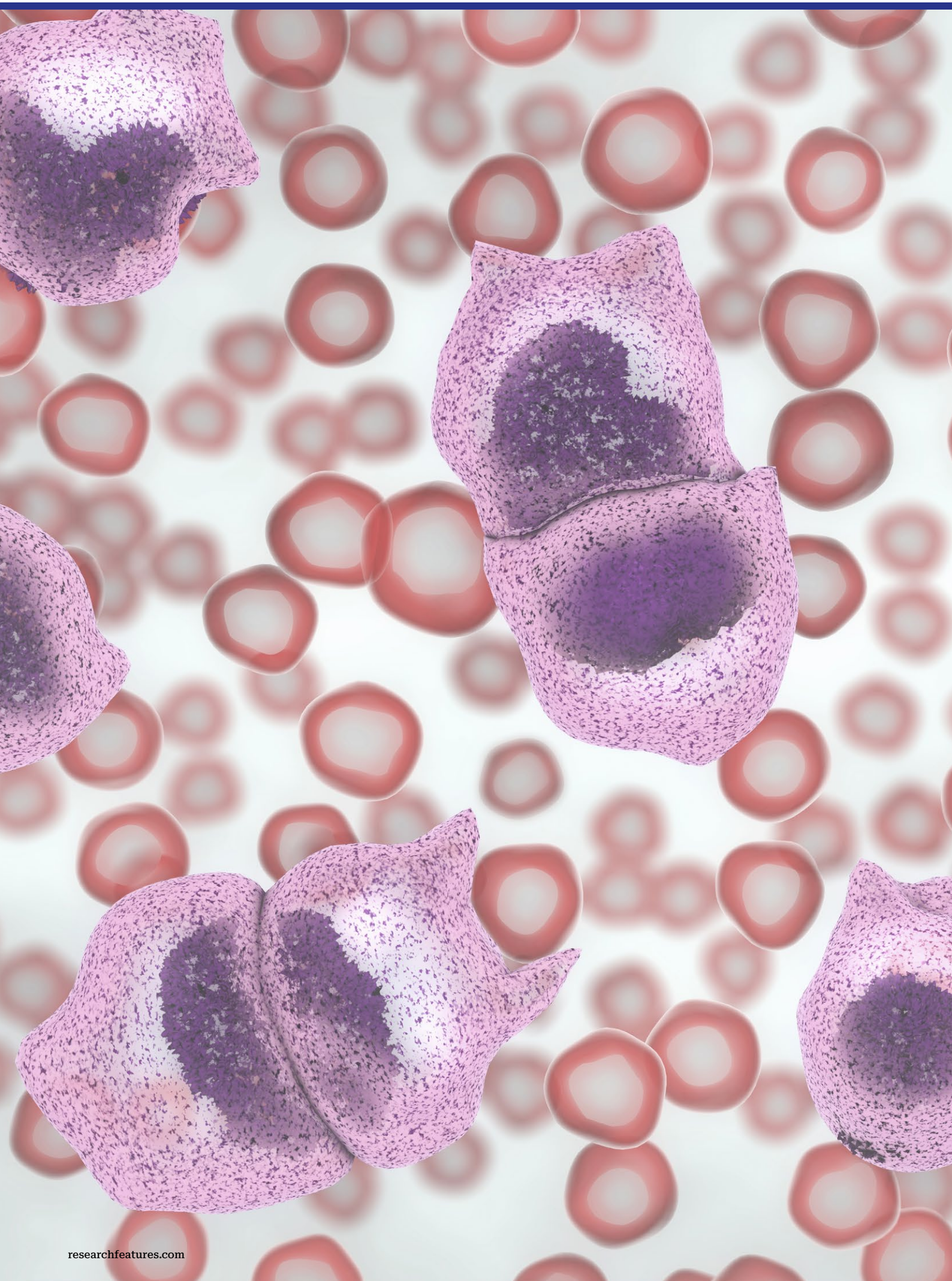


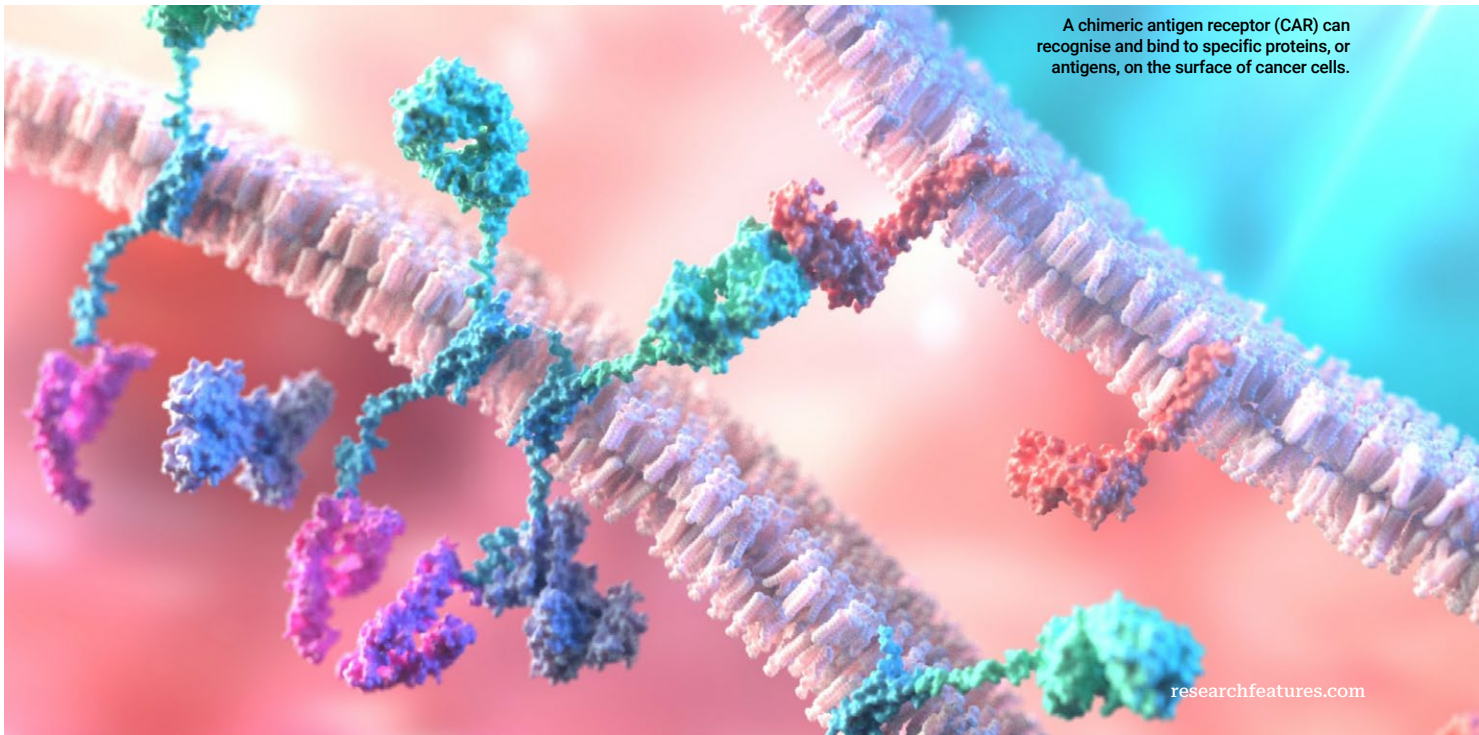
Latest developments in cancer immunotherapies

- B cell cancers have historically been treated with chemotherapy and high-energy radiation.
- Recently, immunotherapy treatments have also been added to the oncology clinician's quiver. Chimeric antigen T cell receptors and bispecific antibodies show promising results against B cell cancers.
- But are these treatments effective, and how can we optimise the way we give them to patients?
- Researching this is Dr Priya Hays of Hays Documentation Specialists, USA, an immunologist, science writer, and expert stakeholder in the field of cancer immunotherapies. She has worked with faculty and served as editor on a well-regarded edited collection on the subject published by Springer Nature.

