In all eukaryotes, transcription of nuclear DNA is carried out by at least three different RNA polymerases (Pols), designated Pol I, II and III. Each RNA Pol catalyzes the transcription of a specific set of genes. The set of transcripts synthesized by Pol II is extremely complex, because it includes all the different protein-coding mRNAs (over six thousands in yeast) and many non–protein-coding RNAs, such as lncRNAs, snRNAs, snoRNAs. By contrast, Pol I and Pol III are specialized in the high level synthesis of protein-noncoding RNA species that are fundamental components of the translation machinery. Pol I synthetizes a single transcript, the precursor rRNA, which is processed into 28S, 5.8S and 18S rRNAs. The most abundant products of Pol III–dependent transcription are different tRNA species and 5S rRNA.

The interplay between the three nuclear RNA polymerase systems is a key aspect of growth control. Pol III synthesizes very abundant, essential RNAs whose levels influence the expression pattern of protein-coding genes in a complex way. Genome-wide study performed in yeast revealed that the reduced levels of Pol III gene products result in an extensive, reprogramming of Pol II genes mediated by Gcn4 transcription factor, responsible for so called general amino acid control. This is probably related to the wide impact exerted on cell physiology by a reduced rate of translation as a consequence of the reduced tRNA levels. The known mechanism of Gcn4 induction by amino acid starvation (involving Gcn2 kinase) was however excluded and the alternative has not been proposed yet.

Recently, we have identified Rbs1 protein physically interacting with Pol III complex and involved in its assembly. Rbs1 sequence contains R3H domain which potentially binds single stranded nucleic acid. This feature suggested that, beside participation in assembly of Pol III complex, Rbs1 might have another function. Our preliminary results indicate that Rbs1 is RNA-binding protein and is associated with the particular sequences in the 5’ and 3’ untranslated regulatory regions in some mRNAs. These data provide strong suggestion that Rbs1 is involved in Gcn4 induction in response to inefficient tRNA synthesis, indicating the molecular mechanism of this induction. Verification of this hypothesis is a main goal of current proposal. Second important function of Rbs1, suggested by identification of its mRNA targets, is control of expression of the gene encoding ABC10β, a common subunit of Pol I, II and III. This regulation, which will be experimentally addressed in this proposal, may be important for control of Pol III complex assembly and its coordination with assembly of Pol I and Pol II.