Personalized medicine best way to treat cancer, study argues

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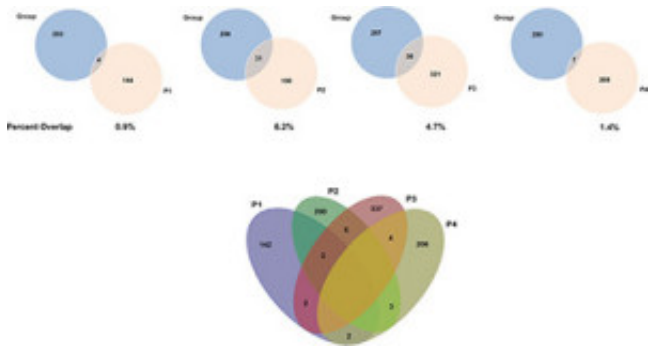

Venn diagrams show the unique, annotated genes identified as significantly differentially expressed in the group analysis and in the personalized analysis(es) of at least 1 patient (P1: Patient 1, P2: Patient 2, P3: Patient 3, P4: Patient 4). Credit: Lili, et al., 2014.

If a driver is traveling to New York City, I-95 might be their route of choice. But they could also take I-78, I-87 or any number of alternate routes. Most cancers begin similarly, with many possible routes to the same disease. A new study found evidence that assessing the route to cancer on a case-by-case basis might make more sense than basing a patient's cancer treatment on commonly disrupted genes and pathways.

The study found little or no overlap in the most prominent genetic malfunction associated with each individual patient's disease compared to malfunctions shared among the group of cancer patients as a whole.

"This paper argues for the importance of personalized medicine, where we treat each person by looking for the etiology of the disease in patients individually," said John McDonald, a professor in the School of Biology at the Georgia Institute of Technology in Atlanta. "The findings have ramifications on how we might best optimize cancer treatments as we enter the era of targeted gene therapy."

The research was published February 11 online in the journal *PANCREAS* and was funded by the Georgia Tech Foundation and the St. Joseph's Mercy Foundation.

In the study, researchers collected cancer and normal tissue samples from four patients with pancreatic cancer and also analyzed data from eight other pancreatic cancer patients that had been previously reported in the scientific literature by a separate research group.

McDonald's team compiled a list of the most aberrantly expressed genes in the cancer tissues isolated from these patients relative to adjacent normal pancreatic tissue.

The study found that collectively 287 genes displayed significant differences in expression in the cancers vs normal tissues. Twenty-two cellular pathways were enriched in cancer samples, with more than half related to the body's immune response. The researchers ran statistical analyses to determine if the genes most significantly abnormally expressed on an individual patient basis were the same as those identified as most abnormally expressed across the entire group of patients.

The researchers found that the molecular profile of each individual cancer patient was unique in terms of the most significantly disrupted genes and pathways.

"If you're dealing with a disease like cancer that can be arrived at by multiple pathways, it makes sense that you're not going to find that each patient has taken the same path," McDonald said.

Although the researchers found that some genes that were commonly disrupted in all or most of the patients examined, these genes were not among the most significantly disrupted in any individual patient.

"By and large, there appears to be a lot of individuality in terms of the molecular basis of pancreatic cancer," said McDonald, who also serves as the director of the Integrated Cancer Research Center and as the chief scientific officer of the Ovarian Cancer Institute.

Though the study is small, it raises questions about the validity of pinpointing the most important gene or pathway underlying a disease by pooling data from multiple patients, McDonald said. He favors individual profiling as the preferred method for initiating treatment.

The cost of a molecular profiling analysis to transcribe the DNA sequences of exons—the parts of the genome that carry instructions for proteins—is about $2,000 (exons account for about two percent of a cell's total DNA). That's about half the cost of this analysis five years ago, McDonald said, and a $1,000 molecular profiling analysis might not be far off.

"As costs continue to come down, personalized molecular profiling will be carried out on more cancer patients," McDonald said.

Yet cost isn't the only limiting factor, McDonald said. Scientists and doctors have to shift their paradigm on how they use molecular profiling to treat cancer.

"Are you going to believe what you see for one patient or are you going

to say, 'I can't interpret that data until I group it together with 100 other patients and find what's in common among them,'" McDonald said. "For any given individual patient there may be mutant genes or aberrant expression patterns that are vitally important for that person's cancer that aren't present in other patients' cancers."

Future work in McDonald's lab will see if this pattern of individuality is repeated in larger studies and in patients with different cancers. The group is currently working on a genomic profiling analysis of patients with ovarian and lung cancers.

"If there are multiple paths, then maybe individual patients are getting cancer from alternative routes," McDonald said. "If that's the case, we should do personalized profiling on each patient before we make judgments on the treatment for that patient."

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