Secrets from a Chameleon-like antimicrobial peptide

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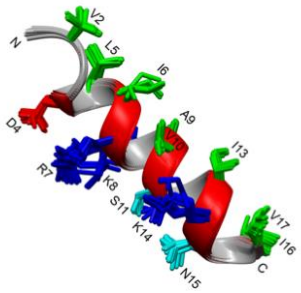
Host defence peptides are components of the innate immune response and are found across most species. Many of these peptides exhibit antimicrobial activity, typically achieved via membrane disruption or by acting on an intracellular target following penetration of the microbial membrane layer. The Uperin 3 peptides are a family of short, 17-amino acid, peptides first isolated from a toadlet*, Uperoleia mjobergii*. They have antibiotic activity towards gram-positive bacteria. These peptides are chameleon-like in several ways, including both an α-helical and β-sheet morphologies after self-assembly into amyloid.

The term amyloid is often linked to neurodegenerative disease, such as Alzheimer's Disease, although it is a generic name for a peptide (or protein) quaternary structure, following self-assembly into twisted aggregates called fibrils. While investigating the solution properties of antimicrobial Uperin 3 peptides, they were found to have a range of diverse fibrillar structures, morphologies as well as varied kinetics of self-assembly into oligomers. Furthermore, the environmental conditions that influenced this process, especially surfaces such as, co-solvents, surfactants, lipid membranes and nanoparticle surfaces influenced the self-assembly process, if placed nearby or in contact with the Uperin 3 peptides. We have used several experimental approaches, as well as molecular dynamics simulations too explore the energy landscape of Uperin peptide assemblies and shown that aggregation and disaggregation processes can be regulated at different stages along the pathway to amyloid.

This presentation will showcase some of the characteristic properties of both amyloid forming and antimicrobial peptides, associated with disease and functional applications. Using several experimental approaches, as well as molecular dynamics simulations too explore the energy landscape of peptide self-assembly. These provided insights into the aggregation and disaggregation processes and clarity into the self-assembly pathway.



Some recent Publications

[1] V. Baltutis, A.N. Calabrese, J.A. Carver, L.L. Martin, "Uperin antimicrobial peptides: structures, activity, and amyloid fibril formation" in *Antimicrobial Peptides: Function, Mechanisms of Action and Role in Health and Disease*, (2021) Ch, 4, Nova Science Publishers. (doi.org/10.52305/CQGC8374).

[2] A.K. Prasad, C. Tiwari, S. Ray, S. Holden, D.A. Armstrong, K.J. Rosengren, A. Rodger, A.S. Panwar, L.L. Martin, *Chempluschem*, (2022) 87(1), e202100408. Doi: 10.1002/cplu.202100408.

[3] T. John, S. Piantavigna, T.J.A. Dealey, B. Abel, H.J. Risselada, LL. Martin, *Chemical Science*, (2023) 14, 3730-41. Doi: 10.1039/D3SC00159H.