

# Connect

ISSUE 05  
APR - JUN 2021



Celebrating Life  
Across The Region

Doctor's Corner  
Dr Francisca Tan

IOC Staff  
Recognition Award

Car-T Cell Therapy  
Treatment for Blood Cancer



## IOC Reaches Out To Cancer Survivors and Caregivers

Started by the National Cancer Survivorship Foundation in USA, 6 June is recognised as National Cancer Survivorship Day, celebrating those who have survived cancer and inspiring others to maintain hope as they battle cancer.

Aimed at motivating patients and their caregivers to stay positive in their journey to recovery, Integrated Oncology Centres (IOC) also echoed the National Cancer Survivorship Foundation's initiative and dedicated the whole month of June to show its support to those who are battling cancer as well as those who have conquered the disease.

Cancer survivorship includes three main facets, mainly caregiving, dealing with recurrence and staying strong in the fight against cancer.

### **Coping with being a cancer caregiver**

The role of caregivers is important in the cancer care management journey. Providing care and support to cancer patients is not an easy task and often gets overwhelming as caregivers juggle with the social and psychological impact of seeing their loved ones go through challenging times. Furthermore, there is also the financial burden that one might face in this journey to consider.

Here are unknown responsibilities that caregivers have to shoulder:

Role Categories	Types of Support	Examples
Support with activities of daily living	Personal care	Assist with bathing, dressing, toileting, movements
	Managing the home	Ensure rent/mortgage and utilities are paid; cleaning, laundry
	Logistical support	Transportation and planning of errands and activities
	Emotional and mental support	Provide support through touching, listening, attention, humor, pragmatism, stoicism; assist with referral to mental health services
Psychosocial support	Social and spiritual support	Respect and support of spiritual needs; empathy
Navigating the healthcare system	Health insurance and social services benefit management	Pay health insurance claims; apply for disability benefits
	Coordination of appointments and visits	Manage schedule related to routine visits for cancer treatment; accompany to healthcare visits
	Transition of care between healthcare institution and home	Organize care after hospital discharge; provide assurance of continuity of care
	End-of-life care	Advocate for patient; communicate patient preferences; provide decision support for palliative and/ or hospice care

Source: Role of Caregivers: <https://www.ahajournals.org/doi/10.1161/>



...continued from page 3

It is important for caregivers to remember that they are not alone in this journey. If caregivers feel overwhelmed, they are encouraged to seek counsel and support from their social network. They can also reach out to healthcare professionals who would be willing to provide advice on how to better manage their emotions and wellbeing. Throughout this journey, it is important for caregivers to remember that self-care should be a priority and caregivers need to take time off for their own physical, mental and emotional well-being as well.

### **Managing cancer recurrence**

As unfortunate as it may seem, cancer recurrence and relapse is not unheard of in cancer patients. While it might be challenging to predict a recurrence, the risks of a relapse are known to increase when the cancer is fast growing and more advanced or widespread.

It is imperative for cancer patients to understand the possibilities of cancer recurrence and associated ramifications so they feel empowered to take charge of their own journey to recovery.

This includes making lifestyle modifications such as changes in diet, exercise, sleep patterns and even stopping habits such as smoking. Cancer patients also need to be educated on the importance of regular screening for early detection of a relapse. Patients also need to follow their doctors' instructions on screening for relapse or continuing on follow-up therapies if needed.

### **Staying motivated throughout your cancer care journey**

The battle against cancer does not come easy for anyone. A cancer survivor has to navigate several challenges in their everyday lives. This includes recovery from the side effects of the treatment, changes in lifestyle, and societal stigmas associated with cancer. Most often, patients may have the urge to jump right back into their daily routines without considering the repercussions. Unfortunately, in most cases, it might be physically stressful and take longer for them to get back to their familiar routines. This sometimes leads to demotivation.

In order to stay motivated and well-informed, cancer survivors should consider steps like lifestyle modification to stay in remission, counselling and regular screening as part of their routines to resume normal life after treatment.

IOC hopes to encourage all cancer survivors to celebrate every milestone achieved throughout their journey to recovery and most importantly to "celebrate life" each day.





