own donor T cells for at least three months. Apparently, there are immature progenitor cells present in the thymus gland which renew themselves in the absence of supply from the bone marrow and from which further T cells can mature. Presumably, the thymus gland serves as a 'reservoir' to make sure that the body does not have to stop its continuous production of these important immune cells if there is a weakness in the bone marrow. Whether this striking observation also applies to humans, is not yet known, but: "The thymus glands of mouse and man are very similar in structural and functional respects," Rodewald explains.

The commonly held assumption that the thymus gland is unable to produce its own T cells on a continuing basis is probably due to the animal models that were available until now: "There were no mice without any T cell progenitors," says Rodewald. "Therefore, we were unable to find out what happens to the thymus when there is no supply."

In a next step, the researchers will try to find out which cells in the thymus gland develop into mature T cells if there is no supply and in which corner of the thymus they hide themselves. “This opens up a whole new research field for us,” says Rodewald. “And I am sure that we are in for more surprises.”

Vera C. Martins, Eliana Ruggiero, Susan M. Schlenner, Vikas Madan, Manfred Schmidt, Pamela J. Fink, Christof von Kalle, and Hans-Reimer Rodewald: Thymus-autonomous T cell development in the absence of progenitor import, Journal of Experimental Medicine, doi: 10.1084/jem.20120846

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 2,500 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg where promising approaches from cancer research are translated into the clinic. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. The center is a member of the Helmholtz Association of National Research Centers. Ninety percent of its funding comes from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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