

# New weapon against cancer

- Natural Killer T (NKT) cells combine the rapid response of innate immunity with targeted adaptive mechanisms, making them a potent force against cancer.
- Derived from the patient's own blood, NKT cells may serve as an adjunctive therapy after surgery, chemotherapy, or radiotherapy.
- The successful application of NKT therapy depends on rigorous quality control, including GMP-compliant cell preparation, sterility tests, and viability assessments, to ensure safety.

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**C**ANCER is an ever-growing problem in modern society. In Malaysia, we are not spared from this disease. A report from the National Cancer Registry Department, examining data from 2017 to 2021, suggests that the lifetime risk for Malaysians is now one in eight.

This disease not only affects the lives of patients. It can also change the lives of those caring for the patients, like their families and friends.

At present, we have robust arsenals to fight against cancer, such as chemotherapy, radiation therapy and surgical resection.

Chemotherapy, which is a collection of different drugs with each having different mechanisms of action, has been a reliable weapon in our fight against cancer. However, these drugs come with a lot of debilitating side effects, some that could be attributed to damage to healthy cells by chemotherapy agents.

Therefore, despite their effectiveness, researchers still seek more effective and targeted therapies with potentially fewer side effects.

## A PROMISING CANDIDATE

Immunotherapy has shown great strides in improving care for patients living with cancer by offering a more targeted treatment. Monoclonal antibodies have shown great success in the care of patients living with cancer.

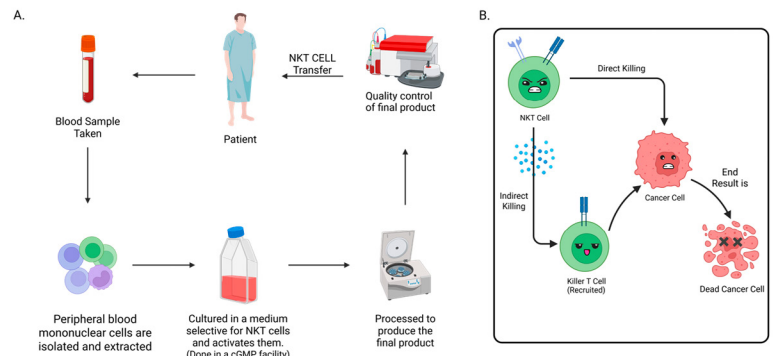
The field of cell-based immunotherapies is one subset of the broader immunotherapy family to examine. Cell-based immunotherapies manipulate the activity of the cellular warriors of our immune system to fight various diseases, including cancer, without requiring antibody production.

This is not a novel idea; we have taken one of our warriors, the T-cell, and genetically modified its receptor to develop the chimeric antigen receptor T cell therapy (CAR-T).

Would it be possible to use another one of our cellular warriors, which is a known destroyer of cancer cells, in the quest to improve cancer care?

**A. Autologous NKT immunotherapy, from blood collection to ex vivo cell expansion and product quality check prior to patient clinical infusions.**

**B. Diagrammatic illustration of anti-cancer killing mechanisms of NKT immunotherapies, both through direct cancer cell killing and indirect recruitment of other immune cells (e.g. killer-type cells) to mediate anti-cancer effects.**



## THE NATURAL KILLER T CELL

Natural Killer T (NKT) cells are a specialised subset of T cells that also exhibit functions similar to those of Natural Killer (NK) cells.

T-cells are typically associated with the adaptive immune system and are a crucial component of the cell-mediated immune response. NKT cells are unique as they are a part of the innate immune system, which does rapid and “non-specific” killing, which is unusual as other T-cells participate in the slow yet specific killing of anything that is “non-self”, which is the hallmark of the adaptive immune system.

Like NK cells, NKT cells are able to kill tumours both without sensitisation by the Major Histocompatibility Complex (MHC) Class 1 molecule and with MHC induction, indirectly killing tumours through activated CD8+ cytotoxic T-cells. Despite sharing similar functions and cell surface markers with NK cells, they have distinct mechanisms that lead to their activation in destroying virus-infected cells and cancer cells.

NKT cells are activated when their T-cell receptor recognises the CD1d molecule on an antigen-presenting cell. At the same time, NK cells are activated by recognising the absence of an MHC class 1 molecule on a cell.

One method of utilising NKT cells in the fight against cancer is through the adoptive transfer of in vitro-expanded NKT cells. These cells are obtained from a peripheral blood sample and then cultured and stimulated with cytokines until a sufficient number of cells is achieved.

Prior to the intravenous infusion of these cells, a flow cytometry analysis is conducted to assess the purity of the NKT cells based on their cell surface markers. To further ensure safety, sev-

eral steps should be taken. Notably, it should be made in a cGMP facility.

A certificate of analysis (COA) should also be prepared, including information on the final cell product, such as quality control sterility tests for fungus, bacteria, endotoxins, and mycoplasma conducted before infusions, as well as tests for cell population purity, viability, and proper batch IDs.

These quality control steps will ensure the final products released for clinical use are free of contamination and possess quality-certificate cells for disease therapy use.

## HOW WILL THIS WEAPON BE APPLIED IN THE FIGHT AGAINST CANCER?

The current goal of using adoptive NKT cell transfusions is to enhance the natural anti-cancer response of the immune system, rather than serving as a stand-alone drug. So, if it gets licensed, it could serve as an adjunctive post-care option following conventional treatments, such as chemotherapy, radiotherapy, and surgery, or other immunotherapies.

There are challenges associated with the use of NKT cells in cell-based immunotherapies. Extracting NKT cells from an autologous source would be a challenge, as the number of these cells in a cancer patient is typically low. Immunosuppressive effects from the tumour microenvironment are also a hurdle that needs to be overcome to boost the efficacy of cell-based immunotherapies.

NKT-based therapies could be stalwart in post-care cancer therapy, especially in preventing relapse and controlling minimal residual disease. These cells could help narrow the gap between innate and adaptive immunity, making them a valuable asset in post-treatment immune surveillance. - **The HEALTH**