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Learning from Viruses

When infected by a virus, a cell uses specific defense mechanisms developed in the course of a long evolution. Thus, it can activate enzymes that disrupt or prevent replication of the viruses within the cell. But viruses, too, have their own strategies against the host cell's defense troups. By closely studying the interaction between cell and virus, scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) are gaining valuable insights for the development of safe and functioning viral vectors for use in oncology.

"Viruses are of special interest for oncology, not only as disease-causing agents, but also as therapeutic tools," said **Professor Martin Löchelt** of the Division of Genome Modifications and Carcinogenesis at DKFZ. Using a cat virus belonging to the spuma (foamy) retrovirus family as a model, working groups headed by Löchelt and Dr. Carsten Münk of the Paul Ehrlich Institute in Langen, jointly with collaborators from Leipzig and Paris, have been studying the mechanisms by which the viruses effectively avoid the host cell's defense.

The feline foamy viruses produce a protein named Bet that neutralizes a key weapon of the host cell against retroviral single-strand DNA, an enzyme called APOBEC3. As a result of Bet expression, the virus can replicate freely within the cell and the infection takes its course. However, if the viral Bet protein is inactivated using a trick, the cell is able to effectively prevent virus replication and thus to fight the infection. Strategies like the Bet protein are also used by other viruses such as HIV to disable cellular defense mechanisms. The interaction between enzyme and viral protein is specific to a species, which is one reason why infections are not easily transmitted from one species to another.

These findings open up new targets for fighting infectious diseases, for example by specific activation and boosting of cellular defense enzymes. Moreover, they are also useful for optimizing viral vectors. Thus, retroviral vectors are used in oncology as Trojan horses to selectively attack cancer cells. The same mechanism by which the virus escapes the cell's defense can save a therapeutically applied viral vector from being destroyed by the target cell, in this case a cancer cell. Martin Löchelt and his working group will further pursue this approach.

Source: Löchelt M, Romen F, Bastone P, Muckenfuss H, Kirchner N, Kim YB, Truyen U, Rösler U, Battenberg M, Saib A, Flory E, Cichutek K, Münk C.: The antiretroviral activity of

APOBEC3 is inhibited by the foamy virus accessory Bet protein. Proc Natl Acad Sci U S A.; May 31, 2005, vol. 102, no. 4933: 7982-7987.

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

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