

The Future of Immunotherapy & Cell-based Therapies

Physician-scientist Antoni Ribas explores anti-PD-1 immunotherapy given before surgery, called neoadjuvant therapy.

April 11, 2024 By [Melanoma Research Alliance](#)

“Melanoma research helped lead the way to a lot of paradigm shifts in cancer treatment,” says Dr. Antoni Ribas, Professor of Medicine, Surgery, and Molecular and Medical Pharmacology at the University of California Los Angeles (UCLA).

Today, Ribas is a world-renowned physician-scientist, an elected fellow of the American Association for Cancer Research (AACR) Academy, the American Society of Clinical Investigation, and the National Academy of Medicine, among others. However, early in his career, Ribas was discouraged from pursuing tumor immunology.

“For a while, people were not keen on anyone who wanted to do research in tumor immunology,” he says. But Ribas was intrigued. He wanted to learn more about the biology of tumors and bring this knowledge to his patients. Tumor immunology studies the relationship between immune function and tumor cells, including the cellular and molecular mechanisms that affect how a tumor interacts with immune system cells, the tumor environment, and how the immune system can be harnessed as a treatment for cancer.

Reflecting on how the field has evolved, Ribas points to the number of therapies that were being studied just ten years ago in clinical trials that have now become standard of care for patients with melanoma. This has particularly been true for anti-PD-1 drugs, which Ribas knows firsthand.

That’s because ten years ago, he was the principal investigator of a large phase 1 trial studying the anti-PD-1 drug and checkpoint inhibitor pembrolizumab, which enables the immune system to better attack cancer. This work demonstrated how the immune system could lead to durable responses in patients and helped pave the way for melanoma treatment as we know it today.

“Another step forward has been the testing of anti-PD-1 antibodies before surgeries,” says Ribas. Currently anti-PD-1 immunotherapy has been approved to be given after surgery, what is called [adjuvant therapy](#). However, what Ribas and others soon realized was that in doing so, they not only removed tumor tissue but also surrounding immune cells that could recognize the tumor. When immunotherapy was given following surgery, these potent anti-tumor immune cells would

no longer be present to respond to anti-PD-1 antibodies.

To explore this area further, Ribas and his collaborator Dr. Sapna Patel (MD Anderson) conducted a study of patients who received three doses of immunotherapy first, underwent surgery, and then continued with immunotherapy. This approach, called neoadjuvant therapy, proved effective with a nearly 50% improvement of survival over adjuvant therapy. “This is another place where melanoma’s leading the way, because the paradigm should be the same for other cancers,” says Ribas. “We hope that patients with other cancers can benefit from immunotherapy before surgery.”

Ribas is exploring other innovative areas of treatment as well, including cell-based immunotherapy. Certain immune cells appear to recognize differences between melanoma and normal healthy cells. Ideally, these cells would be activated naturally by the body to attack cancerous cells. However, in situations where this does not work, scientists like Ribas are studying ways to take the immune system cells out of the body, grow them in a laboratory, and infuse them back into the patient. This is called [cellular therapy](#) for cancer and there are two main groups:

1. Immune cells purified from a surgically removed tumor or biopsy, called tumor-infiltrating lymphocytes or TILs, are expanded in the lab and reinfused back to the patient to elicit a stronger anti-tumor immune response.
2. Immune cells isolated from the patient’s blood are genetically modified to recognize and attack melanoma, and then infused back into the body. This gives the immune system cells a kind of “GPS” to find the melanoma and destroy it.

TIL therapy, first pioneered by Dr. Steven A. Rosenberg at the National Cancer Institute, is a labor intensive process and involves isolating specific immune cells from a surgically removed tumor and then giving nutrients to help them grow to very large quantities. This creates a proverbial army of immune cells that are then infused back into the patient with the goal of supercharging the immune response against and ultimately killing all cancerous cells.

Genetically modified immune cells (as mentioned in the second example above), have acquired new receptors to recognize and attack melanoma. “The key question is, do we have receptors that redirect the immune system to melanoma in a safe way, avoiding the immune system attacking normal cells?” says Ribas. “This has not been the easiest thing to tackle, but progress is being made.”

Once the cell therapies are developed, patients still need to be conditioned with high doses of chemotherapy to deplete their existing immune systems. Once the immune system is wiped out, the new immune system — that has been carefully created for them in the lab — can be infused into the patient. This puts limitations on who can receive cell therapies because of the toll it takes on the body.

“Cell therapies have become the standard of care in patients with lymphomas, leukemias, and multiple myeloma,” says Ribas. “We know that the same principles could work in melanoma,

because of TIL therapy, but more work is still needed to better target those immune system cells.” The U.S. Food and Drug Administration (FDA) has approved one cellular therapy for melanoma: [AMTAGVI \(lifileucel\)](#).

Although there is still more work to be done, it’s incredible to see just how far the field has come. A big contributor of this work has been MRA. “Since its founding, MRA has been the largest non-profit funder of melanoma research,” says Ribas.

“The grants chosen for funding by MRA are reviewed by a panel of experts that include the best in the field. MRA’s early stage grants enable researchers to venture into new fields and are very important to opening up new areas of research,” he says.

“As scientists we try to understand the problems that limit treatments and then we innovate from there, hoping that what we discover can have a beneficial impact on the patients we serve,” says Ribas.

“This approach is what leads to advances both in our scientific understanding but also in improved patient outcomes.”

And it’s working.

“If we look back 10 years ago, less than 1 in 20 patients had a chance to live long-term,” says Ribas. “Now, close to half of the patients with advanced melanoma are living years beyond their diagnosis, and probably many of them have in fact been cured. That’s why we as scientists continue to do what we do. This is the power of research — and I’m proud to be part of it.”

[This post](#) was originally published by the [Melanoma Research Alliance](#). It is republished with permission.