**Opening Lecture**

**Lectures**

**OL**

**Biznes or Science?**

Piotr Chomczynski  
*Molecular Research Center, Inc.*  
e-mail: piotr@mrcgene.com <Piotr Chomczynski>

Science, discovery and commercialization. Economic development requires that these three elements should be effectively integrated. The skyrocketing cost of doing science makes commercialization of its discoveries a necessary prerequisite for adequate support in society. However, in contrast to a scientific discovery, commercialization is not always adequately appreciated and executed. What is necessary for the successful commercialization of a scientific discovery? What does it take to set up your own enterprise based on a discovery? Are some people predestined to establish and run a company? Ten commandments for entrepreneur. How can you stimulate your mind to create new ideas? These questions are currently much discussed in the scientific and business communities. I will present my insights on these subjects based on personal observations.

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**Parnas Lecture**

**PL**

**Transcription termination and polyadenylation of non-coding RNAs in yeast**

Pawel Grzechnik and Joanna Kufel  
*Institute of Genetics and Biotechnology, University of Warsaw, Pawinskiego 5A, 02-106 Warszawa, Poland*  
e-mail: kufel@ibb.waw.pl <Joanna Kufel>

Transcription termination by RNA polymerase II is coupled to the formation of the transcript 3' end. For mRNAs this is carried out by a large cleavage and polyadenylation complex and the addition of polyA tails by the major poly(A) polymerase Pap1p. In contrast, 3' ends of nonpolyadenylated small nucleolar and nuclear RNAs (snoRNA and snRNA) in yeast *Saccharomyces cerevisiae* are formed either by endonucleolytic cleavage by Rnt1 (RNase III), release from excised introns or by termination. This is followed by trimming the 3' ends by the nuclear exosome, a complex of 3'-5' exonucleases, with a specific involvement of its nuclear component Rrp6. Recent analyses of snoRNA genes have shown that their terminators consisted of two elements. First motif is snoRNA-specific, contains Nrd1- and Nab3-binding sites and directs termination mediated by the Nrd1/Nab3 complex, whereas second region resembles mRNA cleavage and polyadenylation sites and depends on components of the mRNA cleavage and polyadenylation machinery.

The role of polyadenylation of many classes of stable transcripts was attributed to degradation of aberrant species by the exosome. It has been reported that in this case exosome activity is stimulated by polyadenylation by the TRAMP complex containing two alternative poly(A) polymerases Trf4/5p. We have shown that transcription termination of independently transcribed, intrinsically non-polyadenylated snoRNAs is linked to polyadenylation of their precursors at both terminators and the role of this activity is not to degrade RNAs but to promote their correct processing. Poly(A) tails are added by Pap1 to both forms, whereas Trf4 adenylates precursors at the major site and this acts as signal for polyadenylation by Pap1. Trf4 also oligoadenylates processing intermediates to facilitate their processing or degradation by the exosome. Surprisingly, another important function of Trf4, independent of its catalytic activity, in is termination at the Nrd1/Nab3 site to enhance Nrd1 association with snoRNA genes. During the final steps of maturation by the Rrp6/exosome snoRNA fate is decided and incorrectly processed or misassembled molecules are degraded by TRAMP and the exosome. Therefore, this last step acts as a surveillance mechanism, removing defective RNAs and safeguarding the quality of mature, functional molecules.

These data show that also Pol II ncRNA precursors become polyadenylated by default and that this process is required for the synthesis of their mature forms. Also, they suggest that polyadenylation of these transcripts is a key event linking their transcription termination, 3' end processing and degradation.