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Editorial

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Amyloids: New Nano Biomaterials, Their Technological Applications and Structural Studies

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In recent years, amyloids have attracted a lot of attention due to their involvement in degenerative disease, as Alzheimer's and Parkinson's diseases [1]. Functional amyloids can stabilize bacterial biofilms, serve as scaffolding for melanin formation, store peptide hormones, and promote interactions among proteins in subcellular condensates [2, 3]. Moreover, non-human functional amyloids may play a role in human disease by facilitating bacterial pathogenicity [4] and promoting the aggregation of human amyloidogenic proteins [5].

Closely related to protein misfolding, amyloid nanofibrils have particular properties that can suggest their application as new nano biomaterials. These biomolecules possess numerous advantageous features and are readily amenable to functionalization. Amyloid fibrils can serve as building blocks for natural and artificial functional materials [6]. They can be applied in several technological field, including but not restricted to, pharmaceuticals, cosmetics, environmental conservation and food sector [7]. The potential uses of amyloid supramolecular assemblages beyond those of synthetic polymers, as the building blocks might confer biological functions alongside mechanical qualities or catalytic activity [8, 9]. The application prospects are of considerable economic and social relevance.

One of amyloids perspective technological application is biocatalysis. Amyloid-like protein nanofibers indeed have enzymatic catalytic functions [10, 11], e.g., glucagon amyloid fibrils may function as catalysts in several biological processes, such as dephosphorylation, lipid and ester hydrolysis [12]. Moreover, some synthetic amyloid proteins have demonstrated catalytic activity and advantages over natural enzymes in terms of stability and reusability. Recently, it was found that amyloids provide distinctive selectivity in enzymatic operations. For example, the azo-stilbene derivative, an amyloid-recognition motif, is integrated into the substrate, enabling the amyloid composed of Bz-Phe-Phe-Ala-Ala-Leu-Leu-NH_2 (BL7) to protect the substrates from the encroaching enzyme [13].

The integration of mechanical and catalytic capabilities of amyloid fibrils facilitates the advancement of novel nano biomaterials [14-16]. Amyloid fibrils can be engineered for next-generation sustainable applications with minimal environmental impact, including: (i) efficient water purification [17, 18]; (ii) adsorbents for the heavy metals removal from wastewater [19]; and (iii) the development of materials with specific applications based on the established amyloid atomic structure, such as capturing carbon dioxide from flue gas, thereby addressing the global issue of excessive anthropogenic carbon dioxide [20].

Since the interest in amyloids functions and applications is constantly increasing, detailed structural studies of amyloid fibrils have come to the forefront [21]. Among others, several advanced methods are suitable for these investigations. Atomic force microscopy (AFM) can provide high-resolution imaging, offering nanoscale lateral resolution and sub-nanometer vertical resolution of amyloid plaques. Furthermore, post-imaging analysis can be employed to extract metrics such as the nanoscale roughness of amyloid networks [22]. AFM tech-

niques facilitate *in vitro* examination of hierarchical organization, enabling manipulation of individual fibrils or protofilaments, as well as the mechanical characterization of their properties [23, 24]. Single-molecule fluorescence microscopy enables the ultrasensitive detection and viewing of individual amyloid fibrils and oligomers by a technique referred to as single-aggregate visualization by enhancement [25, 26].

The capacity to resolve the structure of amyloids has significantly enhanced due to current technological developments, including last generation of synchrotron radiation. In particular, enhanced X-ray beams of 4th generation synchrotrons, along with new beamlines, enable significant gain in resolution. Various modern approaches now illuminate the atomic-level structure of amyloids, uncovering a range of polymorphic configurations that typically conform to the cross-β amyloid pattern. Next, cryo-electron microscopy with its rapid progress in the recent years has appeared valid method for the amyloid structural studies. Both nano-diffraction (X-ray) and cryo-electron microscopy in micro-electron diffraction mode were successfully used to study amyloids fibrils, including those appearing in thin protein multilayers [27-29].

The integration of structural biology data from many approaches and experimental techniques provides new insights into the atomic-level resolution of fibrillar structures formed by individual protein subunits [30].

It is worth noticing not only atomic structure but also comprehending the dynamic of the assembly mechanism of amyloids during fibril production is crucial for devising viable therapeutic approaches and nanotechnological application. For this reason, high-speed real-time atomic force microscopy was utilized to examine the formation of Aβ fibrils at the single-molecule level, concentrating on their interaction with anti-Aβ antibodies [31]. The results revealed that fibril growth comprises alternating phases of elongation and stasis, governed by the sequential incorporation of Aβ monomers into protofilaments. It was discovered that antibody 4396C can selectively attaches to the fibril termini in the stopped state and impede fibril elongation. This offers an enhanced comprehension of fibril assembly through real-time observation of fibril growth and antibody interactions, coupled with molecular simulation, and proposes innovative techniques for Alzheimer's therapy focused on reducing fibril elongation [31].

In conclusion, the research area of amyloids appears now rather waste both for basic life science and for various technological application. The advanced structural methods potentially allow us to achieve the full understanding of mechanisms of amyloid fibrillization, crucial both for diagnostic, therapy and application in nanotechnology.

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