Univerza
v Ljubljani

Fakulteta *za kemijo*
in kemijsko tehnologijo

p.p. 537, Večna pot 113
1001 Ljubljana
telefon: 01 479 80 00
faks: 01 241 91 44
dekanat@fkkt.uni-lj.si

VABILO NA PREDAVANJE
V OKVIRU DOKTORSKEGA ŠTUDIJA
KEMIJSKE ZNANOSTI / INVITATION TO THE
LECTURE WITHIN DOCTORAL PROGRAMME IN
CHEMICAL SCIENCES

Prof. Michael Sattler

Bavarian NMR Center, Department of Chemistry, Technical University of Munich, Garching, Germany

z naslovom / title:

NMR to study molecular recognition and dynamics of biomolecular complexes and in structure-based drug discovery

v sredo, 30. 3. 2022 ob 15. uri / on Wednesday, 30. 3. 2022 at 15.00

v predavalnici 1 v 1. nadstropju Fakultete za kemijo in kemijsko tehnologijo, Večna pot 113 **/ in lecture room 1,** 1st floor at the Faculty of Chemistry and Chemical Technology, Večna pot 113

Vljudno vabljeni! / Kindly invited!

Abstract:

We combine solution NMR spectroscopy and small angle scattering (SAXS, SANS) with crystallography and cryo-EM in integrative structural biology approaches to study the conformational dynamics of multidomain proteins where multiple structural domains are connected by linkers of variable length and rigidity. This allows modulatory of interactions and conformational dynamics to recognize ligands and control biological function. While crystallographic structures provide structural information about snapshots, solution techniques, such as NMR, are crucial to describe conformational dynamics. The molecular functions of these multi-domain proteins often rely on dynamic structural ensembles and can be controlled by population shifts between active and inactive conformations. Posttranslational modifications can further modulate the molecular interactions to regulate the biological activity. Integrative structural biology combining solution techniques, especially NMR spectroscopy, is important to unravel the molecular recognition, dynamics and regulation of protein complexes. Examples are RNA binding proteins (RBPs) involved in splicing regulation or client recognition by the molecular chaperone Hsp90.
NMR also plays an important role in structure- and fragment-based drug discovery. Both protein and ligand-observed experiments allow to screen and identify ligands and characterize the protein-small molecule complexes. Examples of methods and application of structure-based drug discovery will be presented.

References

- Napolitano, V. *et al.* Acriflavine, a clinically approved drug, inhibits SARS-CoV-2 and other betacoronaviruses. *Cell Chem. Biol.* 1–24 (2022) doi:10.1016/j.chembiol.2021.11.006.
- Jones, A. N., Tikhaia, E., Mourão, A. & Sattler, M. Structural effects of m6A modification of the Xist A-repeat AUCG tetraloop and its recognition by YTHDC1. *Nucleic Acids Res.* 1–13 (2022) doi:10.1093/nar/gkac080.
- Lopez, A. et al. (2021) Client binding shifts the populations of dynamic Hsp90 conformations through an allosteric network, *Science Advances*, 7(51) eabl7295
- Softley, C. A., Bostock, M. J., Popowicz, G. M. & Sattler, M. Paramagnetic NMR in drug discovery. *J. Biomol. NMR* 74, 287–309 (2020).
- Kang H-S et al. An autoinhibitory intramolecular interaction proof-reads RNA recognition by the essential splicing factor U2AF2, *PNAS* 117, 7140–7149 (2020).
- Kooshapur, H. et al. Structural basis for terminal loop recognition and stimulation of pri-miRNA-18a processing by hnRNP A1, *Nature Commun* 9, 2479 (2018).
- Mackereth CD et al. Multi-domain conformational selection underlies pre-mRNA splicing regulation by U2AF, *Nature* 475, 408–411 (2011).