Poster Presentation

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Regulation of the ribosome and protein synthesis by RNAi

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In many biological processes, e.g. the development of multicellular organisms, a tight regulation of the protein synthesis is a necessity. Among numerous mechanisms for translational control, RNA interference (RNAi) based mechanisms have been shown to regulate the translation of messenger RNA (mRNA) and hence regulate the synthesis of proteins. The key proteins in all RNAi mechanisms are the argonaute proteins. The only catalytically active argonaute protein is denoted argonaute2 (Ago2) in humans. This single chain protein is comprised of four globular domains arranged in a crescent shape tertiary structure [1]. The guide RNA binding specificity lies within the Mid and PAZ domain while the active site resides in the PIWI domain. In 2011 it was reported that the receptor for activated C-kinase (RACK1), an integral protein of the ribosomal 40S subunit, directly binds the microRNA induced silencing complex (miRISC) [2] and thereby contributes to gene repression through RNAi mediated knockdown. This interaction of RACK1 with miRISC was furthermore shown to be a specific interaction between Ago2 and RACK1. Structural investigation of this interaction will be of great interest to elucidate how Ago2 is positioned in relation to ribosome bound mRNA and if this positioning of Ago2 on the ribosome facilitates mRNA binding to the guide RNA bound in Ago2. In our studies we will co-crystallize recombinantly expressed Ago2 with 80S ribosome from S. cerevisiae [3] and solve the structure by x-ray crystallography. Recent project progress will be presented on the conference poster.

[1] *Schirle, N. and MacRae, I. The crystal structure of human Argonaute2. Science, 336, 1037-1040 (2012),* ***[2]*** *Jannot, G. et al. The ribosomal protein RACK1 is required for microRNA function in both C. elegans and humans. EMBO reports, 12, 581-586 (2011),* ***[3]*** *Ben-Shem, A. et al. Crystal structure of the eukaryotic ribosome. Science, 330, 1203-1209 (2010)*

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