

Model predicts early response to cancer immunotherapy

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Killer T cells surround a cancer cell. Credit: NIH

Researchers have developed a model that could predict early on in treatment whether cancer patients will respond to immunotherapy, according to a report published today in *eLife*.

The model could provide doctors with a way to identify those who will benefit from immunotherapy at an early stage in their [cancer treatment](#) using readily available information from hospital scans and laboratory tests. This would allow patients to receive personalized treatment and could avoid some people experiencing side effects from a treatment that may not work for them.

"Although immunotherapy has transformed survival for a subset of [cancer patients](#), durable treatment effects are still only seen in a minority," says Zhihui Wang, Associate Research Professor of Mathematics in Medicine, Houston Methodist Research Institute, Houston, Texas, US, and one of the co-first and co-senior authors of the study. "Mathematical models can qualitatively or quantitatively discern the underlying complex biological and physical processes in [cancer](#) which may otherwise be missed and can help optimize treatment approaches. We wanted to demonstrate how standard clinical measures, such as images from scans and analysis of tissue biopsies, could be used to build a model that predicts who might benefit from immunotherapy."

The team focused on looking at how patients respond to a class of immunotherapy drugs called [immune checkpoint inhibitors](#). They designed a model to determine changes in relative tumor mass over time after patients start their checkpoint inhibitor therapy. The change in tumor mass is influenced by a complex biological cross-talk between the immune system and [cancer cells](#). They simplified this cross-talk by focusing on three measurements that can be combined into an equation: The ability of malignant tumor cells to grow, the ability of immune cells to kill cancer cells within the tumor environment and the potential effectiveness of checkpoint inhibitor-based immunotherapy treatment.

They first calibrated this model using [clinical data](#) from [clinical trials](#) evaluating a class of checkpoint inhibitors that specifically target the PD-1/PD-L1 pathway. The trials measured changes in tumor volumes

over time in 189 patients with common types of tumors.

The team then checked the results from this model calibration against data from an additional group of 64 patients with non-small cell lung cancer who were treated with an immunotherapy drug called pembrolizumab.

They found that the ratio of immune to tumor cells within the tumor environment, and the potential effectiveness of checkpoint inhibitor treatment, were both significantly different between responding versus non-responding patients. Importantly, the model correctly predicted the treatment response that occurred in 81.4% of patients using only tumor volume measurements and within two months of treatment initiation. This high sensitivity of the model to predict a response at early time points (less than 60 days) suggests that the model could provide valuable early identification of cancer patients most likely to benefit from checkpoint inhibition therapy. There were also minimal false-negative results from the model related to the group of patients predicted to receive the least benefit from therapy. This is important to ensure the model does not wrongly predict that a patient will not benefit from a treatment that might be effective.

"The model introduced here retrospectively investigates the molecular, cellular and biophysical mechanisms behind a patient's individual response to immune checkpoint inhibitor therapy," concludes Eugene Koay, Associate Professor at the Department of Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, and a co-senior author of the study. "We have demonstrated that this [model](#) can reliably use information from routine scans or tissue biopsy analysis, which are easily obtainable as early as the start of treatment. Together, these measurements may serve as early and accurate indicators of the effectiveness of immunotherapy [treatment](#) on an individual patient basis."

More information: Joseph D Butner et al, Early prediction of clinical response to checkpoint inhibitor therapy in human solid tumors through mathematical modeling, *eLife* (2021). [DOI: 10.7554/eLife.70130](https://doi.org/10.7554/eLife.70130)

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