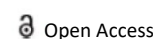




OPINION ARTICLE



Note on Structure and Formation of Amyloids

Maya Bhut*

Department of Pathology, Wollega University, Nekemte, Ethiopia

ARTICLE HISTORY

Received: 02-Mar-2022, Manuscript No. EJMJIH-22-55339;
Editor assigned: 04-Mar-2022, PreQC No. EJMJIH-22-55339 (PQ);
Reviewed: 18-Mar-2022, QC No. EJMJIH-22-55339;
Revised: 23-Mar-2022, Manuscript No. EJMJIH-22-55339 (R);
Published: 30-Mar-2022.

Description

Amyloid is a protein aggregate characterized by a fibrous morphology 7 nm -13 nm in diameter; a secondary structure of beta sheets (β sheets) (known as cross β), and the ability to stain with certain dyes such as congo red. In the human body, amyloid is associated with the development of various diseases. Pathogenic amyloid causes previously healthy proteins to lose their normal structure and physiological function (misfolding), forming fibrous deposits in the amyloid plaques around cells, resulting in tissue and organ health. Amyloids may also have normal biological functions; for example, in the formation of fimbriae in some genera of bacteria, transmission of epigenetic traits in fungi, as well as pigment deposition and hormone release in humans.

Structure

Amyloids are formed of long unbranched fibers that are characterized by an extended beta-sheet secondary structure in which individual beta strands (β -strands) are arranged in an orientation perpendicular to the long axis of the fiber. Such a structure is known as cross- β structure. Each individual fiber may be 7 nm–13 nm in width and a few micrometres in length. The presence of a fibrillar morphology with the expected diameter; detected using Transmission Electron Microscopy (TEM) or Atomic Force Microscopy (AFM), the presence of a cross-secondary structure, determined using circular dichroism, FTIR, and solid-state nuclear magnetic resonance are the main hallmarks recognised by different disciplines to classify protein aggregates as amyloid (ssNMR), X-ray crystallography, or X-ray fiber diffraction (commonly referred to as the “gold-standard” test for determining whether a structure contains cross-fibers) and the capacity to stain with certain dyes as Congo red, thioflavin T, or thioflavin S.

The word “cross” was coined after two sets of diffraction

lines, one longitudinal and the other transverse formed a distinctive “cross” pattern. At 4.7 and 10 ngstroms (0.47 nm and 1.0 nm), respectively, two distinct scattering diffraction signals are formed, corresponding to the inter-strand and stacking distances in beta sheets. The beta sheet “stacks” are small and span the width of the amyloid fibril; the amyloid fibril’s length is made up of aligned -strands. The cross-pattern is regarded as an amyloid structural diagnostic mark.

Formation

Amyloid is made up of hundreds to thousands of monomeric peptides or proteins that are polymerized into long strands. Amyloid formation includes a lag phase (also known as nucleation phase), an exponential phase (also known as growth phase), and a plateau phase (also known as saturation phase). When the number of fibrils is plotted against time, a sigmoidal time pattern emerges, indicating the three separate phases.

Individual unfolded or partially unfolded polypeptide chains (monomers) transform into a nucleus (monomer or oligomer) *via* a thermodynamically unfavourable process that begins early in the lag phase in the simplest model of ‘nucleated polymerization’ (indicated by red arrows in the image below).

Fibrils form as a result of the addition of monomers in the exponential growth of these nuclei. Later on, a new model called ‘nucleated conformational conversion and it was introduced to fit various experimental findings: Monomers frequently transform into misfolded and extremely disordered oligomers that are separate from nuclei. Only later will these aggregates reorganise structurally into nuclei, on which more disorganised oligomers will add and reorganise through a templating or induced-fit mechanism, eventually creating fibrils (this ‘nucleated conformational conversion’ hypothesis).