

Prions

Prions (from *Proteinaceous Infectious Particles*) are **infectious particles** made up only of a protein molecule. The prion theory was formulated in **1982** by *Stanley Prusiner*, who received the Nobel Prize in 1997. **Prions are the cause of neurodegenerative diseases in humans and animals.**

Characteristics of prions

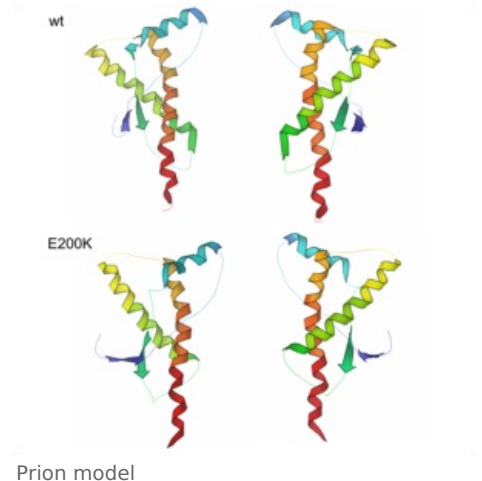
In the human brain, under **physiological** conditions, the product of the PRNP gene on chromosome **20** is the **PrP** (Prion Protein), specifically PrP^C (C - cell) - a normal, wild-type form. Its physiological function is unclear, apparently involved in synaptic transmission and cell differentiation.

Pathogenic prions have the same primary structure (amino acid sequence) but differ in their conformational arrangement. While wild-type PrP^C has a significant predominance of α -helix and only about 5% of a β -sheet, pathogenic PrP^{Sc} (Sc - scrapie) has a β -sheet content of up to 40%. Why aberrant PrP^{Sc} prions are formed is still the question to answer. There are several hypotheses for this.

- **The VIRAL** hypothesis assumes the participation of RNA viruses in the development of transmissible spongiform encephalopathies and thus in the development of infectious prions.
- **The MULTICOMPONENT** hypothesis considers that binding with polyanions and lipids is necessary for the formation of infectious prions.
- **HEAVY METAL POISONING** causes the formation of infectious prions when there is too little or too much copper in the body because a healthy amount of copper is needed for a healthy prion.

Once an infectious prion is formed, it can "imprint" its conformation on neighboring, healthy prions. This mechanism probably spreads the disease through the tissue.

Pathogenic prions are extremely resistant to physical and chemical influences, which results in difficulties with sterilization (an experiment was made - to burn the brains of affected animals at 600°C, about 1/3 of the ash-exposed animals were infected). Highly infectious tissues include the eye, brain, and spinal cord tissue.



Diseases

Prion diseases are caused by pathogens, that are the only ones that do not contain nucleic acid. They can be sporadic, genetic, or infectious (even iatrogenic). The presence of defective proteins causes a condition collectively referred to as **spongiform encephalopathy**. It is a degenerative disease of the nervous system, in which the brain gradually acquires a spongy appearance due to the formation of miniature holes.

Human prion diseases

- **Creutzfeldt-Jakob Disease (CJD)**
 - **Sporadic CJD** - has an incidence of 1-2/1 000 000. In the Czech Republic, more than 10 patients die from this form of CJD every year. Difficulties start around the age of 65. The disease progresses as a rapidly progressing dementia (in the range of 2-3 months), ataxia and myoclonus appear. The patient dies within 5-12 months after the first symptoms.
 - **Iatrogenic CJD** - occurred in patients treated with human growth hormone from cadaveric pituitary glands (now it is prepared recombinantly), by the transmission of the dura mater, pericardium, or cornea. There is also a risk of neurosurgical procedures transmitted by instruments. Prion transfer is probably also possible by transfusion.
 - **Familial CJD** - is a genetic form with a mutation in the PRNP gene and neuropsychiatric symptomatology.
 - **A new variant of CJD** - is characterized by psychiatric symptoms (anxiety, depression, behavioral changes), progressive cerebellar syndrome, myoclonus, chorea, and other neurological symptoms. Unlike the sporadic form, the course is slower and affects younger age groups. Transmission is probably alimentary from the meat of BSE animals. The incubation period is more than 10 years, about 200 people have died worldwide.
- **Kuru** - this contagion occurred mainly in indigenous tribes in New Guinea who practiced the cannibalism ritual. After several years of incubation, the patients developed tremor, ataxia, immobility, and subsequent death. After the suppression of cannibalism, the disease disappeared.
- **Alper's disease**
- **Gerstmann-Sträussler-Scheinker syndrome**

- **Fatal familial insomnia**
- **Sporadic fatal insomnia**

Animal prion diseases

- **Bovine spongiform encephalopathy (BSE)** (mad cow disease)
- **Scrapie**
- **Chronic wasting disease (CWD)**
- **Feline spongiform encephalopathy**
- **Transmissible mink encephalopathy**

Diagnostics

Diagnosis of spongiform encephalopathies is based on clinical and histopathological findings (immunohistochemistry, Western blot), or genetic examination.

The **sporadic form of CJD** is characterized by an EEG (looks like an EKG), on MRI there is an obvious involvement of the basal ganglia and insula, atrophy of the frontotemporal area, and 14-3-3 protein in the cerebrospinal fluid. **Familial CJD** can be diagnosed by determining a mutation in the PRNP gene. Prior to the onset of a **variant form of CJD** prions can be detected in the tonsils, appendix, or spleen; MR involvement is mainly in the thalamus pulvinars, cerebrospinal fluid is negative for 14-3-3 protein.

Spongiform changes (optically empty spaces – appearance of a washing sponge), loss of neurons, and proliferation of astrocytes (astrocytosis) can be found in the histological specimen.

Therapy

Causal therapy does not yet exist.

Links

Relates articles

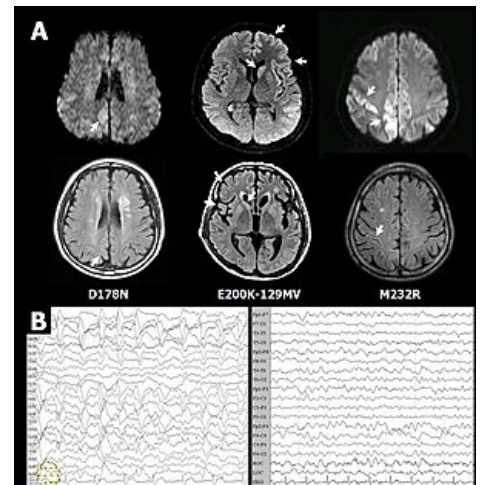
- Causes of pathological conformation of proteins

References

- MATĚJ, Radoslav. *Lidská prionová onemocnění v ČR* [lecture for subject -, specialization Všeobecné lékařství, - Univerzita Karlova]. Praha. 2010.

References

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Magnetic resonance imaging and EEG recording of a person with Creutzfeldt-Jakob disease

Portal: Microbiology Portal: Pathophysiology Portal: Pathobiochemistry Portal: Pathology Portal: Neurology Portal: Biology Portal: Genetics