SYSTEMS BIOLOGY OF GENE REGULATION

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SUMMARY & MISSION STATEMENT

What is the contribution of epigenetic modifications to the transcriptional output of a cell, and how do mutations in epigenetic regulators lead to disturbed gene activity and loss of cellular identity? We aim to answer these question towards identifying novel molecular mechanisms of gene regulation and revealing potential targets for cancer therapy.

OVERVIEW

Cell-type-specific gene expression programs are coordinated by spatiotemporal interactions between regulatory factors and regulatory elements in the genome. Interference or lack of specificity in this process results in loss of cellular identity and gives rise to various cancers. Precise execution of gene expression programs primarily relies on DNA sequence-dependent mechanisms, but chemical modifications of histones and DNA are recognized to orchestrate genome-wide readout of genetic information, independent of DNA sequence.

As a paradigm epigenetic mark, we use DNA methylation - a well-established modification involved in transcriptional repression. Disturbed DNA methylation is a hallmark of many cancers, and factors that regulate methylation are highly mutated in hematological diseases (DNMT3A, TET2, IDH). The cause and consequences of the disturbed methylation patterns, as well as the impact of the identified mutations on the underlying regulatory mechanisms are not fully clear.

We aim to understand how interactions between regulators of DNA methylation and the genome are specified, how these lead to specific DNA methylation landscapes, and how cancer mutations impact targeting of these factors and influence transcriptional output. Towards this we combine various experimental and computational strategies, including genome and epigenome engineering, genome-wide screens, functional genomics and proteomics, single-cell readouts, and computational modelling.

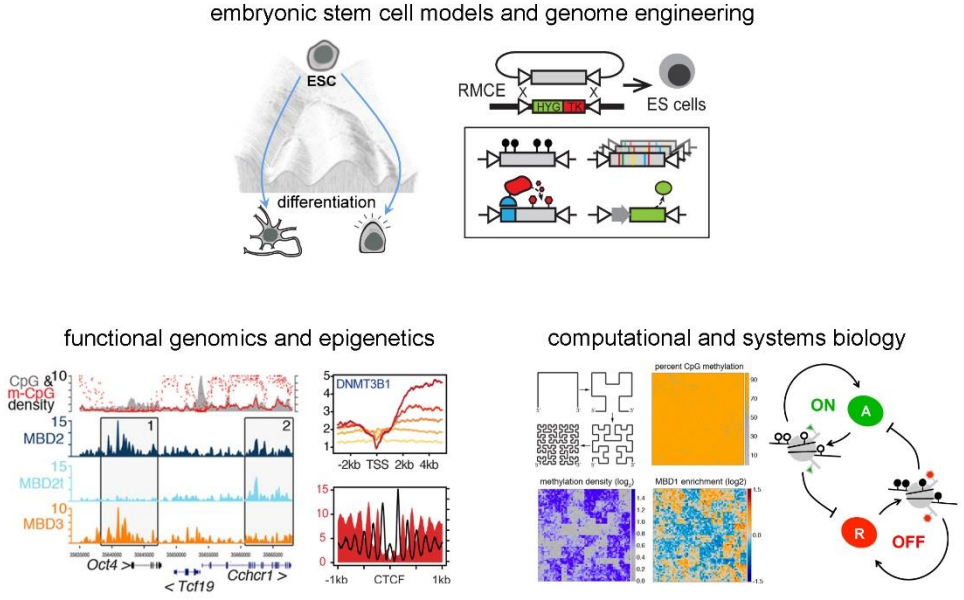
SELECTED CANCER RELATED PUBLICATIONS

Isoform-specific localization of DNMT3A regulates DNA methylation fidelity at bivalent CpG islands. Manzo M, Wirz J, Ambrosi C, Villaseñor R, Roschitzki B, Baubec T. **EMBO J**. 2017 Dec 1;36(23):3421-3434

Dynamics and Context-Dependent Roles of DNA Methylation. Ambrosi C, Manzo M, Baubec T. **J Mol Biol**. 2017 May 19;429(10):1459-1475

Genomic profiling of DNA methyltransferases reveals a role for DNMT3B in genic methylation. Baubec T, Colombo DF, Wirbelauer C, Schmidt J, Burger L, Krebs AR, Akalin A, Schübeler D. **Nature**. 2015 Apr 9;520(7546):243-7.

Methylation-dependent and -independent genomic targeting principles of the MBD protein family. Baubec T, Ivánek R, Lienert F, Schübeler D. **Cell**. 2013 Apr 11;153(2):480-92.



The Baubec Lab combines cellular engineering with functional genomics and computational biology to obtain a quantitative understanding of the molecular mechanisms that regulate chromatin and transcription at a genome-wide level.