

AMYLOIDOSIS - I

DEFINITION, PHYSICAL AND CHEMICAL PROPERTIES OF AMYLOID

Dr.V.Shanthi

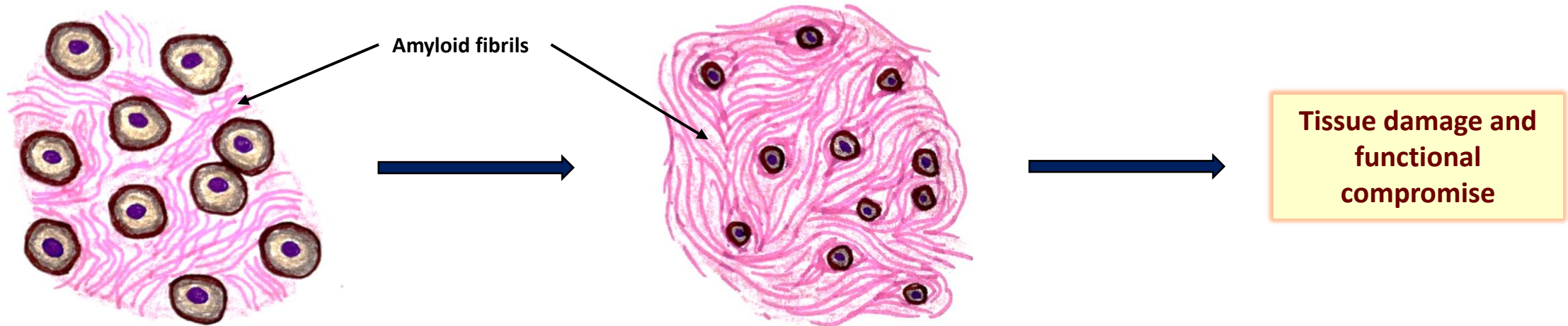
Associate professor, pathology

Sri Venkateswara Institute of Medical Sciences, Tirupathi



AMYLOIDOSIS

Definition - Amyloidosis is a heterogeneous acquired or hereditary disease that results from the predominantly extracellular deposition of abnormal fibrillar protein in various tissues



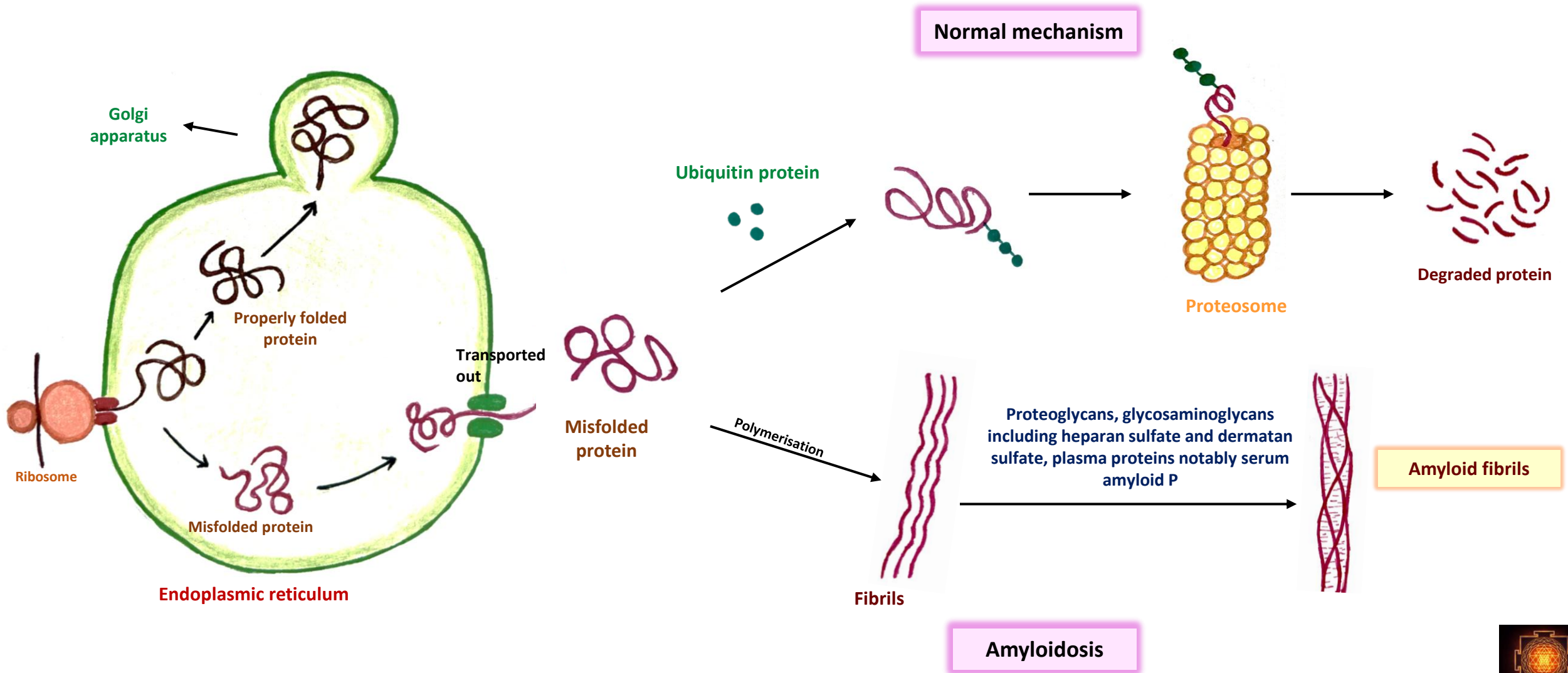
Extracellular deposition of abnormal fibrillar protein

