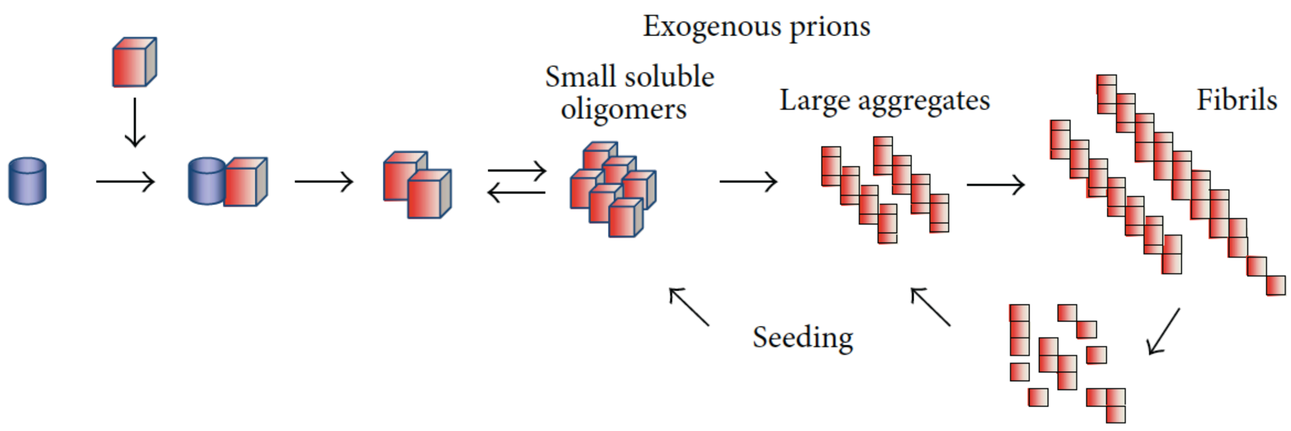
PRIONS IN DIFFERENT ORGANISMS

Fundamentals of prions

A Prion is a missfolded infectious protein that spread by inducing the missfolding of the normal protein.

All known prions induce the formation of an **amyloid fold**, in which the protein polymerises into an aggregate consisting of tightly packed **β-sheets**. Prion aggregates are extremely stable and accumulate in infected tissue, causing tissue damage and cell death. This structural stability means that prions are resistant to denaturation by chemical and physical agents, making disposal and containment of these particles difficult.



FUNDAMENTAL OF PRION DISEASES IN MAMMALS (PrDs)

The infectious form of the prion protein in mamals is called **PrP^{SC}** and the normal cellular prion protein is called **PrP^{C}**. It is a membrane-bound protein that is predominantly expressed in nervous tissue. Although its physiologic function is not entirely known, it probably plays a role in neuronal development and function. Prion infectivity occurs through a mechanism in which the pathogenic PrPSc act as a template to convert PrPC into PrPSc. So when PrPSc, which has mostly β-pleated sheet structure, comes in contact with PrPC, which has mostly α-helical structure, PrPC is misfolded into pathogenic PrPSc. This became an exponential reaction that leadts to neuronal injury and death.

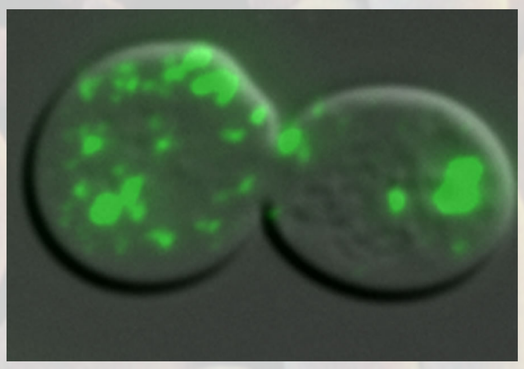
This neurodegenerative diseases produce in the brain to look like a sponge, and the name of Transmissible Spongiform Encephalopathy TSE have been given.

All the known mammalian prions produce prion dieseaes also called **PrD.** [1]

Prions in yeast

- There is no protein with homology to PrP^{C} in yeast, but several yeast proteins have been shown to exist in normal soluble form and transmissible amyloid form, therefore have prion-type behaviour.
- Also there have been found four self-propagation chaperones enzymes that assist refolding of yeast-prion, like Hsp104p.
- Each yeast-prion can form different types of infectious aggregates with distinct conformations and distinct associated phenotypes, called prion variants.

