Amyloid and amyloid deposition in the brain

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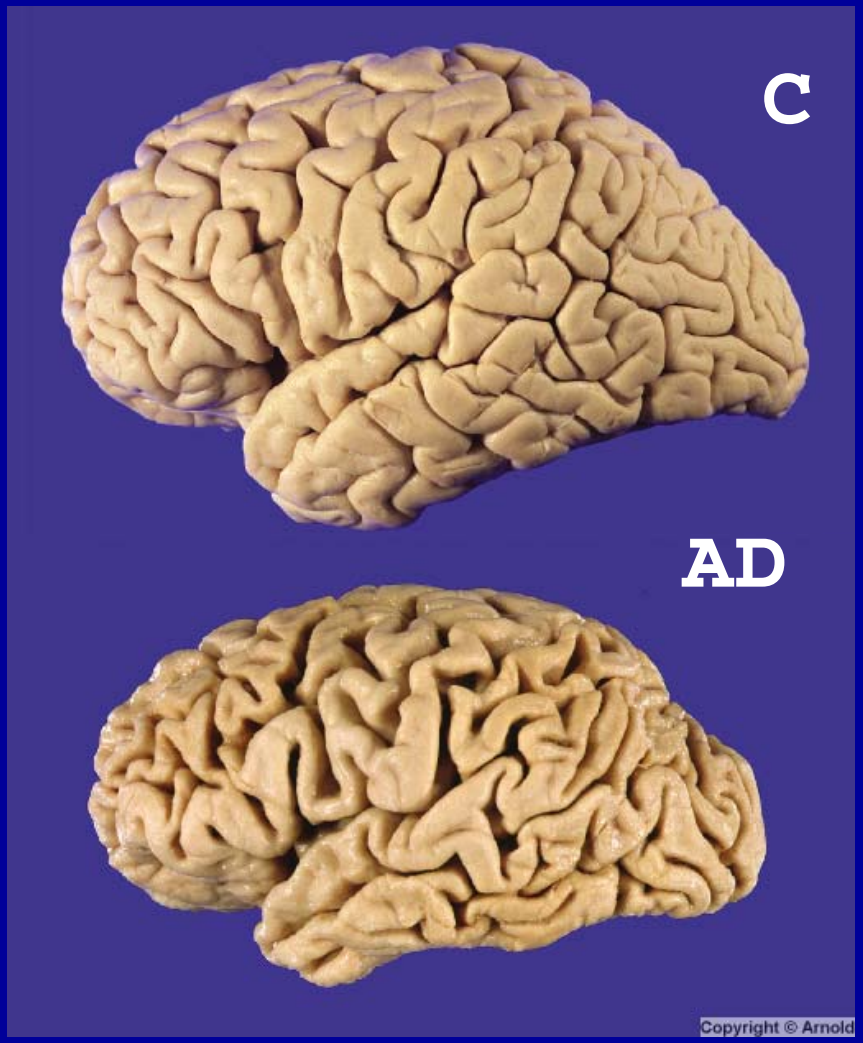
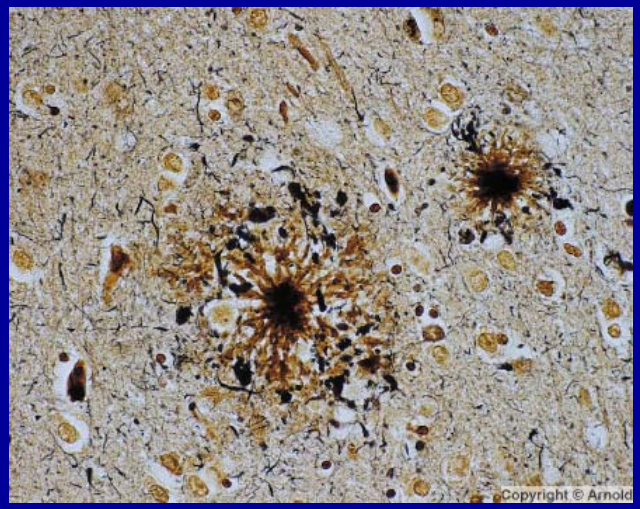
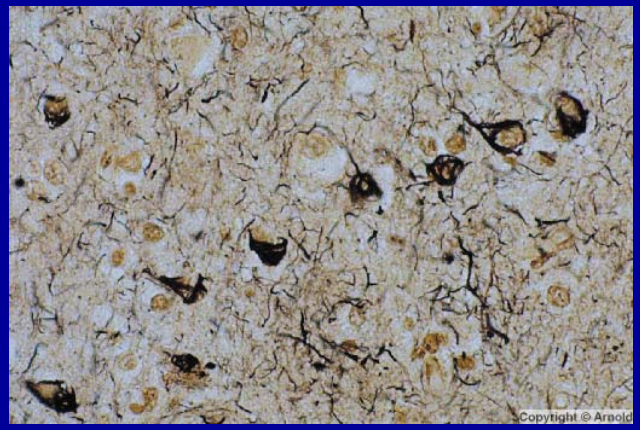
Neuropathological changes of AD



