O-15.3 Short talk

Molecular structure and self-assembly in functional amyloid

Daniel Otzen [1]

[1] Aarhus University, Aarhus, Denmark

Functional amyloid represents a benign way to use the cross-β fold, otherwise associated with neurodegenerative diseases such as Parkinson's and Alzheimer's. The most well-known examples of FuA are the bacterial proteins CsgA and FapC from E. coli and Pseudomonas, respectively. The structure of CsgA, solved by a combination of computational and experimental techniques, reveals a simple repetitive β-solenoid. We have recently solved the cryo-EM structure of FapC which reveals a more complex structure with a Greek Key motif and several layers of inner and outer cores, and will present our latest results underpinning this structure by mutational analysis. Both CsgA and FapC show a remarkable ability to cross-seed pathological amyloid such as Aβ and α-synuclein; Aβ in turn can inhibit inhibition of functional amyloid, hinting at a protective mechanism. Chaperones which target pathological amyloid also inhibit functional amyloid formation, though by different mechanisms; functional amyloid is typically blocked at the monomer/nucleation level and pathological amyloid at later stages. We will also present evidence that the bacterial microbiome has a number of potent amyloid-blockers whose effects extend to include both functional and pathological amyloid. All this suggests a number of common features linking different amyloid classes, both at the molecular and physiological level.