GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

No. 13 April 5, 2004 (JR/Sto)

New Insights into the Mechanisms of Rapamycin

Rapamycin is a new drug which is being used for preventing organ rejection in kidney transplant patients. Since it suppresses the immune response and has a strong cell killing effect, it is a highly interesting substance for potential use in other disease areas such as cancer, autoimmune diseases, and diabetes mellitus. A recent publication of the Deutsches Krebsforschungszentrum (German Cancer Research Center, Heidelberg) provides important new insights into its mode of action.

The name of the protein rapamycin is derived from the native word for Easter Island, 'Rapa Nui'. Rapamycin was first isolated from Streptomyces bacteria found in the soil of Easter Island.

This substance has several qualities which currently draw the attention of pharmaceutical companies. Rapamycin inhibits T lymphocytes and dedritic cells and is thus capable of suppressing immune responses in the initial stages. In addition, it slows down cell growth and kills cells, which opens up further application possibilities in cancer treatment. The growth inhibitory action of rapamycin is already being utilized in the coating of stents – small wire mesh tubes used for holding open narrowed coronary vessels. Rapamycin (under the parallel name of sirolimus) helps prevent the tubes from reclosing as a result of new cell growth.

To date, it has been unclear just exactly how rapamycin unfolds its immunosuppressive and cell killing action. The only thing that was known was that the substance somehow inhibits protein synthesis. The working group headed by Professor Ingrid Grummt of the Division "Molecular Biology of the Cell II" has now found out why this is so: Rapamycin blocks the production of ribosomes – the molecular machines that a cell needs for manufacturing its proteins. Via an intermediate step, rapamycin inhibits a protein which regulates the supply of an important building block of the ribosomes. Blockage of this protein results in a lack of supply for ribosome production. As a result, protein synthesis is arrested, too. Since rapidly growing tissues such as tumors have a particularly great need for ribosomes, these are particularly hit by rapamycin.

There is yet another reason why rapamycin is considered a highly promising substance: It is the only known active substance whose direct target is a single enzyme. As opposed to other compounds which cause undesired side effects alongside the desired effect, rapamycin may thus turn out to be a precision weapon against rapidly proliferating cells.

By the way, the time when researchers had to travel to Easter Island to get rapamycin is long gone. The soil bacteria which produce the promising cell poison can easily be kept in a laboratory.

Christine Mayer, Jian Zhao, Xuejun Yuan, and Ingrid Grummt: mTOR-dependent activation of the transcription factor TIF-IA links rRNA synthesis to nutrient availablitiy. Genes & Development, Feb. 15, 2004, vol. 18 (4): 423-34

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.).

This press release is available at www.dkfz.de/pressemitteilungen

Dr. Julia Rautenstrauch
Division of Press and Public Relations
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968