With progressive accumulation, it encroaches on and produces pressure atrophy of adjacent cells



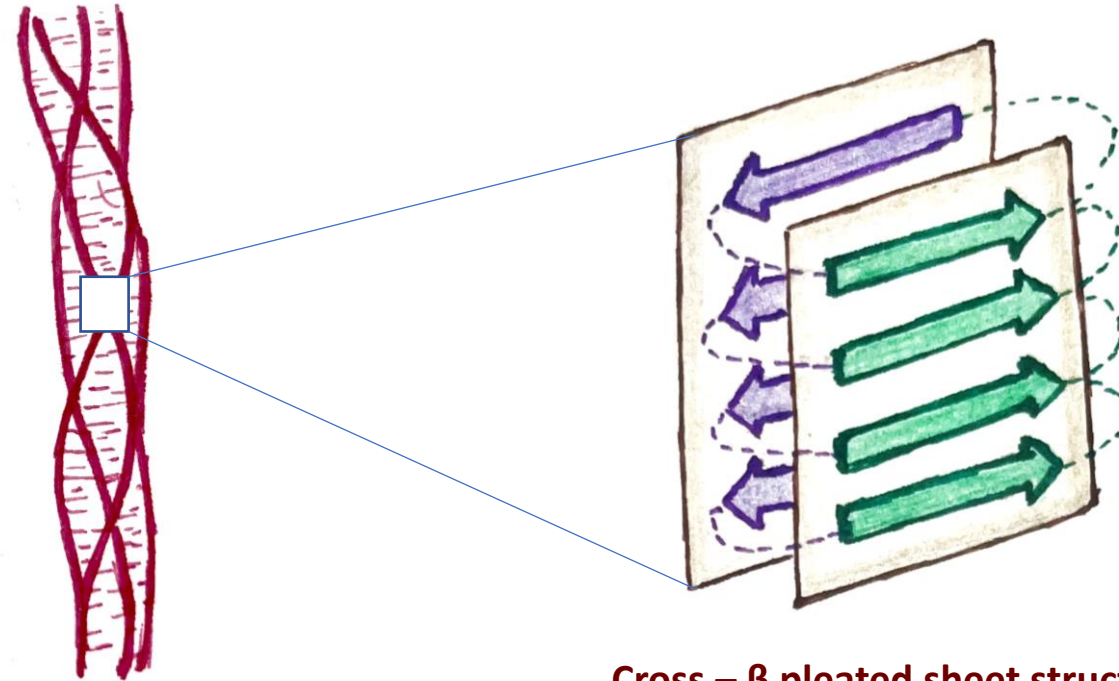
AMYLOIDOSIS

Abnormal fibrillary protein is produced by aggregation of misfolded protein



AMYLOIDOSIS

- Abnormal protein folding leads to a conformational change into a **cross β -pleated sheet secondary structure** which makes the protein hydrophobic, non-functional, insoluble and resistant to degradation