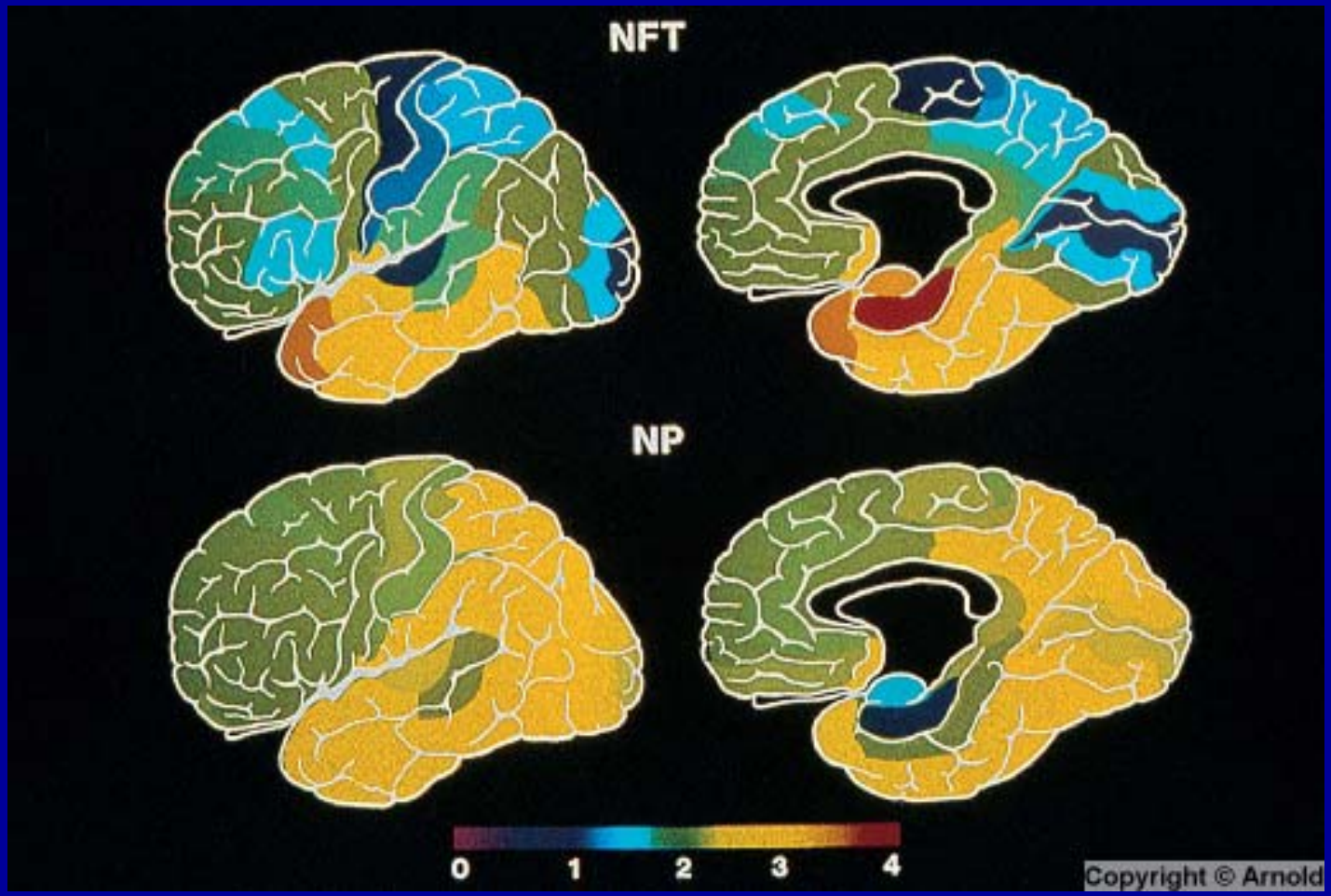


Plaques (Aß)



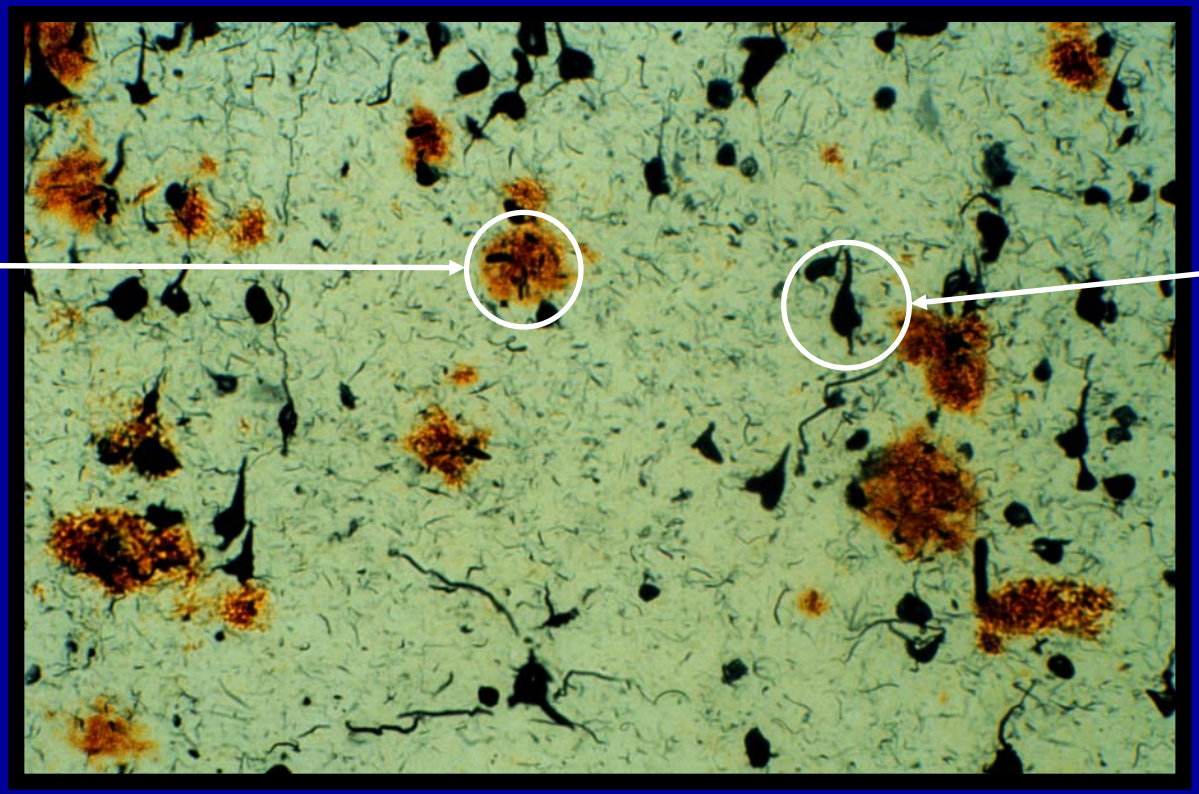
Tangles (p-tau)

