

Patients' Own Autoantibodies May Hold Key to Boosting Cancer Immunotherapy Response

A study finds that some cancer patients can make their “own companion drug,” suggesting a potential template for future treatments.

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SEATTLE — July 23, 2025 — A landmark study has revealed that autoantibodies — immune proteins traditionally associated with autoimmune disease — may profoundly influence how cancer patients respond to immunotherapy.

The study, published July 23 in [Nature](#), offers a potential breakthrough in solving one of modern-day oncology's most frustrating mysteries: why checkpoint inhibitors work for some patients but not others — and how we can extend their benefits to more people.

“Our analysis shows that certain naturally occurring autoantibodies can tilt the odds dramatically toward shrinking tumors,” said senior author [Aaron Ring, MD, PhD](#), an associate professor at Fred Hutch Cancer Center. “We saw some cases where autoantibodies boosted a patient's likelihood of responding to checkpoint blockade by as much as five- to ten-fold.”

The Nature study suggests that autoantibodies could help reveal cancer's weak spots and point to new targets for treatment.

Autoantibodies are proteins produced by the immune system that recognize the body's own tissues. They are most associated with their harmful role in driving autoimmune diseases like lupus or rheumatoid arthritis. However, emerging evidence indicates that in some cases, autoantibodies can surprisingly exert health benefits.

“For years, autoantibodies were viewed mainly as bad actors in autoimmune disease, but we're discovering they can also act as potent, built-in therapeutics,” said Ring, who holds the [Anderson Family Endowed Chair for Immunotherapy](#) at Fred Hutch. “My lab is mapping this hidden pharmacology so we can turn these natural molecules into new treatments for cancer and other illnesses.”

In the Nature study, Ring and his collaborators used a high-throughput assay he developed —

called REAP (Rapid Extracellular Antigen Profiling) — to screen for over 6,000 types of autoantibodies in blood samples from 374 cancer patients receiving checkpoint inhibitors and 131 healthy individuals.

Checkpoint inhibitors have transformed treatment for a wide range of cancers including melanoma and non-small-cell lung cancer by unleashing the immune system to see and attack cancer. But not all patients respond to these treatments and, in many cases, their anti-tumor effects are incomplete and do not result in a cure.

Using blood samples collected from patients and healthy individuals, the REAP analyses revealed that cancer patients had substantially higher levels of autoantibodies compared to healthy controls.

Importantly, certain autoantibodies were strongly linked to better clinical outcomes, indicating their potential role in enhancing the effectiveness of immunotherapy.

For example, autoantibodies that blocked an immune signal called interferon were linked to better anti-tumor effects from checkpoint inhibitors. This finding mirrors other studies showing how too much interferon can exhaust the immune system and then curtail the effects of immunotherapy.

“In some patients, their immune system essentially brewed its own companion drug,” Ring explained. “Their autoantibodies neutralized interferon and that amplified the effect of checkpoint blockade. This finding gives us a clear blueprint for combination therapies that intentionally modulate the interferon pathway for everyone else.”

Not all autoantibodies were beneficial. The team discovered several that were associated with worse outcomes from checkpoint inhibitors, likely because they disrupted critical immune pathways necessary for anti-tumor responses. Finding ways to eliminate or counteract these detrimental autoantibodies could open another promising avenue for enhancing the effectiveness of immunotherapy.

“This is only the beginning,” Ring said. “We’re now extending the search to other cancers and treatments so we can harness — or bypass — autoantibodies to make immunotherapy work for far more patients.”

The study was funded by The Mark Foundation for Cancer Research, The Pew Charitable Trusts and generous donors to Fred Hutch. Ring is the founder and a director of Seranova Bio, the commercial licensee of the REAP technology that was used in this paper.

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