Scientists identify key biomarkers that reliably predict response to immune checkpoint inhibitor therapy for melanoma

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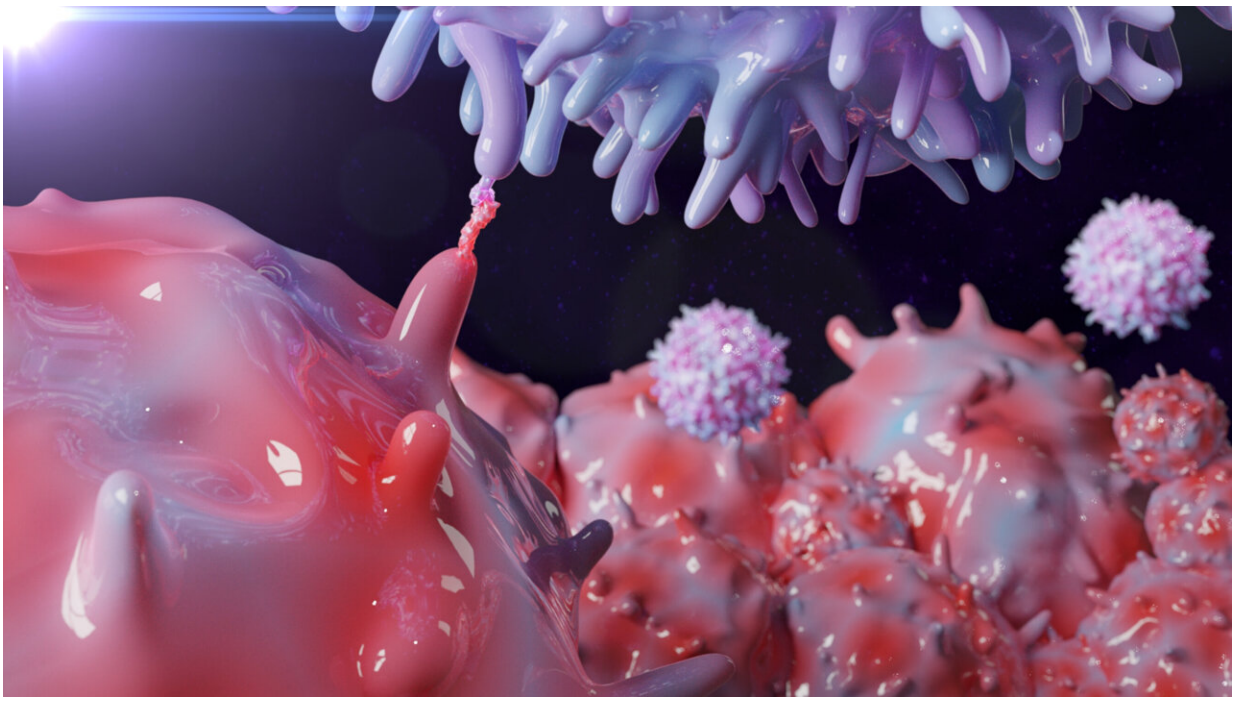

Immune Checkpoint. Credit: Wistar Institute

Immune checkpoint inhibitor (ICI) therapy is a type of treatment for melanoma, the deadliest form of skin cancer, which blocks proteins on tumor or immune cells that prevent the immune system from killing cancer cells.

While this treatment has shown some clinical success in patients with advanced stages of melanoma, its efficacy depends on reliable predictors of a patient's response to the therapy. Currently, the only FDA approved biomarker for ICI melanoma treatment is the tumor mutation burden assay, but the mechanisms linking it to ICI remain unclear.

However, new research now provides evidence of novel, reliable biomarkers that predict therapy response using advanced computer technology.

In a paper published in *Nature Communications*, Noam Auslander, Ph.D., assistant professor in the Molecular & Cellular Oncogenesis Program of Wistar's Ellen and Ronald Caplan Cancer Center, and Andrew Patterson, graduate student in the Auslander lab, identify novel predictors of ICI therapy for melanoma.

In particular, mutations in the processes of leukocyte and T-cell proliferation regulation show potential as biomarkers with reliable and stable prediction of ICI therapy response across multiple different datasets of melanoma patients.

"This work aims to identify better and more biologically interpretable genomic predictors for immunotherapy responses," notes Auslander. "We need better biomarkers to help select patients that are more likely to respond to ICI therapy and understand what factors can help to enhance responses and increase those numbers."

Using machine learning and publicly available de-identified clinical data, researchers investigated why some melanoma patients responded to ICI therapy and others did not. Patterson, first author on the paper, details that their research process involved training machine learning models on a dataset to predict whether a patient responds to ICI therapy, and then confirming that the model was able to continually predict response or

resistance to this treatment over multiple other datasets.

The team found that leukocyte and T-cell proliferation regulation processes have some mutated genes that contribute to ICI treatment response and resistance. This knowledge could be used to identify targets to enhance responses or mitigate resistance in patients with melanoma.

"We were able to better predict if a patient would respond to ICI therapy than the current clinical standard method as well as extract biological information that could help in further understanding the mechanisms behind ICI therapy response and resistance," Patterson explains.

The scientists intend to continue this work with the goals of increasing prediction accuracy, further understanding biological mechanisms underpinning patient resistance or responsiveness to ICI therapy, and determining whether the processes distinguished in the paper can also serve as predictors of ICI treatment response for other cancer types.

More information: Andrew Patterson et al, Mutated processes predict immune checkpoint inhibitor therapy benefit in metastatic melanoma, *Nature Communications* (2022). DOI: 10.1038/s41467-022-32838-4

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