

Peptides and Peptide Conjugates: From Self-assembly Towards Applications in Biomedicine

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Self-assembling peptides and their conjugates offer exceptional potential in nanomedicine. I will present some of our recent work on nanoscale assembled peptides and their conjugates, focussing on lipopeptides and PEG-peptide conjugates. PEGylation is an important technique in the development of conjugates for applications in therapeutics. It is found to greatly influence self-assembly of peptides and proteins - one example from our own work is a peptide which itself forms twisted fibrils but when PEG is attached, self-assembly of the conjugate leads to spherical micelles¹. The conjugate can be enzymatically degraded using alpha-chymotrypsin, releasing the peptide. This nanocontainer delivery and release system could be useful in therapeutic applications. Thermoresponsive telechelic PEG/peptides with hydrophobic dipeptide end groups (di-tyrosine or di-phenylalanine) were developed, one of which shows a de-gelation transition near body temperature and which may be useful in bioresponsive delivery systems². Examples from our recent work on self-assembling lipopeptides will also be outlined. Our focus is to investigate potential relationships between self-assembly and bioactivity, in particular in the fields of regenerative medicine³⁻⁵, antimicrobial systems⁶⁻⁷ and immune therapies⁸.

Representative Publications

1. Castelletto, V.; McKendrick, J. M. E.; Hamley, I. W.; Cenker, C.; Olsson, U., Pegylated Amyloid Peptide Nanocontainer Delivery and Release System. *Langmuir* **2010**, *26*, 11624-11627.
2. Hamley, I. W.; Cheng, G.; Castelletto, V., Self-Assembly of Telechelic Peg End-Capped with Hydrophobic Dipeptides. *Macromolecular Bioscience* **2011**, *11*, 1068-1078.
3. Jones, R. R.; Castelletto, V.; Connon, C. J.; Hamley, I. W., Collagen Stimulating Effect of Peptide Amphiphile C₁₆-Ktks on Human Fibroblasts. *Molecular Pharmaceutics* **2013**, *10*, 1063-1069.
4. Gouveia, R. J.; Castelletto, V.; Alcock, S. G.; Hamley, I. W.; Connon, C. J., Bioactive Films Produced from Self-Assembling Peptide Amphiphiles as Versatile Substrates for Tuning Cell Adhesion and Tissue Architecture in Serum-Free Conditions. *J. Mater. Chem. B* **2013**, *1*, 6157-6169.
5. Castelletto, V.; Gouveia, R. J.; Connon, C. J.; Hamley, I. W.; Seitsonen, J.; Ruokolainen, J.; Longo, E.; Siligardi, G., Influence of Elastase on Alanine-Rich Peptide Hydrogels. *Biomater. Sci.* **2014**, *2*, 867-874.
6. Dehsorkhi, A.; Castelletto, V.; Hamley, I. W.; Seitsonen, J.; Ruokolainen, J., Interaction between a Cationic Surfactant-Like Peptide and Lipid Vesicles and Its Relationship to Antimicrobial Activity. *Langmuir* **2013**, *29*, 14246-14253.
7. Hamley, I. W.; Dehsorkhi, A.; Castelletto, V., Self-Assembled Arginine-Coated Peptide Nanosheets in Water. *Chem. Comm.* **2013**, *49*, 1850-1852.
8. Hamley, I. W.; Kirkham, S.; Dehsorkhi, A.; Castelletto, V.; Reza, M.; Ruokolainen, J., Toll-Like Receptor Agonist Lipopeptides Self-Assemble into Distinct Nanostructures. *Chem. Comm.* **2014**, *50*, 15948-15951.