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AKADEMIE DER WISSENSCHAFTEN

Genes and epigenetic programmes

The scientific and societal relevance of epigenetic concepts

A workshop organised by the
Interdisciplinary research group **»Gene Technology Report«** of the
Berlin-Brandenburg Academy of Sciences and Humanities

Monday, April 16th 2012, 1:00 – 6:30 pm
Berlin, Jägerstrasse 22/23 (Gendarmenmarkt), Einstein-Saal

Genes and epigenetic programmes

The scientific and societal relevance of epigenetic concepts

Members of the interdisciplinary research group »Gene Technology Report«

Bernd Müller-Röber (Chair), Ferdinand Hucho (Vice Chair), Nediljko Budisa, Boris Fehse, Jürgen Hampel, Kristian Köchy, Jens Reich, Hans-Jörg Rheinberger, Hans-Hilger Ropers, Jochen Taupitz, Jörn Walter

The research group »Gene Technology Report« aims to provide a basis for an impartial and open discourse on genetic engineering in Germany. We are acting as an impartial, long-term 'observatory' for almost ten years now to provide careful appraisal of the various applications of genetic engineering and to closely monitor their ethical, political, and social implications.

The workshop will give insight into the importance and intricacies of current epigenetic research. Modern concepts, how gene function is altered by other mechanisms than changes in DNA sequence, have been developed since the mid-20th century. However, the broad relevance of epigenetic modifications for development, adaptation and disease has only fully emerged in recent years. Current research programs on functional genomics all incorporate epigenetics and epigenomics.

The presentations will relate to key topics in current epigenetic research. Each talk will be 30 minutes with an additional 15 minutes for questions and discussion. The concluding plenary session will focus on the overall significance and future applications of this fast-moving field – not just for science, but for culture and society. The workshop is directed at scientists, companies and public bodies who are interested and involved in epigenetic research.

Program

1:00 Welcome and introductory remarks
Jörn Walter

1:15 **»Epigenetic gene regulation in plants«**
Ueli Grossniklaus – *University of Zurich*

2:00 **»Stem cell potency – a panoply of genetic and epigenetic control«**
Hans R. Schöler – *Max Planck Institute for Molecular Biomedicine, Münster and Member of the Berlin-Brandenburg Academy of Sciences and Humanities*

2:45 Break

3:15 **»Non-coding RNAs and epigenetics«**
Nikolaus Rajewsky – *Max Delbrück Center for Molecular Medicine, Berlin-Buch*

4:00 **»Epigenomics – new concepts for functional genomics«**
Jörn Walter – *Saarland University and Member of the interdisciplinary research group »Gene Technology Report«*

4:45 **»The development of epigenetic concepts in the 19th and 20th century«**
»Vanessa Lux – *Center for Literary and Cultural Research, Berlin*

5.30 General discussion

6:30 End of workshop

Prof. Dr. Ueli Grossniklaus

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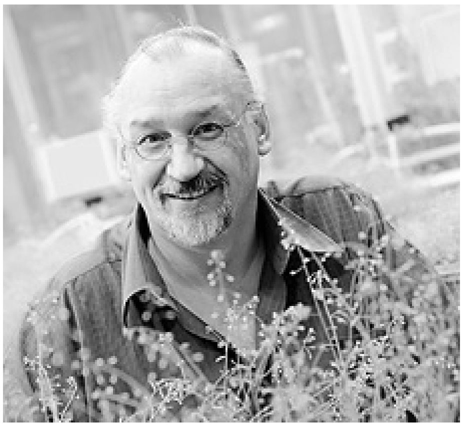

Epigenetic gene regulation in plants

Epigenetic research has a long history in the plant sciences and many fundamental epigenetic processes were first described in plants. In this presentation, I will focus on two selected aspects: genomic imprinting and transgenerational inheritance. Genomic imprinting, which evolved independently in seed plants and mammals, relies on DNA methylation and chromatin modifications in both these groups, illustrating an interesting example of convergent evolution. Comparative studies may thus allow the identification of fundamental aspects of epigenetic gene regulation. In recent years, transgenerational inheritance has become a focus in the media but experimental evidence in mammals including humans is scarce. In plants, transgenerational epigenetic inheritance has unambiguously been demonstrated. A better understanding of these well-described phenomena at the molecular level may provide insights that are relevant also to humans.

