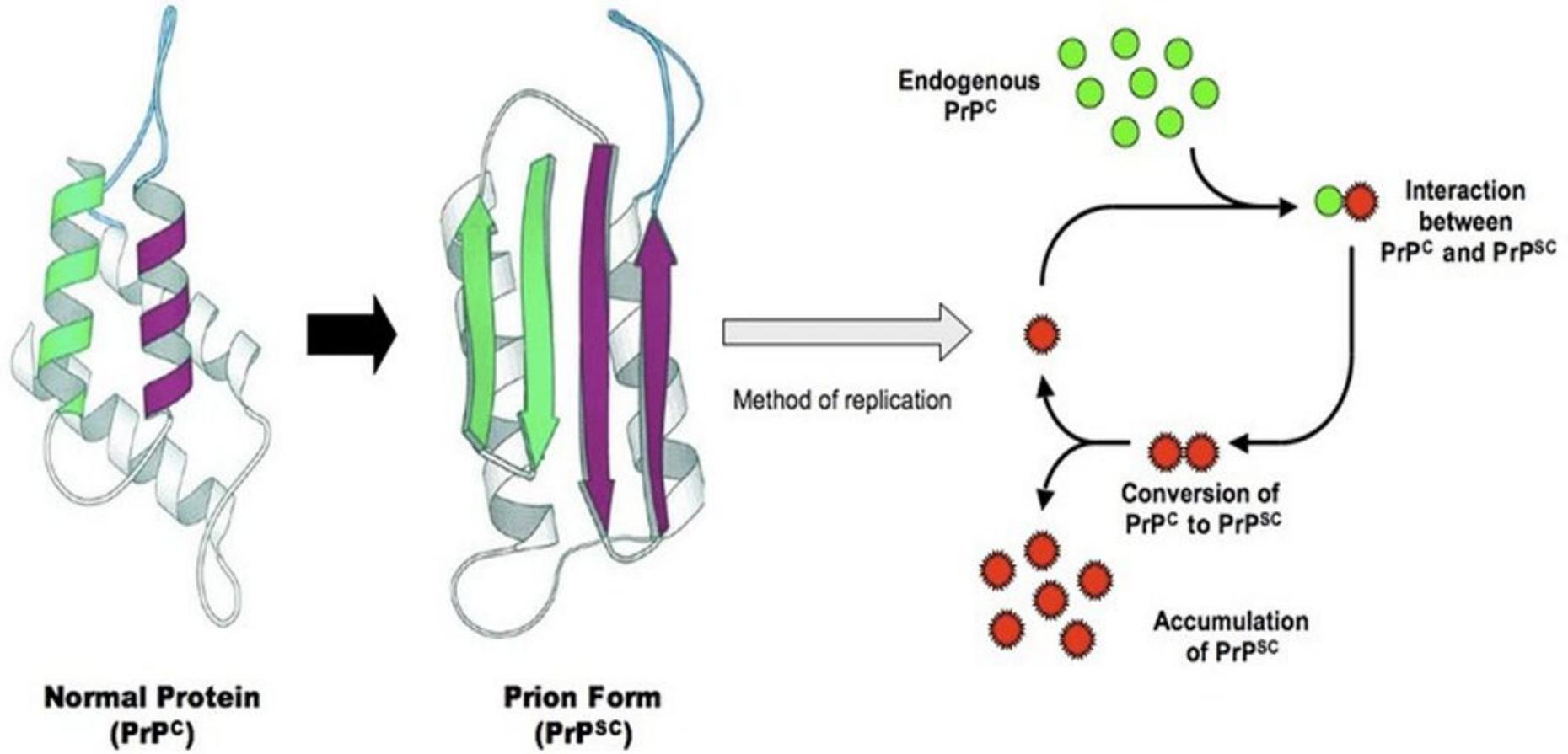
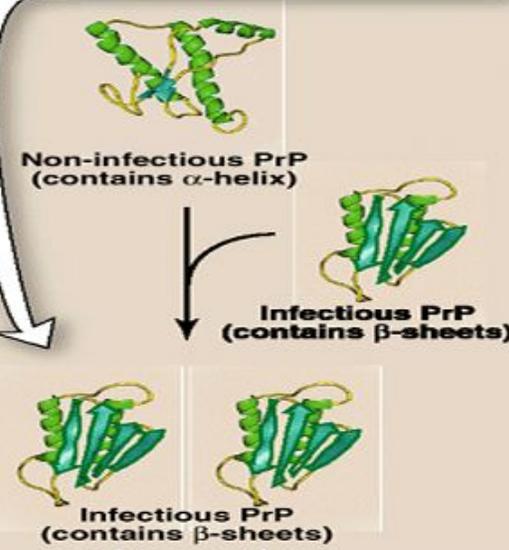


# Prion Disease

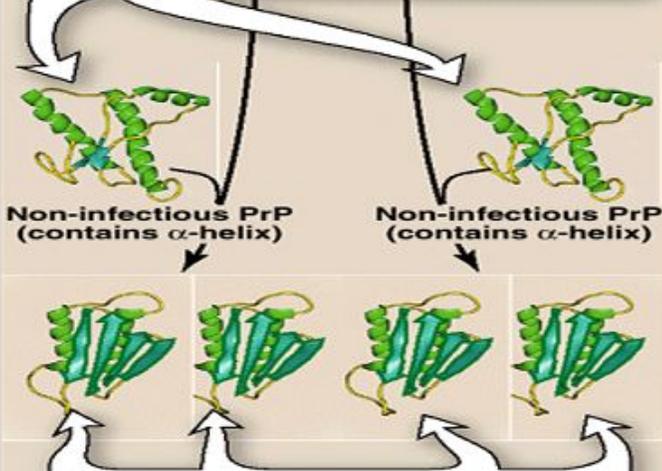
# Prion Protein



**1** Interaction of the infectious PrP molecule with a normal PrP causes the normal form to fold into the infectious form.



