

Project 1.10 Non-canonical functions of ATP in the regulation of gene expression (SONATA BIS-11)

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Background:

The life of every mammal begins with a single cell - the zygote. During development, through multiple divisions and precisely orchestrated processes of gradual differentiation, the zygote transforms into a fully formed organism and then becomes an independent, mature individual. Regulation of gene expression underlies the remarkable precision and reproducibility of this process. Promoters, enhancers, silencers, and insulators are DNA regulatory elements binding transcription factors thereby controlling gene expression. Functional communication between DNA regulatory elements often correlates with increased physical proximity between the elements in the three-dimensional space of the cell nucleus. However, it is not clear what influences the frequency and strength of these interactions. More than 50 years ago it was shown that ATP in high concentrations can act as a solvent that affects the solubility proteins. However, the functional involvement of these noncanonical solvent-like properties of ATP in the control of gene expression is currently unknown.

Aim:

Determine the implication of ATP in the control of interactions between DNA regulatory elements. The PhD students will combine state-of-the-art high-throughput sequencing methods, genome editing technologies, and imaging techniques to better understand the mechanisms controlling gene activity and the contribution of non-canonical ATP functions in the transcriptional regulation of genes.

Requirements:

PhD 1: Master's degree in physics, mathematics, or bioinformatics. The candidate will need to quickly learn essential computational approaches for next-generation sequencing data analysis, he/she will also need to understand the basics of statistics. He/she will develop knowledge in the approaches and algorithms applicable in count data analysis, image processing also tools for clustering, and dimensionality reduction. Ideally, this would be a graduate in mathematics or bioinformatics. That person's job will be to perform bioinformatics analyses of the data generated throughout the project. This person will use R/RStudio, python, Julia, and bash/shell scripting and tools for next-generation sequencing analysis.

PhD 2: Master's degree in cell biology, biotechnology, genetics, or biochemistry/biophysics; This person will carry out the genetic engineering (interrogation of functional promoter-enhancer pairs), work with the TIGRE locus and perform comparative analyses of the level of ATP across different tissues.