Self-Assembled Peptide Nanostructures: A New Frontier in Organic Nanotechnology

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The formation of ordered amyloid fibrils is the hallmark of several diseases of unrelated origin. In spite of its grave clinical consequence, the mechanism of amyloid formation is not fully understood. We have suggested, based on experimental and bioinformatic analysis, that aromatic interactions may provide energetic contribution as well as order and directionality in the molecular-recognition and self-association processes that lead to the formation of these assemblies. This is in line with the well-known central role of aromatic-stacking interactions in self-assembly processes.

Our works on the mechanism of aromatic peptide self-assembly, lead to the discovery that the diphenylalanine recognition motif of the Alzheimer's beta-amyloid polypeptide self-assembles into ordered peptide nanotubes with a remarkable persistence length. Other aromatic homodipeptides could self-assemble in nano-spheres, nano-plates, nano-fibrils and hydrogels with nano-scale order. We demonstrated that the peptide nanostructures have unique chemical, physical and mechanical properties including ultra-rigidity as aromatic polyamides. We also demonstrated the ability to use these peptide nanostructures as casting mold for the fabrication of metallic nano-wires and coaxial nano-cables. The application of the nanostructures was demonstrated in various fields including electrochemical biosensors, tissue engineering, and molecular imaging. Finally, we had developed ways for depositing of the peptide nanostructures and their organization. We had use inkjet technology as well as vapour deposition methods to coat surface and from the peptide "nano-forests".

We are currently using this notion, as well as a novel β-breakage strategy that was developed in our laboratory, for the development of novel inhibitors of the process of amyloid formation by utilizing hetero-aromatic interactions. Our lead compound is a novel chemical entity that inhibits the formation of β-amyloid oligomers *in vitro* and protects cultured cell and isolated cortical neurons from cytotoxic effect of β-amyloid aggregates. Chronic administration of the compound was shown safe and significantly effective in preventing memory impairment in this animal model as assayed by Morris Water Maze experiments. Taken together, our hypothesis provides a new approach to understand the self-assembly mechanism that governs amyloid formation and indicates possible ways to control this process.

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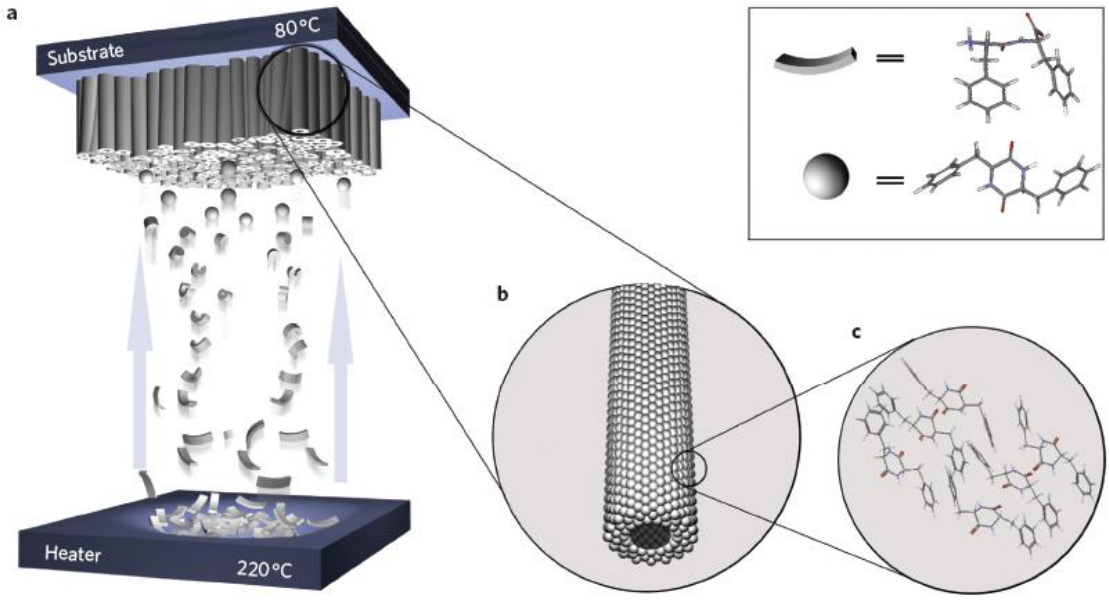

Proposed assembly mechanism for the formation of vertically aligned ADNTs [Taken from Adler-Abramovich et al.(2009) *Nat. Nanotech*. **4**, 849-854].

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