

Immunotherapy for NSCLC

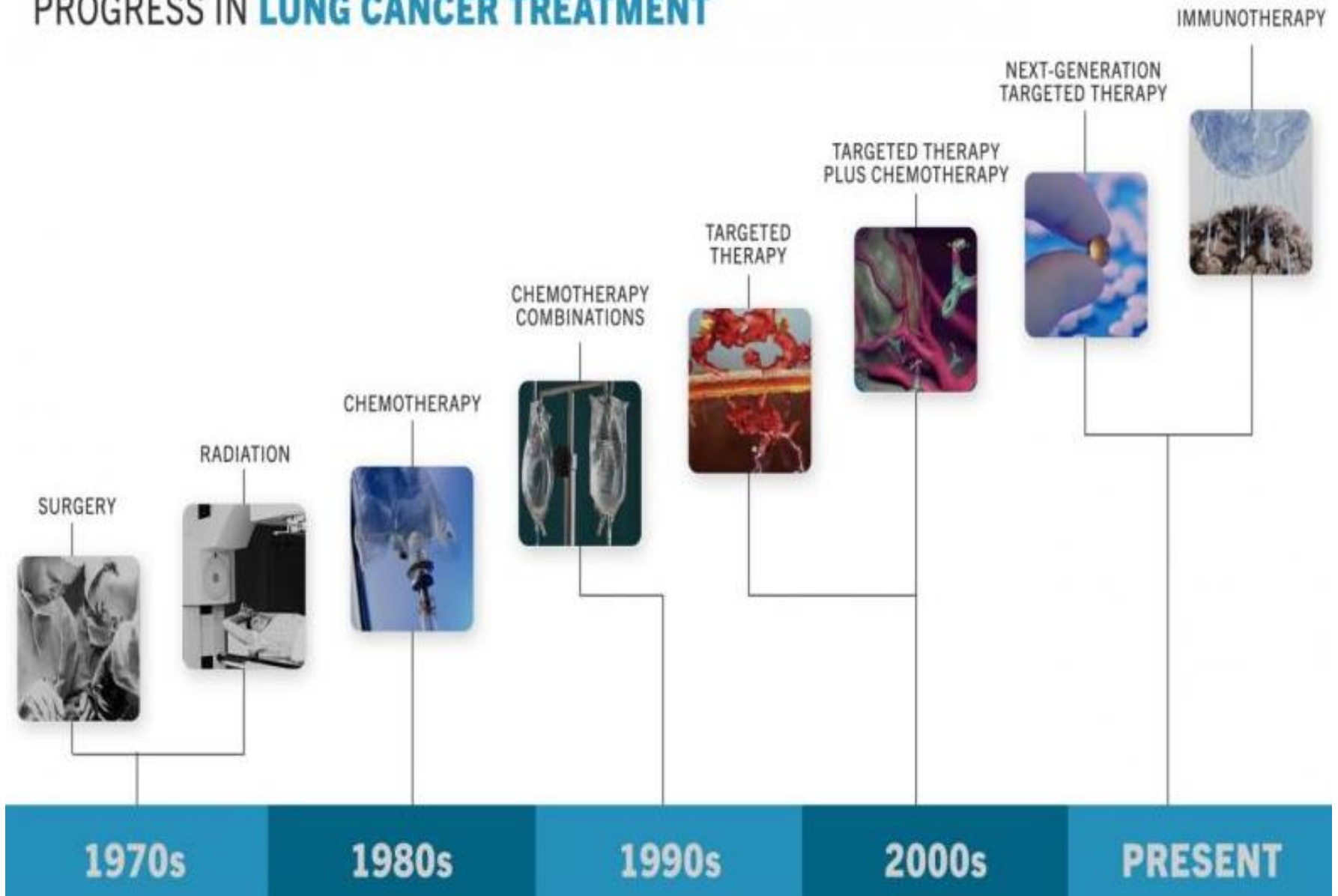
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PROGRESS IN LUNG CANCER TREATMENT

