SFB 960-/RCB-Colloquium

Thursday, February 9th, 2 p.m.

H 53

Prof. Dr. Zbigniew Warkocki

Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznan

Department of RNA Metabolism

"New players in an old game: an update on posttranscriptional regulation of human LINE-1 retrotransposons"

LINE-1 retrotransposons are one of the major constituents of human genomic repetitive sequences. During evolution these retrotransposons accumulated to comprise nearly 18% of the human genome and might still create new genomic insertions in modern humans by a copy-paste mechanism involving RNA intermediates. LINE-1 is tightly regulated by multi-layered regulatory processes to prevent the detrimental effects of LINE-1 insertions on the integrity of the genome. Although transcriptional regulation of LINE-1 expression has been widely studied, the specific influences of general post-transcriptional RNA regulatory processes on LINE-1 are not that well understood. XRN1 is the major cytoplasmic 5' to 3' exoribonuclease which degrades mRNAs decapped by DCP1/DCP2 complex. As the protein is involved in RNA decay, it would be rational to hypothesize that XRN1 could be a potential LINE-1 inhibitor. To test a possible involvement of XRN1 and DCP2 in LINE-1 regulation we used retrotransposition assays under its temporal depletion and in multiple independent clonal wild-type and *XRN1* and *DCP2* knock-out cell lines. Curiously, we observed that the loss of XRN1 or DCP2 decreased the LINE-1 activity by manifolds in both knockdown and knockout conditions. Despite this, they exert differential effects on LINE-1 mRNA steady-state levels and translation of retrotransposonal proteins. By employing various experimental approaches, testing additional RNA decay factors and using specially designed reporters we nailed down the mechanism of the retrotransposition reduction to LINE-1 mRNA 3' end dynamics. We thus demonstrate crucial and somewhat unappreciated role of the 3' end dynamics in LINE-1 biology

Host: Prof. Dr. Gunter Meister, Biochemistry I, gunter.meister@ur.de

Universität Regensburg

Biochemie-Zentrum Regensburg