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datum: 11.10.2017

VABILO

Vljudno vas vabim, da se udeležite sklopa dveh predavanj v okviru tematskega kolokvija z naslovom:

Proteini, ki prepoznavajo ogljikove hidrate

Na kolokviju bomo predstavili dve predavanji:

1) Protein carbohydrate interactions and disease
Prof. Dr. Roland J. Pieters
Department of Chemical Biology & Drug Discovery; Utrecht Institute for Pharmaceutical Sciences, Utrecht, The Netherlands

2) Galectins: intra and extracellular functions
Prof. Dr. Hakon Leffler
Section MIG (Microbiology, Immunology, Glycobiology), Department of Laboratory Medicine, Lund University, Lund, Sweden

Predavanji bosta **v ponedeljek**, **16.10.2017**, ob **15:15** v **predavalnici P4** (3. nadstropje) Fakultete za farmacijo.

Povzetek predavanja z naslovom *Protein carbohydrate interactions and disease,*
Prof. Dr. Roland J. Pieters
The recognition of carbohydrates by proteins is an important phenomenon in living systems and also plays a role in numerous diseases. Interference with these interactions is an important goal towards drug development. Interference is possible by multivalent carbohydrates that greatly enhance inhibitory potency compared to monovalent inhibitors. Bacterial lectins and toxins have been explored with the goal of optimizing inhibition by optimizing the multivalent presentation of the ligands. The optimization process depends on the orientation of the binding sites and different solutions were fond for the pentavalent cholera toxin [1] in comparison with the functionally divalent adhesion lectin LecA of Pseudomonas aeruginosa [2]. Besides lectins, carbohydrates processing proteins are important and we have studied the inhibition of glycosidases by modified iminosugars. These guanidiniums [3] and pseudo-ureas were particularly portent inhibitors of the human beta-glucocerebrosidase with low nanomolar inhibition.

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[3] Sevšek, A; Šrot, L.; Rihter, J.; Čelan, M.; Quarles van Ufford, L.; Moret, E. E.; Martin, N. I.; Pieters, R. J ChemMedChem, 2017, 12, 483-486.

Povzetek predavanja z naslovom *Galectins: intra and extracellular functions, Prof. Dr. Hakon Leffler*

Galectins were discovered in a quest to find proteins binding cell surface carbohydrates and taking part in cell adhesion, and this is indeed one of the roles of galectins. However, they have many other roles. Galectins bind β-galactose containing glycans typically found at the cell surface and inside vesicles. Most studied galectin functions are due to this binding activity, and included formation of cell surface lattices, regulation of glycoprotein traffic and surface exposure of receptor, induction of endocytosis and others, that translate into higher level roles of galectins in immunity, inflammation and cancer. However, surprisingly, it was early discovered that galectins are synthesized as cytosolic proteins, without a signal peptide, and can also have functions in the cytosolic and nuclear compartments, such as interaction with RAS-proteins, ESCRT-complex, centrosomes and roles in transcription and RNA splicing. At the interface between the cytosolic and intravesicular compartments is the now well established carbohydrate-binding dependent rapid accumulation of galectin around disrupted vesicles and coupling of this to autophagy, and also to secretory autophagy. These multiple seemingly unrelated functional effects, suggest roles of galectins in feed back loops regulating membrane turnover and organization or similar.
To help study such galectin related phenomena we have developed binding assays to analyze galectin specificity and aggregation on encounter with natural and artificial ligands. We have generated mutants of galectins with altered fine specificity, permitting coupling of this property to cellular function. We have also developed potent small molecule galectin inhibitors (nM affinities) that can either be readily taken up by cells or not, permitting examination of galectin intracellular roles separate from extracellular roles. Such galectin inhibitors are also in development as therapeutics

S spoštovanjem,

Anderluh Marko

prof. dr. Marko Anderluh