SYDDANSK UNIVERSITET
UNIVERSITY OF SOUTHERN DENMARK

Guest lecture

A new function for an ancient RNA: a cis-acting snoRNA controls snoRNP autoregulation

Time: 7 June 2018 at 10.30 – 11.15

Place: BMB seminar room

Abstract:
Box C/D small nucleolar (sno)RNAs constitute a class of abundant noncoding RNAs that associate with common core proteins to form catalytic snoRNPs. Most of these operate in *trans* to assist the maturation of ribosomal RNA by guiding and catalyzing the 2'-O-methylation of specific nucleotides. snoRNAs arose early in evolution as evidenced by their existence in archaea as well as in eukaryotes. Despite structural and functional conservation, the genomic organization and 'expression strategies' of snoRNA genes are the most versatile in evolution. In humans, the majority of snoRNAs are encoded (hosted) within introns of highly transcribed protein-coding or long noncoding (lnc)RNA genes. This means that the production of a mature snoRNA is critically dependent on the transcription and splicing of its host pre-mRNA. Here, we report that the human intron-hosted box C/D snoRNA *snoRD86* acts in *cis* as a sensor and master switch controlling levels of the limiting snoRNP core protein NOP56. Our results are consistent with a model where *snoRD86* adopts different conformations that dictate the usage of nearby alternative splice donors in the *NOP56* pre-mRNA. Excess snoRNP core proteins prevent further production of NOP56, and instead trigger generation of a cytoplasmic lncRNA that potentially acts as a decoy for these proteins. Our findings reveal a feedback mechanism based on RNA structure that controls the precise coordination between box C/D snoRNP core proteins and global snoRNA levels. On a broader scale, our discoveries illustrate that the positioning of snoRNAs in introns during the course of evolution has allowed co-option of a new function in regulation of splicing. Since the majority of human snoRNAs are encoded by host genes and a substantial fraction of host introns is subjected to alternative splicing, we speculate that snoRNAs may more generally moonlight as *cis*-acting regulators of alternative splicing.

Host
Professor Brage Storstein Andresen, BMB