

Diabetes Center Takes Lead in Investigating Autoimmune Side Effects of Cancer Immunotherapy

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The rapidly expanding field of cancer immunotherapy sparks new hope for many patients coping with advanced forms of the disease. Immunotherapy, which boosts the immune system's ability to detect and attack malignant cells, has extended lives, and in some cases put into remission cancers that previously were considered incurable.

Cancer immunotherapies are significantly less toxic than traditional cancer treatments such as chemotherapy and radiation, but they are not without possible adverse complications. Some patients develop permanent autoimmune side effects, including type 1 diabetes.

These patient experiences caught the attention of Mark Anderson, MD, and Jeff Bluestone, PhD. Together, they and their teams are working to understand which cancer immunotherapy patients risk developing type 1 diabetes and what strategies they can deploy to mitigate potential side effects.

The lessons learned may improve the care of cancer patients while also shedding light on the molecular pathways at the heart of immune tolerance ? lessons that could lead to new treatments for diabetes.

Gaining a Better Understanding of Side Effects

In the Anderson Lab, endocrinology fellow Zoe Quandt, MD, collects blood samples from cancer patients who developed type 1 diabetes while undergoing immunotherapy at UCSF and partnering research institutions. The lab will examine the samples for clues that help explain why the patients experienced this side effect.

In the Bluestone Lab, postdoctoral scholar Arabella Young, PhD, spearheads the creation of a mouse model at high risk for type 1 diabetes. The team will induce the development of cancer

in the animals, treat them with immunotherapies, then determine whether they acquire the same autoimmune side effects that have been reported in humans.

The Anderson and Bluestone teams seek to answer some pressing questions: How similar is immunotherapy-related diabetes to conventional type 1 diabetes? Is therapy-induced diabetes a new disease, or do the patients who develop it have an underlying risk for diabetes that went unnoticed?

Ultimately, the teams hope to develop interventions to protect cancer immunotherapy patients from the autoimmune side effects of the treatment.

Implications for Diabetes Research

Adverse events affecting nearly every organ system have been reported in association with cancer immunotherapies, but the development of type 1 diabetes seems to be most often linked to an immunotherapy that targets a specific pathway.

"The PD-1/PD-L1 pathway is showing itself to be an important player in immune tolerance," said Dr. Quandt. "By studying cancer immunotherapy-related type 1 diabetes and this pathway in particular, we may also learn a great deal about the traditional form of the disease — knowledge that may help us develop strategies for keeping diabetes at bay in all patients."

Dr. Mark Anderson is the Robert B. Friend and Michelle M. Friend Professor of Diabetes Research. Dr. Jeff Bluestone is the A.W. and Mary Margaret Clausen Distinguished Professor of Metabolism and Endocrinology as well as president and CEO of the Parker Institute for Cancer Immunotherapy.

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