# Indonesia

## Adi Husada Cancer Centre



► Inspirational story by a cancer patient



► Motivational quote by a cancer survivor



# Hong Kong

## Hong Kong Integrated Oncology Centre



# Celebrating Life A

The Covid-19 did not dampen our spirits to  
 share more about encouraging stories about  
 Here is a quick snapshot of how I  
 cancer survivors





# Philippines

## Central Luzon Integrated Oncology Centre

### Across The Region

celebrate milestones and our enthusiasm to  
at cancer survivorship in the month of June.  
OC celebrated the milestones of  
ors across Asia:



► Tips for care givers



► Online health education activity



# Vietnam

## Hung Viet Healthcare Network

# Congratulations To The Recipient of IOC Staff Recognition Award 1Q2021

## Nguyen Thi Bich Ngoc, Director of Nursing Hung Viet Cancer Hospital (HVCH), Vietnam

IOC would like to take the opportunity to recognise and celebrate employees who have demonstrated their commitment and dedication in their work with our Staff Recognition Award programme that commenced this year.

Through this programme, employees across IOC are given a chance to nominate any of their colleagues who have made a significant impact in the workplace and have lived out IOC's mission. The panel of judges comprises a team from the IOC corporate head office and committee across the region.

We are proud to announce that the first quarter IOC Staff Recognition Award goes to Ms Nguyen Thi Bich Ngoc, Director of Nursing in Hung Viet Cancer Hospital, Vietnam. She was nominated by Mr Sam Lee, the CEO of Hung Viet Healthcare Network (Hung Viet Cancer Hospital and Hung Viet General Clinic) for her dedication and leadership to the team especially during COVID-19 pandemic.

Over the past two years, new triage policies, visiting restrictions and PPE requirements were implemented in HVCH due to stringent measures taken to contain the spread of COVID-19 in the country. Despite the disruptions and uncertainty during this period, Ms Ngoc was able to lead the team at Hung Viet by making swift decisions and executing actions promptly, taking into consideration the needs of the staff and patients. Even in the midst of the worst COVID-19 period in Hanoi, she still ensured that ward rounds were carried out three times daily to make sure that all patients were well taken care of. When HVCH received a complaint from a patient's family member about the new restrictions, she was the first to stand out and explain to the family member

with great patience.

Her perseverance in delivering seamless care is just one of attributes that make her exceptional. Ms Ngoc is now in her 70s, but age does not stop her from learning about new technology. Due to the Covid-19 pandemic, many new tests, vaccines and treatment protocols were introduced in the hospital but Ms Ngoc was the first group of staff who learnt the new technology. With her deep understanding of the daily clinical operations, she incorporated the new technology effectively into the workflow and led the team to implement the new workflow to tackle the challenges caused by the COVID-19 pandemic.

As a role model and the mentor for younger nurses, Ms Ngoc has taken a lot of effort to train the second generation of nurses for the HVCH. Young nurses have benefited from her knowledge as well as her professional attitude in embracing new technology which is essential in the oncology practice.





◀ Mr Sam Lee, CEO of Hung Viet Healthcare Network (HVHN) presenting the IOC Staff Recognition Award Certificate to Ms Ngoc (left)

“  
The past 17 months have not been easy for everybody. Thank you Ms Ngoc for your energy and dedication in juggling the additional COVID-19 responsibilities and work.  
Thank you for being my inspiration and being part of the team, ”  
- Mr Sam Lee, CEO.



# Doctor's Corner

**Starting from this issue of our newsletter, we will be featuring our specialists across the IOC network and their unique stories on why they chose their profession and specialize in cancer treatment.**

## **Here is the story of Dr Francisca Tan:**

I am Dr. Francisca Tan and Franchy is my nickname. I am a practising Medical Oncologist in Central Luzon Oncology Centre (CLIOC), Philippines. I would like to first share some facts about cancer in Asia. According to the WHO, in the Southeast Asian region, "Cancer is the 4th leading cause of mortality." Thus, the sub-specialty of dealing with cancers does not seem to be an attractive field, right? But then again, at the flipside, it is a very challenging and satisfying endeavour to enter into this sub-specialty.

