Intervening in functional amyloid assembly/disassembly to overcome biofilm-driven microbial resistance

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Abstract

Introduction: Functional amyloids, such as the major subunit CsgA of curli fibers produced by *the Escherichia coli*, exemplify beneficial amyloidogenesis essential for biofilm formation and microbial survival. These extracellular β-sheet-rich fibrils reinforce biofilm structure, increasing resistance to antimicrobials and immune defenses. Modulating the molecular processes of CsgA assembly and disassembly is vital to developing novel anti-biofilm strategies addressing antimicrobial resistance (AMR). **Objectives:** This study aims to (1) identify small molecules that modulate CsgA amyloidogenesis; (2) quantitatively analyze their effects on fibrillation kinetics; and (3) elucidate compound-induced structural changes to guide rational drug design. **Methods:** Recombinant CsgA was expressed in *E. coli* BL21 using a pET-28 vector without affinity tags and purified under denaturing conditions. Amyloid formation kinetics were monitored by Thioflavin T (ThT) fluorescence. Circular dichroism (CD) spectroscopy tracked secondary structure transitions, confirming β-sheet enrichment during fibril formation. **Results and Discussion:** Preliminary results show reproducible ThT kinetics typical of CsgA amyloid assembly. CD spectra indicate progressive β-sheet increase aligning with aggregation phases. These findings provide a solid foundation for screening amyloid modulators and investigating their mechanistic impact on fibril architecture. **Conclusion:** This integrative biophysical approach advances understanding of functional amyloid assembly and offers promising routes for targeted disruption of biofilms to combat AMR. **Funding:** Supported by doctoral scholarships and grants from São Paulo Research Foundation (FAPESP; Proc. 2022/06006-0) and CAPES.

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Programme

10:30 to 11:15 on 11/05/2025
Tucuns/Tartaruga

Institutions

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Track

- Functional protein aggregation in yeast and mammalian systems

Keywords

Functional amyloids

Protein aggregation

Biofilm resistance

CsgA fibrillation

Amyloid assembly and disassembly