Contribution ID: **6** Type: **Contributed Talk (≈20 minutes)**

Nanospectroscopy Study of Amyloid Aggregates Interacting with RNA

Studying structural changes associated with protein aggregation is challenging and often requires a combination of experimental techniques to capture insights at the molecular level across different scales, from nanometers to microns. Studying this process becomes even more complex when aggregation occurs in the presence of molecular co-factors, nucleic acids among them, and when the resulting aggregates exhibit a high structural and morphological polymorphism. Here, we investigate the potential structural effects of RNA on amyloid protein fibrils. To achieve this, infrared (IR) spectroscopy, known for its high sensitivity to structural changes in the cross-β architecture of protein aggregates, was employed. In particular, IR spectroscopic analysis was performed by combining Fourier transform infrared (FTIR) microspectroscopy (micro-FTIR) and IR nanospectroscopy approaches relying on the use of an atomic force microscope (AFM) to probe the supramolecular architecture of aggregates at the nanoscale. Co-incubation with RNA was shown to alter the α-synuclein (α-syn) fibril architecture by promoting the formation of more rigid fibrils and to reduce the structural polymorphism within the fibril population. Additionally, AFM morphological characterization on individual α-syn fibrils demonstrated that RNA modifies the morphological properties of fibrils, reducing their diameter and increasing their persistence length. Remarkably, IR nanospectroscopy experiments demonstrated that RNA had a more pronounced impact on the supramolecular architecture of α-syn ordered fibrils compared to less ordered amyloid aggregates, suggesting that RNA has distinct structural effects depending on the aggregate architecture. This finding suggests that RNA may have varying interaction affinities for different types of aggregates, leading to distinct modifications in their supramolecular architectures depending on their structural organization.

Scholarship elegibility

no

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