

Genes on Demand. International Initiative for Mutation of the Mouse Genome

Institute of Developmental Genetics

What's wrong with our genes when we face disease? An international research consortium wants to answer this question. In the next three to five years scientists will alter virtually all genes of the mouse genome to enable, via generation of mouse models, the functional analysis of human disease-related genes. The mouse genome is 99% identical to the human genome, rendering the mouse an ideal model organism. The mutation of mouse genes allows scientists to gain insight into the mechanisms of genetically determined diseases like Morbus Parkinson, cancer, and cardiovascular diseases.

The international research consortium will use both directed and random approaches to mutate all the mouse genes. The directed mutagenesis strategy, conditional gene targeting, is used to delete genes via homologous recombination, that is, by exchange of DNA sequences. The random approach for gene inactivation, conditional gene trapping, includes the application of a so-called reporter gene whose expression can easily be detected in the mutant organism. The loss of function of the mutated genes allows characterizing their role in the healthy organism. Three research projects, all using targeted mouse gene inactivation strategies, are planning to closely collaborate

in an international effort: the European EUCOMM project and its Canadian partner project NorCOMM were joined in September by another research team, the KOMP project of the American National Institutes of Health (NIH). EUCOMM is funded by the European Community with € 13 million and is coordinated by Professor Wolfgang Wurst, Director of the GSF Institute of Developmental Genetics.

Prior to the establishment of the international research consortium, scientists had to confront a quite unsystematic, fragmented research situation. Some 6,000 of the approximately 25,000 mouse genes were considered to be mutated and available. However, for a large proportion of these genes double or multiple naming had occurred. Furthermore, only 500 of these genes were conditionally mutated, i.e. alterable in a time- and space-controlled manner. In addition, the cost of developing individual mouse models was quite high. "A committee of the international consortium will now coordinate its joint activities and control completeness and efficiency of the mutagenesis effort", says EUCOMM Project Manager Dr. Cornelia Kaloff, GSF-Institute of Developmental Genetics.

A large proportion of the required technology was developed by Professor Wurst and his colleagues in conjunction with the International Gene Trap Consortium and the Wellcome Trust Sanger Institute, Hinxton, UK. Very soon, the international scientific community will be able to, via a central database,



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obtain mouse embryonic stem cells with single mutated genes rapidly and at a reasonable price to create mouse models for any desired genetically determined disease.

Literature:

- J. Auwerx et al.:
The European dimension for the mouse genome mutagenesis program.
Nat. Genet. 36 (2004) 925-927



Dr. Cornelia Kaloff

**EUCOMM Project Manager,
Institute of Developmental
Genetics**

**Telephone +49-89 / 31 87-22 75
cornelia.kaloff@gsf.de**