Distribution of tangles and plaques in Alzheimer's disease



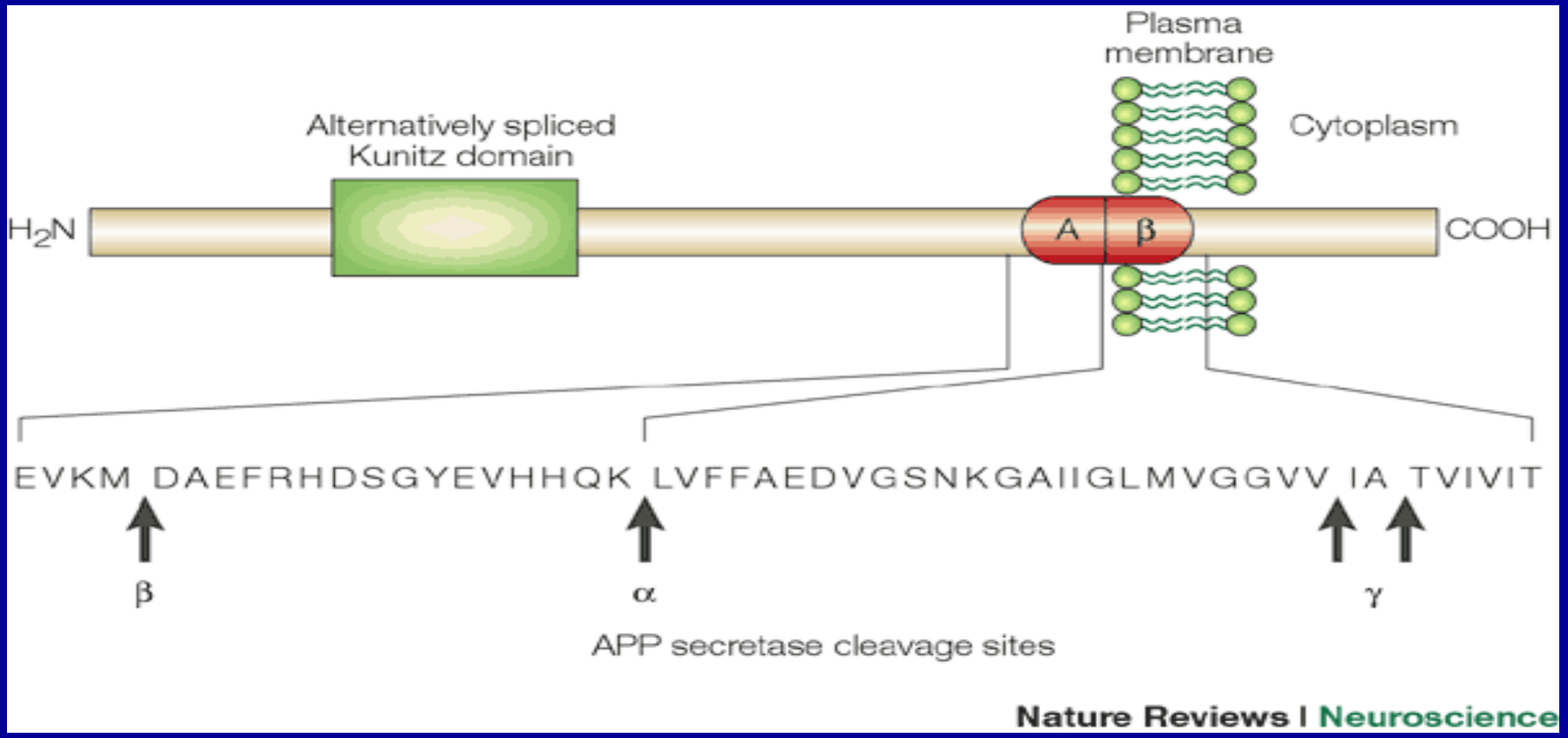
AD: Pathological Hallmarks

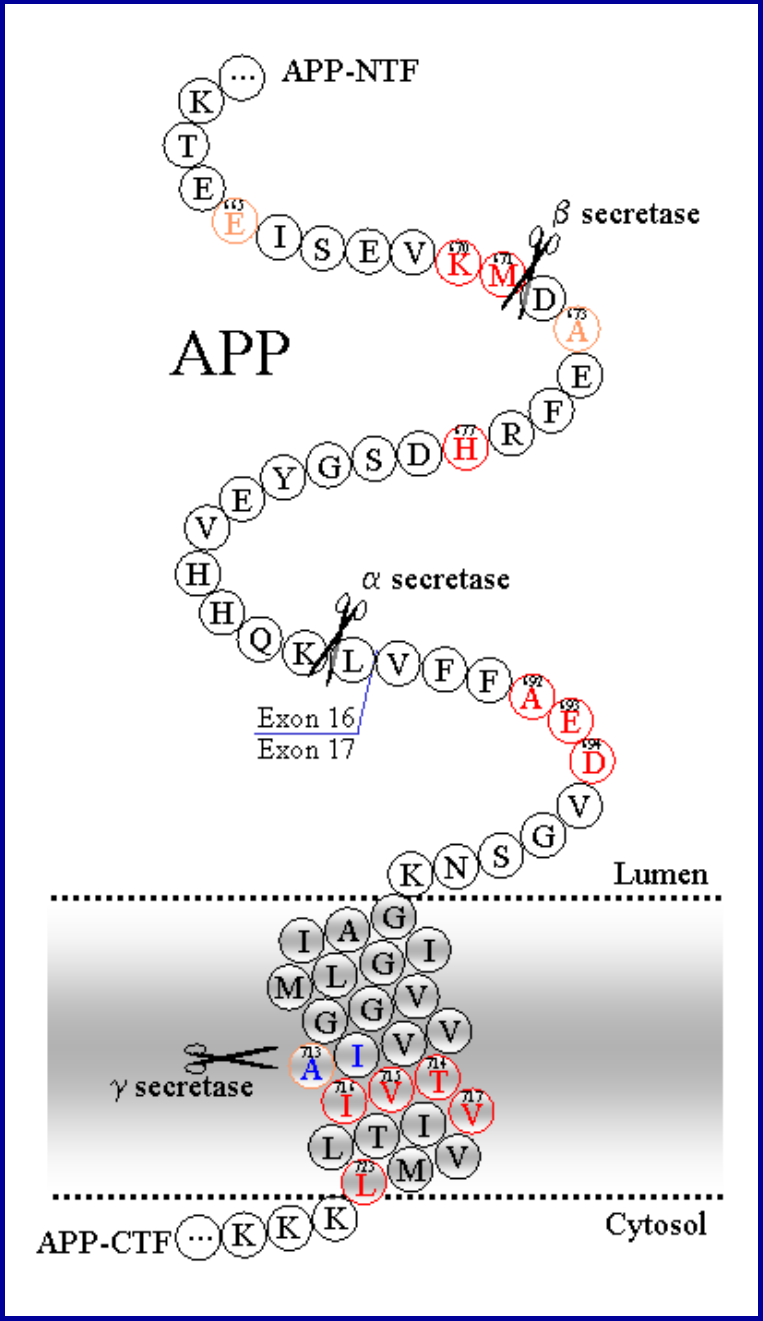
Amyloid Plaques and Neurofibrillary Tangles



