NANO HIGHLIGHT
Functional Organic Nanostructures Engineered using β-Peptides

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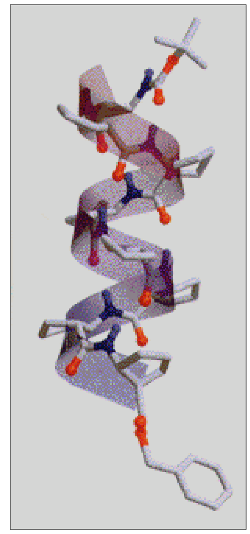
This highlight describes the synthesis of heteropolymeric nanostructures in which functional side chains display unique ordering, in terms of both sequence along the polymer chain and three-dimensional arrangement in space. These nanostructures are opening new frontiers in fundamental nanoscience by combining the properties of rigid rods with unique surface patterning of chemical functionality. This combination is enabling a variety of technological advances in areas such as biological sensing, design of antimicrobial surfaces and gene delivery.



Heteropolymeric nanostructure ("foldamer") formed from non-natural amino acids. Functional groups are presented by the nanostructure in a unique ordering and three-dimensional arrangement in space.

The approach revolves around the engineering of amide-based organic nanostructures (see figure). Nature uses α-amino acid-based polymers to create proteins that are capable of performing a multitude of functions. Our research, although inspired by Nature, is revealing that β-amino acid oligomers and polymers ("β-peptides") represent an exciting opportunity for nanoscience and nanotechnology as their secondary structure (shape) is more stable than that of conventional peptides composed of α-amino acid residues and thus subject to greater rational control.

Two recent accomplishments serve to illustrate the opportunity defined by these novel organic nanostructures. First, at a fundamental level, β-peptide-based nanostructures are providing a new tool box with which to understand the unwritten rules of self-assembly of nano-objects with patterned chemical functionality. Recent results reported in *Journal of the American Chemical Society*[2] demonstrate that subtle variations in chemical patterns presented on the surfaces of β-peptide nanorods can have dramatic effects on their self-assembly. In particular, sequence control was used to manipulate the spatial distribution of charge over the surface of the nanorods, thus unmasking its key role in the expression of long range order, including liquid crystallinity. A second accomplishment is the discovery that β-peptide oligomers that form discrete, globally amphiphilic helices selectively associate with fungal membranes and display antifungal activity [3]. The biological activity of these nanostructures was shown to be strongly influenced by the patterning of chemical functionality on their surfaces. Finally, the folding behavior and stability of individual helices has also been confirmed by using computational methods [4]. These accomplishments, when combined, demonstrate that β-peptides provide the basis of an important opportunity to advance nanoscience and nanotechnology.

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[2] Pomerantz WC, Abbott NL, Gellman SH, *JACS*, 128 (27): 8730-8731, **2006**.
[3] Karlsson AJ, Pomerantz WC, Weisblum B, Gellman SH, Palecek SP. *JACS*, 128(39): 12630-12631, **2006.**
[4] Rathore, N, Gellman, SH, de Pablo, JJ, *Biophysical Journal* 91(9), 3425-3435, **2006.**