The fluorescent green chunks in these yeast cells are prion proteins that have assumed the shape that aggregates into clumps called amyloids. As seen in the picture, prions pass from mother to daughter cell.



- Yeast prions can always reappear because their proteins can misfold and become a pion seed again (the prion protein still present in the non-prion cell can reform the prion).
- This fungal prions do not appear to cause disease in their hosts, however some of those prions have known functions in the yeast cell like Ure2p prion that is a regulator of nitrogen catabolism. [2]

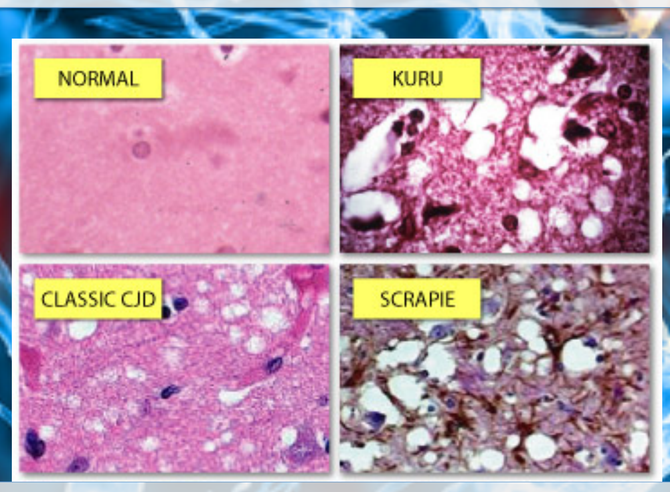
INTERESTING ADDITIONAL DATA

- In bacteria, no prions have been found, however, there have been found some amyloid aggregation.
- In plants, no prions have been found, but there are some studies that suggest that could be vectors for prions. More studies are needed.
- There are other proteins similar to prion (but not PrP^{sc} protein) that produce ontogeny of age-related degenerative disorders such as amyotrophic lateral sclerosis (ALS), Alzheimer's disease, and Huntington's disease.

Prions diseases PrD

PRIONS IN HUMANS

There are three kinds of prion diseases: **Sporadic PrD** which is thought to occur by spontaneous folding of PrP^{C} into PrP^{Sc} (Jakob-Creutzfeldt disease); **Genetic PrD** that are caused by mutations in the prion-related protein gene (PRNP), and they are classified based on the mutation, clinical phenotype, and neuropathological features (genetic JCD, familial fatal insomnia); and **Acquired PrD** In the orally acquired forms of PrD ((kuru, variant JCD, and iatrogenic JCD) through the intestinal epithelium by ingesting contaminated food.



Brain tissue images: We can observe the vacuoles in TSE infected cell. Autophagic vacuoles are a subcellular alteration linked to apoptosis. Vacuoles give sponge brain texture

PRIONS IN ANIMALS

PrDs occur in many species (scrapie in sheep and goats, and bovine spongiform encephalopathy in cattle). But prion protein and TSE have been found also in chicken, mouse (used as model) elk and deer (chronic wasting disease, CWD), mink (Transmissible Mink Encephalopathy, TME) and felines (Feline Spongiform Encephalopathy, FSE).

Prions can jump between species as long as the other specie have similar PrP^{c}.

Basic bibliography: [1]*Prion Diseases*, Leonel T. Takada, MD1 Michael D. Geschwind, MD, PhD; [2] *Prions of Fungi: Inherited Structures and Biological Roles* Reed B. Wickner, Herman K. Edskes, Frank Shewmaker, and Toru Nakayashiki; [3] *From Prion Diseases to Prion-Like Propagation Mechanisms of Neurodegenerative Diseases* Isabelle Acquatella-Tran Van Ba, Thibaut Imberdis, and Véronique Perrier. *Fundamentals of prions and their inactivation (Review)* AkikazuSakudo, YasuhisaAno, TakashiOnodera, KayakoNitta,HideharuShintani, KazuyoshiIkuta and YasuharuTanaka.