Aβ plaques in brain cortex

Production of Aβ from APP

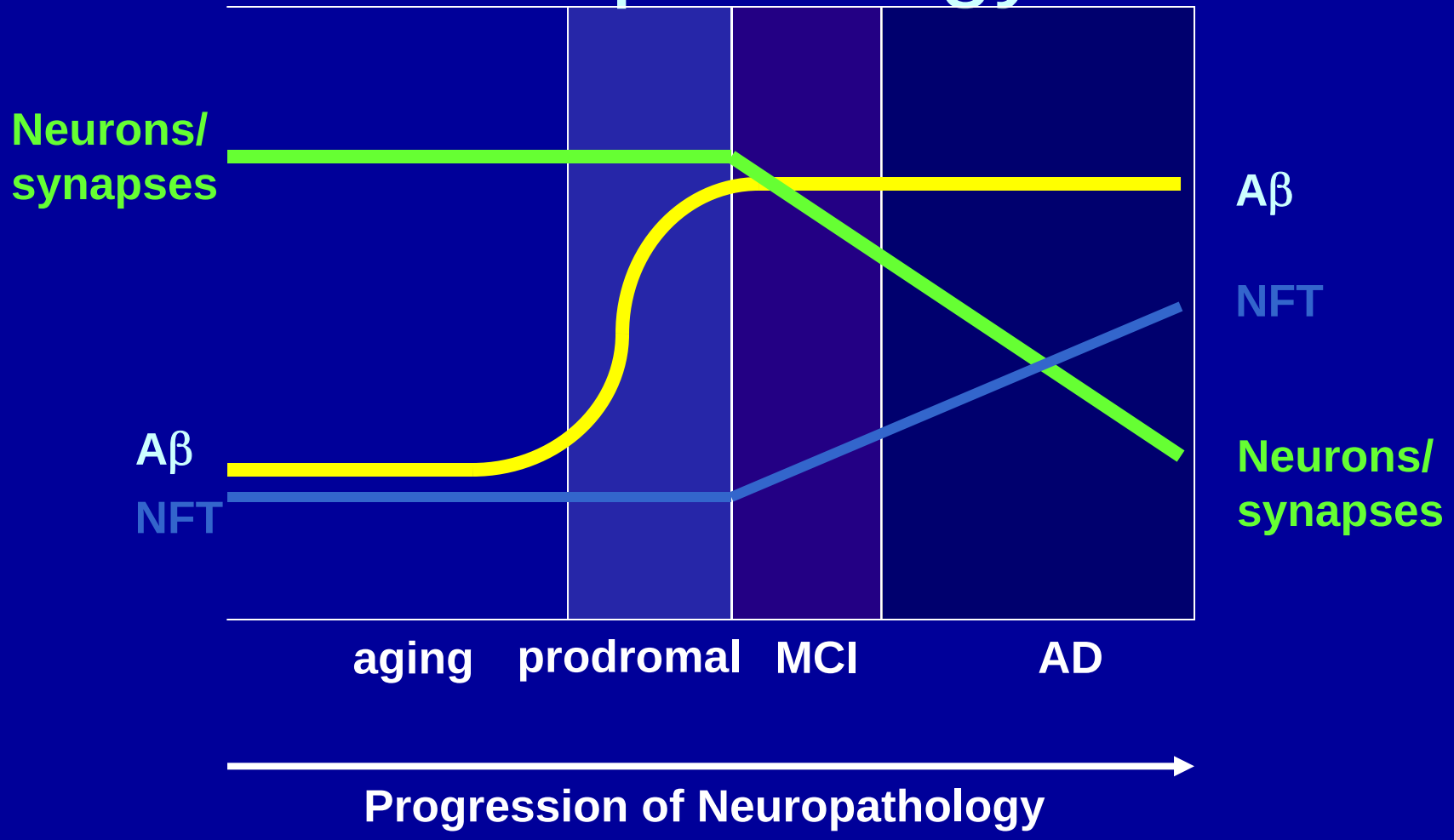




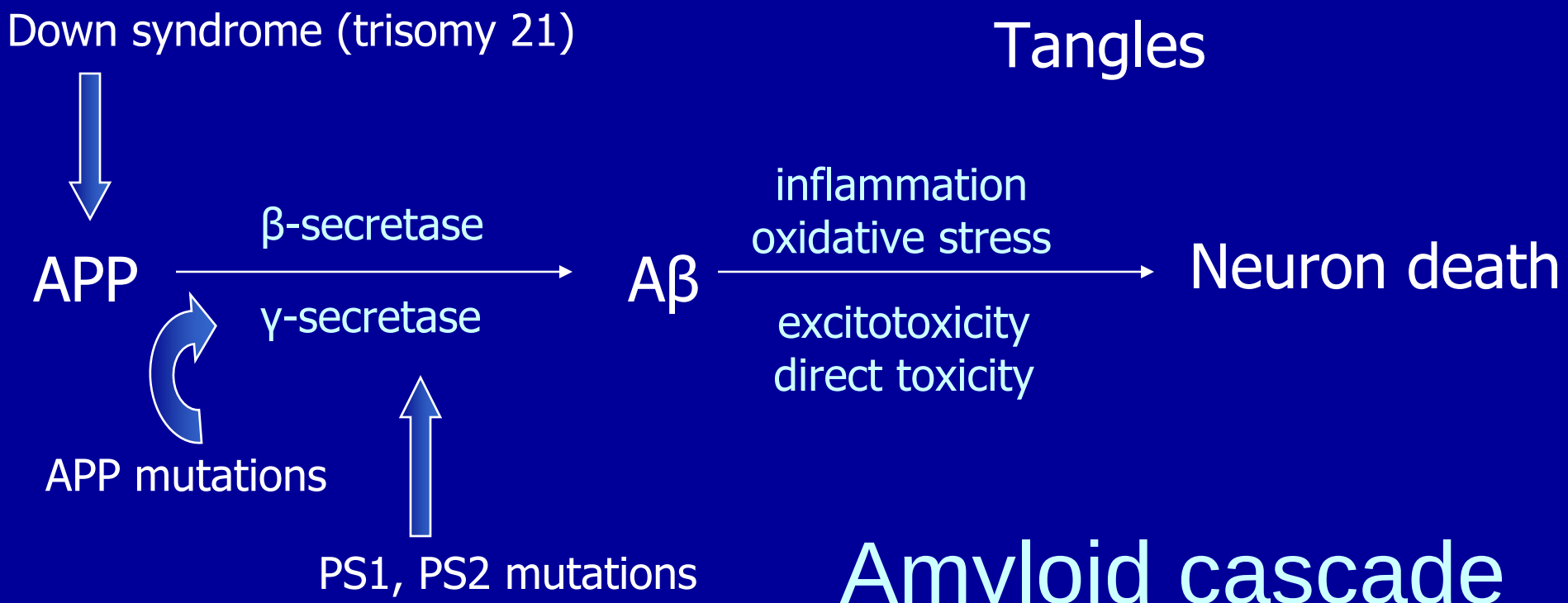
Mutations in APP cause a small percentage of familial Alzheimer's disease

