PRIONS

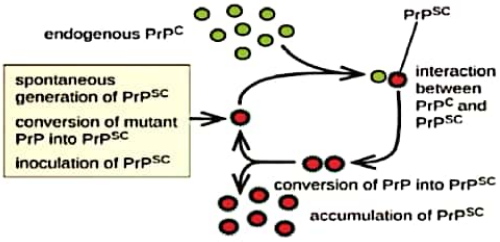
- A prion is a misfolded rogue form of a normal protein found in the cell.

- It was discovered by Stanley B. Prusiner, a doctor, in 1982, while studying Scrapie (a fatal, degenerative disease in sheep) at the University of California, San Francisco, USA. He called it "Proteinaceous infectious Particle" - shortened as "prion". He recieved the Nobel Prize in Physiology or Medicine in 1997. His findings were originally met with resistance because proteins are acellular and don't contain DNA or RNA.

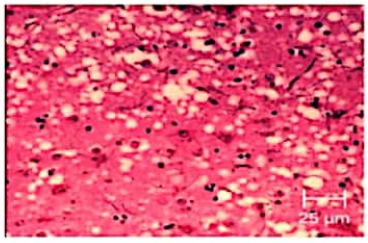
- The protein that prions are made (PrP) is found throughout the body, even in healthy people and animals. They are normal proteins found on the membranes of cells. In human, the PrP has 209 aminoacids and structurally well defined. However, the PrP found in infectious material has a different structure (misfolded) and is resistant to proteases. The normal form of the protein is called PrP^C, while the infectious form is called PrP^{SC} (C refers to 'cellular' in PrP^C while SC in PrP^{SC} is for scrapie, the prototypic prion disease in sheep)

- Prions are known to cause various forms of transmissible spongiform encephalopathy (TSE) in human and animals.
- TSE is a rare degenerative disorder that affects the brain and nervous system. Since, prions are resistant to proteases, they are not broken down as they multiply and instead accumulate within neurons, destroying them. Progressive neuron destruction eventually causes brain tissue to become filled with holes in a sponge-like pattern. This leads to brain damage, loss of motor, coordination, and dementia. The infected individuals are mentally impaired and become unable to move or speak, eventually leading to death within a few months or years.

transmissible spongiform encephalopathy (TSE) in human and animals.



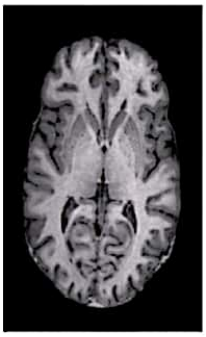
(a)



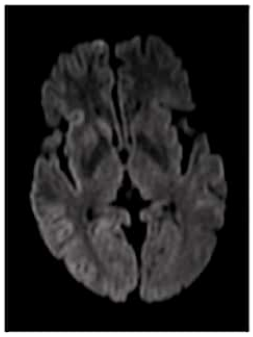
(b)

The endogenous normal prion protein (PrP^C) is converted into the disease-causing form (PrP^{SC}) when it encounters the variant form of protein.

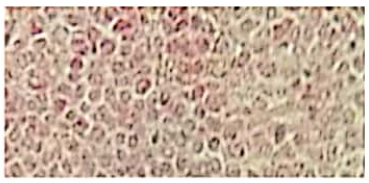
- PrP^{SC} may arise spontaneously in brain tissue, especially if a mutant form of the protein is present, or it may originate from misfolded prions consumed in food that eventually find their way into brain tissue
- TSEs in human include Kuru, fatal familial insomnia (FFI), Gerstmann-Straussler-Scheinker (GSS) disease, and Creutzfeldt-Jacob disease (CJD).
- TSEs in animals include mad cow disease or Bovine Spongiform Encephalopathy (BSE), Scrapie (in sheep and goats), and Chronic wasting disease (in elk and deer)



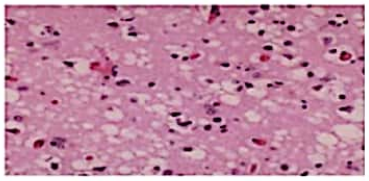
Normal brain



CJD brain



Normal brain tissue



Sponge-like lesions in the brain tissue of a CJD patient

(a) (b)

The brain tissue of CJD patient is full of sponge-like lesions, which results from accumulation of abnormal Prion proteins.

- TSEs can be transmitted between animals and from animals to humans by eating contaminated meat or animal feed.
- Transmission between humans can occur through heredity (as is often the case with GSS and CJD), or by contact with contaminated tissue, as might occur during a blood transfusion or organ transplant. There is no evidence for transmission via casual contact with infected persons.