Researchers report clinical utility of personalized medicine program for cancer patients

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Scientists from the Icahn School of Medicine at Mount Sinai developed and tested a personalized cancer therapy program using an integrated genomic approach that led to therapeutic recommendations for 91 percent of patients. In a paper released today in *Genome Medicine*, they report results of the pilot program and show that multidimensional genomic profiles outperform the targeted cancer panels in use at many clinical labs today.

The genetic variants specific to a patient's tumor are important for guiding the choice of cancer treatment. As DNA sequencing has become more affordable, clinical labs rapidly adopted targeted sequencing panels which scan tumor DNA for some variants known to cause cancer. In the personalized cancer therapy program at Mount Sinai, researchers generated much more data about the genetic makeup of both patients and their tumors to determine whether this in-depth characterization led to better results.

"There is tremendous interest in tailoring cancer treatment for each patient, since every tumor has its own unique signature of genetic variants that shape progression and response to therapy," said senior author of the study Rong Chen, PhD, Assistant Professor of Genetics and Genomic Sciences and Director of Clinical Genome Informatics at the Icahn Institute at Mount Sinai. "We launched this program with the idea that a more comprehensive view of that variant signature would

make a difference in patient treatment, but even we were surprised by just how much is being missed with current testing."

The scientists analyzed whole exomes, gene expression, copy number variation, and gene fusions of both tumor samples and matched normal samples for an initial group of 46 patients. Participants had a wide range of cancer types—including colon, thyroid, and breast—and many were in advanced stages of the disease. In 42 of the 46 cases, the integrated genomic profile led to medically actionable genetic variants with implications about drug response, toxicity, or prognosis. The team also ran commercially available targeted cancer panels for each sample, finding that these tools failed to detect medically actionable variants for many patients. All results were returned to patients and their physicians, and in several cases the information led to changes in treatment.

"The argument against this integrated approach is the added cost of using multiple analysis platforms. But for patients battling cancer, it's hard to put a price on information that may lead to more successful outcomes," said Eric Schadt, PhD, the Jean C. and James W. Crystal Professor of Genomics at the Icahn School of Medicine at Mount Sinai, and Founding Director of the Icahn Institute for Genomics and Multiscale Biology. "We believe labs could maximize benefit by implementing a staggered approach, starting with targeted panels and incorporating multiscale characterization for patients lacking medically actionable variants."

More information: Andrew V. Uzilov et al, Development and clinical application of an integrative genomic approach to personalized cancer therapy, *Genome Medicine* (2016). DOI: 10.1186/s13073-016-0313-0

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