Functional Genomics:
from Gene Discovery to Function in Disease

Summary

Genome research, starting with the Human Genome Project in 1990, has fundamentally changed our knowledge and research in biomedical sciences in two dimensions. First, novel and surprising discoveries such as the low number of classical protein-coding genes but a huge amount of non-protein-coding transcipts opened the gate to an unexpected novel complex layer of gene regulation. Second, as genomics demands genome-wide large-scale efforts, the development of high-throughput technologies was and is still being in demand.

In this Habilitation Thesis, both aspects of genome research, high-throughput technology development and application, are discussed. With the establishment of various microarray platforms for the model organisms *Arabidopsis thaliana*, *Mus musculus* as well as for our species, *Homo sapiens*, genome-wide expression studies for the identification of coding and non-coding genes in distinct disease-related fields could be performed. This resulted in the discovery (i) of novel pathways involved in plant pathogen defense, (ii) of the mode of cancer drug-mediated cell death in chronic lymphocytic leukemia and multiple myeloma, (iii) of novel candidate genes for involvement in osteoporosis, (iv) of which one promising compound emerged to be able to control and reverse osteoporosis, and (v) of a gene with impact in the renewal/differentiation balance of adipose progenitors. Moreover, focusing on the ‘dark matter in biology’, (vi) a microRNA cluster could be identified as novel biomarker of cellular aging, (vii) microRNAs were identified to distinguish and characterize the major subtypes of anaplastic large cell lymphoma to provide novel molecular targets for treatment, (viii) microRNAs with impact on human fat cell development and obesity were found and functionally characterized, (ix) of which one candidate turned out to be able to switch adipocyte differentiation from the energy storing white to the energy combusting thermogenic ‘brite’ phenotype. And last but not least, due to the expanding field of non-coding RNAs as novel gene regulators, (x) a microarray for profiling also long non-coding RNAs has been developed.