Arginine-rich antimicrobial peptides: Self-assembly, Cytocompatibility and Bioactivy

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Self-assembly is the ability of molecules to form well ordered 3D nanostructures without an external stimuli.[1] Understanding the mechanisms of molecular self-assembly is important for a range of areas including the understanding and treatment of pathologies to the development of new novel nanomaterials. Here, I focus on the ability of peptides and peptide conjugates to self-assemble with potential application such as peptide antimicrobials, understanding complex systems, as well as design novel new materials. Small angle-X ray scattering plays a central role in characterisation of these nanostructures, and through modelling it is possible to extract important structural information on these structures.

The increase in prevalence of multi antibiotic-resistant pathogens is of great concern and has been listed by the World Health Organisation (WHO) as one of the biggest threats to modern day healthcare, food security and development. The self-assembly, cytocompatibilty and antimicrobial activity of a group of arginine-rich amphiphilic peptides rich in alanine or phenylalanine is examined.[2,3] As L-arginine is cationic, this amino acid may interact with anionic or zwitterionic lipid membranes, which may lead to pore formation. Peptides with the ability to self-assemble into ordered stable structures may have the ability to self-deliver. Here, the activity of the peptides against several bacteria strains are examined, with the mechanism of interaction probed by the use of bacterial membrane models DPPG and DPPE at various ratios using a series of techniques including SAXS, CD, DSC and Cryo-TEM. The effect of amino acid ordering, amphilicity and sequence are compared to the cytocompatibility, bioactivity and self-assembly behaviour of the peptides.

The self-assembly and cytocompatibility of two telechelic star polymer-peptide conjugates based on poly(ethleneoxide) (PEO) four arm polymers capped with oligo-L-tyrosine is investigated.[4] PEO has previously been proposed to have had the ability to be used as an inert spacer within peptides to improve circulation time for active compounds for applications such as gene delivery, drug delivery and cell signalling. Tyrosine has the ability to form strong π-π stacking interactions, and residues in proteins are involved in numerous signalling cascades due to their ability to be phosphorylated and dephosphorylated by kinase and phosphatase enzymes respectively. Characterisation of the structural assembles using SAXS is discussed, and the use of modelling to determine parameters of these structures. Potential applications of these conjugates include development of enzyme responsive materials.

Finally, I will present the design of a novel designed cell holder, designed to hold hydrogels, precipitates and powders which is compatible with B21, (Diamond Light Source, UK).[5] This cell is customer designed, user friendly, easily disposable with a high degree of versatility. The sample holder was designed using Fusion 360 software and made in situ using a 3D printer. Window material is optimised to produce minimal background scattering as well as ease of use.

References

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[3] Charlotte J.C. Edwards-Gayle, Glyn Barrett, Shyamali Roy, Valeria Castelletto, Francesca Greco, Jani Seitsonen, Janne Ruokolainen, Robert P. Rambo, Ian W. Hamley. "Antibacterial Activity and Lipid Membrane Activity of Arginine-Rich Amphiphilic Peptides" *Submitted*
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