Also: Down syndrome, gene duplication

Temporal course of AD Neuropathology

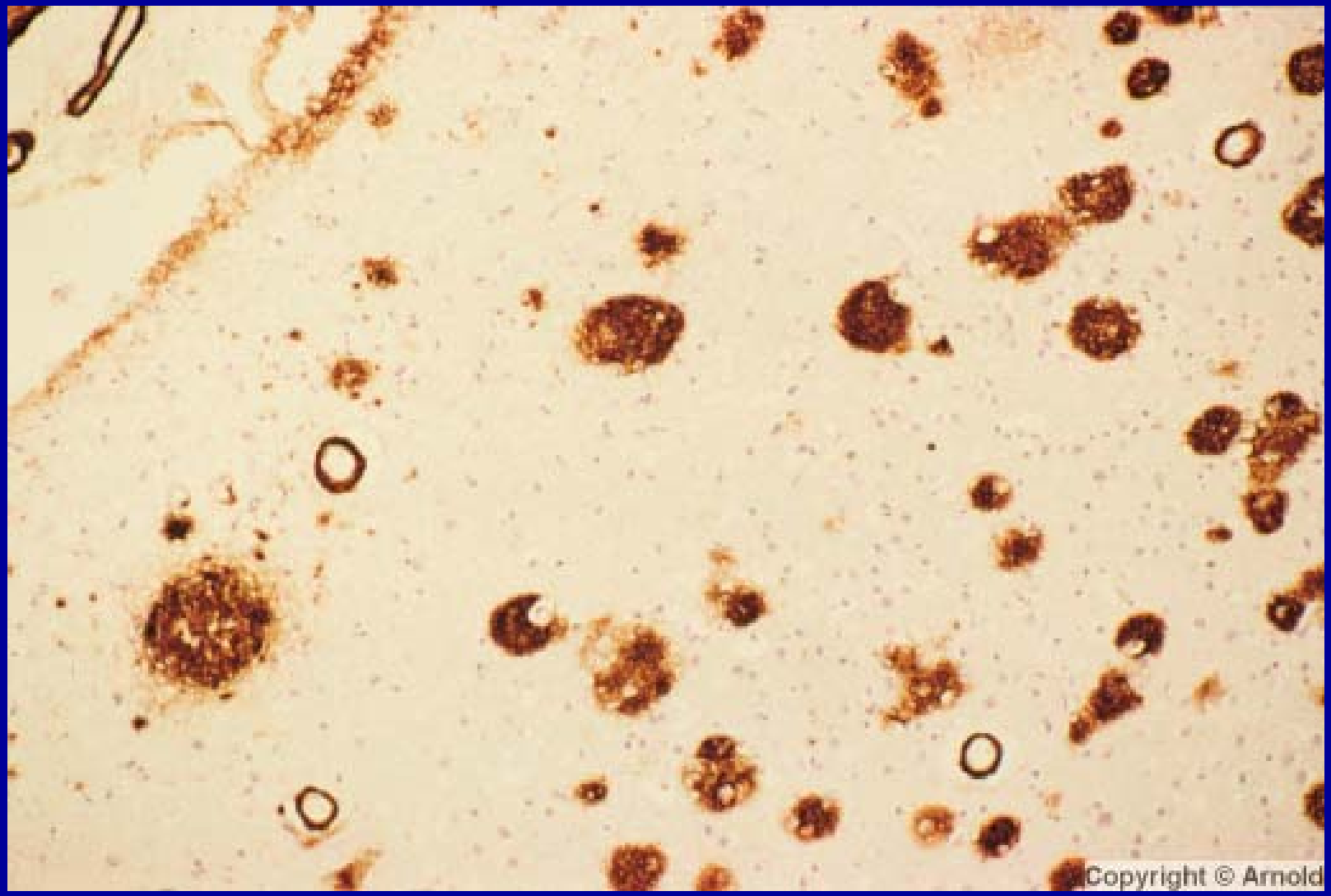


Tangles are downstream of Aβ accumulation

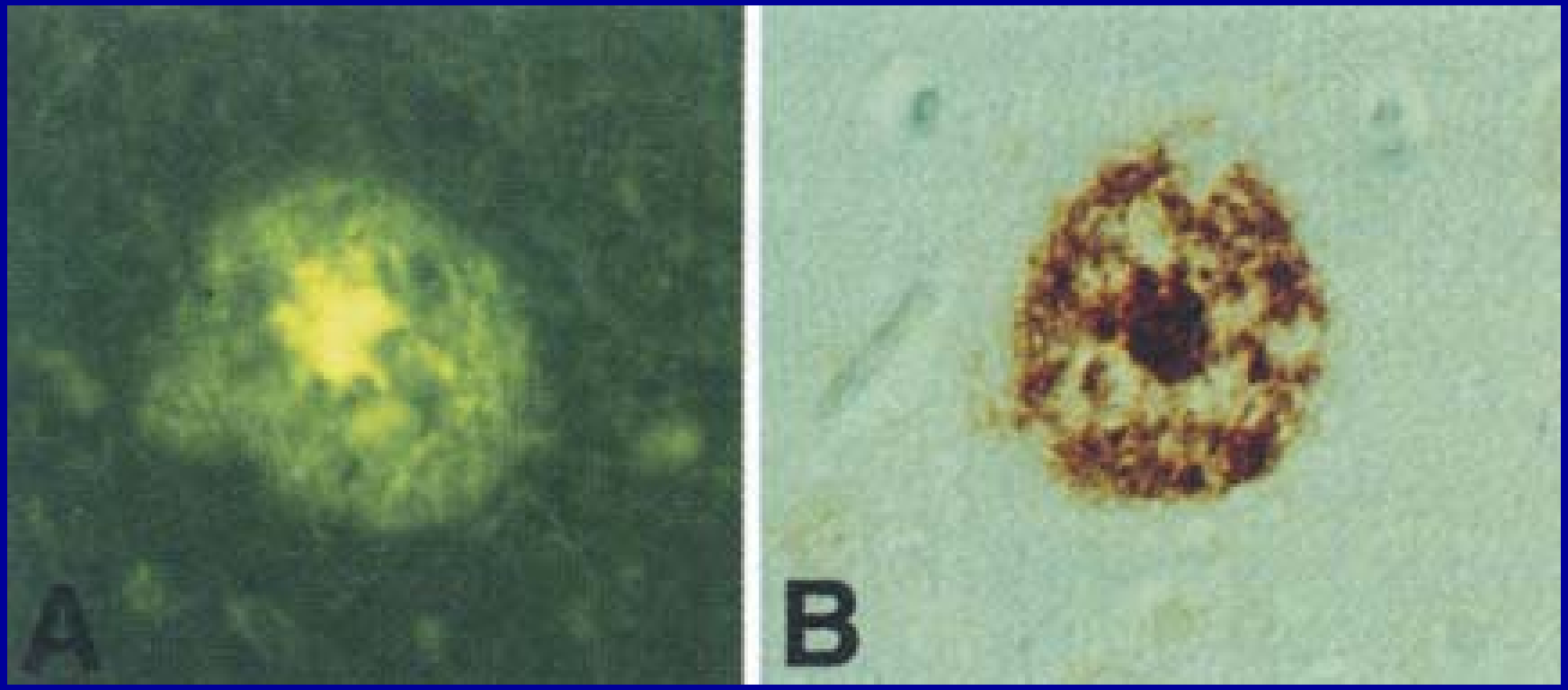


Amyloid cascade hypothesis

Aβ deposition in AD brain



