GERMAN CANCER RESEARCH CENTER
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**Counting Cells That Ensure Gene Balance**

**Two are one too many – this is the motto used by cells of a female organism: These contain two X chromosomes, one of which always becomes inactivated. How does the cell recognize that it contains two of these sex chromosomes and how does it choose which one to turn off? Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), working together with French colleagues, have now been able to elucidate an early step in this complex process.**

Forty-five years ago, British scientist Mary Lyon already described this chromosome inactivation typical of female cells. Lyon proposed a hypothesis: With two copies of the X chromosome, all X-linked genes are present in two copies. However, in a male organism, which is equipped with a set of one X and one Y chromosome, the X genes are present in only one copy in each cell. To restore genetic balance, a female cell inactivates one of its two X chromosomes.

During development of a female embryo, inactivation of either of the X chromosomes, the one inherited from the father or the one inherited from the mother, occurs at random. To coordinate inactivation, the cell first needs to determine whether it contains more than one X chromosome and then make a choice which of the two to switch off. Since the mid-1980s it has been known that a specific region of the X chromosome termed X inactivation center (Xic) is crucial for a correct inactivation process.

**Professor Dr. Roland Eils**, who leads the bioinformatics departments at the German Cancer Research Center and at the Institute of Pharmacy and Molecular Biotechnology of Heidelberg University, suspected that the spatial arrangement of the Xics within the nucleus is key to inactivation. Working together with colleagues of the Curie Institute, Paris, he searched different cells for distinctive features in the distribution of Xic regions. The scientists compared developing female embryonic stem cells of mice just before X inactivation, with mouse cells in which X inactivation had already taken place. Using a 3-dimensional visualization of fluorescent labels of the Xic regions, they observed that the Xics of both X chromosomes in the developing stem cells were located very close to each other in up to 15 percent of cells. In the comparative cell line, this was found in only about three percent of cells, which constitutes a random result. The formation of pairs (co-localization) was particularly noticeable in the stem cells after about one and a half days of development, i.e. shortly before X inactivation.

A specific loss of DNA (deletion) in the Xic region of one of the two X chromosomes prevents the pairing of Xics. In addition, cells that have forgotten how to count show no pairing at all. The scientist postulate that the pairing of Xic regions is a necessary prerequisite for correct chromosome counting, but they cannot give any information yet as to what kind of interaction there is between the two Xic regions during transient co-localization.

C.P. Bacher, M. Guggiari, B. Brors, S. Augui, P. Clerc, P. Avner, R. Eils, and E. Heard: Transient colocalisation of X-Inactivation centres accompanies the initiation of X inactivation Nature Cell Biology, doi: 10.1038/ncb1365

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.).

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

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