BIOCHEMISTRY SEMINAR SERIES

Midstream Presentation - Fall 2020

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"Transcriptional Roadblocks Protect Against Pervasive Transcription, and the Regulation of a Manganese Transporter via the Endoribonuclease Rnt1p"

Part 1- At any point in time a number of biological processes may be occurring on the DNA within close proximity to one another. Research from our lab and others has shown that these processes are able to interfere with one another to some extent: such as DNA bound transcription factors being able to block the progress of upstream transcriptional machinery. Through the analysis of RNA sequencing data we uncovered a pattern showing the appearance of pervasive transcription near tDNA loci after the loss of RNA Pol III binding from the tDNA. Further investigation of this pervasive transcription revealed that a vast majority of these sites contained retrotransposon elements, which may be the source of these pervasive transcripts. We have also found that at many tDNA loci genome wide these pervasive transcriptional events lead to interference with the normal transcriptional activity of nearby genes. One such example is the gene MEP3, which we have shown undergoes the loss of its own transcription corresponding with the appearance of an overlapping antisense transcript after the loss of nearby RNA Pol III binding. This loss of MEP3 transcription results in a phenotype equivalent with that of a MEP3 deletion indicating some biological relevance for the blocking of this pervasive transcription by RNA Pol III. These findings suggest that RNA Pol III activity at tDNA loci genome wide may be acting as a safeguard mechanism against this retrotransposon based pervasive transcription.

Part 2- Rnt1p is an endoribonuclease involved in the regulation of a wide range of biological processes. Yeast strains suffering a deletion of RNT1 are not only exceptionally sick, but also particularly susceptible to metal ion stress. Further analysis of Rnt1p cleavage sites identified a possible Rnt1p target in the manganese transporter SMF1, which is one of the primary manganese transporters for the cell. We have shown that yeast cells with a mutation in the Rnt1p cleavage site in SMF1 are not only more susceptible to toxic metal stress than wild-type cells, but also contain higher levels of toxic metal ions after treatment with toxic levels of metal. Preliminary evidence at the RNA level also indicates that strains with the cleavage site mutation fail to downregulate SMF1 RNA in the presence of excess manganese. Together, these data indicate the existence of a previously unknown regulatory pathway for SMF1 in which Rnt1p plays a critical role.

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via Zoom

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