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Scientists Decipher the Human X Chromosome

Why this chromosome plays a special role

The nearly full sequencing of the X chromosome in humans is a milestone in biology and medicine. The results published today in the renowned specialist journal Nature in a joint article by genome researchers from Germany, the United Kingdom and the USA allow a better understanding of the evolution of the sex chromosomes and to identify the causes of X chromosome linked inherited diseases as well as cancers. Scientists of the Division of Molecular Genome Analysis headed by Professor Annemarie Poustka at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have made major contributions to the unraveling of the X chromosome.

Among the 23 chromosome pairs in humans, the X and Y chromosomes play a special role, since they determine the gender of a person. This pattern of gender determination is relatively new in developmental history. In the course of evolution, this chromosome pair has lost the ability to exchange genetic material and thus to recombine genes. Genes whose function requires simultaneous activation of two copies were probably “moved” by the X chromosome to other chromosomes. Since males possess only one X chromosome, gene defects on this chromosome will have an effect even if they are recessive, while a female must have the abnormal gene on both X chromosomes for it to be expressed.

The X chromosome consists of 155 million base pairs. Scientists have identified 1,098 genes on this strand of genetic material, which represent about 4 percent of all human genes. Although this places the X chromosome among the gene-poor human chromosomes, the number of hereditary diseases it is linked with is more than proportional. Some 10 percent (307) of all known monogenic disorders – i.e. disorders caused by a defect in a single gene – are associated with the X chromosome. The molecular causes of 168 of these disorders are known today. For more than a quarter of the related research work, the availability of the sequence of the X chromosome was already very helpful. For future research projects, it will be vital.

The DKFZ’s contribution to this 12-year international research collaboration has been the complete molecular analysis of a section on the X chromosome spanning about 10 million base pairs called region Xq28. Professor Annemarie Poustka has pursued this research project as a model project for the systematic analysis of complete chromosomes and the whole human genome. Back in 1987, Poustka started by developing novel, modern cloning systems that facilitate efficient production and multiplication of specific chromosome sections and by establishing the first chromosome-specific gene libraries. From early on she has achieved a synergy of new molecular-biological technologies and specific biological-medical questions. These studies have resulted in a very detailed knowledge of the base sequence in the chromosomal region under investigation, the nearly complete identification of all genes contained in this region and the unraveling of a multitude of X-linked inherited disorders. For numerous serious conditions such as neurological disorders of the MASA/CRASH Syndrome or the Fragile X Syndrome, which leads to mental disability, Annemarie Poustka and her co-workers have obtained essential scientific findings explaining their development and progression and providing diagnostic possibilities at a molecular level. The results obtained by the genome researchers at the DKFZ are also of great relevance for understanding a number of other diseases including adrenoleukodystrophy, primary muscle disorders in myotubular myopathy, signal transduction disorders in Incontinentia Pigmenti and multisystem disorders in Dyskeratosis Congenita.

The work now presented in Nature demonstrates once more the enormous value of systematic and internationally coordinated high-throughput studies for answering fundamental questions of biology and medicine and for our knowledge about disease mechanisms. The German contribution to this project has been funded by the Federal Ministry of Research and Education within the German Human Genome Project as well as by the Deutsche Forschungsgemeinschaft (DFG). The groups involved from Jena (Institute of Molecular Biotechnology), Berlin (Max Planck Institute for Molecular Genetics), Munich (Medical Genetics Section of the Ludwig Maximilian University) and Heidelberg (German Cancer Research Center) joined forces in 2001 within the National Genome Research Network and are working towards close interconnections between genomic and clinical research.

*Mark T. Ross et al.: “The DNA Sequence of the Human X Chromosome”, Nature, 17 March, 2005, Issue 7031, Volume 434.

This press release is available at www.dkfz.de/pressemitteilungen

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