



Department of Molecular and Cellular Biology



FACULTY CANDIDATE

Biochemistry

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Synthetic Host Defence Peptides to Combat Antimicrobial Resistance

Tuesday, July 23, 2019

2:30p.m.

SSC 2315

The alarming rise in antibiotic resistance around the world coupled with a lack of new antibiotics in the drug development pipeline has created a global health emergency that requires urgent and immediate action. Host defence peptides (HDPs) are short polypeptide sequences found in virtually all living organisms that have garnered significant attention as alternatives to antibiotics. Originally appreciated for their direct antibacterial effect, HDPs also exhibit a wide range of biological activities including antibiofilm, antiviral, anticancer and immunomodulatory functions. In principle, synthetic peptides could be optimized for a specific biological purpose if sufficient sequence information were available to predict the activity of novel peptides. Unfortunately, beyond the generic properties of HDPs (eg. positive charge and amphipathicity), our current understanding of the chemical space occupied by biologically active HDPs is limited. To address this knowledge gap, high throughput peptide screening and activity-guided design strategies were used to explore the activity landscapes of synthetic HDPs in depth. Subsequently, these results were leveraged to identify new peptides with enhanced antibiofilm and immunomodulatory activities *in vitro*. The most promising therapeutic peptide candidates demonstrated *in vivo* efficacy in a murine abscess infection model resulting in a reduction in abscess size and lowering bacterial burden in this chronic infection model. Looking forward, an improved understanding of HDP activity landscapes will provide valuable insights into the biological role of natural HDPs in health and disease while also unlocking their therapeutic potential as new weapons against antimicrobial resistance.

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