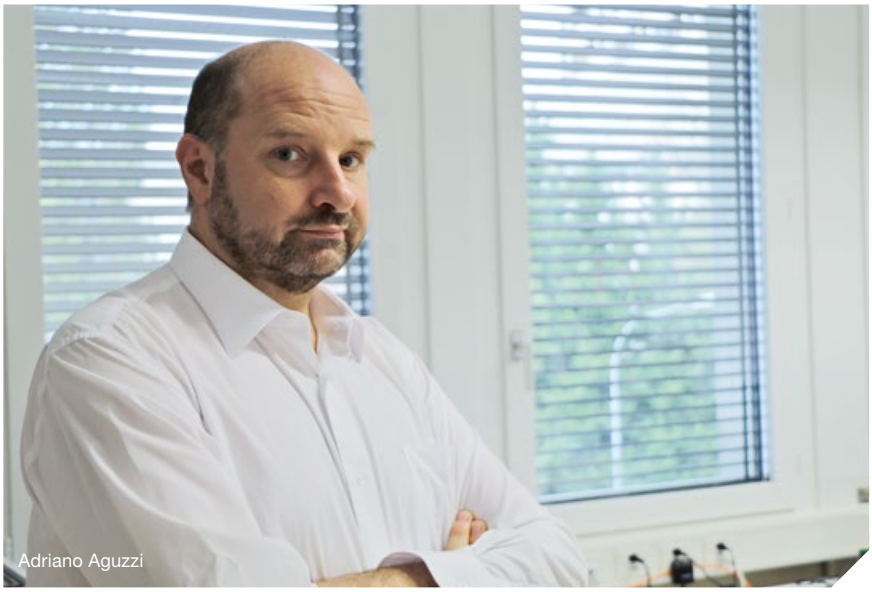
7. PrionX – Why do proteins infect other proteins?

Prions are proteins that are responsible for a number of brain diseases in humans and other mammals. So far, however, very little is known about their growth mechanisms. The PrionX project therefore seeks to learn more about these aggressive proteins.

The term *prion* stems from the words **pr**otein and infect**ion,** and refers to the virus-like properties of these types of proteins. Prion diseases gained publicity in the 1990s due to the BSE crisis. It was feared that this "mad cow disease" could be transferred to humans through the consumption of beef products. After the crisis subsided, however, the talk of these mysterious proteins once again died down.

Prion diseases, including BSE, are caused by the misfolding of proteins. The prions induce other proteins to change their shape, and these abnormal prions build up in the brain, leading to cell death. The brain's tissue becomes riddled with holes, and a spongy structure develops; a pattern that is also observed in other diseases such as Parkinson's. It is mostly the elderly who are affected, and no effective therapies exist to date. The reason for this is an incomplete understanding of the biochemical and cellular networks involved in the course of the disease.

A deeper understanding of these processes is precisely the goal of the researchers working on the MRD Project PrionX. The interdisciplinary team is planning to tackle this problem using the latest advances in genome editing (CRISPR) and microscale liquid handling. These technologies make it possible for the scientists to selectively suppress or eliminate individual genes.


Adriano Aguzzi

"The basic idea is to infect cells with prions while suppressing each gene individually in order to see what influence this has on the production of prions," explains Adriano Aguzzi, professor at the University Hospital Zurich. "And when we've made our way through the whole genome, we will be left with a picture of prion replication." Since there are around 30,000 genes in a cell, the vast extent and ambition of the study becomes evident.

A major obstacle for previous research in this area was that prions are barely active *in vitro.* Normally, when cells are infected with prions, they replicate vigorously. But *in vitro,* hardly any replication takes place. "I suspect the cells support the multiplication of the prions. This is why replication doesn't take place in a cell-free sample," speculates Aguzzi. "Once we learn more about this replication, we'll be able to tackle it therapeutically."

Aguzzi is confident that the team will find evidence of prion replication. "We're on a journey of discovery. So far, we've found a number of very interesting things that we would like to examine more closely, and which could significantly deepen our understanding of prion diseases."

PrionX at a glance

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Approved SystemsX.ch funds (2015–2018): CHF 1.347 million

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