Researchers identify biomarkers to predict patient response to immunotherapy treatment for melanoma

February 17 2022

David R. Soto-Pantoja, Ph.D., associate professor of surgery and cancer biology at Wake Forest School of Medicine, and Elizabeth Stirling, graduate student, were part of a team of researchers who discovered blood biomarkers that can potentially predict patient response to immunotherapy for melanoma. Credit: Wake Forest School of Medicine

Melanoma, a type of skin cancer, is often curable when detected and treated in its early stages. However, the disease can rapidly spread to other organs in the body and become deadly. According to the American Cancer Society, more than 7,600 people die of the disease each year in the United States.

Thankfully, immune checkpoint inhibitors (ICI), a type of immunotherapy, have transformed the treatment of certain cancers, including melanoma, and improved patient care. But despite the availability of this immunotherapy, doctors have been unable to predict who will benefit from ICI and who will not.

Now, a team of researchers at Wake Forest School of Medicine, led by David R. Soto-Pantoja, Ph.D., associate professor of surgery and cancer biology, has discovered blood biomarkers that can potentially predict patient response.

Results from the study are published online in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

"When immunotherapy works, it can be very successful and improve overall survival. About 20% to 40% of patients will respond," Soto-Pantoja said. "But predictive biomarkers are urgently needed to guide treatment decisions and to develop new approaches to therapeutic resistance."

For the study, scientists analyzed blood samples of two patient groups before treatment, both with stage III and IV melanoma. One group of patients responded to ICI treatment and had a complete or partial response. The other patient group did not respond to ICI treatment and had disease progression.

Scientists examined the bioenergetics or cellular metabolism of

circulating immune cells called peripheral blood mononuclear cells and the metabolomic profiles of plasma.

Cancer cells consume abnormal nutrients and release factors that can be sensed by blood circulating cells. According to Soto-Pantoja, it's possible that mitochondria of circulating cells can sense these metabolic changes. Soto-Pantoja's team also examined how this organelle changes function in patients' blood cells.

"We found functional and molecular metabolic biomarkers, which are associated with ICI response, can be detected in blood before treatment," Soto-Pantoja said.

The circulating immune cells of patients who responded to treatment had an increased extracellular acidification rate, a measure of glucose metabolism. Investigators also found changes in mitochondrial shape and structure changes that were linked to the response. In addition, the team identified a common metabolic signature that distinguished responders and non-responders—increased lactate levels to pyruvate (specific lipid and amino acid metabolites) and an elevated glucose receptor in patients who responded to treatment.

"Our study shows new insight in the treatment of melanoma that can be extended to other cancer types," Soto-Pantoja said. "These biomarkers can potentially lead to personalized treatment strategies to improve overall survival."

More information: Circulating Immune Bioenergetic, Metabolic, and Genetic Signatures Predict Melanoma Patients' Response to Anti–PD-1 Immune Checkpoint Blockade, *Clinical Cancer Research* (2022).