Cross – β pleated sheet structure



AMYLOIDOSIS

HISTORY

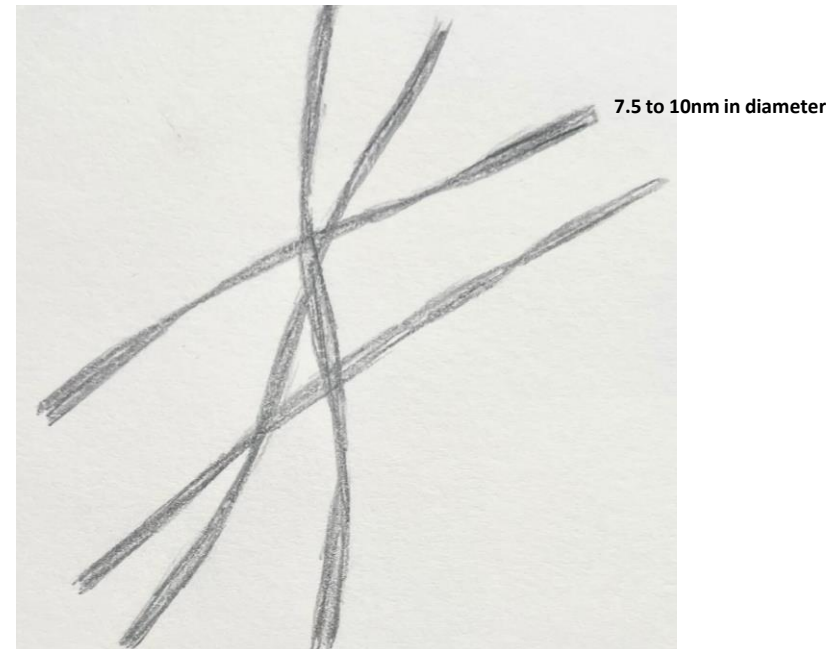
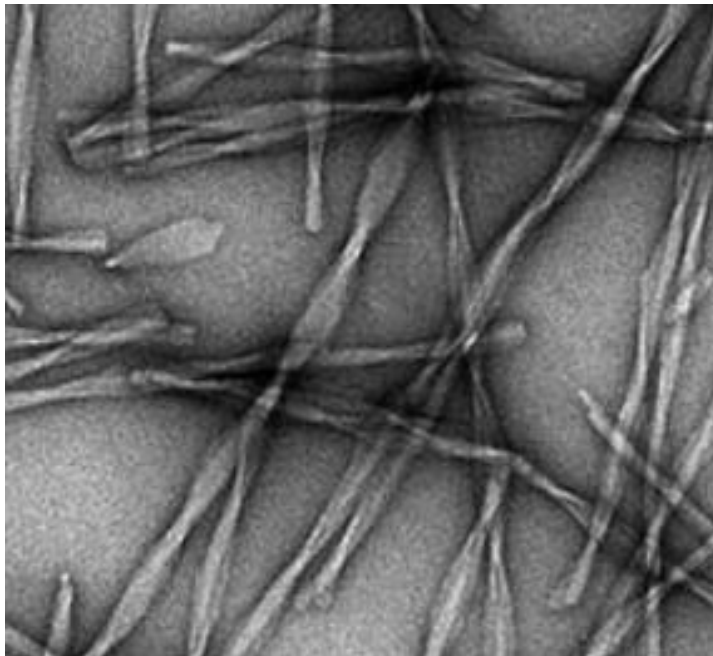
- Presence of abundant charged sugar groups in these adsorbed proteins give the deposits staining characteristics that resemble starch. Hence named as amyloid.
- Derived from **Greek word “Amylon”** and **“Amylum” in latin** – which means cellulose or starch like
- First described by **Rokitansky** in **1842**
- Term **Amyloidosis** was first used by **Rudolf Virchow** in **1854** based on color produced by staining with crude iodine
- Later it was recognized as protein by **Freidreich and kekule** in **1859**



AMYLOIDOSIS

PHYSICAL NATURE OF AMYLOID

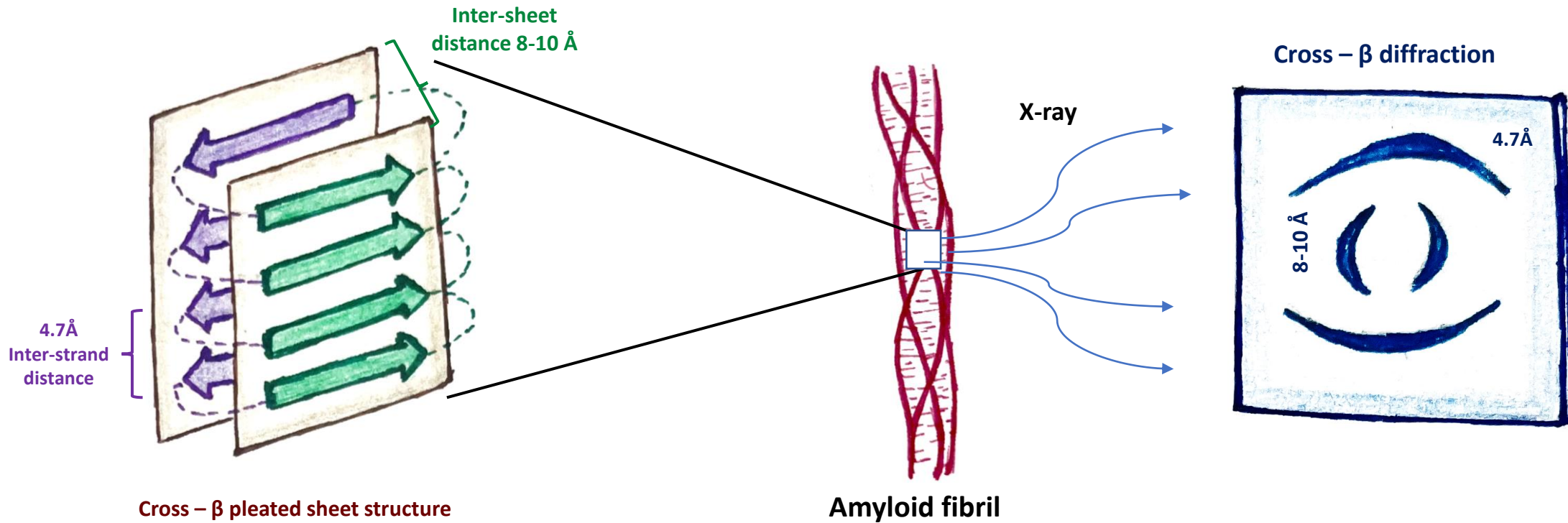
Electron microscopy - irrespective of type of amyloid, fibrils consist of continuous, non-branching fibrils with a diameter of approximately 7.5 to 10nm