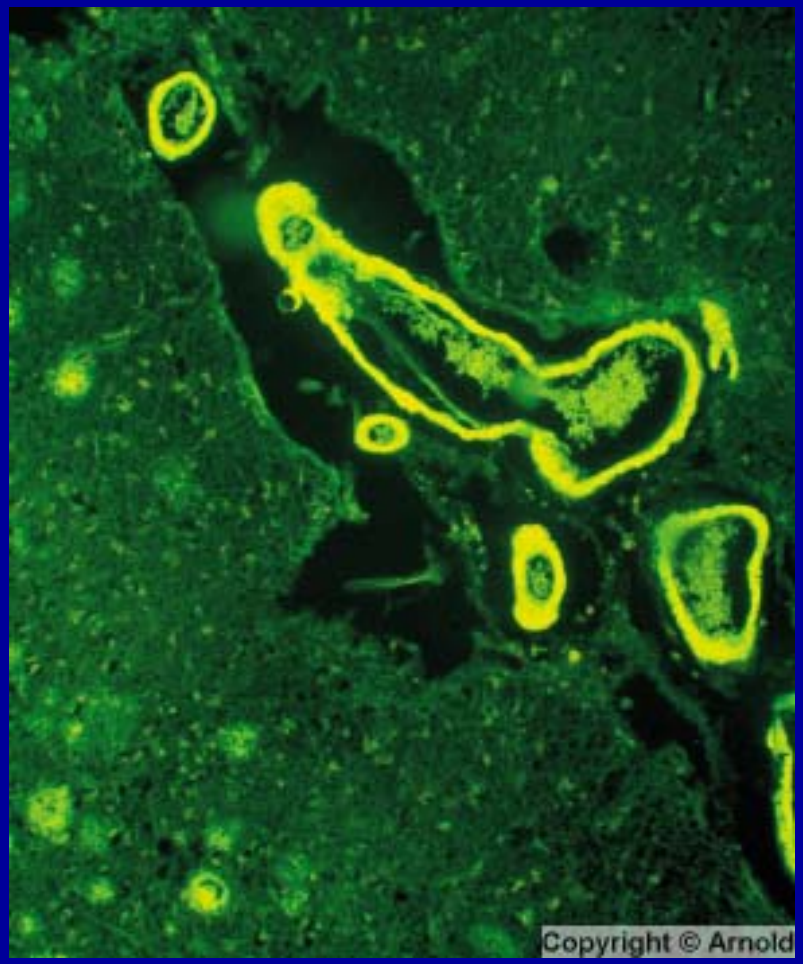
Staining for Aβ plaques



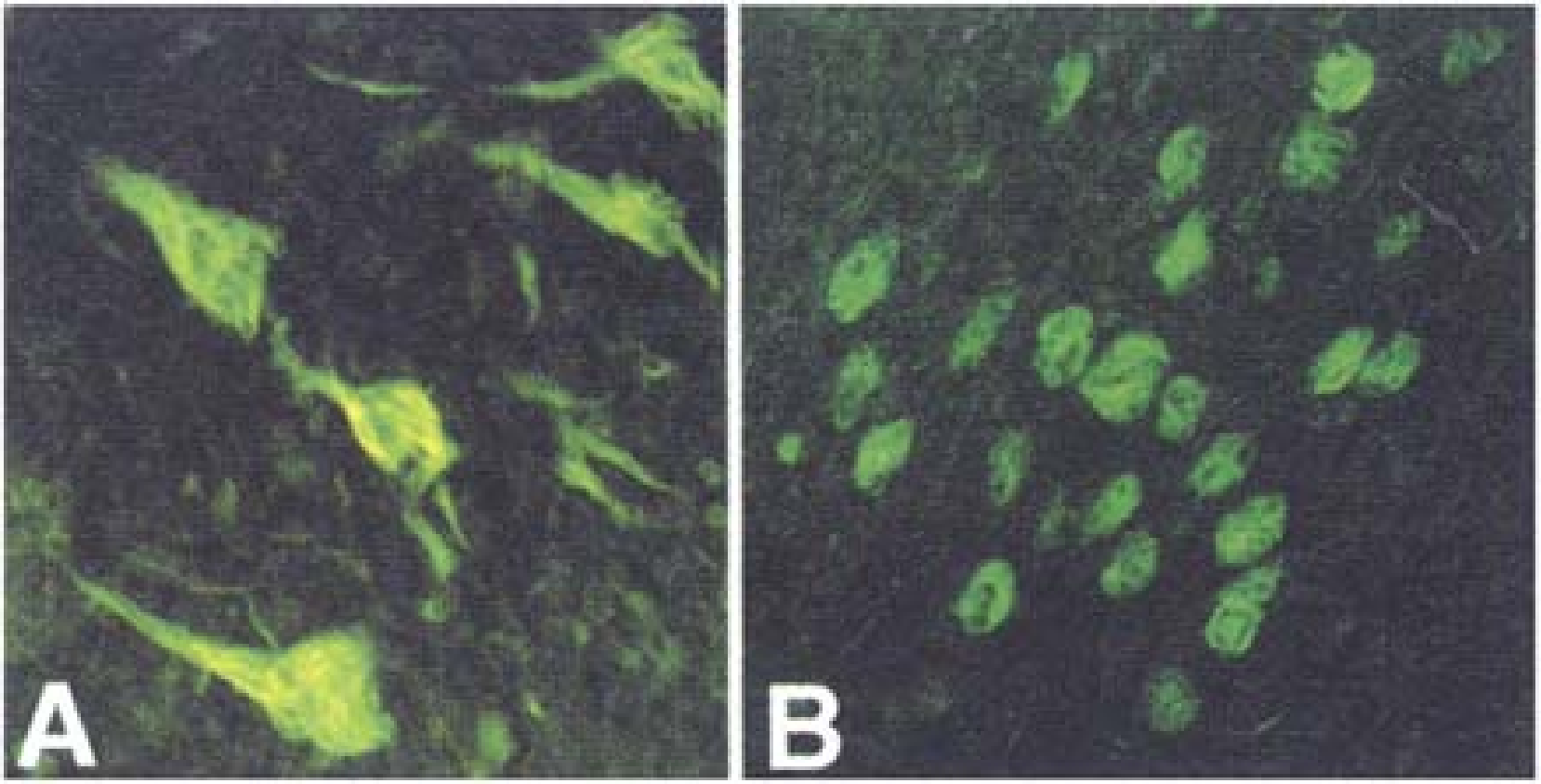
Thioflavin S

Aβ immunostain

Aβ amyloid in blood vessels



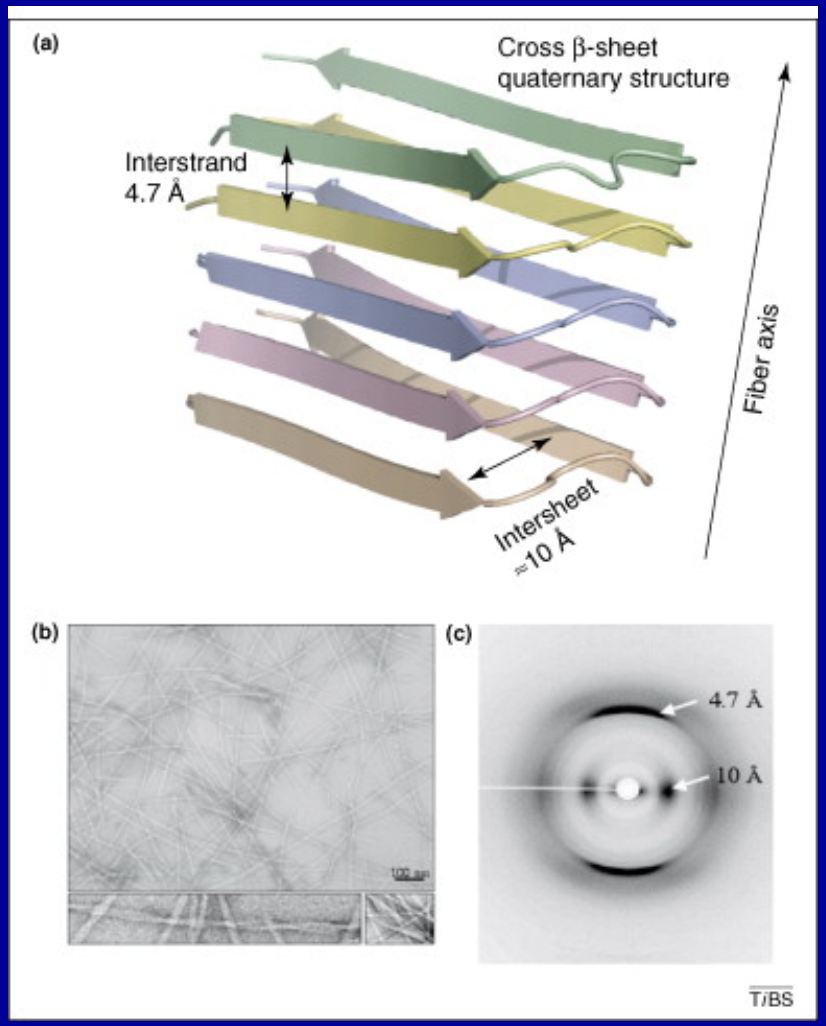
Neurofibrillary Tangles (NFT)



