Lipids help to fight leukemia

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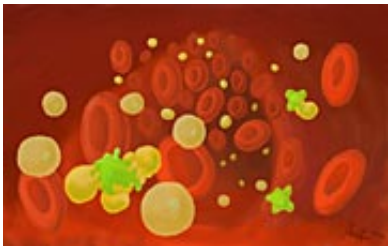

T cells (yellow) recognize and attack leukemia cells (green). Credit: University of Basel, Artem Kalinichenko

T cells use a novel mechanism to fight leukemia. They may recognize unique lipids produced by cancer cells and kill tumor cells expressing these lipid molecules. A study conducted by researchers at the University of Basel shows that a tumor-associated lipid stimulates specific T cells, which efficiently kill leukemia cells both in vitro and in animal models. The results have been published in the *Journal of Experimental Medicine*.

Leukemias are cancer diseases affecting blood cells . Acute leukemias prevent development of normal bold cells and thereby are severe life-threatening diseases. Current therapy for acute leukemias is based on chemotherapy that eradicates tumor cells followed by bone-marrow stem cell transplantation that reconstitutes the patient with healthy blood cells. In some cases, leukemia cells survive this treatment and start to re-grow. A major aim of many studies is finding novel and efficient ways to detect and eradicate leukemia cells before a second outbreak of the disease.

More punch against tumor cells

T lymphocytes are major contributors to fight against leukemias. T cells may recognize and become activated by tumor-specific protein antigens in some instances produced in large amounts only by tumor cells. These protein antigens are also called tumor-associated antigens (TAA) and stimulate specific T cells, which in turn kill leukemia cells. However, protein TAA accumulation can be drastically reduced by variant leukemia cells and some TAA may change their structure, thus preventing recognition by T cells and facilitating tumor immune evasion.

Prof. Gennaro De Libero and his team from the Department of Biomedicine at the University of Basel has identified a new approach that might help to make the immune system more efficient in recognizing leukemia cells. His research team is studying T cells that specifically recognize lipid antigens since several years. Together with colleagues in Italy, China and Singapore, the Swiss team has identified a new lipid that accumulates in leukemia cells and that stimulates specific T cell responses. The new lipid methyl-lysophosphatidic acid (mLPA) is very abundant in several forms of human leukemias and is the first example of a lipid TAA.

Therapeutic implications in human leukemia

The published study also shows that it is possible to isolate human T cells that specifically recognize and kill mLPA-expressing leukemia cells in in vitro tests. When these T cells were transplanted into mice, they also displayed great in vivo therapeutic efficacy against leukemia cells.

An important feature of mLPA is that differently from protein TAA, it does not change its structure, and remains abundant in leukemia cells. The Swiss team is now investigating, whether mLPA can be used to

target leukemia cells in addition to protein TAA. This type of immunotherapy may be extremely beneficial in preventing relapses of the disease after chemotherapy and bone marrow transplantation. It opens new avenues to novel non-invasive cancer immunotherapies.

More information: Marco Lepore, Claudia de Lalla, S. Ramanjaneyulu Gundimeda, Heiko Gsellinger, Michela Consonni, Claudio Garavaglia, Sebastiano Sansano, Francesco Piccolo, Andrea Scelfo, Daniel Häussinger, Daniela Montagna, Franco Locatelli, Chiara Bonini, Attilio Bondanza, Alessandra Forcina, Zhiyuan Li, Guanghui Ni, Fabio Ciceri, Paul Jenö, Chengfeng Xia, Lucia Mori, Paolo Dellabona, Giulia Casorati, and Gennaro De Libero, A novel self-lipid antigen targets human T cells against CDc+ leukemias The *Journal of Experimental Medicine* (2014) DOI: 10.1084/jem.20140410

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