AMYLOIDOSIS

PHYSICAL NATURE OF AMYLOID

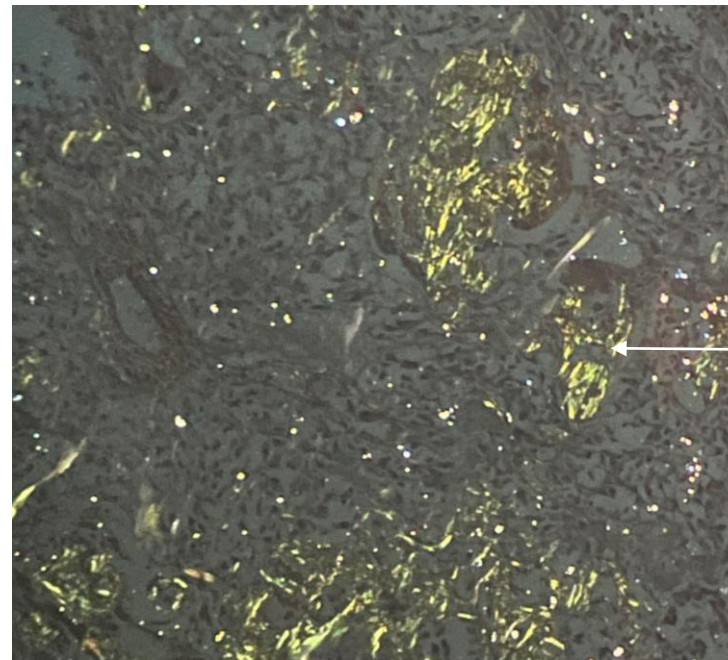
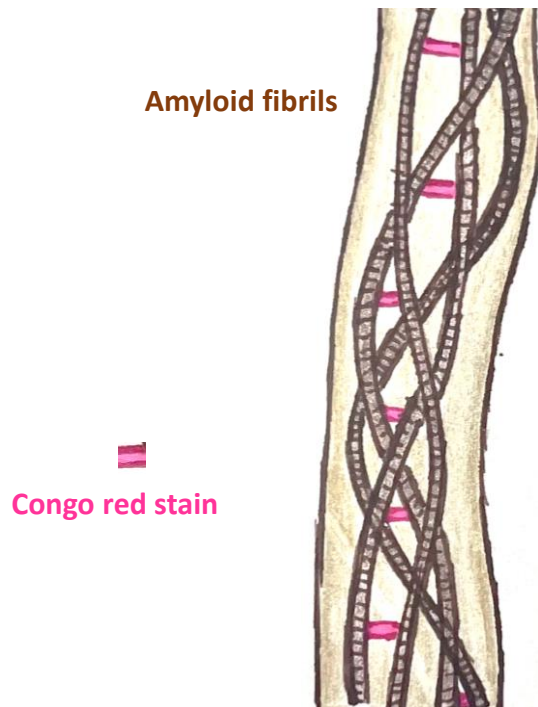
X-ray crystallography and infrared spectroscopy demonstrates a characteristic cross- β pleated sheet conformation



AMYLOIDOSIS

PHYSICAL NATURE OF AMYLOID

- Cross- β pleated sheet conformation of amyloid is responsible for the distinctive **Congo red staining** which gives pink red color on light microscopy and **apple green birefringence** on polarized microscopy