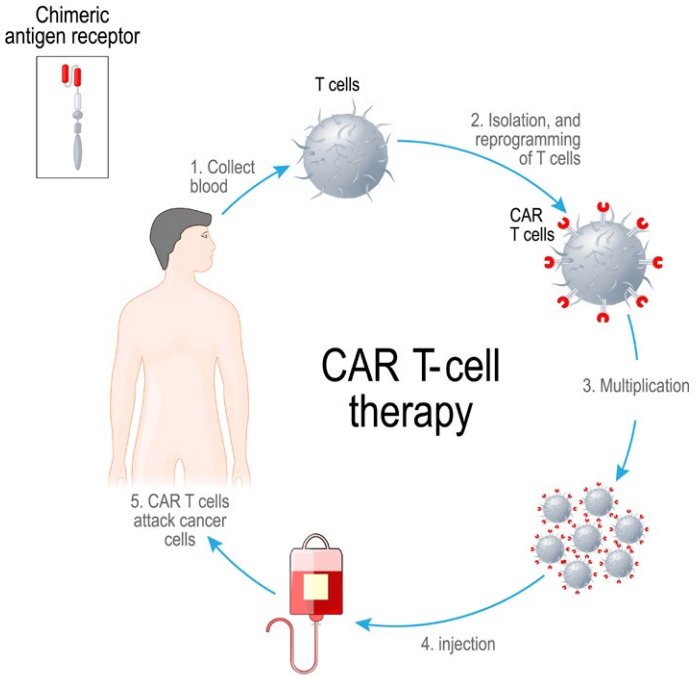
The immune system is the sum of all our body's defence mechanisms against bacteria, viruses, and cancer. It is a complex system that employs white blood cells or leukocytes – a variety of cells that can fight off intruders. The type of leukocytes that can produce antibodies are called B-lymphocytes or B cells. B cells are produced in the bone marrow but can also be found in the blood and in the organs of our body's lymphatic system which includes lymph nodes, pea-sized structures scattered across our body, and our spleen, an organ positioned in the left upper corner of our abdomen. The immune system is divided into innate immunity and adaptive immunity. Innate immunity is in response to acute infection and consists of cells such as natural killer cells, neutrophils and macrophages. Adaptive immunity constitutes the 'memory' of the immune system; it reacts to foreign antigens that have presented earlier and consists of T cells and B cells. The immune system works through antigen presenting cells, also known as dendritic cells that present immunoglobulins and T cells to antigens on the surface of tumour cells, viruses and bacteria or any other form of non-self.

The cancers that start from our B cells are called B cell cancers or B cell malignancies. B cell malignancies are divided into lymphomas, a type of cancer that grows in the lymphatic system, and leukaemias, a cancer of the bone marrow and blood. There are a number of oncology treatments available for treating B cell cancers. These include traditional chemotherapy agents which are agents that directly kill cancer cells; radiotherapy, which kills tumour cells with the help of high-powered energy beams; and also a number of novel and recently developed treatments such as cancer immunotherapies which use our immune system to fight off cancer. These newer treatments include immune checkpoint inhibitors, which target key mechanisms of the immune system; chimeric antigen T cell receptors, which improve the

CAR T-cell therapy helped minimise the disease in 83% of patients with acute lymphoblastic leukaemia.



A chimeric antigen receptor (CAR) can recognise and bind to specific proteins, or antigens, on the surface of cancer cells.



Chimeric antigen T cell receptors (CAR T-cell therapy).

immune cell ability to kill cancer cells; and bispecific antibodies that are developed to target the cancer cells and kill them or make them easier to kill.

These new treatments have dramatically changed the way doctors treat these cancers and are already making a huge difference in care by increasing patients' survival. But how efficient and safe are these new treatments? Dr Priya Hays, CEO of Hays Documentation Specialists has researched the different treatment plans that involve these newer drugs as well as their efficacy and toxicities.

How checkpoint inhibitors work

T-cells are another type of leucocyte with the ability to defend our body against diseases. T cells are divided into T regulatory cells, CD4+ T cells and CD8+ T cells (CD stands for cluster of differentiation and is a type of cell surface marker). CD8 T cells are the cytotoxic T cells that are responsible for anti-tumour activities.

New treatments are dramatically changing the way we can now treat cancers.

T cells are covered in molecules called checkpoint proteins that can turn an immune response on and off. One of them, the anti-programmed death-1 (PD-1) protein, turns T-cells off when they are not needed, thus preventing them from destroying healthy cells and tissues. Some cancer cells can take advantage of this function by sending a signal to turn the PD-1 button off. This deactivates the T cells which can no longer recognise and kill cancer cells. Programmed death 1 (PD-1) inhibitors are drugs that block this cancer cell signal and prevent them from switching the PD-1 button off. This keeps the T cells active and able to detect and kill the cancer cells. The drugs have been found work against solid tumours such as lung cancer and melanoma (skin cancer). More specifically, recent trials have shown that most of the patients with solid tumours that had treatment with a PD-1 inhibitor called nivolumab had a good result with their disease decreasing or becoming inactive. Nivolumab was well tolerated by most patients with only 1 in 5 reporting side effects, one of the most severe ones being inflammation of the lungs.

