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VABILO NA PREGLOV KOLOKVIJ / INVITATION TO THE PREGL COLLOQUIUM

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Velika predavalnica Kemijskega inštituta / Lecture Hall

at the National Institute of Chemistry; Hajdrihova 19, Ljubljana

Swirling your way into the plasma membrane: the pore-forming toxin Aerolysin

Pore-forming toxins are the largest class of bacterial toxins. Pore-forming proteins are however found in all kingdoms of life from bacteria to plants and mammals. The seminar will be divided into two parts. Since pore formation is a very ancient form of attack cells have developed means to respond to their permeabilizing effects. Recent findings related to cellular responses will be reported. The second, and major, part will be focused on the structure of. Aerolysin, which is the founding member of a super-family of ß-pore forming toxins for which the pore structure is unknown. The mechanisms leading to biosynthetic folding into the soluble state will be discussed. We have also combined X-ray crystallography, cryo-electron microscopy (EM), molecular dynamics and computational modeling to determine the structures of aerolysin mutants in their heptameric forms, trapped at various stages of the pore formation process. A dynamic docking approach based on swarm intelligence was applied whereby the intrinsic flexibility of aerolysin extracted from new X-ray structures was utilized to fully exploit the cryo-EM spatial restraints. Using this integrated strategy, we obtained a radically new arrangement of the prepore conformation and a near-atomistic structure of the aerolysin pore, which is fully consistent with all biochemical data available so far. Upon transition from the prepore to pore, the aerolysin heptamer shows a unique concerted swirling movement, accompanied by a vertical collapse of the complex, ultimately leading to the insertion of a transmembrane ß-barrel.

Vljudno vabljeni! / Kindly invited!

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