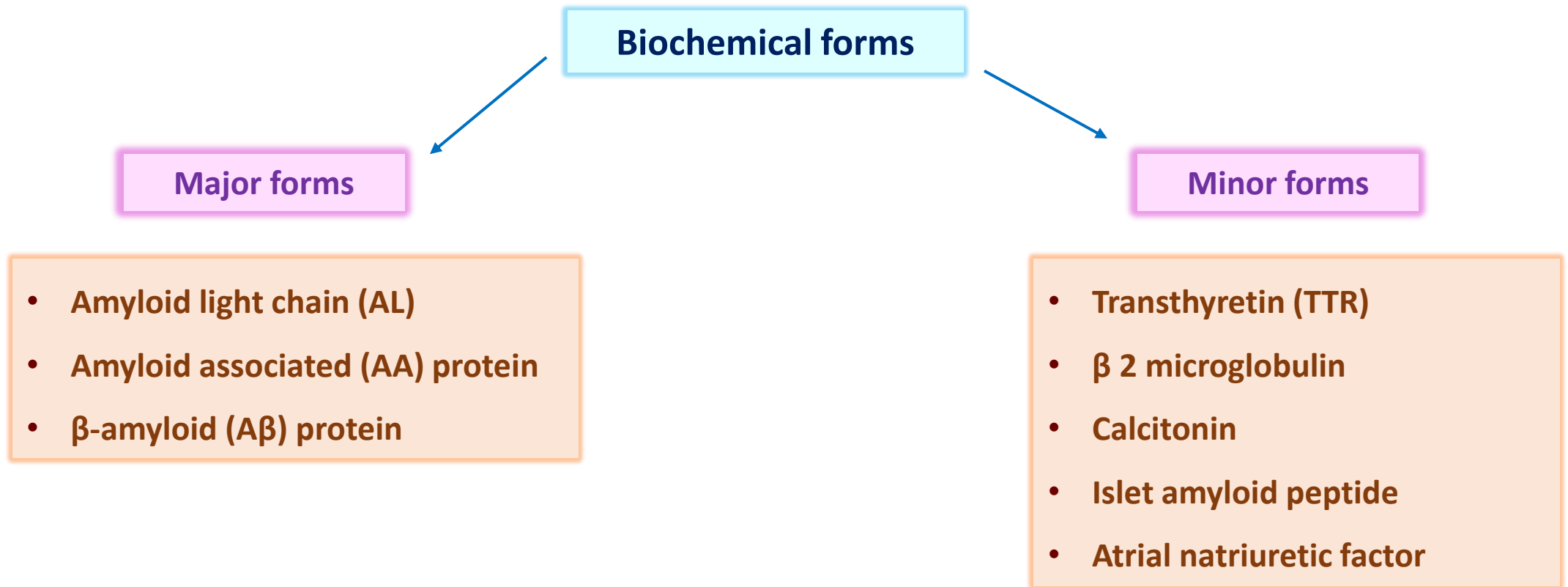


Apple green birefringence on polarized microscopy



BIOCHEMICAL PROPERTIES OF AMYLOID

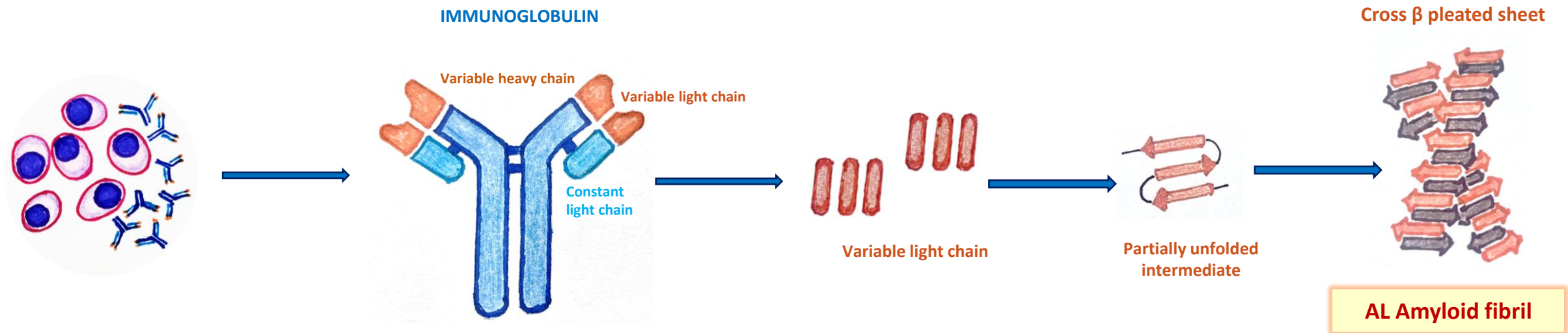
Amyloid is not a single chemical entity but contains 20 different proteins which aggregate to form amyloid



BIOCHEMICAL PROPERTIES OF AMYLOID

Amyloid light chain (AL)