Prof. Dr. Hans R. Schöler

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Stem cell potency – a panoply of genetic and epigenetic control

The pluripotent and multipotent states of stem cells are governed by specifically expressed transcription factors forming a highly interconnected regulatory network in concert with more widely expressed transcription factors. The transcriptional network exhibits a hierarchical structure, with a small number of transcription factors playing an essential role in maintaining cellular potency and controlling the more numerous auxiliary transcription factors. When the set of master transcription factors comprising Oct4, Sox2, Klf4, and Myc is expressed ectopically in somatic cells, the transcriptional network is propelled to organize itself in such a way as to support a pluripotent state. Instead, when Oct4 is replaced by Brn4, another member of the POU family of transcription factors, fibroblasts are converted into multipotent neural stem cells. Apparently, these transcription factors play distinct but interdependent roles in remodelling gene expression by influencing the local chromatin status during reprogramming.

Prof. Dr. Nikolaus Rajewsky

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Non-coding RNAs and epigenetics

A major lesson from recent genomics is that metazoans share to a large degree the same repertoire of protein encoding genes. It is thought that differences between cells within species, between species, or between healthy and diseased animals are in many cases due to differences in when, where and how genes are turned on or off. Gene regulatory information is to a large degree hardwired into the non-coding parts of the genome.

Our lab focuses on decoding transcriptional regulation (identification and characterization of targets of transcription factors in non-coding DNA) and post-transcriptional control mediated by a class of small, non-coding RNAs (microRNAs). microRNAs are a recently discovered large class of regulatory genes, present in virtually all metazoans. They have been shown to bind to specific cis-regulatory sites in the 3' untranslated regions (3' UTRs) of protein-encoding mRNAs and, by unknown mechanisms, repress protein production of their target mRNAs. Our understanding of the biological function of animal microRNAs is just beginning to emerge, but it is clear that microRNAs are regulating or are involved in a large variety of biological processes and human diseases, such as developmental timing, long-term memory, signalling, homeostasis of key metabolic gene products such as cholesterol, apoptosis, onset of cancer, Tourett's syndrome, and others.

Prof. Jörn Walter, PhD

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Epigenomics – new concepts for functional genomics

Epigenetic concepts have greatly influenced our view on mechanisms of genetic regulation and modes of inheritance. Epigenetic control involves multiple layers of molecular information including DNA-methylation, histone modifications and non-coding RNAs. Each cell type of a multicellular organism contains characteristic patterns of such epigenetic modifications. During development the single genome of an organism is epigenetically “translated” into hundreds of cell type specific **epigenomes**. Recently large NGS based programmes have started to precisely map and interpret cell specific epigenomes. The data are amendable in public browsers and already start to revolutionize our view on functional genomics. Because of the complexity of epigenomic data the development of novel computational methods will play a major role to functionally understand and link the role of epigenetic control in biological systems. Moreover the combinatorial complexity of epigenomic information, i.e. the combined action of multiple epigenetic signals along chromosomes, already indicates that a simple separation of epigenetic signals into “on or off” categories may have to be reconsidered. The recent discovery of novel DNA-modifications such as hydroxymethylcytosine and carboxy-methylcytosine indeed points in this direction and challenges „traditional“ concepts put forward for DNA-methylation. In my presentation I will highlight major goals and challenges of epigenomic mapping initiatives worldwide and discus recent discoveries in in the field of DNA-methylation in the context of development and disease.

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The development of epigenetic concepts in the 19th and 20th century

“The fact that the word ‘epigenetics’ is reminiscent of ‘epigenesis’ is to my mind one of the points in its favour”. With this response to a critical commentator (published in 1956 in *Nature*), C.H. Waddington not only positions his ‘epigenetics’ in opposition to preformationism. He implicitly draws a line to several key debates in the history of heredity and evolution concerned with interrelations between phylogeny and ontogeny, between nature and culture, and between generations. Within this pre-genetic and pre-Weismannian heritage a whole range of epigenetic concepts is buried. During the era of genetic reductionism most of theses concepts were put under the label of Lamarckism and excluded from further scientific debate. The currently rising field of ‘post-genomic’ epigenetics inherits these issues. By revisiting the constellations in which epigenetic concepts developed in the 19th and 20th century some of the challenges for current epigenetic research are discussed.