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A new gold standard to improve cancer genome analysis

When various labs are asked to investigate cancer cell genomes in search of mutations, their results can sometimes show significant variations, a team of scientists from the International Cancer Genome Consortium (ICGC) found out in a worldwide interlaboratory test. The researchers have now provided a sequencing data record as a "gold standard" as well as guidelines for bioinformatic evaluation in order to create uniform worldwide standards in the search for cancer-relevant mutations. The study was led by scientists from the German Cancer Research Center (DKFZ) in Heidelberg and the Spanish National Center for Genome Analysis (CNAG-CRG) in Barcelona.

Oncologists are increasingly using information obtained from investigations of the tumor genome in order to find individualized therapies for patients. They specifically search the hereditary information of cancer cells for mutations that drive malignant growth. By now, targeted drugs against many of these cancer-typical cellular alterations have become available.

However, how precisely and reliably do the numerous laboratories that specialize in this search around the globe identify individual cancer mutations? And how does the quality and type of sequencing influence results? A team of experts collaborating within the International Cancer Genome Consortium (ICGC) launched an interlaboratory test to find this out. They distributed the DNA of a tumor to five ICGC laboratories and compared the quality of the resulting sequencing data records. The data record that had the highest quality was subsequently sent out to another 17 ICGC institutes for bioinformatic evaluation.

The investigators found significant variations both in sequencing and evaluation results in some of the cases. Only 40 percent out of one thousand small mutations, which each affected the exchange of only a single DNA base, were identified uniformly by all participating teams. The outcome for small DNA losses and insertions was even less favorable: Only a single one out of 337 of these genomic changes was identified by all of the centers.

The team of experts led by Ivo Gut from the Spanish National Center for Genome Analysis* and Roland Eils from the German Cancer Research Center therefore devised measures to improve this situation.

The DNA sequence from the circular experiment, which the participating ICGC labs have by now sequenced up to 300 times and analyzed with almost unprecedented precision, has now been made available for download. It serves as a kind of gold standard. Laboratories that start out in the field of genome analysis can use this data record as a basis to check whether the bioinformatic methods that they are using are capable of detecting all mutations concealed therein. In addition, the team developed evaluation guidelines that stipulate, among others, threshold values for detecting a particular mutation.

"Since tumor genome analysis is becoming increasingly common in cancer medicine, rigorous quality control is necessary – like in any other diagnostic method," says David Jones. "After all, whether or not a patient survives may depend on the detection of a particular mutation that can be treated efficiently with a drug that is already available." Ivo Buchhalter from the DKFZ, who is one of the first authors of the present study, is very pleased: "Several groups have already been able to substantially improve their results thanks to our measures."

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A picture is available at:
http://www.dkfz.de/de/presse/pressemitteilungen/2015/bilder/CNAG-094-WIJ_1739.jpg
Source: Centro Nacional de Analisis Genómico, (CNAG-CRG)

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 3,000 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg, where promising approaches from cancer research are translated into the clinic. In the German Consortium for Translational Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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