

Press Release

Prions and retroviruses – an unholy alliance? - Expression of endogenous retroviruses is changed after prion infection

In work originating from the Bavarian Research Cooperation Prions (FORPRION), which ended in 2007, a team led by the scientist Prof. Dr. Christine Leib-Mösch has been able to show that prion proteins may activate endogenous retroviruses in infected brain cells. In the Institute of Molecular Virology of the GSF – National Research Centre for Environment and Health in Neuherberg/Munich (Helmholtz Association of German Research Centres) the group is continuing to search for cellular components whose make-up is changed as a result of a prion infection. In collaboration with colleagues from the Technical University of Munich and the University of Heidelberg, the group used micro-array technologies – micro-arrays are chips with thousands or tens of thousands of DNA or protein probes - and could demonstrate that the expression of endogenous retroviruses is influenced by infectious prion proteins in tests with mouse cells.

Prions – an abbreviation for proteinaceous infectious particles – work as a trigger to a set of diseases of the brain and nervous system, the so-called spongiform encephalopathies. These include BSE in cattle, scrapie in sheep and Creutzfeldt Jakob's Disease in humans. Prions are structural variants of a normal protein found in healthy tissues – especially in the brain. The devastating effect of infectious prions is that, once they have entered the organism, they can modify the normal "healthy" prion proteins to create more infectious prions, and thus cause the illness to progress.

However, as yet, little is known about the molecular mechanisms of pathogenesis, the role of co-factors and the interaction of prion proteins with cellular components.

Retroviruses insert their genetic information into the genome of host cells. In the case of endogenous retroviruses, this involves retroviral infections from long ago, which were transmitted through many generations by means of the germ line. Nearly ten percent of the genome of mice and humans consists of endogenous retroviral sequences that have accumulated during the course of evolution. Indeed, most structural genes of endogenous retroviruses are inactive, but many regulatory elements, such as binding sites for transcription factors, often remain active and can influence neighbouring cellular genes.

The GSF scientists infected mouse neural cells kept in culture with infectious prion proteins and subsequently analysed the expression patterns of endogenous retroviruses. The results showed that the expression of a set of endogenous retroviral sequences is influenced by the prion infection: in comparison with uninfected cells, the expression partly increased but also partly decreased – depending on the cell line and the type of endogenous retroviruses. These effects could be suppressed by pentosan-polysulphate, an anti-prion drug, which means that the influence of the expression can be attributed to the prions and not to some secondary effects.

These observations suggest that prion proteins may stimulate the production of retroviral particles by activation of endogenous retroviruses. Subsequently, these retrovirus-like particles could transport prion proteins from cell to cell, and thus spread the infection.

These studies were carried out within the scope of the “Bavarian Research Cooperation Prions” (FORPRION; www.abayfor.de/forprion/) in the Association of Bavarian Research Cooperations (www.abayfor.de). FORPRION was founded in 2001 following the appearance of the first BSE cases in Bavaria and was financed equally from the budgets of the Bavarian State Ministry for Science, Research and Art, and the Bavarian State Ministry of Health Food and Consumer Affairs.

Through basic and applied research the consortium aims to make progress in the diagnosis and therapy of human and animal prion diseases, as well as in the field of preventive consumer protection. FORPRION linked up 25 projects, based at five Bavarian universities and in institutes of the Max Planck Society. The financial support of the Bavarian Research Cooperation Prions FORPRION ended in June, 2007.

Literature:

A. Stengel, C. Bach, I. Vorberg, O. Frank, S. Gilch, G. Lutzny, W. Seifarth, V. Erfle, E. Maas, H. Schätzl, C. Leib-Mösch, A. D. Greenwood: Prion infection influences murine endogenous in neuronal cells. *Biochemical and Biophysical Research Communications* 343 (2006) 825–831

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Neuherberg, 22 August 2007