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Biomolecular NMR spectroscopy in medicinal chemistry

Raphael Stoll*
Faculty of Chemistry and Biochemistry, Ruhr University of Bochum, Germany

Biochemistry seeks to understand life at a molecular level by examining the relationship between the structure and function of biomolecules, such as proteins, nucleic acids, and lipids. To achieve this, we use a variety of techniques, particularly biomolecular NMR spectroscopy, in order to determine the three-dimensional structures and dynamics of biomolecules as well as how they interact with each other and other molecules in solution at near-physiological conditions.

Cancer cells are hallmarked by the ability to divide unrestrictedly, posing an often lethal threat to an organism. Thus, the development of selective small antagonistic ligands tailored to bind to crucial protein targets is paramount to be able to treat cancer effectively. In order to achieve this goal, the molecular mechanism of a potential therapeutic effect needs to be elucidated at atomic resolution.

Our research focuses in the main on medically-relevant proteins, specifically those involved in the development of cancerous tumours, in order to better understand the causes of the condition and propose more effective treatment strategies. Examples include oncogenic proteins, tumour suppressors as well as proteins involved in malignant melanoma, to name but a few. Other current areas of investigation also cover the structure, function, dynamics, and interaction of proteins associated with the transduction of physiological signals as well as bioenergetics.

In particular, we would like to understand structure-function-relationships of MDM2, p53, Ras as well as Rheb GTPases, and the melanoma inhibitory activity (MIA) proteins. Our additional research efforts in medicinal chemistry include an “SAR by NMR”-like approach in order to develop potential lead structures of small molecular antagonists for these medically-relevant proteins. This presentation will cover recent advances from our research endeavours.

Biography:

Raphael Stoll is Professor of Biomolecular Spectroscopy in the Faculty of Chemistry and Biochemistry at the Ruhr University of Bochum, Germany. He studied Physiological Chemistry and Biochemistry at the Universities of Tübingen, Germany, and Oxford, UK, as a fellow of the „Studienstiftung” and DAAD. Supported by a fellowship from the FCI, he carried out his doctoral research at the Max Planck Institute for Biochemistry in Munich and received his PhD from the Technical University of Munich. After a stay as a research associate at The Scripps Research Institute, CA, USA funded by first a DAAD- and then an Emmy-Noether fellowship, he initially joined the Ruhr-University of Bochum as Junior professor. His research focuses in the main on structure-function-relationships of medically-relevant proteins, specifically those involved in the development of cancerous tumours, in order to better understand the causes of the condition and propose more effective treatment strategies.