Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

# Basic Principles of Cancer Immunotherapy

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Second appointment in Microbiology and Immunology

NCI Designated Comprehensive Cancer

AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

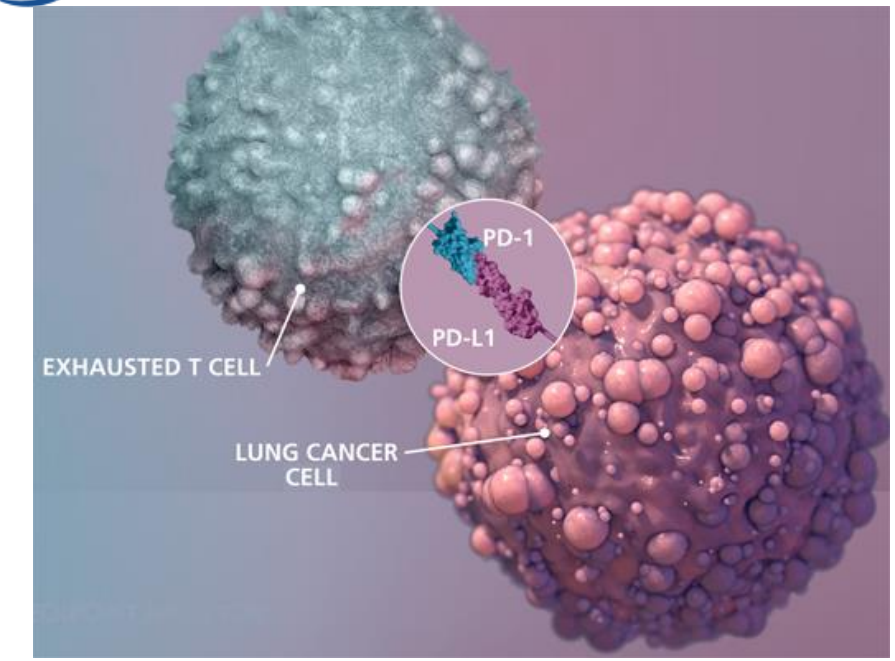
Society for Immunotherapy of Cancer

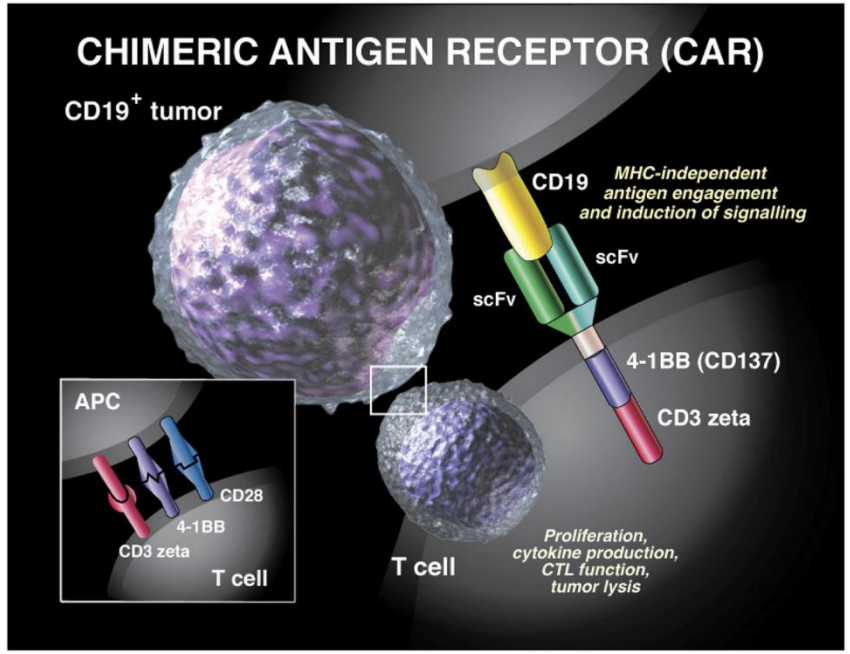
# Disclosures

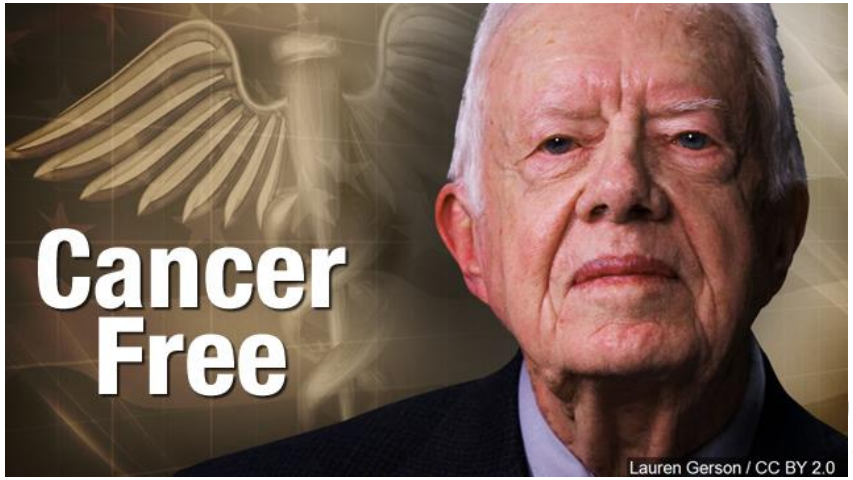
- Royalty: Ares Immunotherapy
- IP Rights: Ares Immunotherapy
- Contracted Research: Ares Immunotherapy, Obsidian, Lycera, FisherScientific
- Ownership Interest Greater Than 5 Percent: Ares Immunotherapy

- I will be discussing non-FDA approved indications during my presentation.

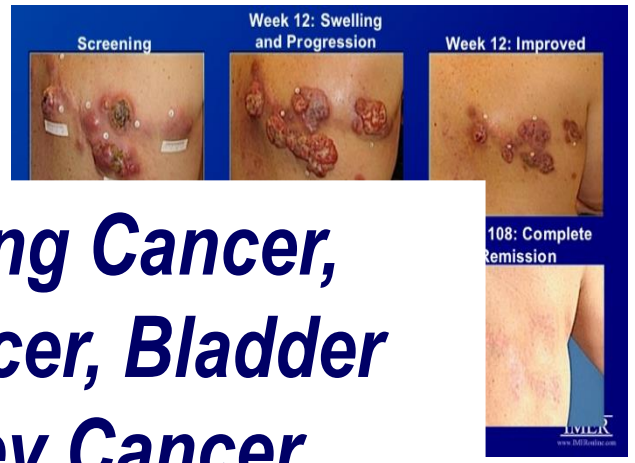
# Top Breakthrough



# Cancer Immunotherapy:
## Remarkable Success


***Melanoma, Lung Cancer, Head/Neck Cancer, Bladder Cancer, Kidney Cancer, Hodgkin's Lymphoma, Merkel Cell Carcinoma, MSI-H or dMMR Tumors***

⬆ Anti-PD

)y


⬆ T cell therapy (natural)


CAR-T cell therapy
(T cell with synthetic receptor)
FDA APPROVED

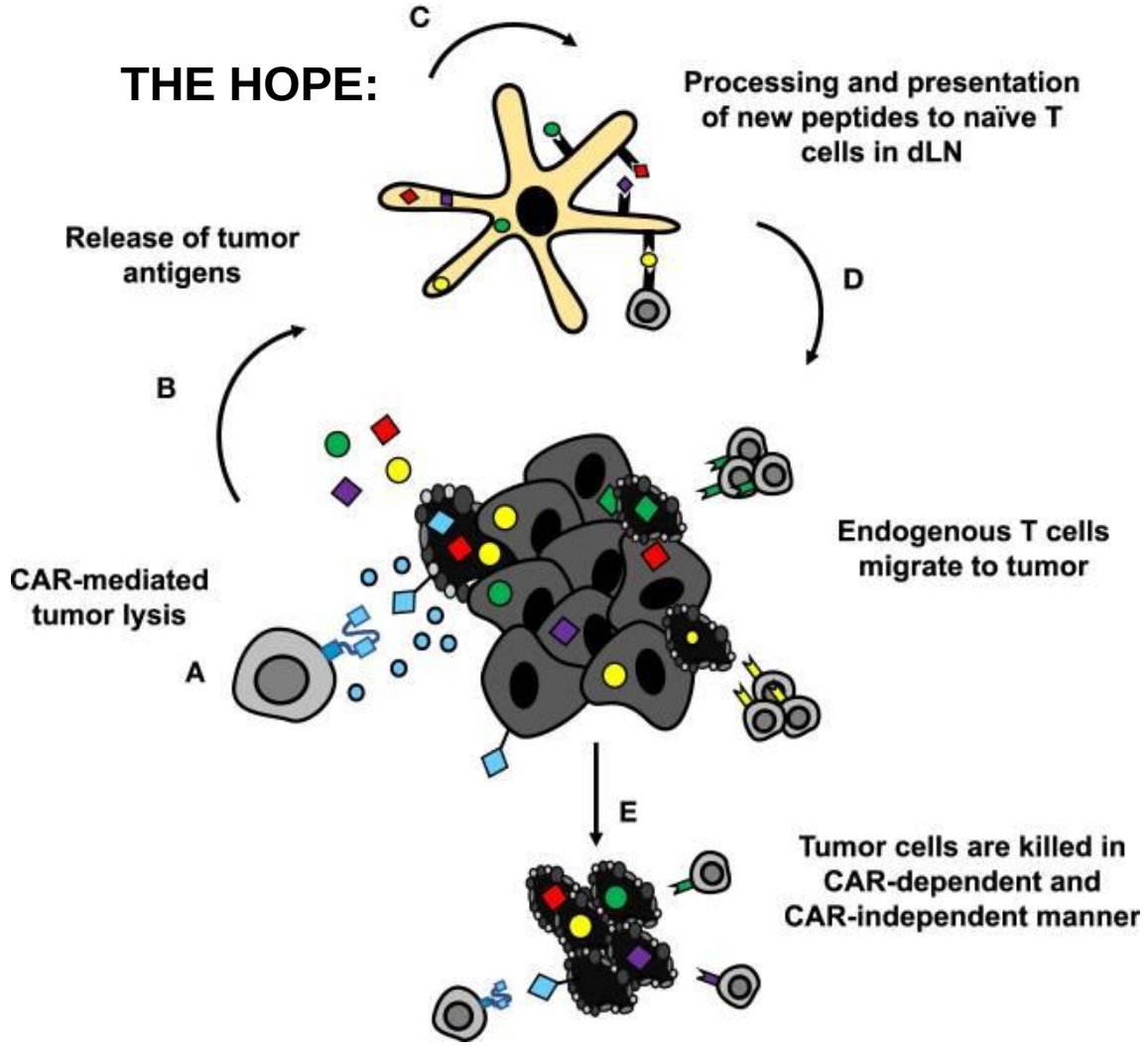
# Cancer Immunotherapy Premise

- Normally, the immune system eliminates precancerous and malignant cells

- Tumors evolve mechanisms to locally disable the immune system.

The goal of the immunotherapy field is to develop medicines that restore the capacity of the patients' immune system to recognize and kill cancer.

# Two mechanisms of tumor immune escape




## 1: Render immune dysfunction:

-T cells become exhausted via chronic stimulation

-Tumors upregulate molecules that cause T cell dysfunction.

## 2: Avoiding an immune response:

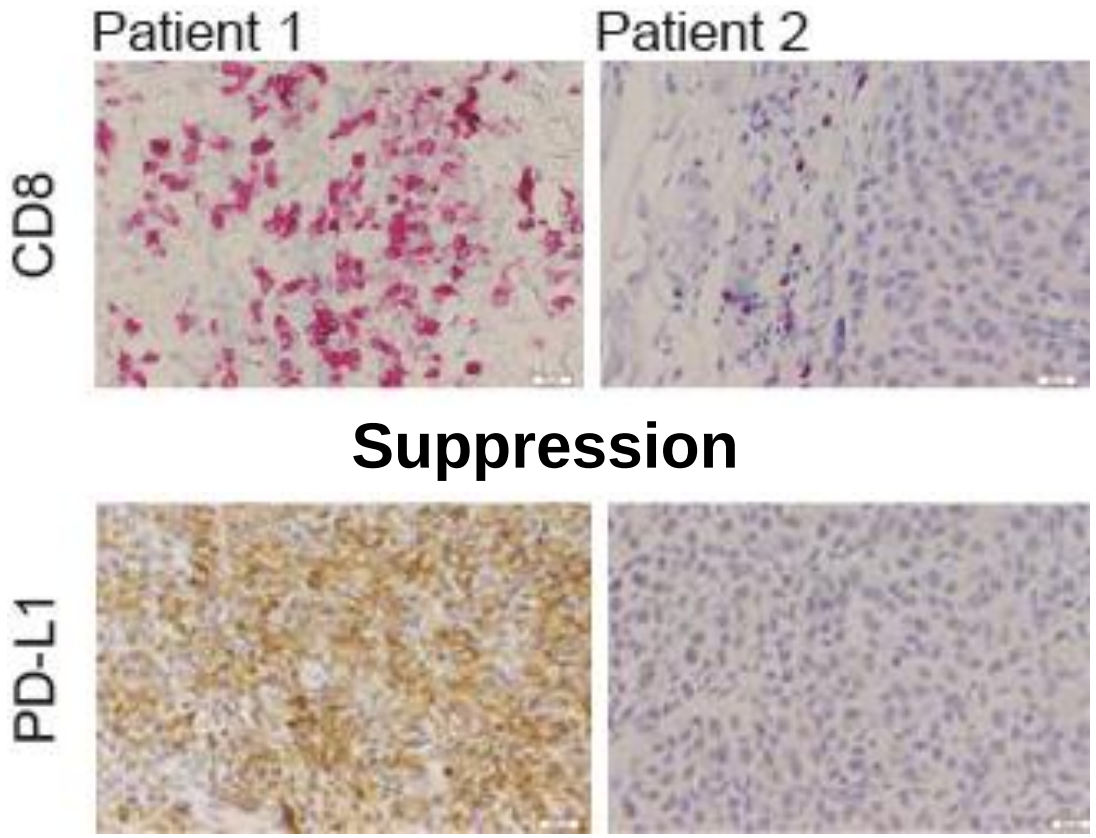
-Tumor remains invisible

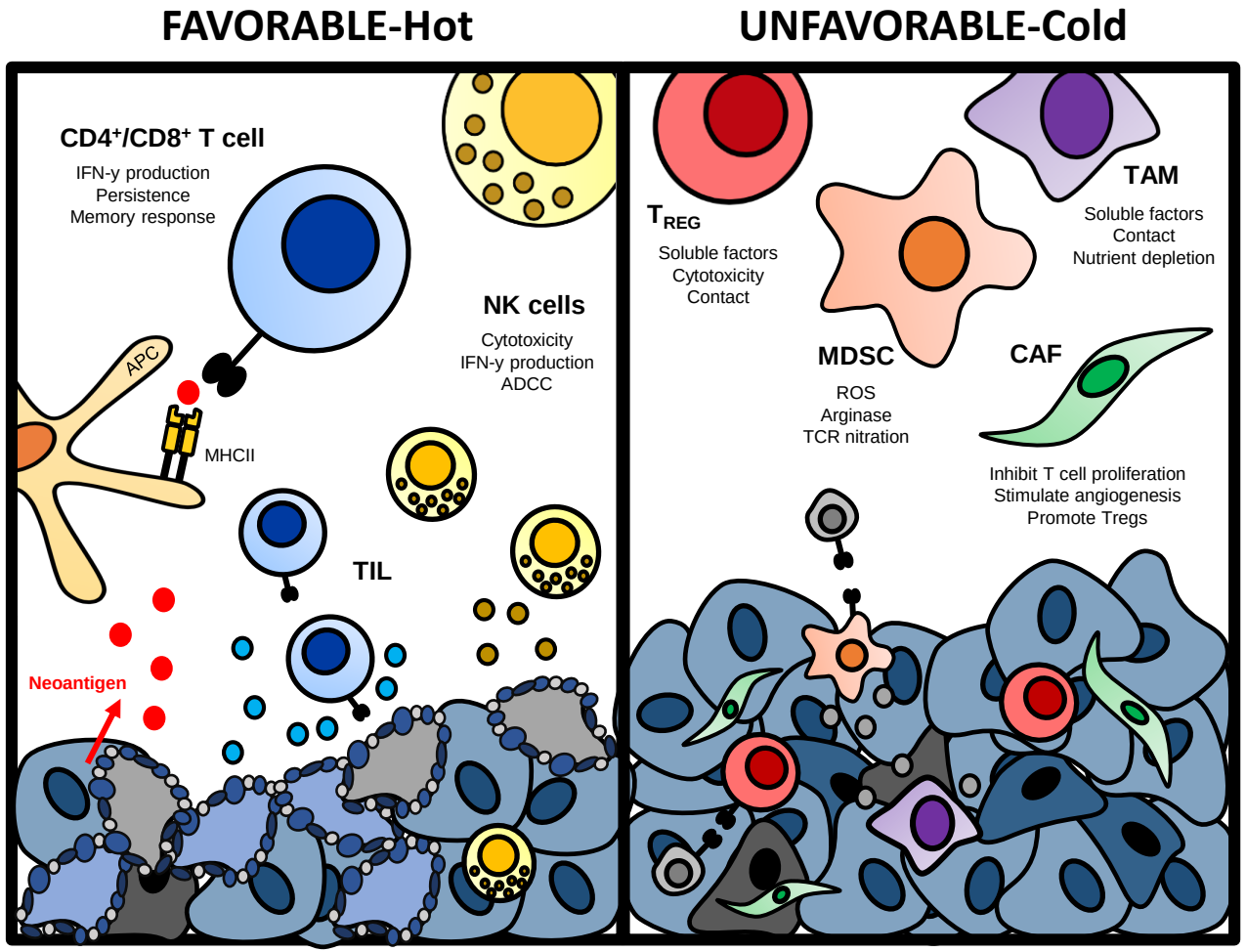
-Lack of antigens (T cells don't "see" tumor)

Knochelmann HM, et al. Frontiers in Immunol 2018

# Immune evasion – Hot *vs* cold tumors

## TILs



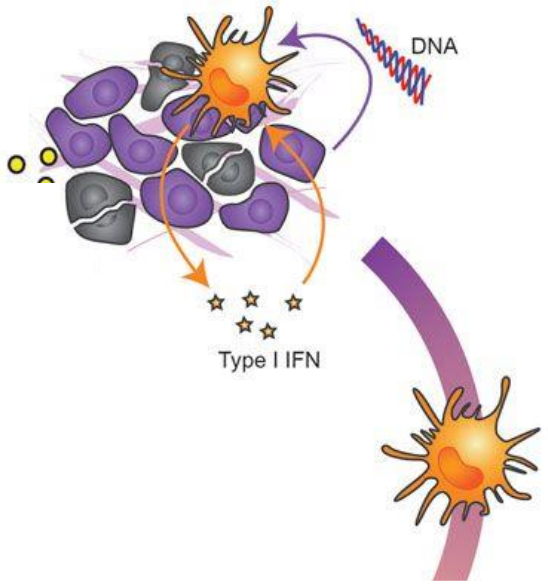




Knochelmann HM, et al. Frontiers in Immunol 2018

Ascierto P.A., Paulos CM, JITC 2019
Horton J, Knockelmann HM, et al. Trends in Cancer 2018

# Initiating innate immunity

Innate immune sensing (i.e. Sting activation)

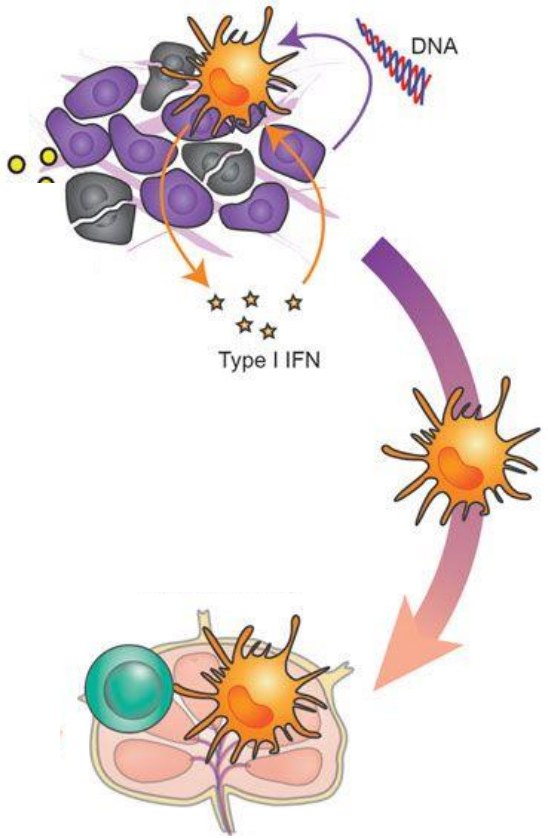



APC maturation
&
Transport to lymph node

Modified from Corrales et al. Cell Res. 2017

# Results in T cell activation

Innate immune sensing (i.e. Sting activation)




APC maturation
&
Transport to lymph node

Cytotoxic T cell activation

Modified from Corrales et al. Cell Res. 2017

# T cell are activated if there are 3 signals

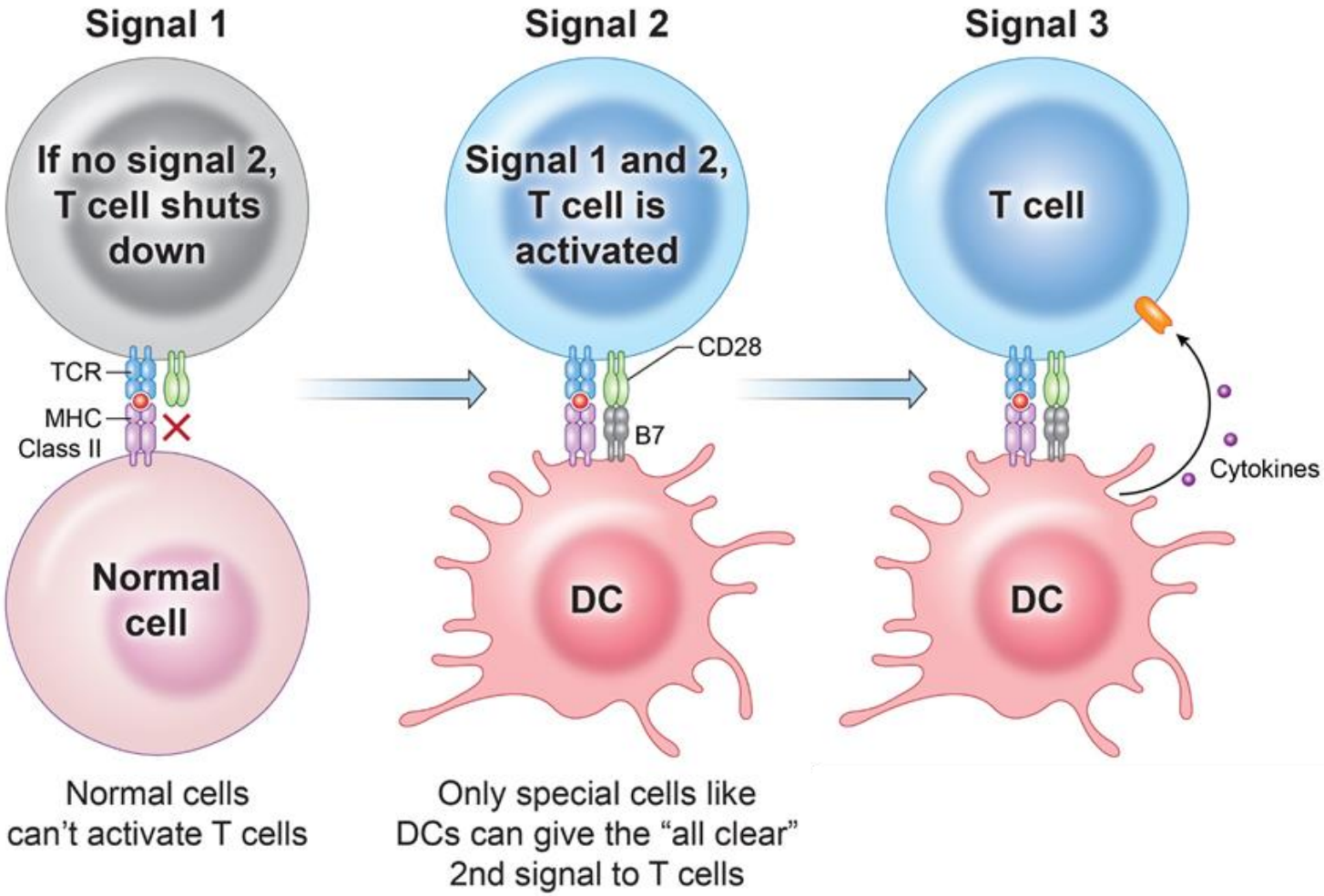
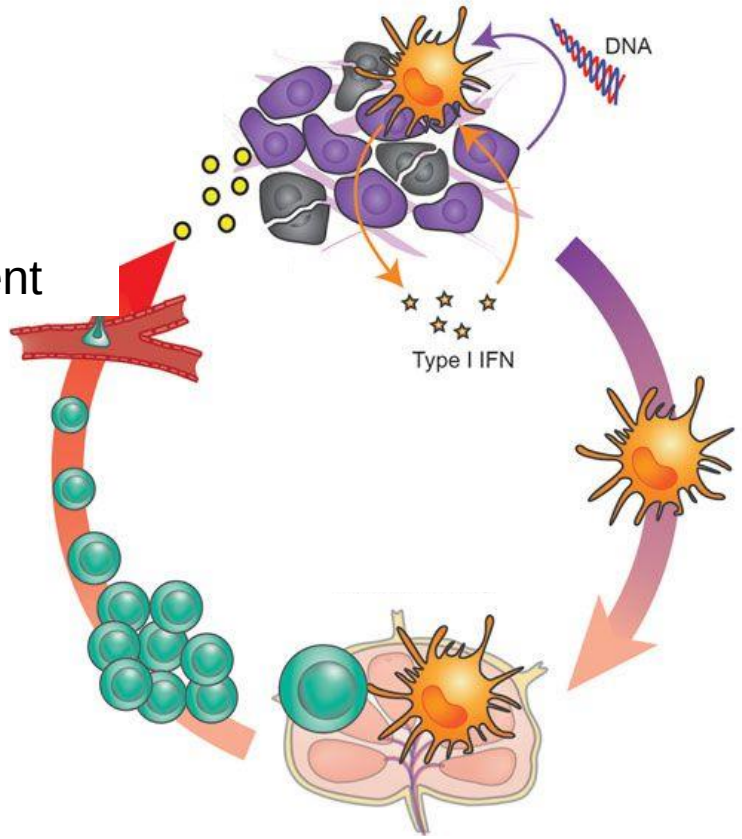



Image courtesy of NCI

# Mediating T cell proliferation & migration to tumor

Innate immune sensing (i.e. Sting activation)