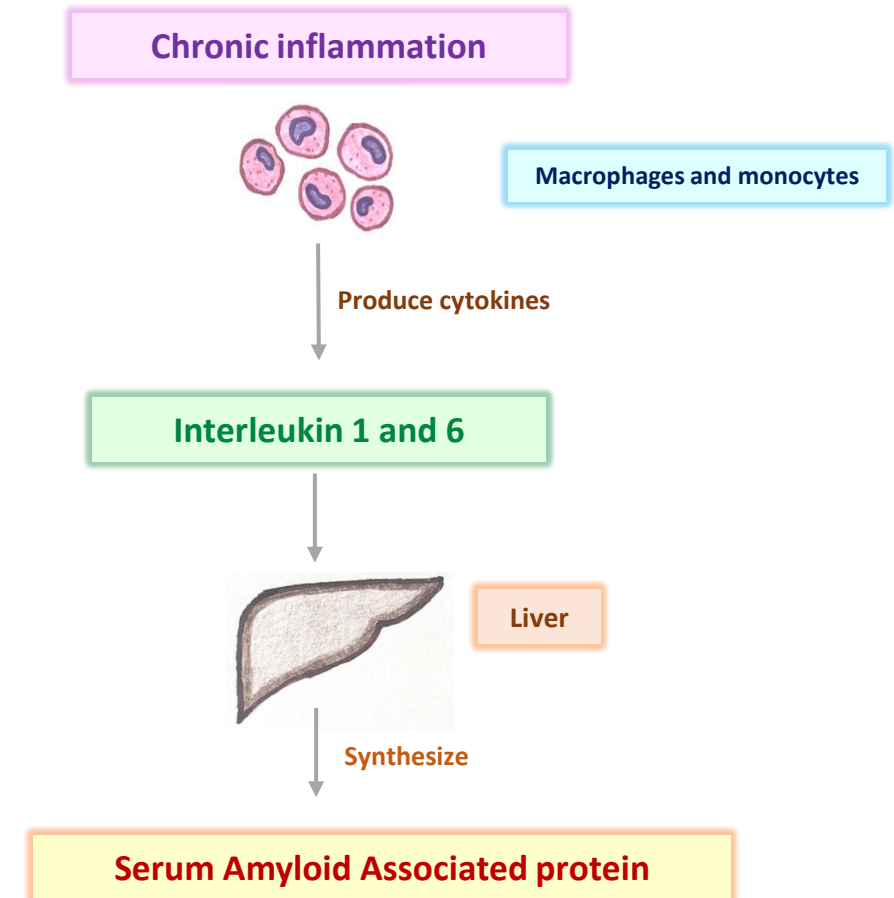
- **Precursor protein** - complete immunoglobulin light chain, amino terminal fragment of light chain or both
- Most of the AL protein analyzed are composed of λ light chains or their fragments
- **Condition with AL protein deposition** - plasma cells tumors (Excess of light chains are produced by tumor cells)



BIOCHEMICAL PROPERTIES OF AMYLOID

Amyloid associated (AA) protein

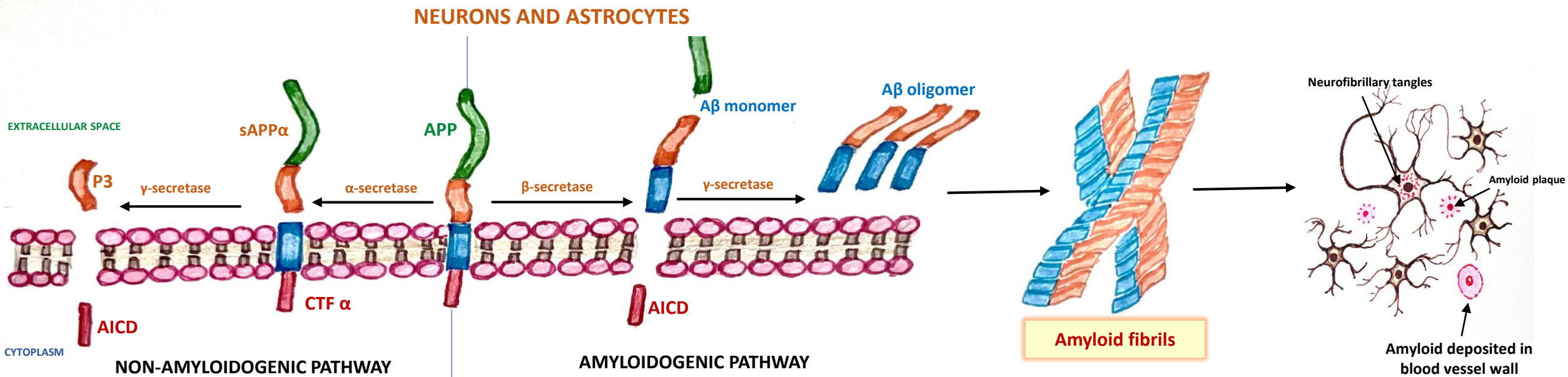
- Precursor protein- SAA (Serum Amyloid Associated) protein (non-Ig protein)
- Source of SAA- liver produced as acute phase protein in chronic inflammation
- Proteolysis of a large precursor protein called SAA (Serum Amyloid Associated) protein, produces amyloid associated protein
- Condition with AA protein deposition – chronic inflammation



BIOCHEMICAL PROPERTIES OF AMYLOID

β - Amyloid (A β) protein

- **Precursor protein** - transmembrane glycoprotein in neurons and astrocytes called Amyloid Associated protein (AAP)
- Derived by proteolysis of much larger transmembrane glycoprotein called amyloid precursor protein
- **Condition with A β protein deposition – Alzheimers disease** (It constitutes the core of cerebral plaques as well as deposited in walls of cerebral blood vessels)