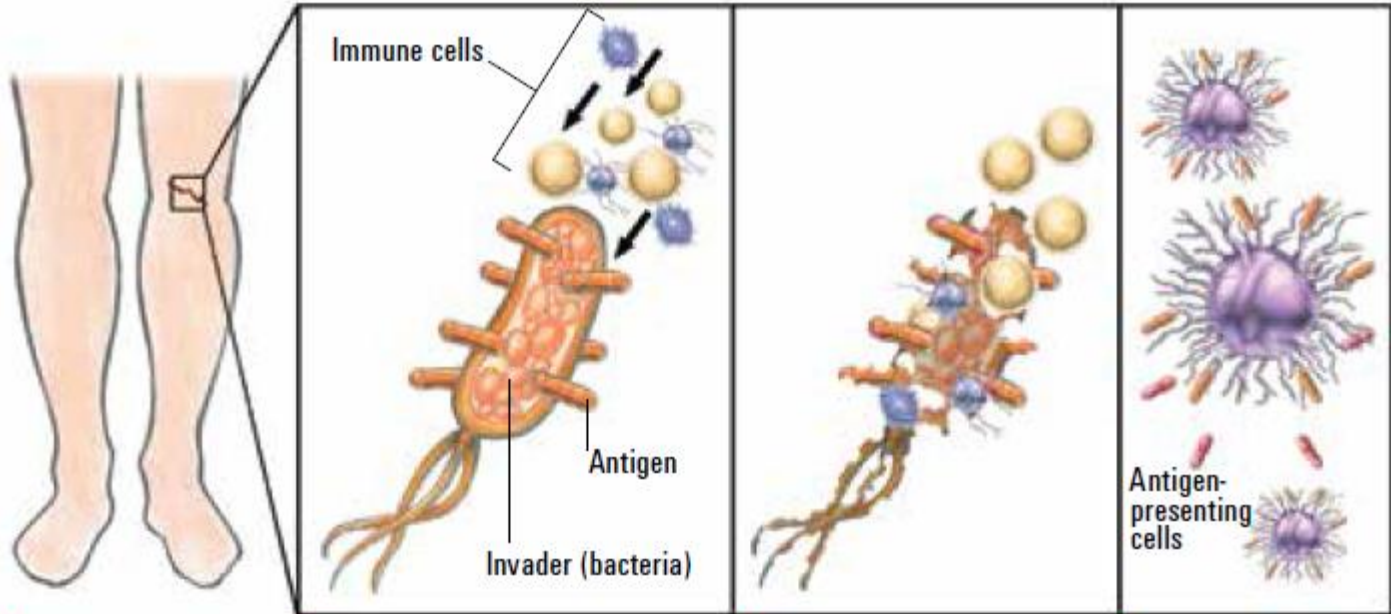


Newer Approaches

- ◆ Immunotherapy is a type of cancer treatment that works by stimulating the body's own immune system to fight cancer
- ◆ Because cancer cells have the ability to evade the immune system by using a number of clever techniques, immunotherapy uses different strategies to restore the immune system's ability to destroy tumors.
- ◆ Immunotherapy is novel and unique, differing from any previous “standard” treatment

How does IMMUNOTHERAPY work?

▲ NORMAL IMMUNE RESPONSE



▲ Skinned knee: First barrier of protection is broken.

▲ An invader enters the body through the cut, where immune cells have begun to gather to protect the body.

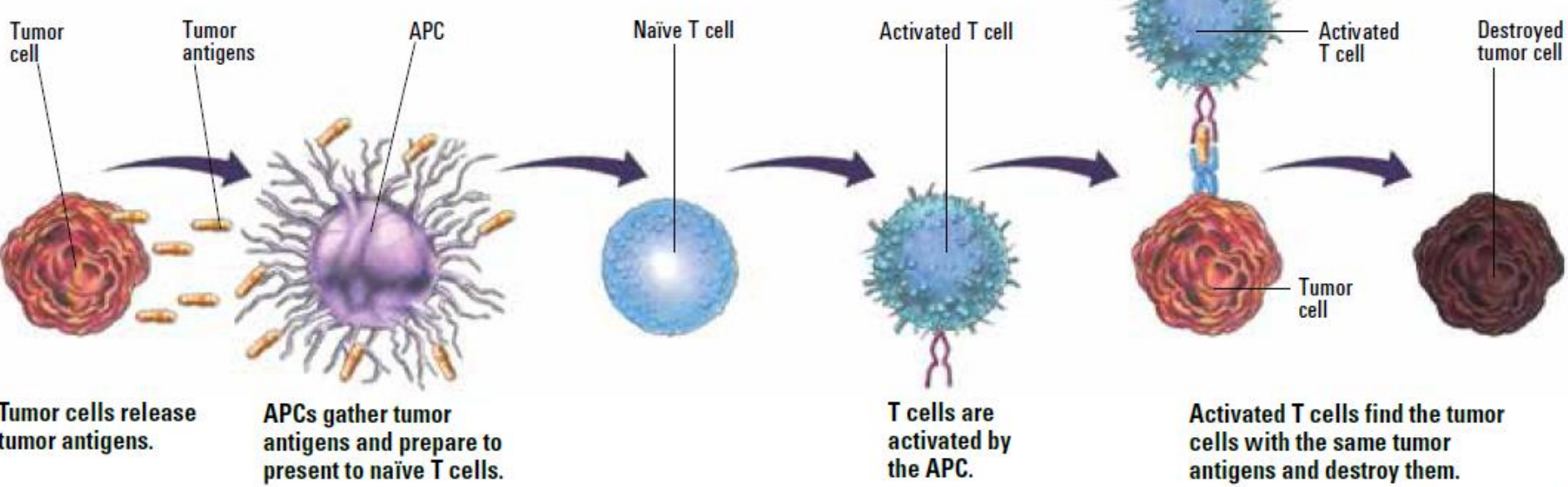
▲ The immune cells begin to destroy and digest the invader and its antigens.

