Universität Basel

Research Project

Analysis of the stability of the neuronal differentiation states

Third-party funded project

Project title Analysis of the stability of the neuronal differentiation states
Principal Investigator(s) Becskei, Attila ;
Organisation / Research unit
Departement Biozentrum / Synthetic Microbiology (Becskei)
Project start 01.04.2019
Probable end 31.03.2023
Status Active
The understanding and control of cellular differentiation has become a major focus of molecular life sciences and biomedical therapy. While animal cells are less plastic than plant cells, an increasing number of molecules, especially transcription factors, have been identified that are capable of reprogramming cell lineages. ă

This plasticity is, however, associated with an inherent instability of the differentiated or reprogrammed states. Therefore, it is of major interest to unravel mechanisms that can stabilize the desired cell phenotypes. Transcriptional positive feedback loops have been often suggested to stabilize phenotypes, a claim supported by well-characterized molecular mechanisms to support bistability in simpler organisms. Recent evidence suggests, however, that chromosomal regulatory landscapes can also support epigenetic inheritance and differentiation. This project aims at unveiling whether and to what extent these two mechanisms contribute to the neuronal differentiation and the stability of neuronal phenotypes.

By focusing on neurogenic transcription factors, we will examine whether they orchestrate transcriptional feedback loops and assess their ability to support bistable phenotypes. Concurrently, we will explore the correlation between phenotypic diversity and the changes in the chromosomal regulatory landscape. In the second subproject, we will use tools of synthetic biology to dissect the components of the chromosomal regulatory landscape to characterize the minimal set of elements that can promote phenotypic diversification through the control of the interdependence in the stochastic expression of the genes in a chromosomal segment.ă ă

Our experimental systems analysis will shed light on the control principles that can stabilize differentiated or reprogrammed cell states, which will help to engineer neurons with precise functioning for ex vivo studies and for therapeutic applications.ă

Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners