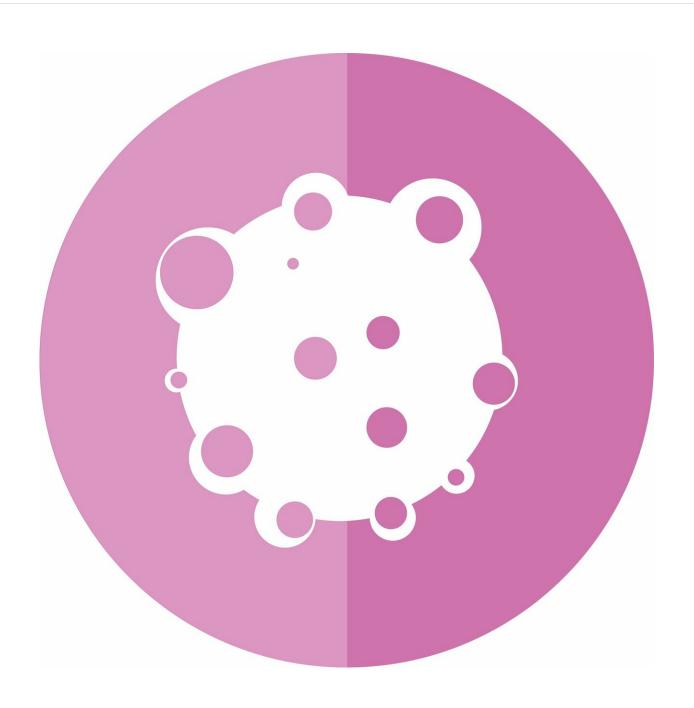


Study suggests tumor mutational load may be useful metric to predict response to checkpoint-inhibitor immunotherapy

January 15 2019, by Bob Yirka





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A large team of researchers affiliated with Sloan Kettering Cancer Center, Weill Cornell Medical Center and Columbia University Medical Center has found that the mutational load of a tumor may be a useful way to predict a response to checkpoint-inhibitor immunotherapy across different types of cancer. In their paper published in the journal *Nature Genetics*, the group describes their study of over 1,500 patients with advanced cancer who had undergone checkpoint-inhibitor immunotherapy, and what they found.

Checkpoint-inhibitor immunotherapy is a type of treatment for cancer patients whereby an attempt is made to prevent cancer cells from suppressing the body's natural immune response, allowing it to fight tumor development. Unfortunately, for some patients, it does not work as well as for others. In their search to understand why this is the case, medical scientists have also been trying to figure out which patients would benefit from such treatment and which will not. Doing so would save precious time for those patients who will not benefit from it, allowing doctors to prescribe a more effective treatment. In this new effort, the researchers found what they believe is a reliable way to test patients prior to administration of treatment—testing their mutational load. A mutational load, also known as tumor mutation burden, is a number that describes the rate of DNA faults in a tumor, which is a way of quantifying mutation rates in tumors.

The study consisted of sequencing cells from a very large number of cancer patients, both those who had undergone checkpoint-inhibitor immunotherapy and those who had not, and looking for a pattern that



would indicate differences. They found that those patients with higher mutational loads responded better to checkpoint-inhibitor immunotherapy than did those who had smaller load readings. They also found that different types of cancers had different load thresholds. The team notes that they do not know why a high mutation rate makes patients better candidates for checkpoint-inhibitor immunotherapy, but they do have a theory. They think it might be because higher mutation rates tend to result in cell proteins that are more mangled and easier for the immune system to recognize.

More information: Robert M. Samstein et al. Tumor mutational load predicts survival after immunotherapy across multiple cancer types, *Nature Genetics* (2019). DOI: 10.1038/s41588-018-0312-8

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