Here are some of my reasons: I realized on my first day of fellowship training that I was offering hope to patients. Secondly, it is very humbling to talk with patients who "think" they are the end of their ropes, but when I explain the options of treatment and dispel their fear of "dying soon," their demeanour changes and their eyes light up with expectations. My third reason is that in the past decade, so many advancements have been made in the treatment, diagnosis and surveillance of the different kinds of cancer. And, in the past 20 years, the death rates for many types of cancer are steadily decreasing. Every patient I encounter is unique and every case is a challenge in treatment.

I would also like to share a little bit about myself and why I chose to become a doctor. I grew up in a family of doctors, my grandfather, both parents (although my dad died when I was 6 years old), my older sister, and brother were all doctors. I even have cousins who are doctors. So, naturally, it was easy to decide to go into medicine, even though I excelled in economics while I was in Highschool.

Putting personal facts aside, it is not an easy task to deal with cancer patients. This is because, you not just handle the patient, but also the impact on his/her family, and even protection of the family from their risk of acquiring cancer. Being diagnosed with cancer is life-changing. The patient and his/her family's emotions, routine, and finances, will be greatly affected by the cancer care and treatment. I usually witness some form of distress and trauma in each patient and their families. They really appreciate it when I take the time to listen to their stories, even when they just talk about their kids, their grandchildren and their daily routines.

So, back to my question as to what it is like to care for a cancer patient? As a doctor, the experience of treating a cancer patient is very daunting because our responsibilities are heavy. The patient is entrusting us with the task to cure the cancer, decrease the rate of recurrence or to prolong life for those in advanced stages. But now, given all the new arsenals in treating cancer, it is a very hopeful field. And for those who have loved ones and friends who do have cancer, I applaud you for your patience amidst your own stress. Do not give up on your battle.

I am very happy and thankful to have a wonderful and supportive team here at CLIOC, so I can focus on giving my best to all the cancer patients. I hope to continue with my mission to give quality cancer care to all patients.

**DR FRANCISCA ROSARIO E. TAN,**

MD, MSc, FPCP, FPSMO, FPCGM  
Medical Oncologist  
Central Luzon Integrated Oncology Centre (CLIOC)



“

As a doctor, the experience of treating a cancer patient is very daunting because our responsibilities are heavy. The patient is entrusting us with the task to cure the cancer, decrease the rate of recurrence or to prolong life for those in advanced stages. But now, given all the new arsenals in treating cancer, it is a very hopeful field. ”

A 3D digital illustration of a CAR-T cell, shown as a large, white, textured sphere with numerous thin, white, hair-like projections extending from its base. A bright red, textured spherical cancer cell is attached to the top of the white cell. Two other red cancer cells are shown floating in the dark blue background. The text 'What is CAR-T cell therapy?' is overlaid in white on the central part of the image.

# What is CAR-T cell therapy?

## Introduction

The four traditional pillars of cancer therapy have been surgery, radiation therapy, chemotherapy and targeted therapy. In the recent years, cellular therapy for cancer treatment has emerged as the fifth pillar of therapy.

Amongst cellular therapy, a specific form of treatment known as CAR (chimeric antigen receptor) T-cell therapy has gained attention worldwide for its use in the treatment of various forms of blood cancers. To date CAR-T cell therapy has demonstrated significant benefit in the treatment of conditions such as B-cell acute lymphoblastic leukaemia, B-cell lymphomas and multiple myeloma. Several forms of CAR-T cell therapy have been licenced by the US FDA over the last few years for clinical use.

## What is CAR-T cell Therapy?

T-cells are a form of white cells in our body which play an important role in the recognition and clearance of foreign bodies, including cancer cells. However, in patients with aggressive forms of cancer, the T-cells can sometimes be ineffective in clearing the cancer, due to the fact that they cannot effectively recognise the cancer cells, or they may not be able to infiltrate areas where the tumour is.

**Chimeric antigen receptor (CAR) T-cell therapy** is a way to get T-cells to fight cancer more efficiently by genetically modifying them in the laboratory. These gene-modified CAR T-cells are able to express a tumour specific receptor on their cell surface which allows them to identify and destroy specific cancer cells with highly potent activity.

After CAR-T cells are infused into a patient, they act as a “living drug” against cancer cells. When they come in contact with their targeted cancer cell, CAR-T cells bind to it and become activated, then proceed to proliferate and become cytotoxic.

