Oncogenic signatures mapped in TCGA a guide for the development of personalized therapy

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Clinical trial design for new cancer therapies has historically been focused on the tissue of origin of a tumor, but a paper from researchers at Memorial Sloan-Kettering Cancer Center published on September 26 in *Nature Genetics* supports a new approach: one based on the genomic signature of a tumor rather than the tissue of origin in the body.

It is well known that the emergence of cancer is a multi-step process, but because of the efforts of The Cancer Genome Atlas (TCGA), funded by the US National Institutes of Health, and other large-scale cancer genomics efforts, for the first time this process can be viewed in exquisite molecular detail, mapping mutations and other molecular events affecting any of the 20,000 genes in a human cell.

Now, two major hypotheses have been confirmed from the genomic analysis of more than 3000 samples from 12 different tumor types: a limited number of specific genetic events appear to cause most tumor subtypes and tumors can be grouped by the oncogenic signatures they contain, no matter what the tissue of origin. That these oncogenic signatures are largely independent of the particular tissue in which the cancer arises indicates that certain drug combinations may be beneficial for select patients with different types of cancer.

"In future clinical trials, we envision that patients with a certain type of endometrial cancer, for example, may be enrolled in the same trial as patients with a subtype of colorectal cancer, and that patient selection for clinical trials can be guided by cancer genomics profiling in the clinic," stated Chris Sander, one of the principal investigators of Memorial Sloan-Kettering's Genome Data Analysis Center. "This work is intended to help in the design of such trials and the development of more-personalized cancer therapies."

The ability to reveal sets of cancer-causing events in molecular detail is based on three major technical and scientific developments in the last decade. New high-throughput genomic technologies and lower operating costs have enabled the collection of genetic data from many thousands of tumors. The experience and knowledge accumulated in cancer genomics in many laboratories has taught us which of the many molecular alterations in cancer are likely to contribute to oncogenesis. Linking data and knowledge, new algorithms and methods for large data analysis in the field of computational biology provide the ability to find the proverbial needles in the haystack: to derive cancer-causing molecular genetic signatures and link them to tumor subtypes and potential therapies on the background of extremely high levels of informational noise.

The Memorial Sloan-Kettering team and their colleagues in TCGA and the International Cancer Genome Consortium plan to expand these comprehensive analyses to tens of thousands of tumor samples. A glimpse of the molecular tumor landscape in more than 13,000 tumor samples is already accessible in the cBioPortal for Cancer Genomics at http://www.cbioportal.org.

Principal authors on the study are Giovanni Ciriello, Nikolaus Schultz, and Chris Sander of the Computational Biology Center at Memorial Sloan-Kettering.

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