Self-assembly of tripeptides into rigid supramolecular materials

Hema Kuntrapakam, Elma N. Estepa, Avishek Dey, Crisol A. Ortiz, Rein V. Ulijn*
Advanced Science Research Center, City University of New York

The structural diversity, biocompatibility, and wide range of mechanical properties of protein-based materials have been used for making functional biomaterials with a wide array of biotechnology applications. Typically, such materials are made from self-assembled peptides. Silk and amyloids possess β-sheet structure as a common structural motif. On the other hand, collagen, the most abundant protein in mammals, contains a helical arrangement of molecules. In our group, we are interested in understanding the nature of short peptides and translating the knowledge for understanding the properties of the complex molecules in nature. Among the 8000 tripeptide sequences possible from 20 amino acids, Pro-Phe-Phe (**PFF**) is believed to be the most aggregation-prone tripeptide. The crystals of **PFF** exhibit high mechanical rigidity with Young's modulus value comparable to enamel. The crystal structure of **PFF** shows a helical-like sheet that is stabilized by the hydrophobic interfaces of Phe residues. Here, we aim to study the effect of replacing Phenylalanine residues with tryptophan.

The project is focused on understanding how ultrashort (tri) peptides with different aromatic sequences will impact the self-assembly mechanisms and result in different topologies which in turn alter their rigidity and mechanical strength. The four tripeptides (*Figure A-D*) **PFF**, **PWF**, **PFW** and **PWW** showed a strong aggregation nature and formed crystals with rigid morphology. To gain molecular-level insights, I crystallized these peptides (*Figure F*). The **PFF** results in an aromatic zipper topology wherein all the phenyl units are arranged together to form zippers whereas **PWW** did not exhibit any zipper-like topology. The tryptophan units of a peptide face the proline and peptide backbone of the neighboring peptide. Currently, I am working towards probing the mechanical strength of these peptides using nanoindentation. Thus, the project helps in providing correlation between molecular packing to the mechanical strength of peptides. Moreover, these short peptides could be developed into high-strength functional biomaterials and have high potential for applications such as piezoelectric materials due to their easy and low-cost preparations.

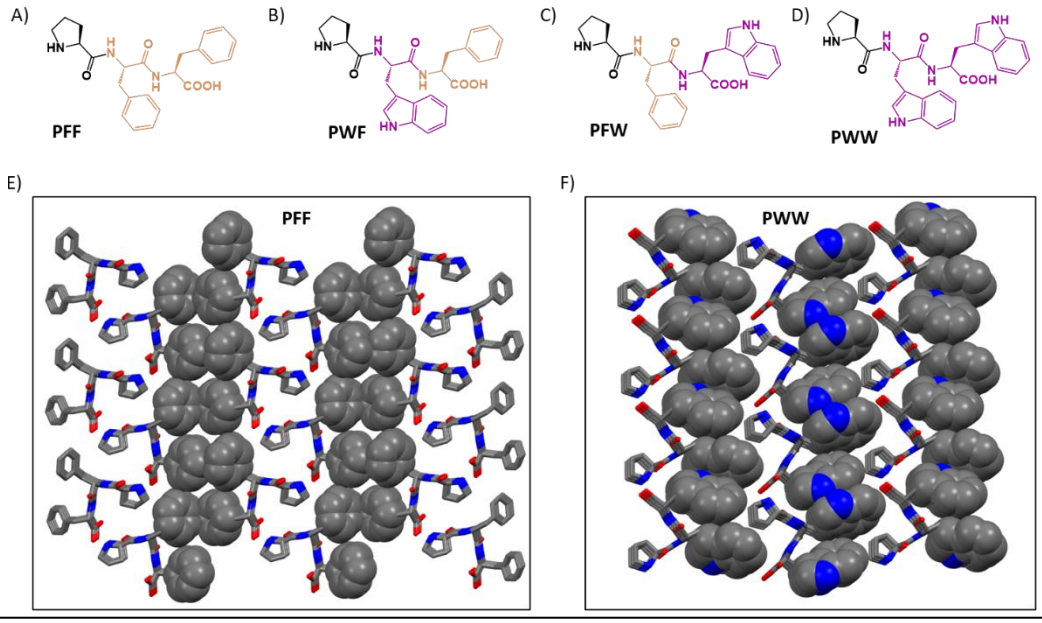

Figure: *A-D) Chemical structures of the tripeptides in the study **PFF**, **PWF**, **PFW** and **PWW** (Abbreviations: **P**-proline, **F**-phenylalanine, **W**-tryptophan); Crystal structures of D) **PFF** and E) **PWW** showing the difference in the arrangement of aromatic side chains. **PFF** shows the formation of aromatic steric zipper topology whereas tryptophan does not form any zippers.*