Chimeric antigen T cell receptors

Chimeric antigen T cell receptors (CAR T-cell therapy) are cell surface receptors used to engineer the patient's own T cells. These lab-engineered T cells are left to multiply and are then given back to the patient to help fight off cancer cells more efficiently. This revolutionary method of treating B cell malignancies helped minimise the disease in 83% of patients with a specific type of B cell leukaemia called acute lymphoblastic leukaemia. CAR T-cell therapy was also shown to work on patients with B cell lymphomas since 82% of them had fewer signs and symptoms of the disease after an average 14.5 months of treatment, and 52% of them were alive at least 18 months after treatment.

Despite its promising results, CAR T-cell therapy is not without its toxicities. Some of the reported side effects include fever, loss of appetite, and damage to the heart, liver, and kidneys. The treatment can also affect the brain and nerves, but these symptoms were found to be short-lived and easy to control with anti-inflammatory medicines such as steroids.

Novel combination treatments

Researchers have recently managed to combine the two treatments described above by using bispecific antibodies attached to engineered T cells. These are lab-made antibodies that can simultaneously bind to both the T cells and the cancer cells, bringing them together and helping the immune system to kill the cancer cells. These types of immunotherapies combine CD3-CD19 epitopes – connecting cytotoxic T cells with antigens on the tumour cell surface. Treatments using bispecific antibodies have proven to be that effective against B cell cancers, such as acute lymphoblastic leukaemia.

What happens next?

The initial trial results for both checkpoint inhibitors and CAR T-cell therapy have been positive, showing both efficacy and safety when used on patients with B cell cancers and solid tumours. Most of the side effects were reversible and the treatments were both tolerated well by patients. These groundbreaking methods have recently revolutionised oncology care; however, it's clear that further and longer studies are needed to evaluate the long-term benefit and survival for these patients, as well as to optimise treatment plans and doses to minimise the drug toxicities as much as possible.

Both checkpoint inhibitors and CAR T-cell therapy have been positive, showing both efficacy and safety when used on patients with B cell cancers and solid tumours.

Personal response

What inspired you to investigate the available immunotherapy treatments?