Hippocampus

Basal forebrain

Amyloid consists of proteins containing β sheets



Amyloid dyes

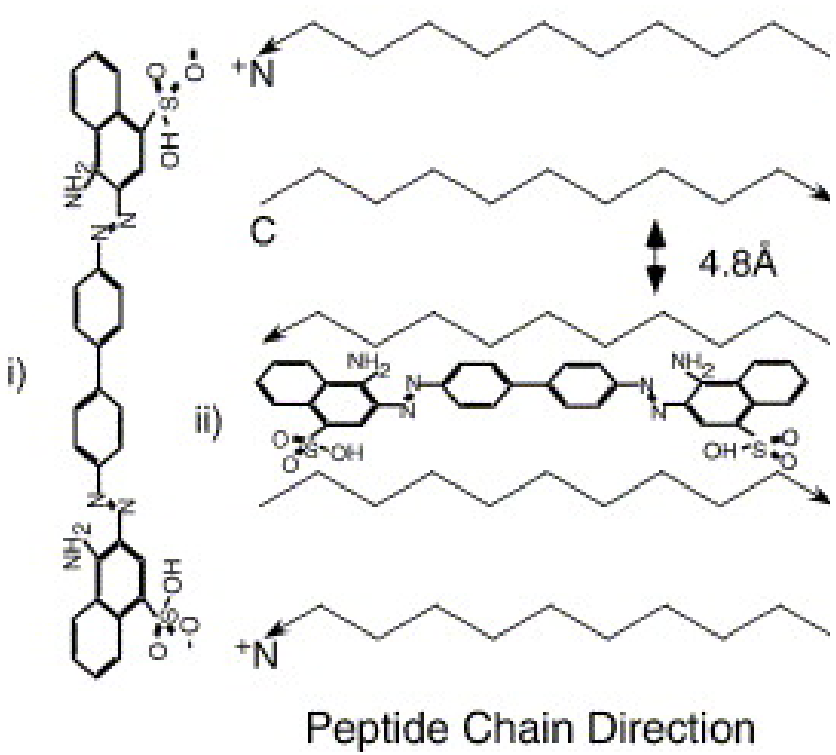
Congo Red

Thioflavin S

Methyl violet

Fowler et al, TIBS 2007

Binding of amyloid dyes

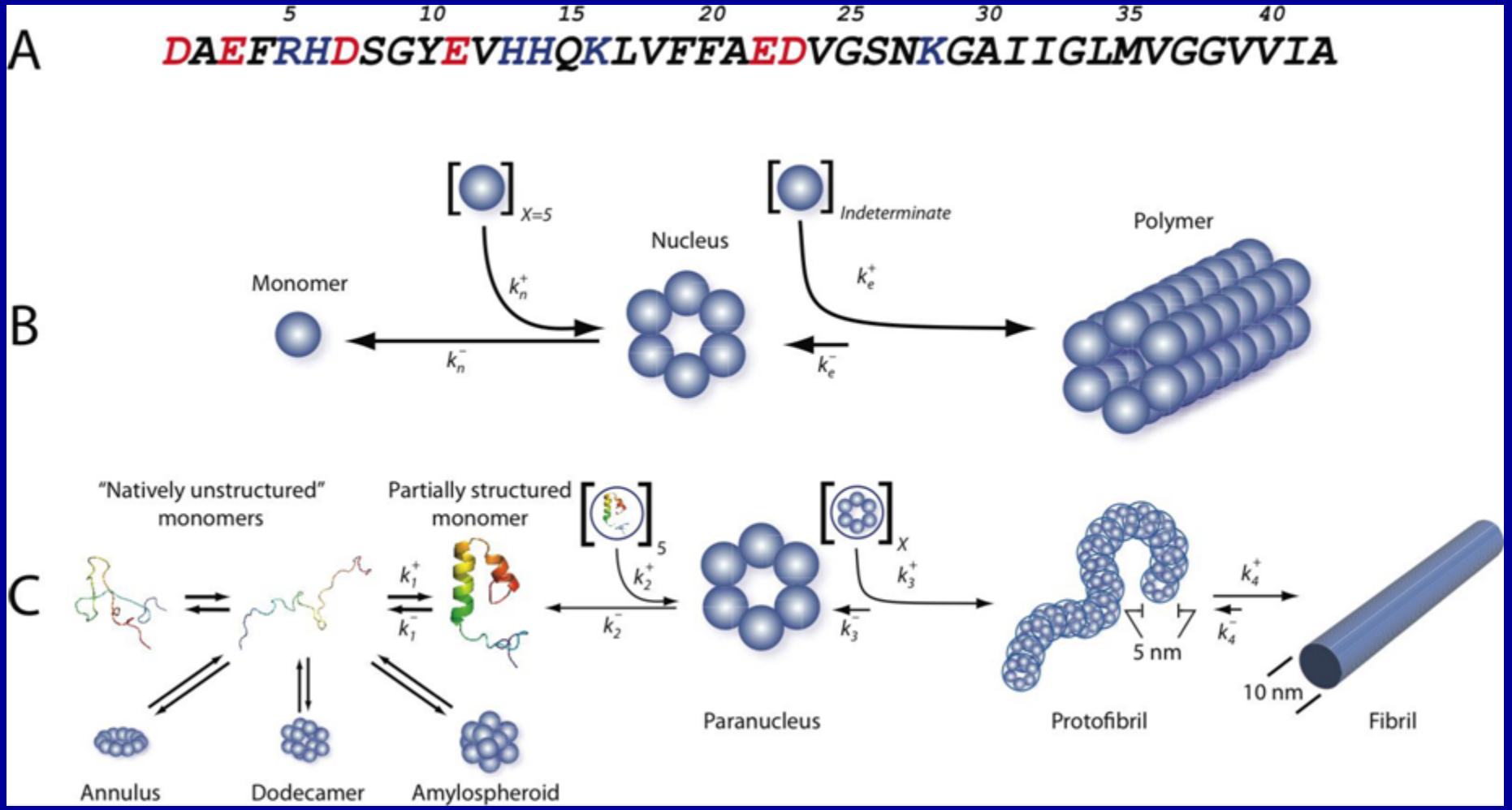


Some non-amyloid staining.

May interfere with amyloid formation.

Frid et al. Brain Res Review 2006

Aβ assembly into amyloid



Roychaudhuri et al (2008) Amyloid β-protein assembly and Alzheimer's disease. J. Biol. Chem., *in press.*

Amyloid-forming proteins

CNS

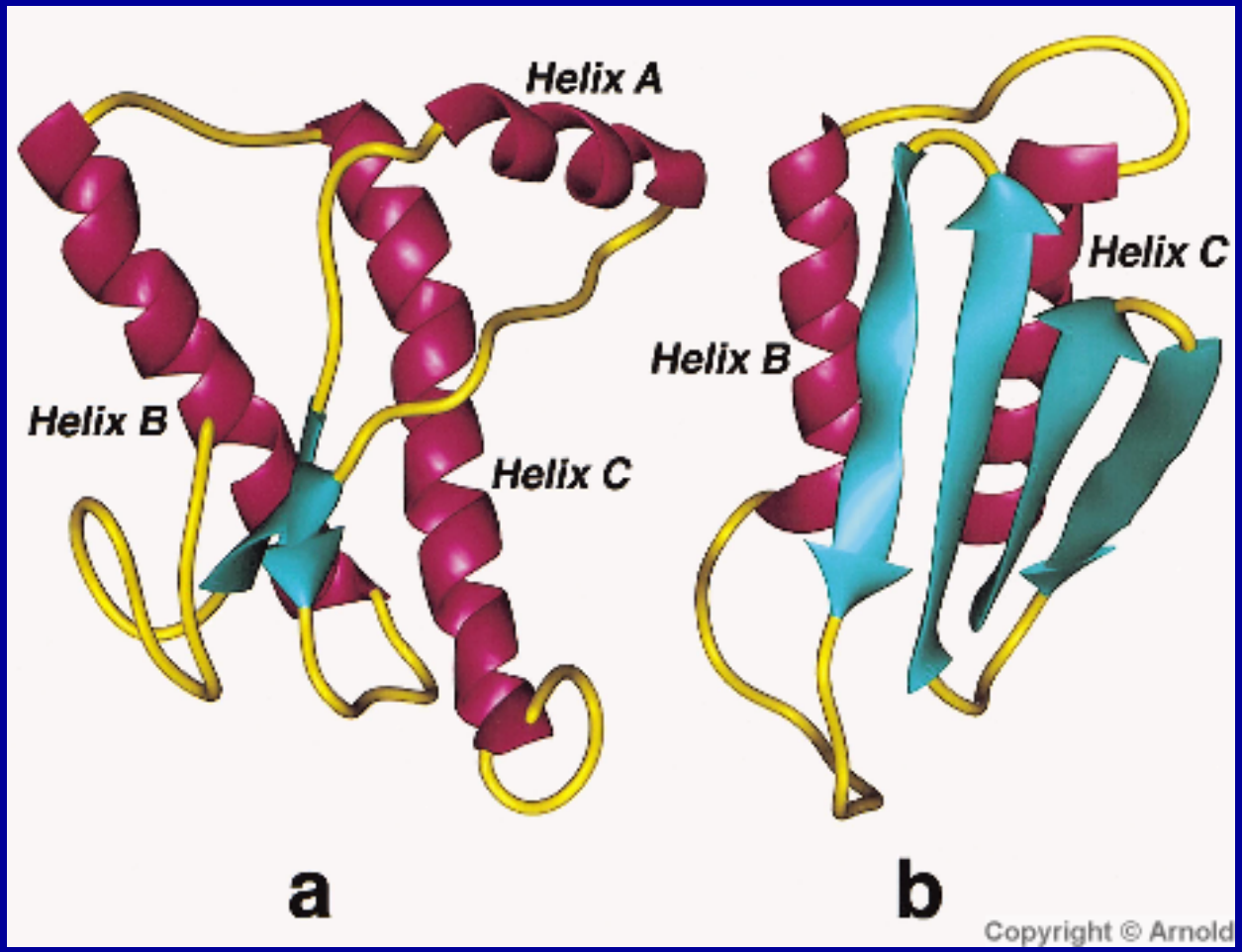
- Aβ
  - Plaques
  - Blood vessels
- tau
- α-synuclein (Parkinson's)
- polyQ (Huntington's)
- Prion protein
- Cystatin C
- Abri/ADan

