A Correlative Light-Electron Liquid-Phase Microscopy for Elucidating Mechanism, Dynamics, and Assembly of Dipeptides

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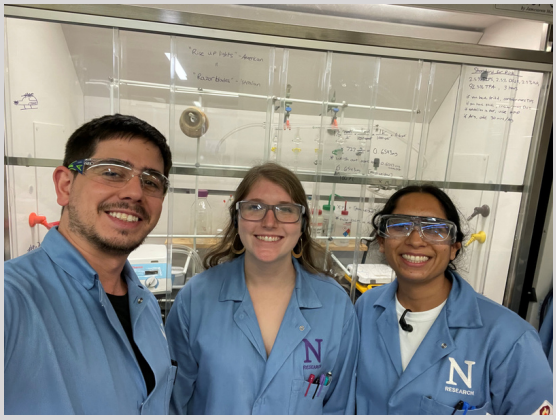

Dan and collaborators in the Gianneschi lab

In nature, supramolecular self-assembly is a key process that extends across multiple length scales in biological systems. The diphenylalanine peptide (FF) is a short self-assembling peptide that forms well-ordered nanotubes. The FF derivatives have been shown to self-assemble into a wide range of morphologies such as tubes, spheres, and gels, with diverse physical properties. These peptides based structures, physical and chemical properties, could be tailored by varying the peptide sequences to obtain different desirable results. However, there is still a gap in our understanding of the relationship and effect of peptide sequence and preparation on the obtained structures properties. In this research our goal was to study the underlying mechanisms involved in the assembly and growing of different peptide based structures while elucidating the results via multiple imaging and characterization platforms. In order to probe these differences in the assembly mechanisms we have performed initial liquid cell transmission electron microscopy (LCTEM) experiments which were possible with the Gianneschi group's cutting-edge expertise in the field, in order to probe the structures assembly and phase transition. LCTEM has the potential to differentiate between different peptides assembly with nanometer spatial resolution and sub-second temporal resolution thus allowing us to quantify the difference in kinetics, molecular motion, diffusion speed, nucleation, growth of the structures. Furthermore, in order to enable the correlation of the LCTEM results with other microscopy methods we have synthesized fluorophores for tagging of the peptides and imaging them via both confocal laser scanning microscopy (CLSM) and super-resolution CLSM. The fluorophores were synthesized, purified, characterized and conjugated to peptides using both solid and liquid phase coupling reactions while utilizing the group's chemical synthesis expertise and equipment. The fluorescently labeled peptides could then be used either to corroborate the results from the LCTEM or to allow the studying of multicomponent peptide system and tracking of the individual peptides. Future research collaborations in between the Adler-Abramovich (TAU) and Gianneschi (NU) might include further probing of peptide supramolecular systems assembly using LCTEM microscopy, CLSM, and mutual validation of the results between these advanced microscopic techniques.

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