The present generation of CAR T-cells are largely constructed using T-cells from patients themselves (autologous T-cells). This can pose logistical challenges, as patients who are requiring T-cells are often heavily pre-treated, and sometimes it

is hard to harvest an adequate amount of T-cells to manufacture the CAR-T cell product. The next generation CAR T-cells will involve certain products which may be ‘off-the shelf’ cellular therapy products made using pre-harvested and produced cells from carefully selected donors (allogeneic T-cells).

## What are the Indications for CAR-T cell therapy?

The initial development of CAR T-cell therapies focused largely on Acute Lymphoblastic leukaemia (ALL), which is the most common form of cancer in children. More than 80% of children are diagnosed with ALL that arises in B cells. One of the great success stories of modern cancer therapy is that with present day chemotherapy combinations, children with ALL have a 5-year overall survival of 80-90%.

However, in the minority of children with more aggressive forms of ALL, relapsed ALL remains a leading cause of death from childhood cancer. Targeted antibody treatments as well as allogeneic haematopoietic stem cell transplantation have been existing forms of rescue options for these patients. In recent years, CAR T-cell therapy for B-cell ALL in children and adolescents has produced excellent results with initial response rates of 70-90%.

The most significant clinical results have come from CAR-T cell trials studying autologous CD19-specific CAR-T cell therapies, starting with remarkable initial clinical results in recurrent chronic lymphocytic leukemia (CLL). Subsequent reports have shown impressive results using CD19 CAR-T cells in B-cell acute lymphoblastic leukemia (ALL) with some patients having durable remissions at 5 years post therapy, and in B cell lymphoma – progression free survival at 5 years of 31% in refractory diffuse large B-cell lymphoma, and 43% in refractory follicular lymphoma in recently updated results.

To date, the US Food and Drug Administration (FDA) has approved 5 chimeric antigen receptor (CAR) technologies. The different agents utilize slightly different methods of genetic engineering to transform the patient's T cells into CAR-T cells.

- **Kymriah™ (tisagenlecleucel)** is for the treatment of children and young adults up to the age of 25 years with B-cell precursor acute lymphoblastic leukemia (ALL).
- **Yescarta™ (axicabtagene ciloleucel)** approved for the treatment of adults with diffuse large B-cell lymphoma (DLBCL) and was granted accelerated approval for the treatment of adult patients with relapsed or refractory follicular lymphoma in February 2021.
- **Tecartus™ (brexucabtagene autoleucel)** was approved in July 2020 for the treatment of advanced Mantle Cell Lymphoma.
- **Breyanzi (lisocabtagene maraleucel)** On February 5, 2021, the FDA approved Breyanzi (lisocabtagene maraleucel) for the treatment of adult patients with relapsed or refractory large B-cell lymphomas.
- **Abecma (idecabtagene vicleucel)** a BCMA CAR T-cell directed therapy for adults with relapsed/refractory multiple myeloma was approved in March 2021.





## How are CAR-T Cells Manufactured

The present autologous CAR-T products use a complex process that requires collection from each individual patient and “bespoke” manufacturing with full release testing for each individual patient product.

CAR T-cell therapy production involves the following phases:

1. **Evaluation:** The patient undergoes a series of tests to evaluate if CAR T-cell therapy is an appropriate option.
2. **Collection:** The T-cells are collected from the patient’s blood. The procedure is known as apheresis or leukapheresis.
3. **Engineering:** The collected T-cells are sent to a laboratory to be genetically engineered into the CAR T-cells.
4. **Multiplication:** The modified CAR T-cells are grown and multiplied in the laboratory. These cells are then frozen and sent back to the clinic for the treatment. This process of multiplying the CAR T-cells can take several weeks.
5. **Conditioning:** Before the new CAR T-cells are infused into the patient’s body, the patient will have a brief course of chemotherapy. This will help to improve the chances of the body accepting the new CAR T-cells.
6. **Infusion:** Shortly after the chemotherapy, the modified CAR T-cells are infused into the patient through a process similar to a blood transfusion.
7. **Recovery:** After the CAR T-cell infusion, the patient may experience some side effects for the first 30 days after the infusion, and the recovery of the body’s immune system may take several months.





