Pellach M., Atsmon-Raz Y., Simonovsky E., Gottlieb H., Jacoby G., Beck R., Adler-Abramovich L., Miller Y., Gazit E. Spontaneous structural transition in phospholipid-inspired aromatic phosphopeptide nanostructures. ***ACS Nano*****.** 2015; 9: 4085-4095.

Abstract: Phospholipid membranes could be considered a prime example of the ability of nature to produce complex yet ordered structures, by spontaneous and efficient self-assembly. Inspired by the unique properties and architecture of phospholipids, we designed simple amphiphilic decapeptides, intended to fold in the center of the peptide sequence, with a phosphorylated serine "head" located within a central turn segment, and two hydrophobic "tails". The molecular design also included the integration of the diphenylalanine motif, previously shown to facilitate self-assembly and increase nanostructure stability. Secondary structure analysis of the peptides indeed indicated the presence of stabilized conformations in solution, with a central turn connecting two hydrophobic "tails", and interactions between the hydrophobic strands. The mechanisms of assembly into supramolecular structures involved structural transitions between different morphologies, which occurred over several hours, leading to the formation of distinctive nanostructures, including half-elliptical nanosheets and curved tapes. The phosphopeptide building blocks appear to self-assemble via a particular combination of aromatic, hydrophobic and ionic interactions, as well as hydrogen bonding, as demonstrated by proposed constructed simulated models of the peptides and self-assembled nanostructures. Molecular dynamics simulations also gave insight into mechanisms of structural transitions of the nanostructures at a molecular level. Because of the biocompatibility of peptides, the phosphopeptide assemblies allow for expansion of the library of biomolecular nanostructures available for future design and application of biomedical devices.