IMG

Institute of Molecular Genetics
of the Czech Academy of Sciences

Regular Wednesday IMG seminar

Prof. Dr. Reinhard Lührmann

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"The cascade of snRNP remodeling steps leading to the formation of the spliceosome's active site"

The spliceosome is a highly dynamic, large RNP machine that catalyses pre-mRNA splicing. Spliceosomes assemble de novo by the stepwise recruitment of the snRNPs U1, U2 and U4/U6.U5 and a plethora of auxiliary splicing factors to the pre-mRNA substrate yielding the pre-catalytic B complex. For the transformation of the B complex into an activated (Bact) complex, the spliceosome undergoes dramatic structural rearrangements, initiated by the Brr2 RNA helicase, which involve the formation of a catalytically active U2/U6 RNA structure, and the exchange of about 50 proteins. To investigate the assembly pathway of the U2/U6 RNA active site and the mechanism whereby proteins aid its proper folding, we have blocked spliceosome assembly at novel intermediate stages of activation and, in collaboration with Holger Stark, determined the cryo-EM structures of two distinct, human pre-Bact complexes that lack a mature, catalytic U2/U6 RNA structure. These pre-Bact structures, coupled with biochemical analyses, provide new insights into the order of protein recruitment and release during Bact formation. They also elucidate how spliceosomal proteins and their mutually exclusive interactions ensure the correct order of RNP rearrangements needed to generate the U2/U6 catalytic RNA. I will also discuss the substantial structural rearrangements that 17S U2 and 25S U4/U6.U5 snRNPs undergo during their integration into the spliceosome, highlighting a general principle of the spliceosome, that is, chaperoning away reactive RNA sites during spliceosome assembly until they are needed and made available by RNA helicases.

The seminar will be held

on Wednesday 7th February 2024 at 15:00

in the Milan Hašek Auditorium at IMG

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)