Contribution ID: **18** Type: **not specified**

Functional supramolecular structures in infectious diseases mechanisms and therapy

Thursday 28 January 2021 16:30 (30 minutes)

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Protein fibrils that perform physiological activities, such as functional amyloids, could provide new therapeutic venues, mostly due to their roles as key virulence determinants in microbes, antimicrobial activities, and possible involvement in systemic and neurodegenerative diseases. Moreover, they display unique stability and tunable self-assembly, which could be used to design therapeutics with enhanced endurance, bioavailability and shelf-life, as well controlled activity. Yet, these fibrous proteins present great challenges in structural and functional studies due to their aggregative and partially disordered nature, and structural polymorphisms observed in similar and even identical sequences. Using X-ray micro-crystallography, we determined the first high resolution structures of bacterial amyloids involved in cytotoxicity, antibacterial activity and biofilm structuring [1-4]. The similar structures of biofilm-associated and human pathological amyloidogenic regions led to repurposing of anti-Alzheimer's compounds to act against Salmonella biofilm. Moreover, the structural similarity implies on possible inter-species interactions that could have bearing on amyloid diseases by the creation of transmissible agents. In addition, we offer atomic-resolution insight into three fibril-forming antimicrobial peptides from bacteria, an amphibian and human [5-6], which featured unique morphologies, including novel types of protein fibrils composed of densely packed helices (Fig. 1). The self-assembly is critical for the antibacterial activity. We expect that a detailed molecular understanding of functional fibrils will provide the foundation for antimicrobial translational research and for elucidation of the etiology of and interactions between microbial and human 'amylomes'in health and disease.

The crystal structures of fibrils of two antimicrobial peptides from human (left) [5] and an amphibian (right) [6] are shown. Transmission electron micrographs show the interactions of the fibrils with bacterial cells.

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[6] Salinas N., Tayeb-Fligelman E., Sammito M., Bloch D., Jelinek R., Noy D., Uson I., and Landau M. The Amphibian Antimicrobial Peptide Uperin 3.5 is a Cross-α/Cross-β Chameleon Functional Amyloid. PNAS 118 (3) e2014442118; 2021

Short info on the speaker

Academic Positions
2020-Present Visiting Group Leader
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2019-present Associate Professor
The Faculty of Biology at the Technion –Israel Institute of Technology

2012-2018 Assistant Professor
The Faculty of Biology at the Technion –Israel Institute of Technology

2013-2015 David and Inez Mayers Career Advancement Chair in Life Sciences Fellow
The Faculty of Biology at the Technion –Israel Institute of Technology

Professional Positions
2019-present Visiting Scientist on one-year Sabbatical
Centre for Structural System Biology (CSSB) at the DESY campus, Hamburg, Germany
Affiliation: The European Molecular Biology Laboratory (EMBL)
Hosts: Profs. Kay Grünewald and Matthias Wilmanns

2007-2012 Post-doctoral scholar
University of California, Los Angeles, USA.
Adviser: Prof. David Eisenberg
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2002-2007 Research assistant (support research with computational aspects)
The laboratory of Prof. Uri Seligsohn at the Amalia Biron Research Institute of Thrombosis and Hemostasis, Chaim Sheba Medical Center, Tel-Hashomer and Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

Research Field: Functional fibrils, microbial amyloids, antimicrobials, X-ray crystallography, cryogenic electron microscopy

Presenter: LANDAU, M. (CSSB/EMBL, Technion Haifa)

Session Classification: PETRA III Session