Periphery

- Transthyretin
- Serum amyloid A
- Immunoglobulin light chain
- Islet amyloid polypeptide
- Lysozyme
- Gelsolin
- Lactoferrin
- β2-microglobulin
- ApoAI

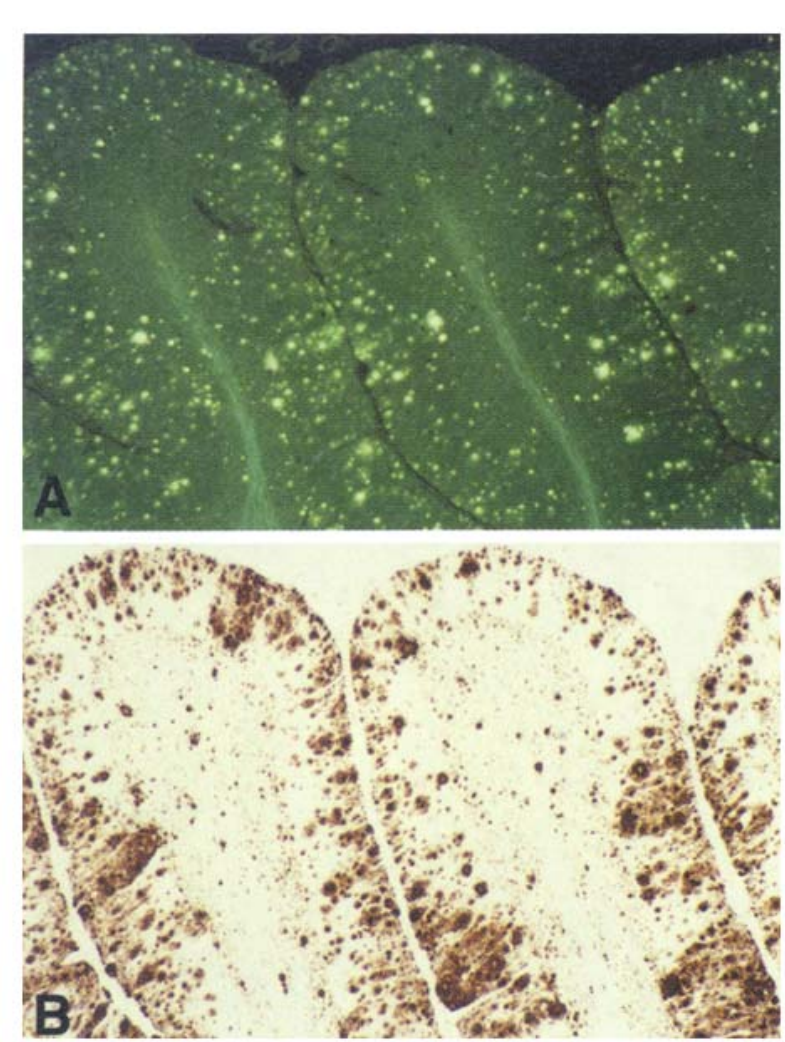
Prion protein

normal folding amyloid

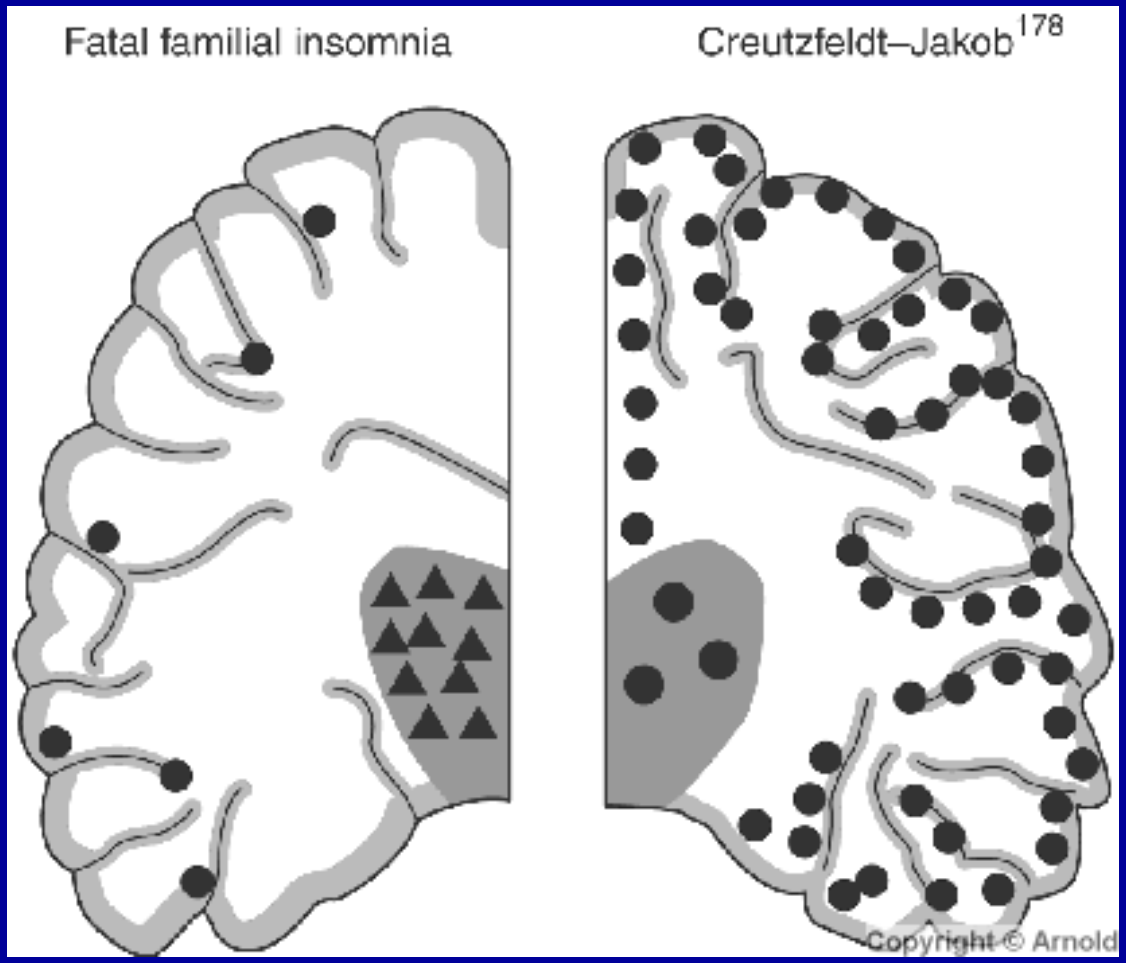


β sheet

Prion protein in cerebellum



Distribution of prion protein in two diseases



Conclusions

- Alzheimer's disease is characterized neuropathologically by plaques (made up of Aβ) and tangles (made up of tau).
- Accumulation of Aβ is a primary event in Alzheimer's disease.
- Aβ plaques can be detected by amyloid binding molecules.
- Other proteins also form amyloids.