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SYLICA LECTURE: Human mitochondrial RNase P and its multiple faces

You are cordially invited to the lecture delivered by

Assoc. Prof. Walter Rossmanith

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WHEN: 07/11/2013, 2 p.m.
WHERE: seminary room A11/205, University Campus Bohunice

Abstract:

The human mitochondrial genome is transcribed into long polycistronic precursor RNAs, encoding the tRNAs interspersed among the rRNAs and mRNAs. Endonucleolytic processing at the level of the tRNAs thereby determines the concomitant release of all the RNAs required for mitochondrial protein synthesis. RNase P is the endonuclease that cleaves at the boundary of tRNAs and their 5' flanking sequences. For long human mitochondrial RNase Phad remained elusive and its identification in 2008 finally revealed an enzyme that, unlike any previously identified RNase P, did not contain an RNA as a central catalytic subunit, but was composed of proteins only (Holzmann et al., 2008). The nature of its protein components moreover indicated that the holoenzyme or some of its subunits could have further functions in mitochondrial tRNA biosynthesis. In fact, a subcomplex of two subunits of mitochondrial RNase P constitutes the methyltransferase responsible for methylation of purines at position 9 (Vilardo et al., 2012), a modification supposed to be crucial for the proper folding of some mitochondrial tRNAs. The human mitochondrial enzyme again is unusual because of its ability to methylate both A and G. Moreover, in contrast to related methyltransferases, it requires an additional subunit, which on its own is a short---chain dehydrogenase, involved in the degradation of branched---chain fatty and amino acids and thus with no obvious connection to tRNA maturation. The tRNA cleavage, tRNA methylation, and dehydrogenase activities, physically associated in human mitochondrial RNase P, are nevertheless uncoupled and independent from each other. Thus, human mitochondrial RNase P is a multifunctional complex gathering diverse enzymatic activities related to tRNA maturation and beyond.

Holzmann, J., P. Frank, E. Löffler, K. L. Bennett, C. Gerner, and W. Rossmanith (2008). RNase P without RNA: identification and functional reconstitution of the human mitochondrial tRNA processing enzyme. Cell 135,462-74.

Vilardo, E., C. Nachbagauer, A. Buzet, A. Taschner, J. Holzmann, and W.ossmanith (2012). A subcomplex of human mitochondrial RNase P is a bifunctional methyltransferase – extensive moonlighting in mitochondrial tRNA biogenesis. Nucleic Acids Res. 40, 11583-93.

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