## What are the Potential Side-effects of CAR T-cell Therapy?

The common side effects of CAR T-cell therapy include:

### Cytokine release syndrome (CRS)

In some cases, patients may develop flu-like symptoms such as fever, chills, headache, nausea, vomiting, loose stools, and muscle or joint pains. These side effects are due to the release of cytokines by the immune cells during CAR T-cell therapy. Up to 70-90% of patients can develop some form of CRS, but these symptoms are usually mild, and short-term lasting 5-7 days.

### Neurological events or CRES (CAR T-cell related encephalopathy syndrome)

CRES typically occurs around 2-5 days after infusion. Patients may present with confusion, difficulty speaking, agitation, and in more severe forms: seizures, drowsiness, altered state of consciousness and encephalopathy (brain injury and malfunction). Patients need to be monitored pre-emptively for any neurological disturbances, and sometimes patients will need to be taken to intensive care for stabilisation (with sedation and mechanical ventilation) in more severe grades of neurotoxicity.

Factors influencing the severity of CRS/CRES include the baseline tumour burden at time of CAR-T cell therapy, presence of underlying medical issues (such as prior neurological co-morbidities), as well as the type of CAR-T cell product infused.

There is now consensus criteria on the grading of severity of CRS/CRES with concurrent guidelines on the management of patients with differing severity of CRS/CRES. Experience of the treatment centre in recognising and early treatment of symptoms is an important determinant affecting outcomes.

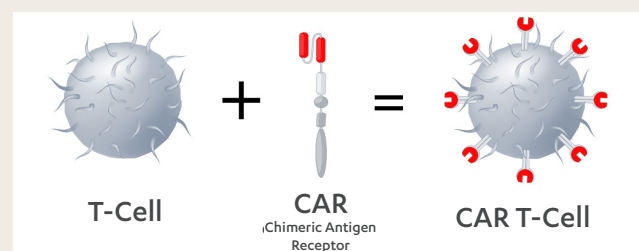
## What is in the Future for Cellular Therapy for Cancer?

Although the initially approved anti-CD19 CAR-T therapy has produced impressive outcomes, setbacks such as high relapse rates and resistance have been reported. Next generation CAR-T cells such as bispecific CAR-T cells like anti-CD19/CD22 and anti-CD19/CD20 are promising options that are currently in clinical trials.

CAR T-cells have also presently been applied in clinical trials for the treatment of solid tumours including hepatocellular carcinoma and mesotheliomas.