▲ Some of the immune cells transform into antigen-presenting cells that tell other immune cells about the invader.

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How does IMMUNOTHERAPY work?

HOW THE IMMUNE SYSTEM ATTACKS CANCER



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Lung Cancer Immunotherapy

GOAL: Enable T cells to recognize and kill tumor cells

There are many possible approaches:

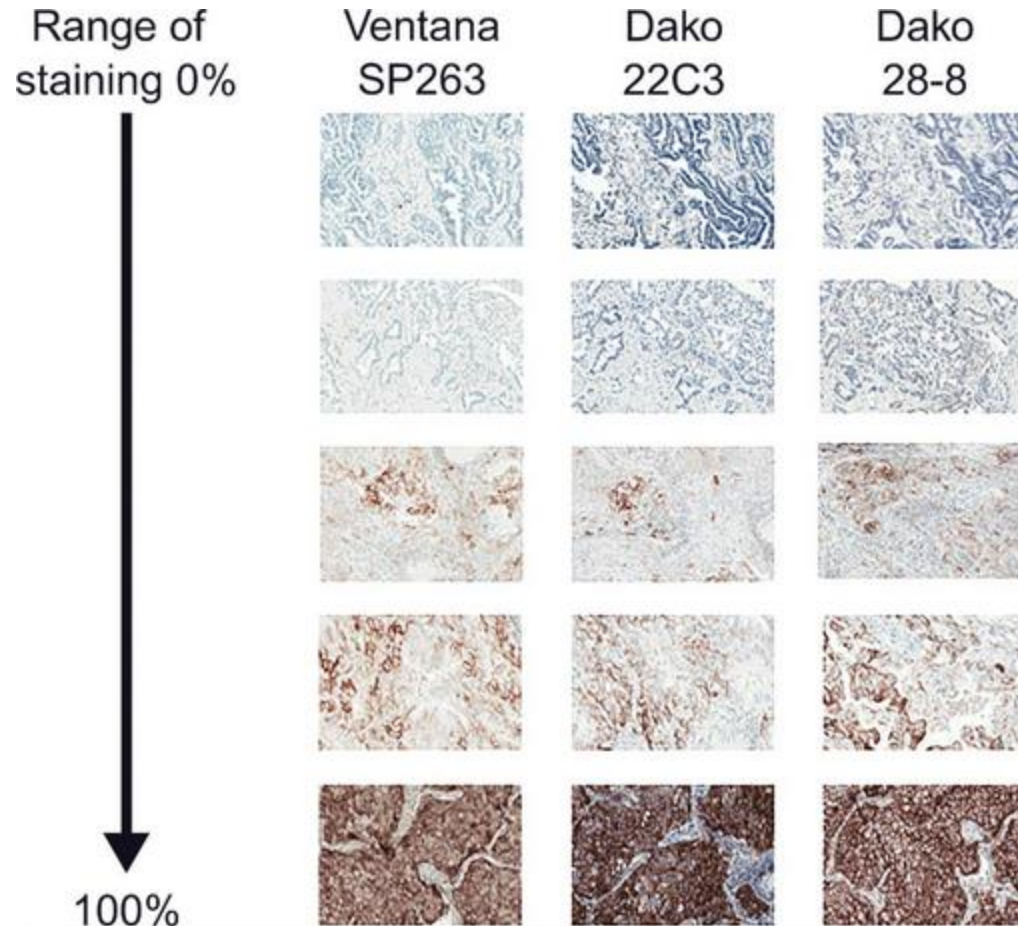
- Checkpoint inhibitors
- Vaccines
- Monoclonal Antibodies
- CAR T cells

What is an immune checkpoint?

