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Pure Chance or Is There a System? Computer Program to Uncover Non-Randomness in Genome Sequence Distribution

For some years now, scientists throughout the world have been in a position to use the complete base sequence of the human genome for their analyses. A question often encountered is whether or not specific sequence motifs have a special function. This is likely in cases where the motif is found in a particular place more often than mere chance distribution would suggest. So far, such calculations have only been possible using time-consuming computer simulations.

Scientists at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and the National Center for Tumor Diseases (NCT) Heidelberg, collaborating with colleagues in Paris and London, have been able to develop a mathematical basis for these calculations, which is being further developed into a user-friendly and rapidly working computer software.

The researchers have tested their mathematical model in a real case from clinical practice: In the development of gene therapies, a commonly used transport vehicle for therapeutic genes is a virus that integrates its genetic material into the genome of a cell. Frequently it is not known whether the virus prefers specific sequence motifs for its integration. The software now makes it possible to search the genome sequence in the vicinity of already integrated viruses for a conspicuous distribution of particular sequence patterns.

“This has practical consequences,” says **Professor Dr. Christof von Kalle**, head of the Division of Translational Oncology of the German Cancer Research Center. “Unfortunately, there have been cases where viruses used in gene therapy have activated cancer genes in their direct vicinity. Yet if we know the preferred integration places of the virus, we can check for genes with a high danger potential in their immediate surroundings.” Therefore, von Kalle sees a multitude of possibilities for use of the program, particularly in the area of clinical trials.

The software will soon be made available to the scientific community free of charge.

Ulrich Abel, Annette Deichmann, Cynthia Bartholomae, Kerstin Schwarzwälder, Hanno Glimm, Steven Howe, Adrian Thrasher, Alexandrine Garrigue, Salima Hacein-Bey-Abina, Marina Cavazzana-Calvo, Alain Fischer, Dirk Jäger, Christof von Kalle, Manfred Schmidt: Real-Time Definition of Non-Randomness in the Distribution of Genomic Events. PloS One, DOI: 10.1371/journal.pone.0000570

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

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