

Press Information

New Method for Identifying the Causes of X-Linked Genetic Disorders



Neuherberg, June 22, 2010. An international consortium of scientists of Helmholtz Zentrum München and the University of Toronto has identified previously unknown potential disease genes in humans and mice. Genes on the X chromosome, which regulate embryonic development, are the focus of the current publication in the renowned journal Genome Research.

Men have only one X chromosome, and therefore mutations on this chromosome disproportionately affect males, frequently leading to serious diseases such as hemophilia, muscular dystrophy and

mental retardation. Scientists of Helmholtz Zentrum München led by Dr. Heiko Lickert, principal investigator at the Institute of Stem Cell Research, in cooperation with the group led by Professor Janet Rossant at the Hospital for Sick Children in Toronto, investigated which X-linked genes are relevant to disease. They reported their findings in *Genome Research*, a leading journal on human genetics.

In cooperation with the Gene Trap Consortium coordinated by Professor Wolfgang Wurst of the Institute of Developmental Genetics, 58 genes were tested. That corresponds to 10 percent of the syntenic* genes on the X chromosome. 17 of these 58 genes are essential for embryonic development and for 9 of these genes, mouse models for human diseases were generated. These models will be studied in detail in follow-up studies in order to gain new insights about the causes of human diseases.

For the first time, the effect of the respective mutation on embryonic development could be shown without generating individual mouse models. Until now, mutation screens were essential to close such knowledge gaps, but such screens are associated with much effort and expense. "This study brings us much closer to our goal of understanding the genetic causes of all X-linked diseases," Dr. Lickert said.

Background

Except for the sex chromosomes, the chromosomes in the human genome occur in pairs. While women have two X chromosomes, men have only one X chromosome and one considerably smaller Y chromosome. That is why for a multitude of genes, men do not have a second copy which could inactivate mutations. In men, X-linked mutations lead to an above-average number of diseases.

* Synteny: Commonalities in the sequence of genes or gene fragments on different chromosome segments when comparing different species (here human and mouse).

Further Information:

Original Publication: Brian J. Cox et al., Phenotypic annotation of the mouse X chromosome; *Genome Research* 2010; Published in Advance June 14, 2010, doi: 10.1101/gr.105106.110

The **Institute of Stem Cell Research** investigates the main regulatory elements of cell fate and cell proliferation in different organ systems. The scientists study stem cells of different organs, for instance of the nervous system or of the lung and the pancreas, to elucidate the molecular and cellular mechanisms responsible for the key characteristic common to all stem cells. Another main focus is the regulation of the generation of specific cell types from stem cells with respect to a reconstituting therapeutic approach.

Helmholtz Zentrum München is the German Research Center for Environmental Health. Our aim is to develop an individualized medical approach to the prevention and treatment of widespread common diseases such as diabetes mellitus, lung diseases and diseases of the nervous system. As one of the world's leading centers with a focus on Environmental Health, we investigate the interaction of genetic disposition, environmental factors and lifestyle. Helmholtz Zentrum München has approximately 1800 staff members; its head office is located in Neuherberg to the north of Munich on a 50-hectare research campus. Helmholtz Zentrum München belongs to the Helmholtz Association, Germany's largest research organization, a community of 16 scientific-technical and medical-biological research centers with a total of 26,500 staff members. – www.helmholtz-muenchen.de

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