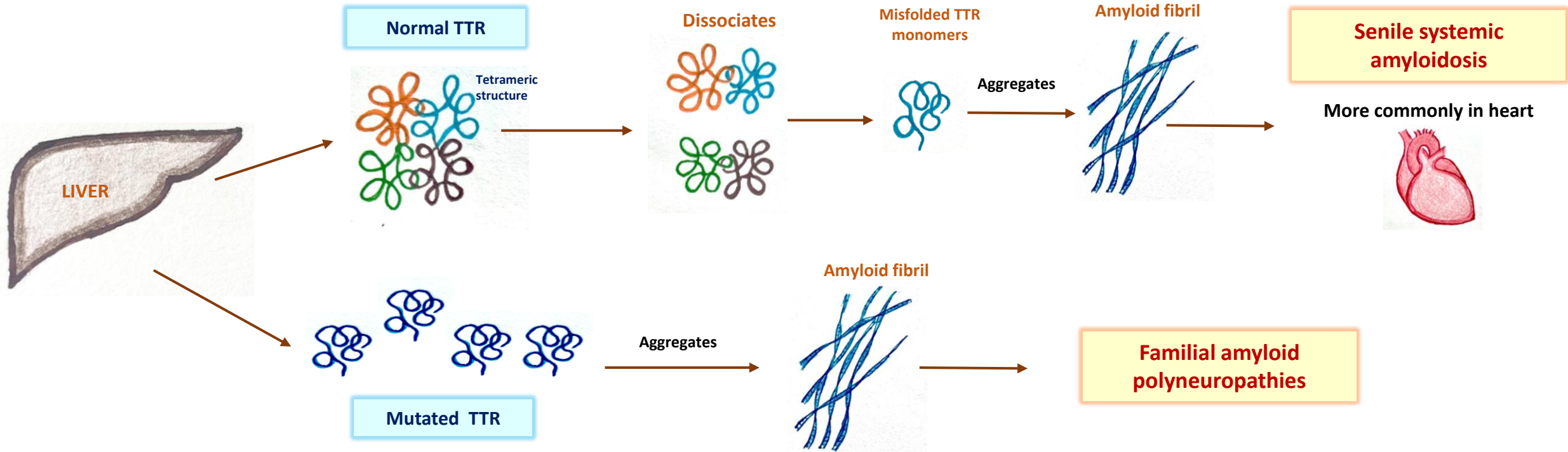
APP- Amyloid precursor protein; CTF-C-terminal fragment; sAPP α - soluble APP α ; AICD- APP intracellular domain; A β – β Amyloid



BIOCHEMICAL PROPERTIES OF AMYLOID

Amyloid Transthyretin (ATTR)

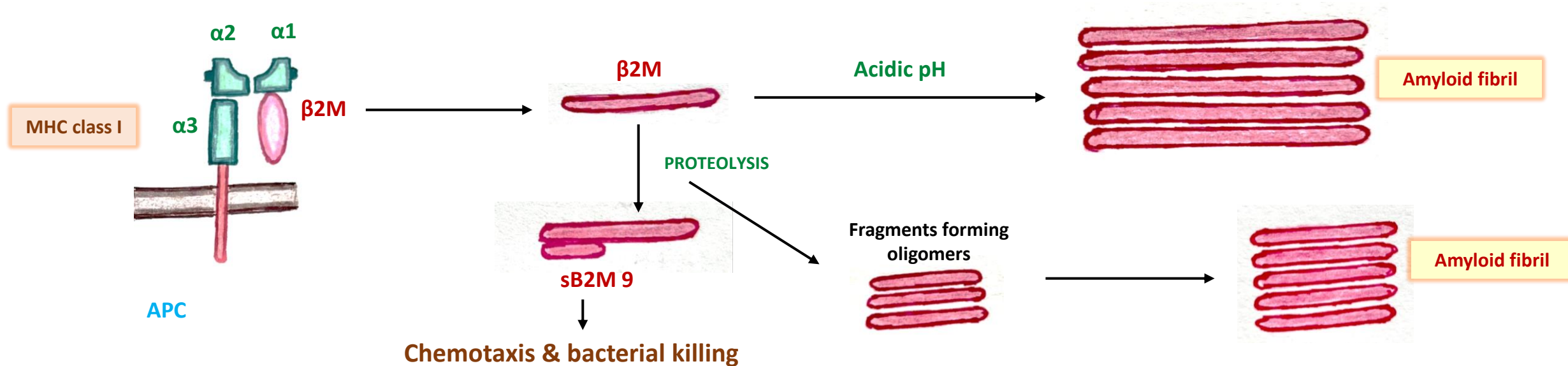
- **Component** – Transthyretin - Normal protein that binds and transports thyroxine and retinol
- **Two forms that are deposited are**