**2** These two molecules dissociate, and convert two additional non-infectious PrP molecules to the infectious form.



**3** This results in an exponential increase of the infectious form.

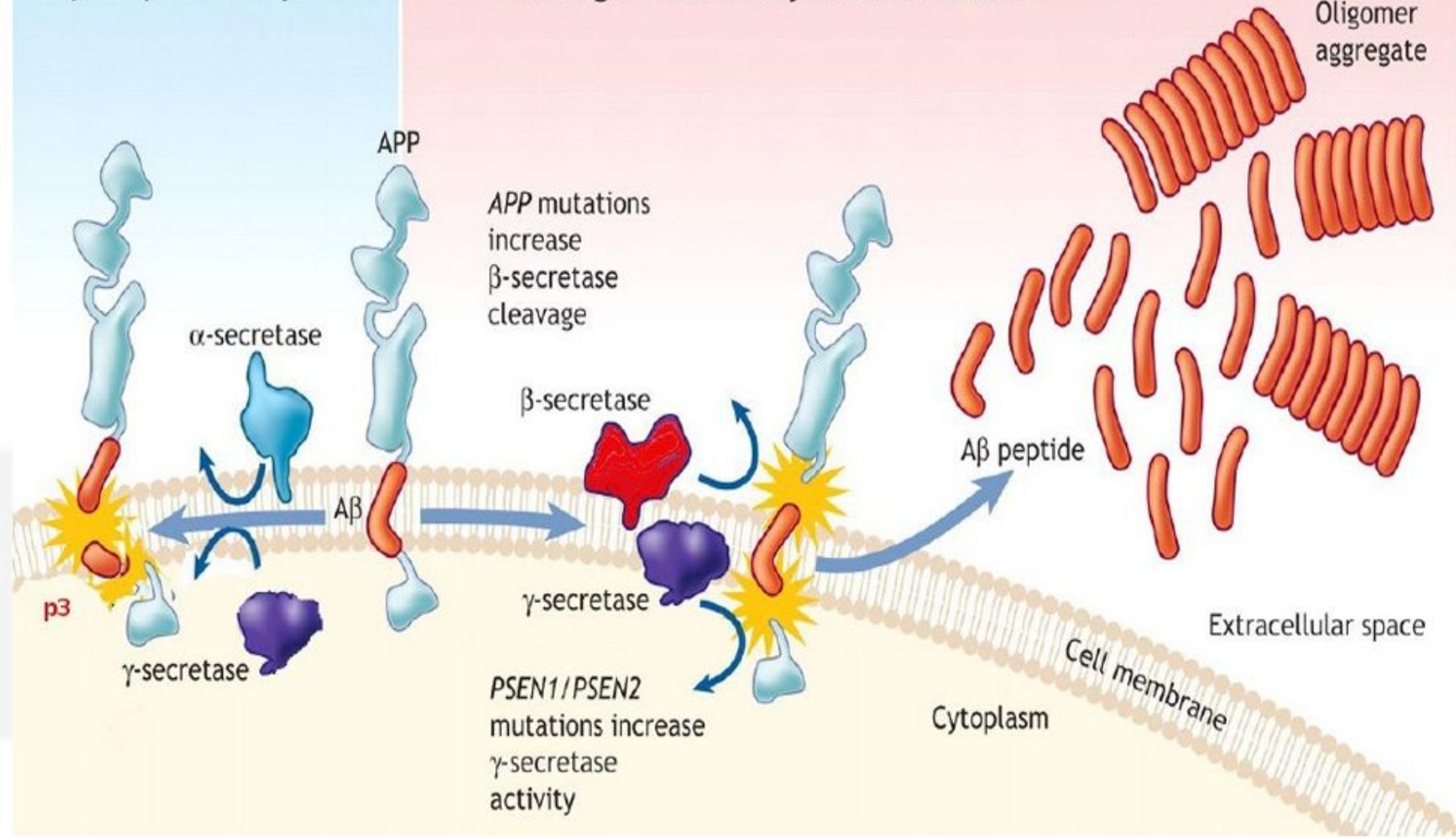
# Prion Protein(PrP) & Prion disease

- PrP is a host protein.
- Present on the surface of neurons and Glial cells.
- **Infective Prion Protein**
  - No any change in amino acid and gene sequences
  - No change in primary structure differences
  - No any alternate post-translational modifications
  - changes in the three-dimensional conformation
  - number of  $\alpha$ -helices noninfectious PrP (PrP<sup>c</sup>) are replaced by  $\beta$ -sheets in the infectious form(PrP<sup>sc</sup>).
  - highly resistant to proteolytic degradation
  - Accumulation of insoluble aggregates of fibrils

# Amyloidosis

Normal cleavage of amyloid precursor protein

Abnormal cleavage of amyloid precursor protein leading to excess amyloid accumulation



# Amyloidosis = Alzheimer's disease

- Accumulation of **amyloid  $\beta$  ( $A\beta$ )**, 40 – 42 A.A. = “Amyloids”
  - Neurodegenerative disorder = “**Alzheimer disease**”.
  - Found in the **brain parenchyma** & around blood vessels.
  - Neurotoxic & leading to the cognitive impairment
  - Abnormal proteolytic cleavage
  - Formation of long fibrillar protein =  $\beta$ -pleated sheets.
- 
- Second factor = Accumulation of neurofibrillary tangles
  - **Tangle protein = Role in assembly of the microtubular structure.**
  - Abnormal form of tangle protein = **tau ( $\tau$ ) protein**
  - Abnormal neurofibrine actions