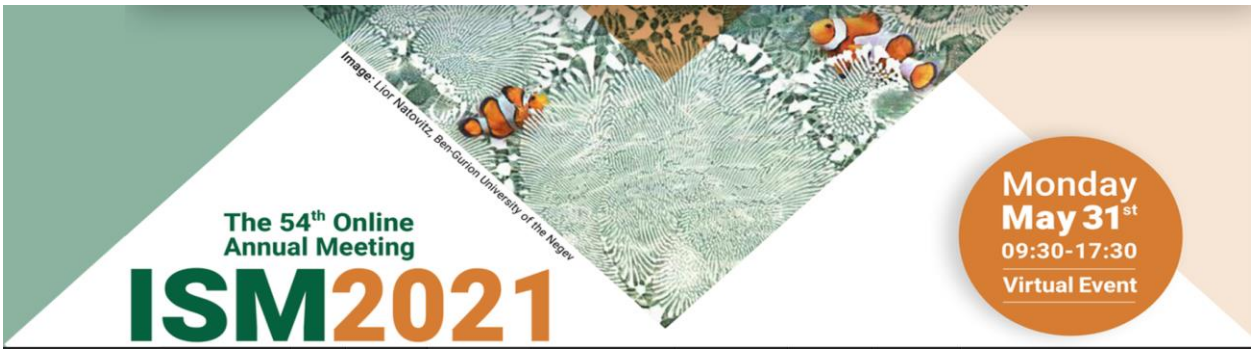

ATOMIC STRUCTURE OF THE LL-37(17-29) HUMAN ANTIMICROBIAL PEPTIDE REVEALS FUNCTIONAL HELICAL FIBRIL WITH A NOVEL ARCHITECTURE

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Antimicrobial peptides (AMPs) are canonical part of the innate immune system of many organisms in all kingdoms of life. Interestingly, certain AMPs assemble into well-ordered fibrils that resemble amyloids, which are proteins associated with neurodegenerative and systemic diseases. LL-37 is an AMP which is expressed by various mammalian cells and is considered to play an important role in the first line of defense against pathogens. Recently, fibrillation of human LL-37 (hLL-37) was found to be critical for binding DNA and affecting receptors in the immune system. hLL-37 is cleaved in-vivo into many active derivatives which show a diverse array of selectivity against microbial strains, and additional functions within the immune system. The hLL-3717-29 13-residue derivative was suggested to serve as the active core of hLL-37. Using X-ray micro-crystallography and electron microscopy techniques, we revealed the supra-helical, thermostable, fibril structure of hLL-3717-29, and correlated between its self-assembly and antibiotic activity. Based on these findings, we are working towards the design novel fibril-forming AMPs with improved shelf life and stability. In addition, we are developing an approach to allow the control over their activity and selectivity upon demand.

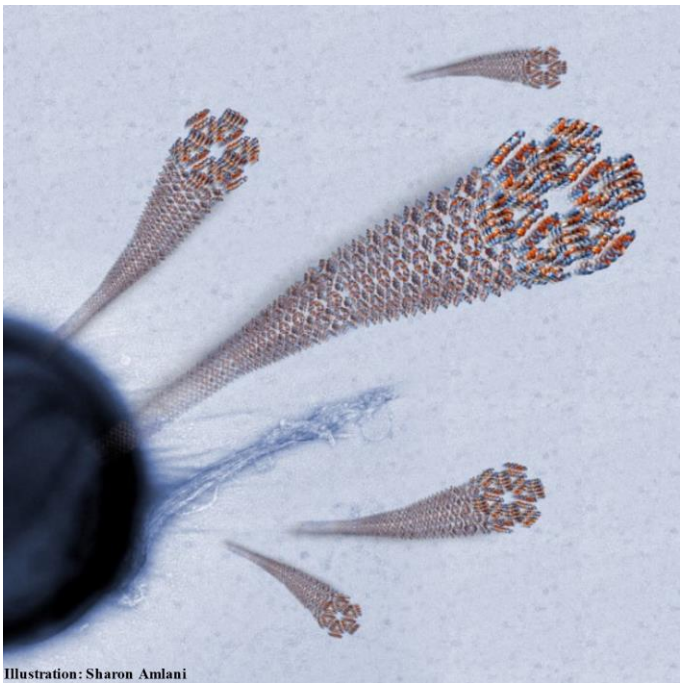
Illustration: Sharon Amlani

Reference: Y. Engelberg and M. Landau. *Nat Commun* 11, 3894; 2020