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another structure for inactive receptor. However, despite considerable similarities, these RTKs have different hydrophobicity distributions along helices, that can be important in terms of preferable lipid environment. The work was funded by the Russian Academic Excellence Project '5-100' and Russian Foundation for Basic Research grant 18-54-15007.

P-27-069
Nisin/lipid II interaction in bacterial membrane: molecular dynamics study

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The worldwide rapid emergence of resistant bacteria put at threat the efficacy of antibiotics, thus the development of novel antibacterial agents is urgently needed. The cell wall precursor lipid II consisting the chemically conservative pyrophosphate group represents a promising pharmaceutical target. Antimicrobial peptides, that target lipid II, i.e. lantibiotic nisin, could be excellent prototypes for new generation antibiotics due to their low liability to develop resistance. Understanding of molecular mechanism of initial stages of membrane-bound lipid II recognition by water-soluble nisin is indispensable, in order to improve the peptide structure and properties into pharmaceutically applicable form. Here, we present a molecular dynamics simulation study of initial stages of the aforementioned recognition. In membrane environment, lipid II adopts very few conformations characterized by unique spatial arrangement of hydrogen bond acceptors in the pyrophosphate group at the bilayer surface. These acceptors are efficiently captured by NH groups of nisin, thus explaining its high selectivity to lipid II. Similarly, rings A and B of nisin, which are known to recognize lipid II, adopt the only stable conformation in the presence of dimethylpyrophosphate, which mimics the binding determinant of lipid II. Finally, we propose molecular model of nisin (rings A and B) / lipid II complex in bacterial membrane, which may be employed for design of novel antibiotic prototypes. Acknowledgements: "Molecular and Cellular Biology" RAS Programme, Russian Foundation for Basic Research (19-04-00350).

P-27-070
Structural and biochemical studies of an odorant binding protein from the malaria vector *Anopheles gambiae*

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Anopheles gambiae is the primary mosquito vector responsible for the transmission of malaria, *causing* more than 1 million *deaths* each year. Mosquitoes rely on *olfaction* to find mates, food, and sources of blood meals. Odorant binding proteins (OBPs) that mediate the initial steps in the transduction cascade of olfactory signals in insects have been suggested to play an essential role in the detection and transportation of semiochemicals to odorant receptors (ORs), and thus, they constitute promising targets for the design of novel repellent/attractant molecules. Therefore, a detailed knowledge of their 3D structures and functionalities may provide a valuable tool for the structure-based discovery of novel olfactory disruptors of insect host-seeking behavior to be used in more effective mosquito control strategies. Herein, we present the novel 3D crystal structure of AgamOBP, an OBP that displays the highest levels of expression in the female antenna. These levels also appear to be affected by the circadian cycle as they dramatically reduced in constant dark (DD) conditions compared to light-dark (LD) circles. Furthermore, co-crystallization and *fluorescence displacement experiments* revealed the ligand-binding site of AgamOBP as well as the binding modes and specificities of various natural volatile compounds with repellent properties. This information will contribute to the better understanding of the molecular basis of odorant perception. In addition, it will guide the generation of OBP-structure-based "olfactophore" models to be used in extensive virtual screening processes for the identification of novel candidate disruptors of host-seeking mosquito behavior. Such compounds, with enhanced binding affinity and specificity for a key OBP can be used at lower concentrations and be detected over longer distances, thus providing new effective repellents for the prevention of mosquito-borne diseases.

P-27-071
Structural insight into DAPK2 inhibition by 14-3-3 protein binding

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DAPK family of human calcium/calmodulin (Ca^{2+}/CaM) dependent serine/threonine kinases includes five proteins which regulate several biological functions in cell. They are most known for regulation of autophagy and apoptosis in caspase dependent or independent manner. The shortest member of the family, DAPK2, is 370 amino acid long protein with only three domains: catalytic domain (CD), autoregulatory domain (ARD), dimerization domain (DD) and unstructured N- and C- terminus. In basal conditions DAPK2 forms inactive homodimers. Prerequisites of this conformation is autophosphorylation on S318 in the ARD which happens to be primary Ca^{2+}/CaM binding site. In inactive conformation of DAPK2, S318 is buried deep in the basic loop of CD, preventing access of substrate. Canonical model of DAPK2 activation suggests that binding of Ca^{2+}/CaM pulls out the ARD from the CD, however in Ca^{2+}/CaM independent model of activation, phosphorylation on S299 is enough for DAPK2 to be catalytically active. Recently has been discovered that autoinhibitory conformation of DAPK2 is stabilized by interaction with 14-3-3 protein. Interestingly, 14-3-3 binding site, is predicted to be in the C-terminus, only 40 AA from Ca^{2+}/CaM binding site. Thus, primary focus of this study is to describe molecular mechanism of how DAPK2 is negatively regulated by 14-3-3 protein binding and how this interaction affects steps of DAPK2 activation by Ca^{2+}/CaM. Our preliminary data showed that 14-3-3 binds with a high affinity towards DAPK2 and that phosphorylated T369 is crucial for the interaction. Stoichiometry of 14-3-3/DAPK2 complex is 2:2 with K_D in nanomolar range. Stability of the complex can be further stabilized using small molecules like fusicoccin. Thus, this study not only provides mechanistic insight into DAPK2 regulation but also presents DAPK2 as possible, easily and specifically modulable drug target during cancer treatment. This work was supported by Charles University project UNCE SCI/014.