

Mondal, S.\*, Adler-Abramovich, L.\*, Lampel, A., Bram, Y., Lipstman, S., Gazit, E. **\*Both authors contributed equally to the work.** Formation of functional super-helical assemblies by constrained single heptad repeat. *Nature Commun.*; 2015: 6, 8615.

**Abstract:** Inspired by the key role of super-helical motifs in molecular self-organization, several tandem heptad repeat peptides were used as building blocks to form well-ordered supramolecular nano-assemblies. However, the need for stable helical structures limits the length of the smallest described units to three heptad repeats. Here we describe the first-ever self-assembling single heptad repeat module, based on the ability of the non-coded  $\alpha$ -aminoisobutyric acid to stabilize very short peptides in helical conformation. A conformationally constrained peptide comprised of aromatic, but not aliphatic, residues, at the first and fourth positions formed helical fibrillar assemblies. Single crystal X-ray analysis of the peptide demonstrates super-helical packing in which phenylalanine residues formed an ‘aromatic zipper’ arrangement at the molecular interface. The modification of the minimal building block with positively charged residues results in tight DNA binding ascribed to the combined factors of helicity, hydrophobicity and charge. The design of these peptides defines a new direction for assembly of super-helical nanostructures by minimal molecular elements.