



VABILO NA PREDAVANJE / INVITATION TO LECTURE

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Velika predavalnica Kemijskega inštituta / Lecture Hall at the
National Institute of Chemistry; Hajdrihova 19, Ljubljana

Insights in the structure and mechanism of TSLP and MyD88 using classical and less classical structural biology approaches

Abstract:

TSLP is a cytokine that plays important roles in epithelial barrier immune responses, and is central in atopic dermatitis and allergic asthma. We present the crystal structure of the TSLP receptor complex and reveal its mechanism, leading to development of potent inhibitors. MyD88 is an essential signaling adapter of Toll-like receptors and IL-1 family members, with crucial roles in innate immunity. However, hyperactivating mutations in MyD88 can drive B-cell malignancies. Using massive mutagenesis and the MAPPIT two hybrid system, we identify the interaction surfaces of the TIR domain of MyD88 for its oligomerization and activation. Using data driven docking, we present a helical MyD88 assembly that helps to explain the activation mechanism of MyD88, its regulation by phosphorylation and its hyperactivation by oncogenic mutations.

Vljudno vabljeni! / Kindly invited!