BIOCHEMICAL PROPERTIES OF AMYLOID

Amyloid β 2 microglobulin

- Precursor molecule - component of MHC class I molecule
- This form of Amyloid β_2 microglobulin is deposited in and around the joints or soft tissues of patients on long term dialysis
- During dialysis β_2 microglobulin cannot be filtered through the membrane. Hence the serum levels of this protein increases, and it gets deposited in various tissues (recent filters are able to remove it hence incidence has reduced)



BIOCHEMICAL PROPERTIES OF AMYLOID

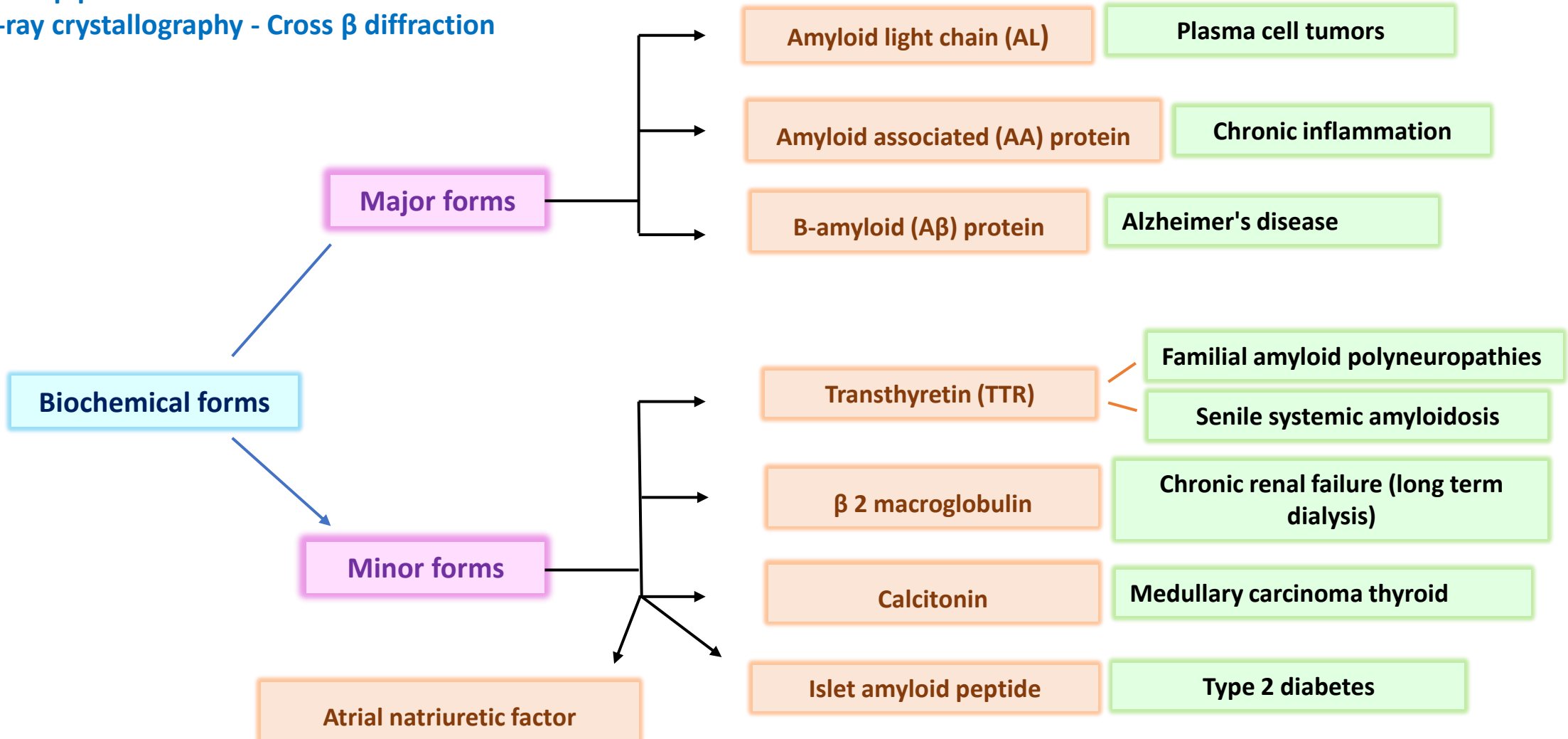
- **Other rare forms include**
 - **Calcitonin** – medullary carcinoma thyroid
 - **Islet amyloid peptide** - Pancreatic islet tumor and type 2 diabetes
 - **Atrial natriuretic factor**
 - **Serum Amyloid P component**
 - **Apo-lipoprotein – E**
 - **Sulfated glycosaminoglycans**



DEFINITION - accumulation of misfolded protein fibrils mostly in extracellular space

PHYSICAL NATURE –

- EM - continuous, non-branching fibrils(7.5 – 10nm)
- Cross β pleated structure
- X-ray crystallography - Cross β diffraction



A decorative border of watercolor-style flowers, including pink and red lilies and peonies, with green leaves, framing the central text.

THANK YOU

