Tumor sequencing study highlights benefits of profiling healthy tissue as well

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As the practice of genetically profiling patient tumors for clinical treatment decision making becomes more commonplace, a recent study from The University of Texas MD Anderson Cancer Center suggests that profiling normal DNA also provides an important opportunity to identify inherited mutations that could be critical for patients and their families.

Preliminary findings from this ongoing study will be presented by Funda Meric-Bernstam, M.D., professor and chair, Investigational Cancer Therapeutics, on June 1 at the American Society for Clinical Oncology 2015 Annual Meeting in Chicago.

The MD Anderson research team sequenced tumor and normal DNA from patients with advanced cancer, with the goal of sharing results with patients to better educate them going forward. Sequencing normal tissue is not routinely done in the research environment, but comparing tumor versus normal DNA can distinguish between germline, or inherited, mutations and those found only in the tumor.

"This is an opportunity to identify germline mutations that could have contributed to a patient's cancer development and may be a heritable cancer syndrome that would put the patient's family members at risk," says Meric-Bernstam, who is also medical director of the Khalifa Institute for Personalized Cancer Therapy. "Therefore, it would be important to inform the patient and their family members so they can get further testing, genetic counseling and risk-reducing efforts as needed."

In this study, researchers performed targeted sequencing of 202 genes, including a panel of 19 genes for which mutations are implicated as a significant cancer risk. The American College of Medical Genetics and Genomics recommends that harmful mutations in these genes, including TP53, BRCA1, BRCA2, PTEN and RB1, be shared with patients because of that risk. Of the 1,000 patients analyzed, 99.9 percent had at least one germline variant in one of these 19 genes.

Further analysis revealed 43 of these patients had mutations considered likely to be pathogenic. Importantly, more than half (23) of these patients were previously not known to have mutations, highlighting the utility of this approach. All mutations were confirmed in a clinical laboratory, with 100 percent agreement.

Although the data is valuable to the care of patients, not all research protocols take into account how best to share this information, explains Meric-Bernstam. In this study, 99 percent of patients said they would like to be informed of harmful mutations. Those with pathogenic germline mutations are now being brought back for formal genetic counseling, a critical component of the study.

"Patients have been very interested and, overall, grateful to be part of this protocol, recognizing the importance of this finding, especially for their families," says Meric-Bernstam.

Once family members are made aware of the possibility of harmful inherited mutations, they can get tested for specific mutations in the gene(s) in question. Depending on those results, they can enroll in high-risk screening programs that may detect the disease early and may offer risk-reduction measures.

Meric-Bernstam does not suggest all cancer patients should have their tumors sequenced. But for those already having sequencing performed,

"it is important to consider analyzing the normal data as well in order to capitalize on the opportunity to inform the patients and their families of the findings."

Going forward, the research team will complete analysis of additional patients included in the study to identify those with potentially harmful mutations and build upon their experience in reporting those results in order to clarify the best way to utilize data obtained from this approach.

Provided by University of Texas M. D. Anderson Cancer Center