Strategies for the fight against major diseases

the International Human Epigenome Consortium

Professor Jörn Walter of Saarland University is the coordinator of DEEP. DEEP’s objective is to conduct systematic analyses of the epigenetic causes of common metabolic diseases such as fatty liver disease (steatosis), obesity, and inflammatory diseases of the joints and the intestine. Project researchers are tracking epigenetic changes in select human cells and tissue samples. The technologies developed for the efficient management of data and bioinformatic analysis are providing the basis for the disease-related analysis of the acquired datasets. DEEP is a key BMBF pilot project in the fight against major diseases. It will help to successfully integrate Germany’s successful medical epigenome research into a wider global research context.

www.deutsches-epigenom-programm.de/en/home/

The Data Grid offers a way to easily visualize available datasets. The different complex datasets can be displayed by clicking on the coloured cells. (Source: IHEC website)

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Cardiovascular diseases, cancer, or neurodegenerative diseases affect people everywhere in the world – and the number of patients is on the steady rise. The only way to curb this trend is through improved disease prevention and control strategies. This requires an in-depth knowledge about the origins of major diseases. The International Human Epigenome Consortium (IHEC) conducts systematic research on the molecular causes of these diseases. This major international biomedical research project brings together hundreds of prestigious researchers from different countries in the European Union, Japan, South Korea, Canada and the USA. The Federal Ministry of Education and Research (BMBF) provides €20 million in funding for Germany’s participation in IHEC.

**Challenge: mapping the molecular causes of major diseases**

Errors in the human genome are the frequent cause for major diseases. Mutations, small changes which concern the sequence of the four building blocks of DNA, have long been known to trigger diseases. However, recent research results have shown that external factors such as nutrition, stress and pollutant exposure, as well as ageing processes can leave molecular fingerprints on the DNA of human cells. Such changes may affect gene activity. Misregulation due to false signals in the cells can result in the outbreak of disease. These irregularities are very significant in the context of major diseases. This high complexity area which research must consider from a number of different perspectives. Researchers have therefore stepped up efforts to investigate the factors, mechanisms and correlations which regulate gene activity in the human genome.

**Epigenome – the levels of cell regulation**

Every cell in the human body normally contains the same genetic information, yet the more than 200 different types of cells perform different functions. For example, the metabolic processes in a liver cell are different than in a blood cell. A hair cell has tasks and a structure that are distinct from the nerve cell. These differences emerge because the information in the genome is retrieved specifically for every cell type. A discrimination is only possible with sophisticated regulation of the cellular gene activity. The word “epigenome” is a broad term for all the mechanisms which specifically control the gene activity in a given cell type. Accordingly, the epigenome of a diseased cell is different to that of a healthy cell.

**Strategy – Focussing on misregulation in the cell**

IHEC is drawing up a comprehensive catalogue of epigenetic changes in human cell types which are associated with major diseases. This can only be accomplished by pooling experimental resources and expertise. Vast amounts of data must be recorded, stored and analyzed to compile the epigenetic catalogue. All of the researchers in the consortium apply state-of-the-art high-throughput technologies which enable the recording of many large datasets at a time. Data is examined with a view to the interactions of certain molecules in genes and their influence on the regulation of gene activity.

The programme aim is to make a total of 1,000 human epigenome maps available as reference data for future research. Based on comparative analyses of biological materials from both healthy and diseased patients, including blood or tissue samples, the researchers hope to gain critical knowledge about the origin and course of major diseases. Ten research groups in IHEC are currently focusing on the most widespread major diseases.

**Objective – individualized medicine for major diseases**

Epigenetic testing has not been common in clinical practice up to now. The outcome of IHEC aims at changing this situation in the medium-term. All of the research networks in IHEC have therefore defined common standards and quality benchmarks for every working step. This is a monumental task which enables efficient and sustainable international research in the first place. The collected data will be stored centrally and in uniform format. The datasets on epigenetic changes provide the basis for all subsequent functional analyses.

**German’s contribution – cooperation at many levels**

The BMBF provides funding within IHEC for the interdisciplinary research network “German epigenome programme - DEEP”. The programme’s various projects are located throughout Germany at different research institutions. The research and funding concept “e:Med – Paving the Way for Systems Medicine” provides the strategic framework of the BMBF research funding.

The results of IHEC will be made accessible to other research groups to encourage and promote medical epigenomic research. Epigenetic maps will enable earlier and more precise diagnoses and improve treatments. In future, epigenomic analysis will become a standard element of individualized medicine, granting every individual optimized and tailor-made treatment.