

Functional Genome Research: Key Technologies

Systematic Methodological Platforms

The cross-disease and systematic approach of human genome research is represented by so-called Systematic Methodological Platforms (SMPs). Here, functional genome analysis is carried out on a large scale by using high-throughput techniques.

To achieve the goal of comprehensive analysis the five most capable German institutes in the field of high-throughput genome research, the German Cancer Research Center (DKFZ) in Heidelberg, the Max-Planck Institute for Molecular Genetics (MPI) and the Max-Delbrück-Center for Molecular Medicine (MDC) in Berlin, the National Research Center for Environment and Health (GSF) in Munich and the German Research Center for Biotechnology (GBF) in Braunschweig, have joined forces with other resource institutes, universities and small and medium-sized enterprises. Both, the technologies established and the data generated in the projects are available to all scientists within the NGFN. The SMPs are a necessary supplement to the clinical research performed in the disease-oriented genome networks.



Bioinformatics

Bioinformatics in the NGFN includes e.g. genomic annotation and knowledge management, the prediction of gene products, structure and function, the modeling of cellular and disease processes, the collection and interpretation of high-throughput data as well as the development of visualization and data mining tools. The SMP established the NGFN bioinformatic infrastructure, including databases for functional data and animal data, a central web server and analysis platforms for gene expression, SNP and sequencing data.



Genotyping

A major focus of the NGFN is the identification of genes involved in complex diseases. Positional cloning is now widely used to achieve this aim. The SMP-DNA provides substantial support in high-throughput genotyping for the NGFN partners. Gene mapping and genotyping are performed with the following methods: genome wide scans with STR markers and SNPs, candidate gene SNPs, comparative sequencing, gene mutation analysis, CGH and matrix CGH.



RNAi

The main emphasis of the RNAi technology is placed on the establishment of high resolution high-throughput functional screens in tissue culture. In addition RNAi technology will be implemented for functional assessment in vivo, e.g. the study of embryonic and adult physiology in mouse models. These technologies promise to speed up functional annotation and validation of disease candidate genes and will therefore have a major impact on the molecular dissection of disease mechanisms.



Resource and Service Center of Genome Research

The RZPD is a service platform for sharing material and data, contributing an immense portfolio of validated clones, clone collections, services and other research resources that are stably maintained for open access. All these materials can be instantly used for systematic functional genomic research as well as for medical research. All validated materials are linked to available scientific data and may be retrieved by reference to the underlying gene.



Proteomics

Proteome centers examine the type and quantity of proteins in a biological system, their post-translational modifications, which are crucial for the protein's biological function and the protein's local context within the cell, i.e. intracellular localization and its interaction with other proteins. New approaches for sample preparation, for multi-dimensional combined electrophoretic and chromatographic separation techniques and for efficient mass spectrometric analysis are developed and implemented.



Expression Profiling

Gene expression profiles and tissue arrays are being analyzed in a high-throughput manner. Systematic and disease-driven analysis of gene expression patterns in humans and mice are performed. The participating institutions have an impressive track record in the area of chip technology, which is the central method of this platform. Data created here are highly relevant for disease-oriented genome networks.



Antibody Factory

The production of binding reagents to a large number of gene products (ORF) is essential for a systematic study of expression patterns, intracellular distribution and complex formation of the respective proteins. For the research needs of clinical networks and industrial partners, in particular, a high-throughput antibody generation will be offered. An example is a set of antibodies against human transcription factors and signal molecules, with the ultimate goal of using the antibodies both individually and on array.



Chemical Genomics

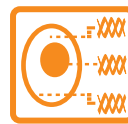
The Chemical Genomics platform for NGFN implements the application of micro-array technology for rapid and systematic identification of small molecule effectors of protein function.

The screening of synthetic compound micro-arrays for interaction with known proteins or the use of synthetic peptide micro-arrays presenting fragments of disease proteins for interaction with organism/tissue specific recombinant protein domains displayed on bacteriophage comprise part of the work.



Genetic Epidemiology

Experts in genetic epidemiology give important support to those studies in the NGFN, which follow the paradigm of a disease-driven research approach on the basis of well-diagnosed patient and family samples. Tasks of the centers for Genetic Epidemiological Methodology (GEM) are methodological support and standardization of phenotype and genotype information.



Cellular Localization and Functional Assays

Starting from full-length cDNAs the intracellular localization of novel proteins is analyzed to obtain first insights into the function of the proteins. In addition automated functional assays addressing the cell cycle and other disease-relevant cellular pathways are established and applied in a high-throughput manner to identify candidate proteins for diagnostics and therapy. Downstream functional genomics and proteomics studies are carried out along with the bioinformatic analysis and mining of the data generated.



The German Mouse Clinic

The Mouse is used as a model system for the molecular understanding of human health and disease. The NGFN has established a large resource of gene-driven and phenotype-driven mutants. A platform for standardized mouse phenotyping, the "German Mouse Clinic (GMC)", brings together specialists from various disease areas in the fields of mouse phenotyping. In addition the "European Mouse Mutant Archive (EMMA)" serves as an archive for the valuable mouse mutants produced in this integrated project.

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