- ◆ Immune checkpoints are designed to suppress the immune system so healthy organs are not damaged
- ◆ Cancer cells can take over these checkpoints so the immune system does not target them
- ◆ PD-1/PD-L1 are checkpoints that are used by cancer cells
- ◆ **Blocking the PD-1/PD-L1 checkpoint allows the immune system to recognize the cancer cells and attack them**
 - Pembrolizumab
 - Nivolumab
 - Atezolizumab
 - Durvalumab
- ◆ All of these drugs are given by an infusion into the veins

Who can receive immunotherapy?

- ◆ We can measure PD-L1 expression with a tumor biopsy
 - This is done as part of standard routine process



Who can receive immunotherapy — Stage IV

- ◆ **Patients with the highest levels of PD-L1 expression (>50%) have a greater chance of response to immunotherapy**
 - May be able to avoid chemotherapy
 - But only about 30% of patients with advanced NSCLC have very high levels of PD-L1 expression
- ◆ **For patients with level between 1-49%, we often combine chemo and immunotherapy**
- ◆ **It should be noted that if the biopsy shows no PD-L1 expression, this does not always mean that immunotherapy will not work**
- ◆ **For patients with level <1%, we can still proceed with**
 - combination chemo + immunotherapy
 - and there may be role for combination immunotherapy (i.e. combine 2 immunotherapy inhibitors)

Who can receive immunotherapy — Stage IV

- ◆ **Recently, we found that combining chemo and immunotherapy improved outcomes even for patients with squamous cell cancer- a subset where this combination was not a possibility before**
- ◆ **Both nivolumab and atezolizumab are approved for all patients with advanced NSCLC after first receiving chemotherapy regardless of the levels of PD-L1 expression (often called 2nd line setting)**

Who can receive immunotherapy — Stage III

- ◆ Recent data show that **CONSOLIDATION** immunotherapy for one year after receiving chemoradiation therapy for Stage III lung cancer
 - improves outcomes, and
 - decreased the incidence of the cancer returning
- ◆ Here, we use a drug called **Durvalumab**, which is FDA approved

Who can receive immunotherapy — SMALL CELL

- ◆ We now combine chemotherapy with Atezolizumab in first line setting of small cell lung cancer, as that has shown to result in superior survival
- ◆ We also heard data on combining another drug, Durvalumab in combination with chemotherapy for first line treatment of SCLC. *Not currently FDA approved*
- ◆ Lot of exciting stuff!

What about patients with actionable mutations?

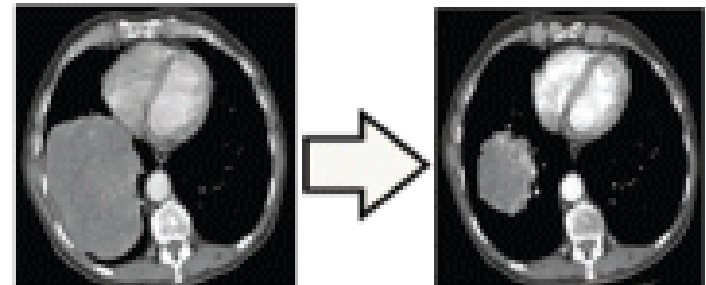
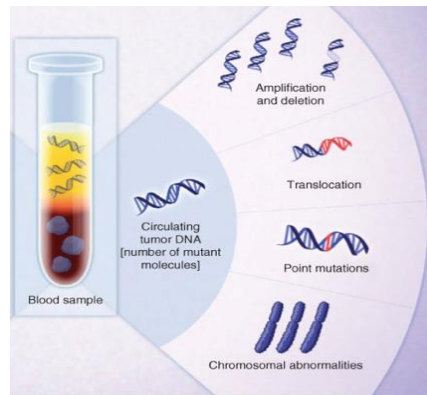
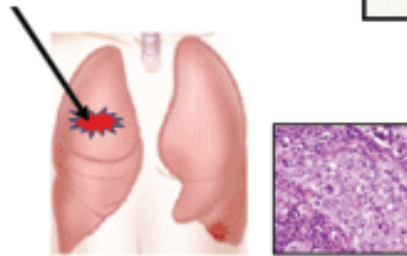
- ◆ Patients with a lung tumor with *EGFR* or *ALK* gene mutations should be treated with targeted therapy rather than immunotherapy initially
- ◆ There is a higher chance that targeted therapy will shrink the tumor than that immunotherapy will work

Not everyone benefits from immunotherapy

- ◆ We are just scratching the surface of understanding what factors can be used to identify the patients who may benefit the most from immunotherapy
 - One of the factors we are looking at is the number of mutations in a tumor

Diagnostic biopsy

- Adequate tissue for biomarker testing and archiving (core)



