



**GSF – National Research Center
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Mutations uncover disease genes

GSF scientist coordinates world-wide largest project towards functional analysis of disease genes

Although the genomes of humans, mice, and other organisms are sequenced, the function of most genes is not known. Thus, the elucidation of gene functions underlying health and disease is a major actual challenge. An important approach towards this aim is the mutation of genes, as this causes a loss of functions in the organism and thereby highlights the role of the respective unaltered genes.

The mouse is the model organism of choice for gene function analysis, inter alia, as about 99 percent of the human and mouse genomes are identical. The mutation of mouse genes and the establishment of mouse models will provide scientists an insight into the development of our widespread diseases.

EUCOMM (The European Conditional Mouse Mutagenesis Program) is an ambitious research program which has now been initiated by the European Union. In the framework of EUCOMM, up to 20,000 mouse genes will be conditionally mutated, corresponding to approximately 70 percent of the entire mouse genome. This challenging aim can only be achieved via intensive cooperation of high-ranking international research teams.

The GSF National Research Center for Environment and Health plays a leading role in this effort. Professor Wolfgang Wurst, Director of the GSF Institute of Developmental Genetics, is coordinator of EUCOMM, which is supported by the EU (FP6) with 13 million Euros. EUCOMM will be launched on Friday, 14 October 2005.

In the framework of EUCOMM, mouse genes will be inactivated by two different methods, i.e. conditional "gene trapping" and "gene targeting". In the case of "gene trapping" genes are switched off by random mutagenesis, in the case of "gene targeting", however, they are modified in a directed manner. 'Conditional' means that the mutations can be generated at a defined timepoint and in a defined tissue. Professor Wurst is one of the internationally leading scientists in this research field. In EUCOMM, his research group will use both mutagenesis strategies to generate mutant mouse embryonic stem (ES) cells.

The international scientific community will, via a database, have free access to the EUCOMM resource of mutant mouse ES cells. These cells will allow the cost-effective and standardized production of mouse mutants in any suitable laboratory,

so that the impact of defective genes – particularly with respect to human disease – can be investigated in an entire organism. In addition, the EUCOMM resource will contribute to a faster and cheaper development of new therapies and drugs.

To date, the EU project EUCOMM is the world-wide largest platform for conditional mutagenesis of the mouse genome. In the field of mouse functional genomics, Europe is a global leader. Furthermore, it plays a major international role in the elucidation of the genetic basis of human disease.

A Canadian project (NorCOMM), complementing the EUCOMM effort, is currently being launched, and the US National Institutes of Health (NIH) are planning a similar research program (KOMP). Both the scientists and the funding organizations involved in these three initiatives will cooperate closely on an international level to optimize complementation of the programs and to avoid overlaps. The eventual common target of the three projects is to mutagenize virtually all genes of the mouse genome. "We are planning to reach this ambitious goal together with the Americans within the next 3 to 5 years", says Wurst.

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