Universität Basel

Research Project

Genome-wide prediction of coactivator-controlled transcriptional networks using data from ultrahigh-throughput sequencing technologies

Project funded by own resources

Project title Genome-wide prediction of coactivator-controlled transcriptional networks using data from ultrahigh-throughput sequencing technologies
Principal Investigator(s) van Nimwegen, Erik ;
Co-Investigator(s) Handschin, Christoph ;
Project Members Salatino, Silvia ;
Organisation / Research unit
Departement Biomedizin / Pharmakologie (Handschin)
Departement Biozentrum / Growth & Development (Handschin)
Departement Biozentrum / Bioinformatics (van Nimwegen)
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Gene regulation in higher eukaryotes is a complex process involving the concerted action of transcription factors and coregulators. The dynamic formation of multiprotein complexes on promoter and enhancer elements mediates a coordinated modulation ofă biological programs, which together contribute to physiological and pathological plasticity on the cell or organ level. However, because of the complexity, the mechanistic aspects of this coordinated regulation are poorly understood. Recentă technological advances now allow the study of the binding of regulator complexes to their cognate sites on a genome-wide scale. ChIP-Seq combines chromatin immunoprecipitation (ChIP) with ultra high-throughput parallel sequencing and thusă provides a technical platform for global mapping of the interactions between protein complexes and DNA elements with high resolution. This methodology generates large datasets that pose significant challenges for storage, processing and interpretation,ă particularly for the bioinformatical inference of transcriptional networks obtained from DNA binding data of protein complexes rather than individual transcription factors. We plan to study the regulation of gene expression by the peroxisome proliferator-activated receptor gamma coactivator 1alpha (PGC-1alpha) in skeletal muscle as a model to infer, validate and refine the genome-wide prediction of transcriptional networks using ChIP-seq together with other complementary techniques. PGC-1alpha is a transcriptional coactivator that modulates the expression of whole gene families and thereby drives the plastic adaptations of a number of tissues following external and internal stimuli. In muscle, PGC-1alpha levels are regulated by motor neuron activity. In turn, PGC-1alpha controls the expression of genes that are required for exercise adaptation, including mitochondrial, myofibrillar and other genes. Interestingly, interaction of PGC-1alpha with a whole panel ofă transcription factors is dynamic and can be modulated by relative levels of the binding partners as well as posttranslational modifications.

Keywords transcription regulation, coactivators, PGC-1alpha, regulatory site prediction, deep sequencing
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Other funds

Add publication

Published results

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