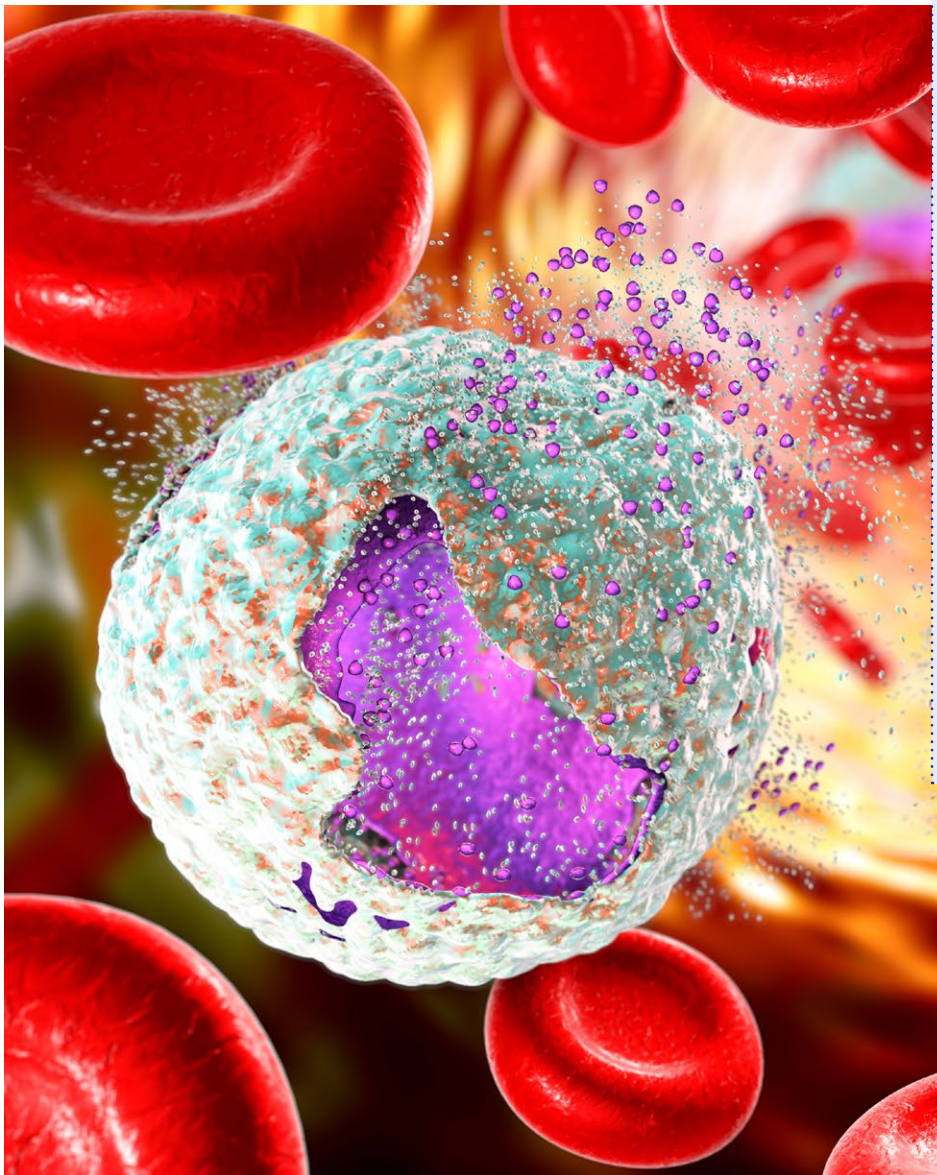
I took a course at a local university in immunology after being introduced to CAR T-cell therapies at a pharmaceutical company. The course was fascinating with excellent instruction. At that time immune checkpoint inhibitors were being introduced to the field. Springer Nature, an international publisher of medical books, invited me to submit my research to their *Cancer Treatment and Research* series. I submitted a proposal on cancer immunotherapies and with the help of the Society for Immunotherapy of Cancer, I was able to corral experts in the field who wrote excellent chapter contributions. The series editor is Steven Rosen, MD, of the City of Hope, California, who is one of the outstanding clinician/mentors in the field, and invited me to contribute a chapter on bispecific antibodies in the edited collection. This collection *Cancer Immunotherapies: Solid Tumors and Hematologic Malignancies* has over 17,000 downloads and 17 citations.
I continued to publish in the field, and now have membership in the American Association of Immunologists.

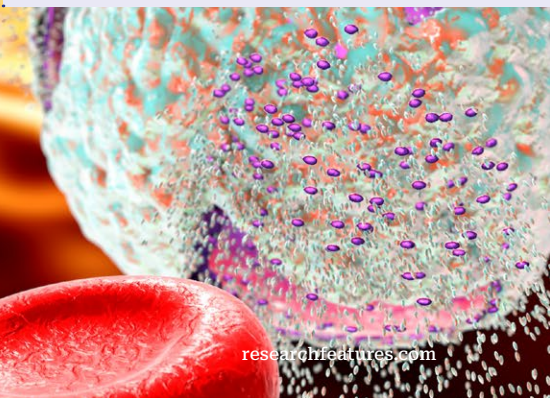
What does your review and its findings add to the current literature?

I wrote and published two articles on cancer immunotherapies within the last year on cancer stemness and immune checkpoint inhibitor efficacy and next generation immunotherapy agents for tumours that do not respond to anti-PD-1 agents. This was preceded by my work on CAR T-cell therapies for B cell malignancies. These papers discussed the clinical trial landscape for these therapies and adverse events associated with them and their management.

What will be your next step in this research?

I am writing new research on immunopathology and bispecific antibodies-cytokine therapy combinations in the near future.





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Bio

Priya Hays, MS, PhD is an accomplished science writer, having written and published five books as well as having authored over sixteen publications in scientific and medical journals. She has also served as editor for a volume on cancer immunotherapies. She is an Elected Member of the American Assocation of Immunologists; an Elected Member of Medical Societies (as Allied Physician/Doctoral Scientist of the American Society of Clinical Oncology; as Affiliate Member of the American College of Medical Genetics and Genomics; and as Member of the Society for Immunotherapy of Cancer). Her latest book *A Dialectical Mind: Essays in Literary Studies, Science and Medicine* was just released by Eliva Press.

Further reading

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Competing interest statement

Priya Hays has relevant stock ownership.