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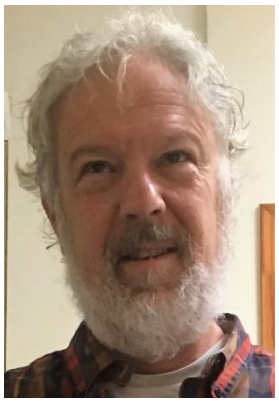

Regulation of gene expression: a system view

New students and post-docs are welcome.

Please send your inquiry to the following mail: choder@technion.ac.il

We are using the most advance technologies to study the regulation of gene expression, and uncovered novel mechanisms and concepts.

Please visit our website http://choder.net.technion.ac.il for more detailed description of the new concepts emerged from our work

Our work in lay terms

Each one of us carry a large set of genes, each one is stored as a memory unit consists of nucleotide sequence in our DNA. Understanding how these memory units control our life in health and disease - i.e., how each gene is "expressed"- is a major aim in biology and medicine. Thousands of groups around the world have discovered that proper expression of a gene involves various stages. Each stage can be viewed as an application for the production of biological molecules. Together all these molecules are required to produce the final products - RNAs and proteins that control our life. Evidently, then, the process is so complex that it requires a number of different applications. It is currently believed that there is a hierarchy among the applications, and some are more critical for the decision whether to express a gene or not (e.g., transcription) and some play just secondary roles.

Our group has found that the various applications (i.e., stages of the mRNA lifecycle) are connected by an additional application. This application (involves various mechanisms discussed in the next paragraph) connects all the other applications and integrates them into a system. Our findings led us to propose that all the components participate in a "brain storming" activity and together they decide what is best for the organism. We hypothesize that what really matters in the cell is not the function of individual factors but the network of interactions (physical and/or functional) among **all** factors.

More "professional" summary

The cross-talk between the various stages of gene expression is a new field, in which my group has been at the forefront. Analogous to the whole-genome view,

obtained in recent years by zooming-out from single gene to gene networks, we have shifted our attention from studies of the distinct steps of gene expression (e.g., transcription, translation) to the integration of all these processes. Hence, our work tries to unravel the cross-talks between all distinct processes. This integration is critical for ability of the cell to function as a system. These studies have led us to propose the following novel concepts:

- "**mRNA imprinting**", which results from co-transcriptional binding of factors to nascent transcripts; this phenomenon affects the functionality and the fate of the imprinted transcripts in the cytoplasm (1). Using novel proteomic and genomic approaches, we have recently found dozens of proteins that bind nascent transcripts co-transcriptionally.
- "**Synthegradases**", which are factors that enhance, or repress, both mRNA synthesis and decay simultaneously. These factors play key roles in determining RNA levels in the cells, and are also capable of imprinting these RNAs (2).
- "**Synthegradosome**", which is a two-arm machinery that comprises of many transcription factors (including Pol II subunits) and mRNA decay factors; the synthegradosome shuttles between the nucleus, where it mediates mRNA synthesis, and the cytoplasm, where it mediates mRNA demise (3).
- **"mRNA coordinators"**, which are factors that integrate all stages of the mRNA lifespan into a system (4). We have recently discovered that many factors constitute the coordinator complex; among them are factors known to function in a specific stage (e.g., translation) that we found to function in all stages (e.g., (i) transcription, (ii) mRNA processing, (iii) transport, (iv) translation and (v) decay).

These concepts should help us obtaining a "bird eye" view of regulation of gene expression.

For further readings and references see http://choder.net.technion.ac.il

Selected publications

1. Choder, M. (2011). mRNA imprinting: additional level in the regulation of gene expression. ***Cellular Logistics*** **1**, 37-40.
2. Bregman, et al. (2011). Promoter elements regulate cytoplasmic mRNA decay. ***Cell,*** **147**, 1473-83.
3. Haimovich, et al. (2013). Gene expression is a circular: factors for mRNA degradation also foster mRNA synthesis. ***Cell***, **153**, 1000-1011.
4. Harel-Sharvit, et al. (2010). RNA polymerase II subunits link transcription and mRNA decay to translation. ***Cell***, **143**, 552-563.