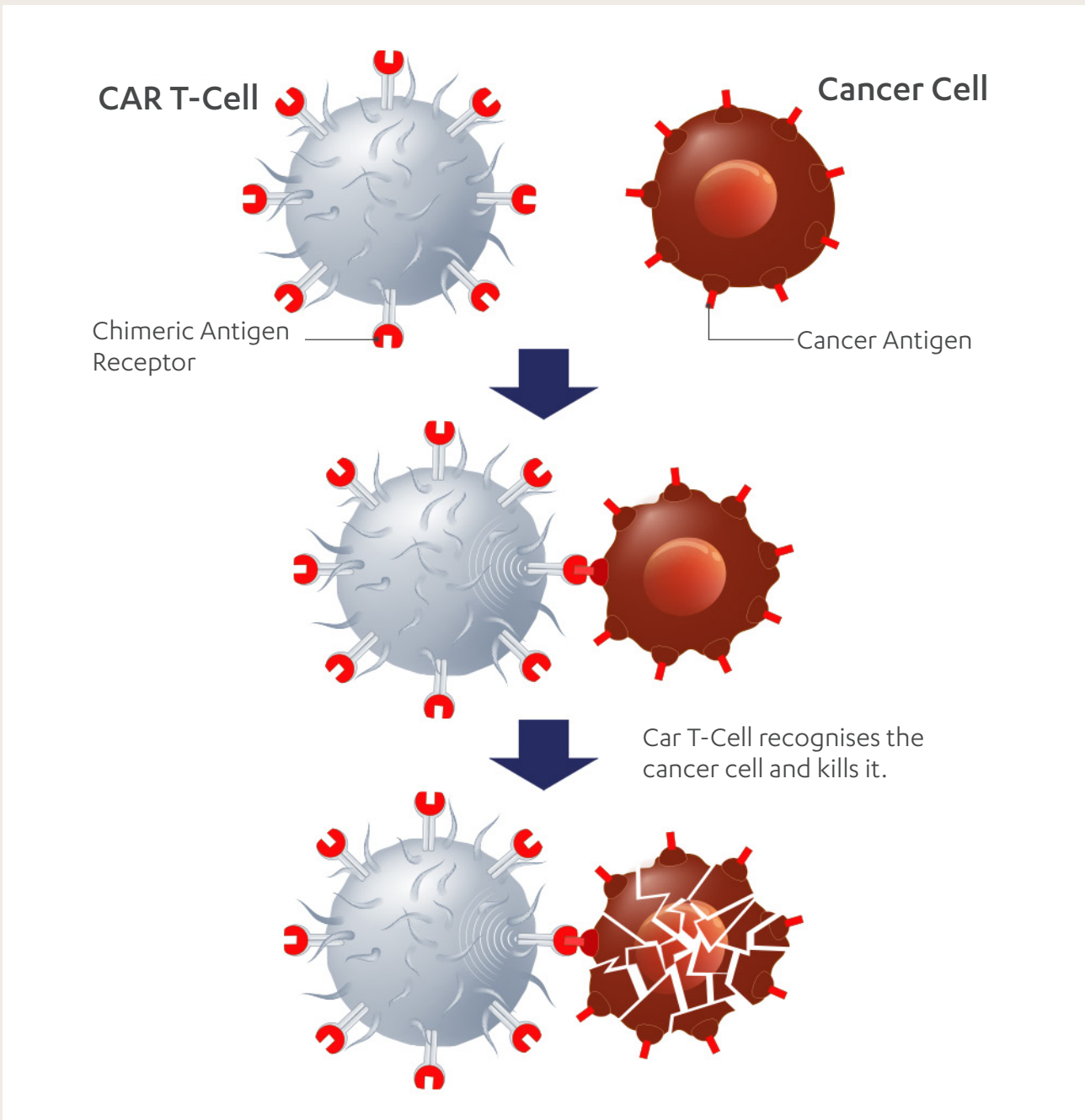
Chimeric antigen receptors have been also introduced in NK cells as another form of cellular immunotherapy, which can also cause cytotoxicity to cancer cells.

In summary, cellular therapy has become firmly established as the fifth pillar of cancer therapy. CAR T-cell therapy is leading the way in cancer-directed cellular therapy with very impressive results in patients with haematological cancers. The presently approved products are but the early first wave of CAR-T cell treatments that will transform cancer therapy, and there is excitement over the next generation of CAR T-cell products and other cellular therapies for cancer.



