# KOLLOQUIUM
## Institut für Molekulare Biowissenschaften
## Summersemester 2024

GOETHE UNIVERSITÄT FRANKFURT AM MAIN

Science in progress

**Tuesday, May 14th, 2024, 17:15, Biocentre, N260 Room 313**

**Julian von Ehr and Uwe Bodensohn**

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Julian von Ehr

### Molecular basis of alternative splicing regulation through SRSF6 isoforms

The human serine-arginine rich splicing factor 6 (SRSF6) is part of the SR-protein family consisting of 12 members. SRSF6 is involved in (alternative-) splicing regulation and can itself exist in at least three isoforms. It is composed of an N-terminal RRM domain, followed by a pseudo RRM and a C-terminal serine-arginine rich disordered domain. With SRSF6 being an integral part of the splicing machinery, all three domains have been implicated in interacting with RNA and/or proteins, but individual interactions mediating SRSF6 specificity remain poorly understood. Therefore, our goal was to structurally and biochemically analyze single domains as well as their combinations to decipher their RNA interaction sites as well as their sequence requirements. To this end, we used nuclear magnetic resonance (NMR) spectroscopy combined with electrophoretic mobility shift assay, fluorescent polarization, and x-ray crystallography, applied to recombinant SRSF6 variants. In particular, we used RNA Bind-n-Seq to obtain RNA consensus motifs for the single and tandem RRMs. We found the two single RRMs to have significantly different binding affinities and sequence requirements towards RNA: RRM1 binds to cytosine- and adenine-rich RNAs in a canonical way, whereas RRM2 prefers purine-rich sequences in a non-canonical mode of interaction. To understand the latter on an atomistic level, we solved the crystal structure of RRM2 both in the apo- and RNA-bound forms, which confirm our NMR data in non-canonical RNA-binding mediated by RRM2's α-helix 1. Additionally, we found the linker between RRMs to play an important part in increasing affinity towards RNA in concert with RRM2.
Altogether, our data provide a strong structural basis for understanding the functions and target specificity of SRSF6 as opposed to the other 11 members of the SR protein family on a molecular level.

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More Information: https://tinygu.de/kolloqmbw

Uwe Bodensohn

## GET3B the central ATPase of the stromal GET pathway

Proper protein targeting and insertion into membranes are essential for cellular organization and organelle function. The Guided Entry of Tail-anchored (GET) pathway facilitates the post-translational targeting and insertion of tail-anchored (TA) membrane proteins. In plants, Arabidopsis thaliana has four GET3 homologues, including AtGET3B and AtGET3D localized to chloroplasts. Plastids, the photosynthetic organelles, possess complex membrane systems, and the mechanisms underlying plastid protein targeting and membrane biogenesis are not fully understood. This study investigated the role of GET3B in chloroplast biogenesis and its interaction with ALB3 and ALB4, which mediate protein integration into the thylakoid membrane. Physical interactions were observed between GET3B and the C-terminus of ALB3 and ALB4, indicating a role for GET3B in protein targeting and membrane integration within chloroplasts. Additionally, genetic interactions were found between GET3B and components of the STIC pathway, implicating GET3B in thylakoid membrane biogenesis. Notably, disruption of GET3B had a significant impact on chloroplast biogenesis and function. These findings enhance our understanding of GET3B's involvement in chloroplast protein targeting and membrane biogenesis, shedding light on the intricate processes of organelle-specific protein sorting in plants.

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*Science in progress* represents talks of institute members. Either post docs or advanced PhD students present and discuss their recent data.

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