CAR T cell therapy

T-Cell Therapy Puts Leukemia Patients in Extended Remission

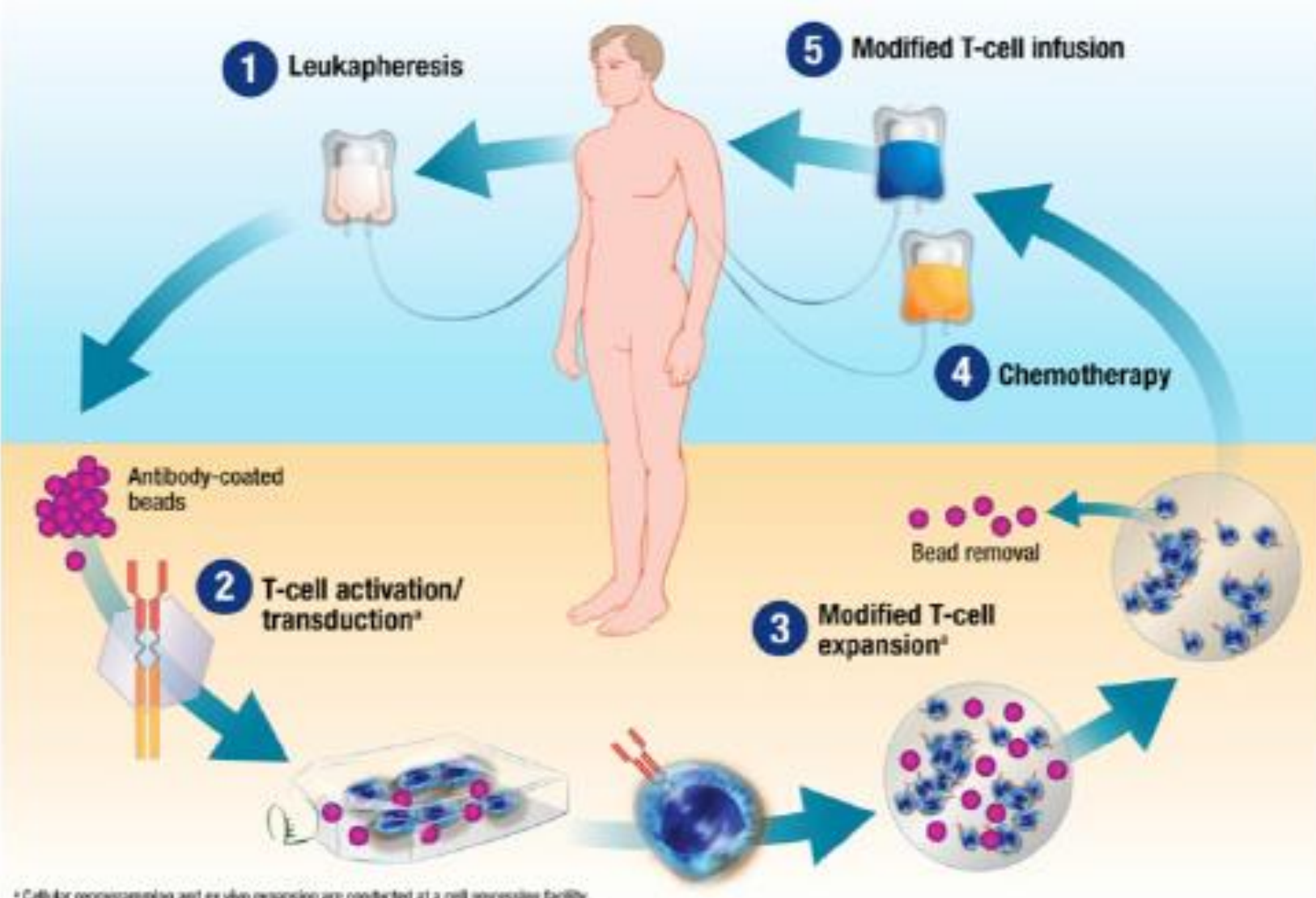
Denise Grady



Modified T-cells in the freezer at the Clinical Cell and Vaccine Production Facility at the University of Pennsylvania. Peggy Peterson Photography/Penn Medicine



CAR T cell therapy



CAR T cell therapy

- **Advantages:**

- Harness power of both arms of immune system
- Very targeted therapy
- Very effective in animal models

- **Disadvantages**

- No brakes
- Cancer can change
- Very expensive



Summary

- ◆ An increasing number of clinical trials for immunotherapy of lung cancer are underway at Penn and at other places which are starting to show success



At the heart of all of this is YOU



Thank you!

Charu Aggarwal, MD, MPH

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