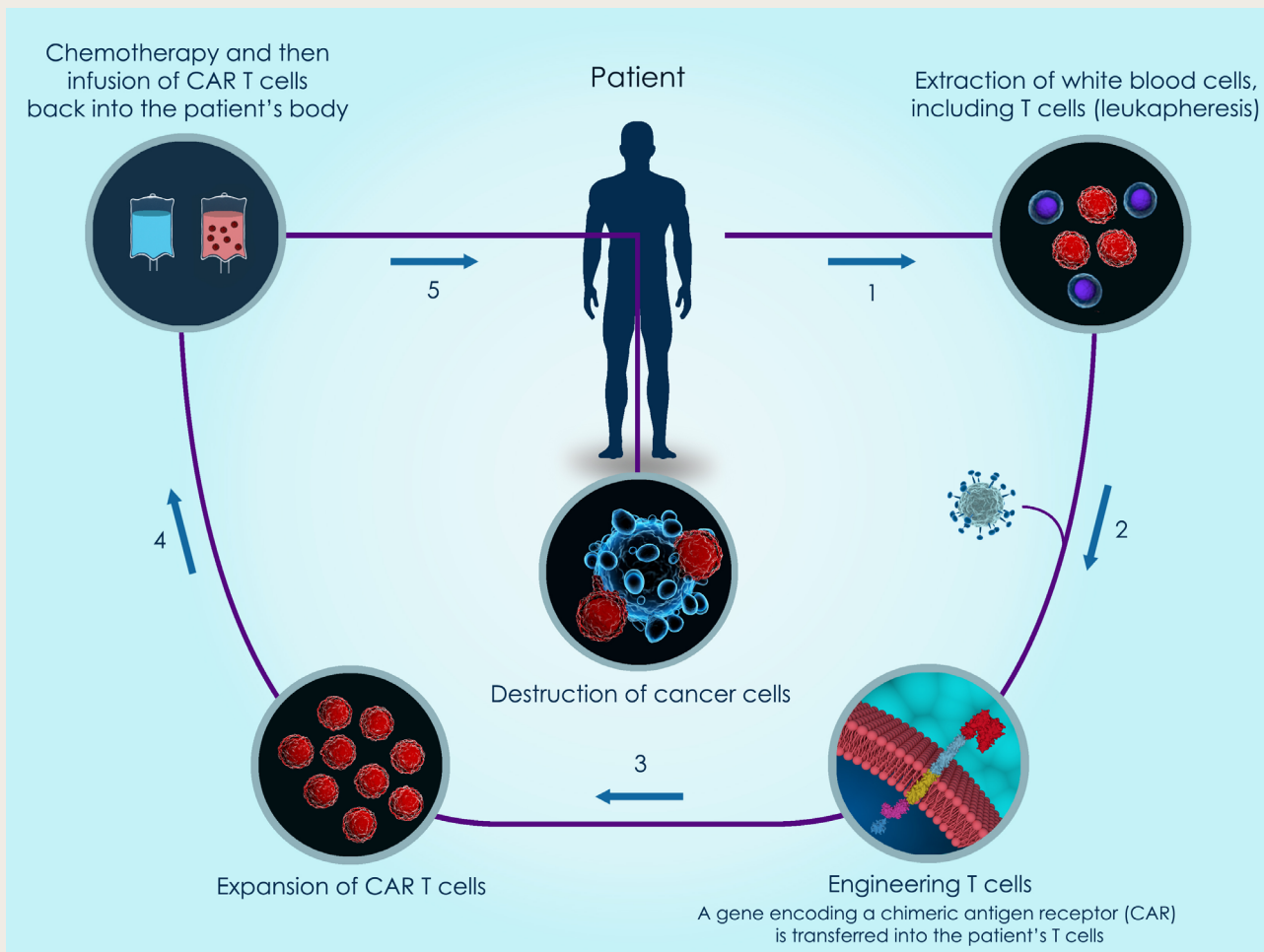
► CAR-T therapy involves the genetic engineering of T-cells from patient (autologous) or healthy donors (allogeneic). After cell modification, the T-cells will express the CAR-T receptor on the cell surface.

Source : CFCH website



► The chimeric antigen receptor expressed on the surface of the CAR T-cells allows the genetically modified T-cells to identify and bind to antigens (proteins) on cancer cell surfaces. Once the CAR-T cells are bound to the cancer cells, they are activated to 1) rapidly expand to generate a significant T-cell response, 2) directly kill the cancer cells in the vicinity

Source : CFCH website



► Outline of the process for CAR-T cell manufacture

This article is contributed by Dr Lim Zi Yi.

Dr Lim Zi Yi is the Medical Director of CFCH and a Senior Consultant in Haematology. He has a specialist interest in Haemato-oncology and Haematopoietic Stem Cell Transplantation. He received his medical degree from the University of Edinburgh, UK and subsequently underwent specialist training in haemato-oncology at Kings College Hospital, London where he helped to develop it into one of the largest allogeneic haematopoietic stem cell transplant centres in Europe. He subsequently returned to Singapore in 2012, where he led the development of several haematological services in the public and private sector.

Dr Lim is passionate about approaching patient care in a holistic manner, utilising state of the art diagnostic tests together with novel treatment protocols to develop personalized treatment strategies for his patients.



# Our centres across the Asia Pacific region



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Integrated Oncology Centres (IOC Head Office) |  
Solis Breast Care & Surgery Centre |  
Luma Women's Imaging Centre/ Medical Centre

## Philippines

Central Luzon Integrated Oncology Centre

## Hong Kong

Hong Kong Integrated Oncology Centre |  
Hong Kong Adventist Hospital Oncology Center

## Indonesia

Adi Husada Cancer Center

## Vietnam

Hung Viet Cancer Hospital |  
Hung Viet General Clinic

## Malaysia

Beacon Hospital



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