idw - Informationsdienst Wissenschaft
Nachrichten, Termine, Experten

Pressemitteilung

Max-Delbrück-Centrum für Molekulare Medizin (MDC) Berlin-Buch

Barbara Bachtler

25.11.2005

http://idw-online.de/de/news138358

Forschungsergebnisse, Wissenschaftliche Publikationen
Biologie, Ernährung / Gesundheit / Pflege, Informationstechnik, Medizin
überregional

Master Switch for Blood Cell Development Detected

E m b a r g o ed until: Sunday, November 27, 2005, 1 pm EST, 6pm GMT, 19:00 CET Blood cells develop from blood stem cells in the bone marrow. Their development is regulated by roughly 20 gene regulators or transcription factors. One transcription factor, called PU.1, plays a central role in this vital process. It steers the development of two major blood cell lines of the immune system, namely the lymphocytes and the myeloid blood cells. In addition, PU.1 regulates the blood stem cells own development thereby ensuring that new blood cells are produced as needed. Yet, the question remains, "What regulates the regulator?" Now, Dr. Frank Rosenbauer, a cell biologist who recently moved from the Harvard Institutes of Medicine (Boston, USA) to the Max-Delbrück Center for Molecular Medicine (MDC) Berlin-Buch supported by the Initiative and Networking Fund of the President of the Helmholtz Association to which the MDC belongs, has detected a master switch which regulates PU.1. This master switch, termed URE (upstream regulatory element), not only turns the gene regulator on or off but also tunes it. As Dr. Rosenbauer demonstrated for the first time, URE can up- and down regulate PU.1, and, thus, determine whether B- or T-cells develop from lymphocyte progenitor cells. Animals that lack URE develop various forms of leukemias and, consequently, die within a few months. The research of Dr. Rosenbauer and his colleagues in the USA and at the MDC has now been published online in the journal Nature Genetics* (November 27, 2005, doi:10.1038/ng1679).

With respect to the development of T-cells, Dr. Rosenbauer and colleagues could also show that the master switch is part of the wnt-signalling pathway. This pathway plays a crucial role in the healthy development of complex organisms. It reaches from the cell surface down into the cell nucleus with the genetic control station. If signals cannot be transmitted correctly via this pathway malformations or tumours develop. During T-cell development, this pathway normally is switched off. Thus, the master switch URE turns off the gene regulator PU.1. However, if this signalling pathway is disturbed, PU.1 is not turned off properly and T-cells cannot mature. "The deregulation of PU.1 prepares the platform for further mutations in the blood stem cells and the precursor cells, respectively, and thus for the outbreak of various forms of leukemia", so Dr. Rosenbauer. Now, together with clinicians from the Charité Medical School Berlin, they plan to study the blood of leukemia patients to see whether the findings in mice also hold true for blood cell development in humans.

* Lymphoid cell growth and transformation are suppressed by a key regulatory element of the gene encoding PU.1

Frank Rosenbauer1,2,9, Bronwyn M Owens1,9, Li Yu3,8, Joseph R Tumang4, Ulrich Steidl1, Jeffery L Kutok5, Linda K Clayton6, Katharina Wagner1,8, Marina Scheller2, Hiromi Iwasaki7, Chunhui Liu3, Björn Hackanson3, Koichi Akashi7, Achim Leutz2, Thomas L Rothstein4, Christoph Plass3 & Daniel G Tenen1

1Harvard Institutes of Medicine and Harvard Stem Cell Institute, Room 954, 77 Avenue Louis Pasteur, Boston, Massachusetts 02115, USA. 2Max Delbrück Center for Molecular Medicine, Robert-Rössle-Str. 10, 13092 Berlin, Germany.

3Internal Medicine, Division of Hematology/Oncology, The Ohio State University, Columbus, Ohio,USA. 4Department of Medicine, Evans Memorial Department of Clinical Research, Boston University Medical Center, Boston, Massachusetts, USA. 5Department of Pathology, Brigham and Women's Hospital, Boston, Massachusetts, USA. 6Laboratory of Immunobiology and 7Department of Cancer Immunology and AIDS, Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA. 8Present addresses: Department of Hematology, Hemostaseology and Oncology, Hannover Medical School, University of Hannover, Hannover, Germany (K.W.); Department of Hematology, 301 General Hospital of PLA, Beijing, China (L.Y.). 9These authors contributed equally to this work. Correspondence should be addressed to F.R. (f.rosenbauer@mdc-berlin.de) or D.G.T. (dtenen@bidmc.harvard.edu).
Press and Public Affairs
Max Delbrück Center for Molecular Medicine(MDC) Berlin-Buch
Barbara Bachtler
Robert-Rössle-Str. 10
13125 Berlin
Phone: +49/30/9406-38 96
Fax.: +49/30/9406-38 33
e-mail: bachtler@mdc-berlin.de
http://www.mdc-berlin.de