



EPIGENETIC GENE REGULATION OF THE EUKARYOTIC GENOME: SYSTEMS BIOLOGY APPROACHES USING SYNTHETIC CELL SYSTEMS

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Epigenetic gene control is a major mechanism for cell-type specific commitment in multicellular organisms. Epigenetic regulatory mechanisms are directly linked with transcriptional regulation and domain-wide changes in chromatin structure. Current understanding of this complex process is predominantly qualitative.

We analyzed the role of epigenetic regulatory proteins involved in gene silencing on the establishment of higher order chromatin structure in mammalian cells using advanced microscopy techniques taking two complementary experimental strategies: (i) interference with epigenetic regulatory proteins using a dominant negative approach and (ii) in vivo targeting of epigenetic regulatory proteins via lac repressor tagging to an amplified chromosome region carrying arrays of lac operator sites.

To understand the epigenetic and spatial-temporal mechanistic interactions underlying the transcription rate of single genes we use a systems biology approach combining quantitative cell biological experiments with mathematical modeling. We created synthetic epigenetic cell systems enabling to toggle the chromatin state and measure the causal effect on epigenetic gene control. We aim to determine how epigenetic mechanisms control gene activity and identify the parameters allowing for robust regulation while maintaining low molecular noise propagation. This research is proof-of-principle to create more complex synthetic epigenetic systems with virtually any desired property including properties as multistability or oscillation and opens an unexplored field of research with great potential for medicine.

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