T cell recruitment

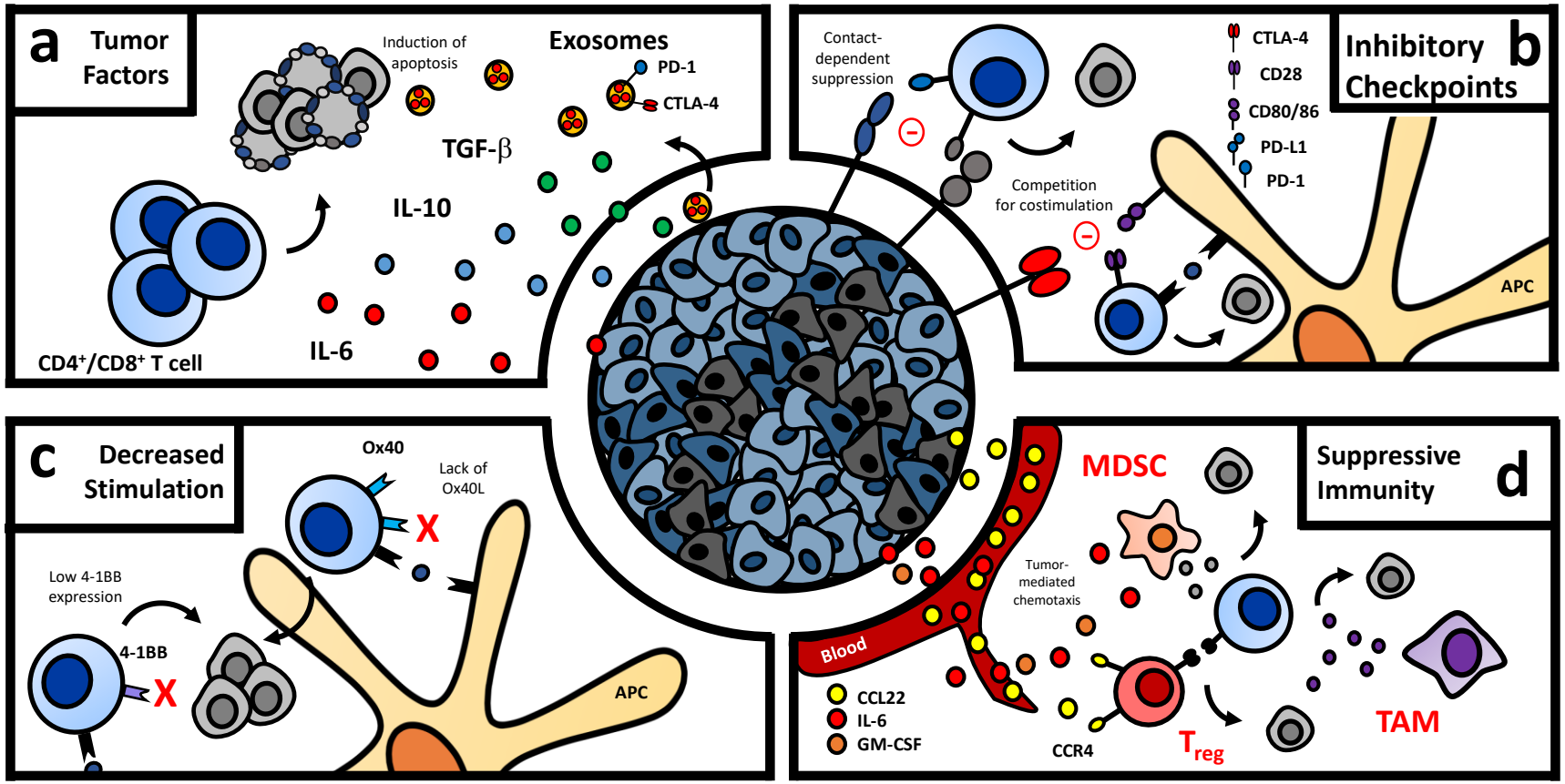



APC maturation
&
Transport to lymph node

Cytotoxic T cell activation

Modified from Corrales et al. Cell Res. 2017

# Many problems remain….

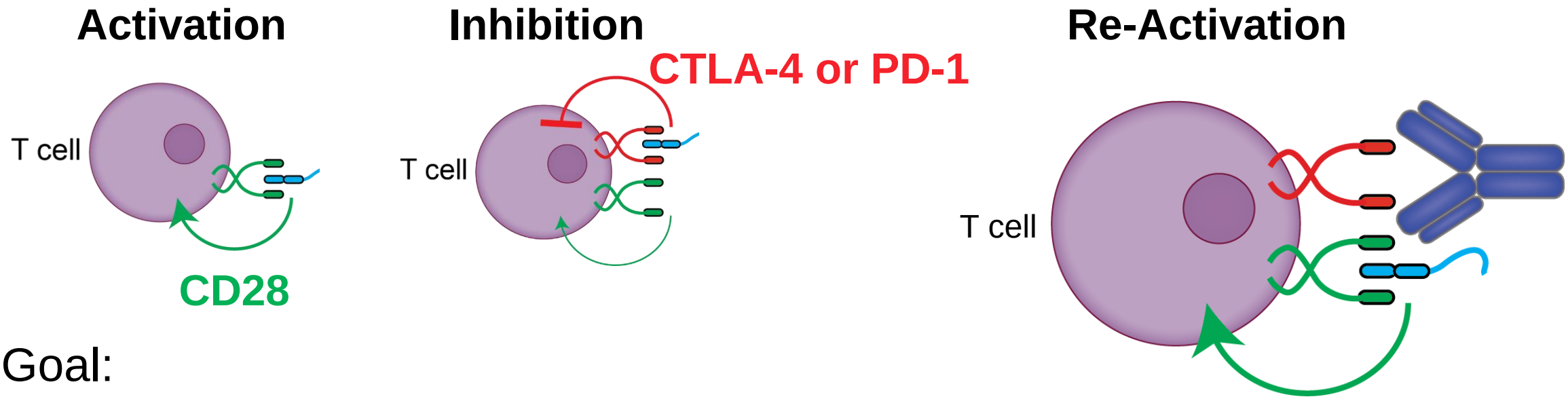



Knochelmann HM, et al. Frontiers in Immunol 2018

# But there are some solutions…

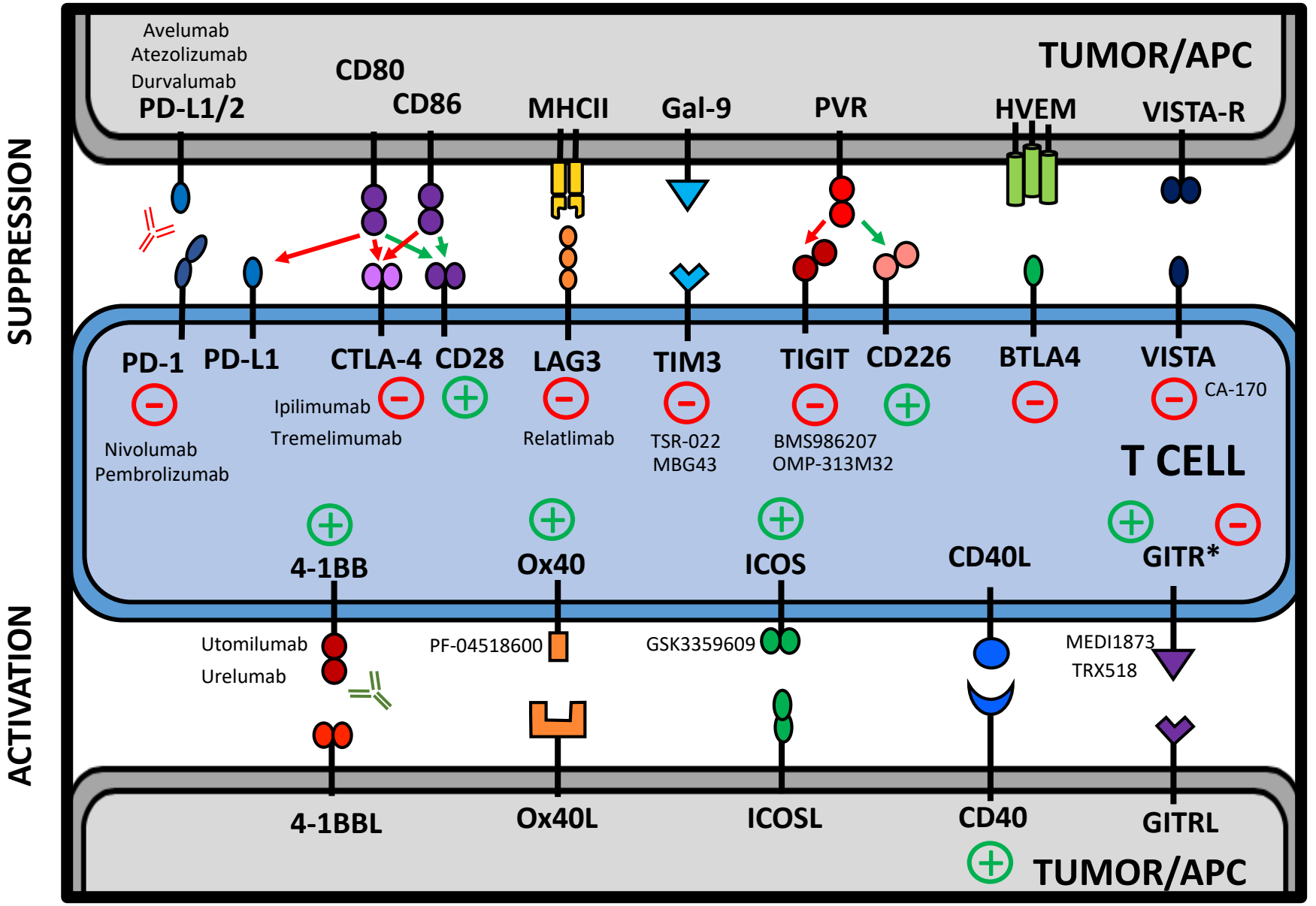
- Checkpoint blockade immunotherapy
- Cancer vaccines
- Adoptive cell transfer
- Oncolytic viruses

# Checkpoint blockade unleashes the “brakes”




Goal:

Regain effector T cell activity by reducing inhibitory signals and/or enhance stimulatory signals




Horton J, Knochelmann HM, et al. Trends in Cancer, 2019

# Therapeutic Cancer Vaccines

Goal:

To increase the immunogenicity of antigens to generate more tumor-specific T cells.

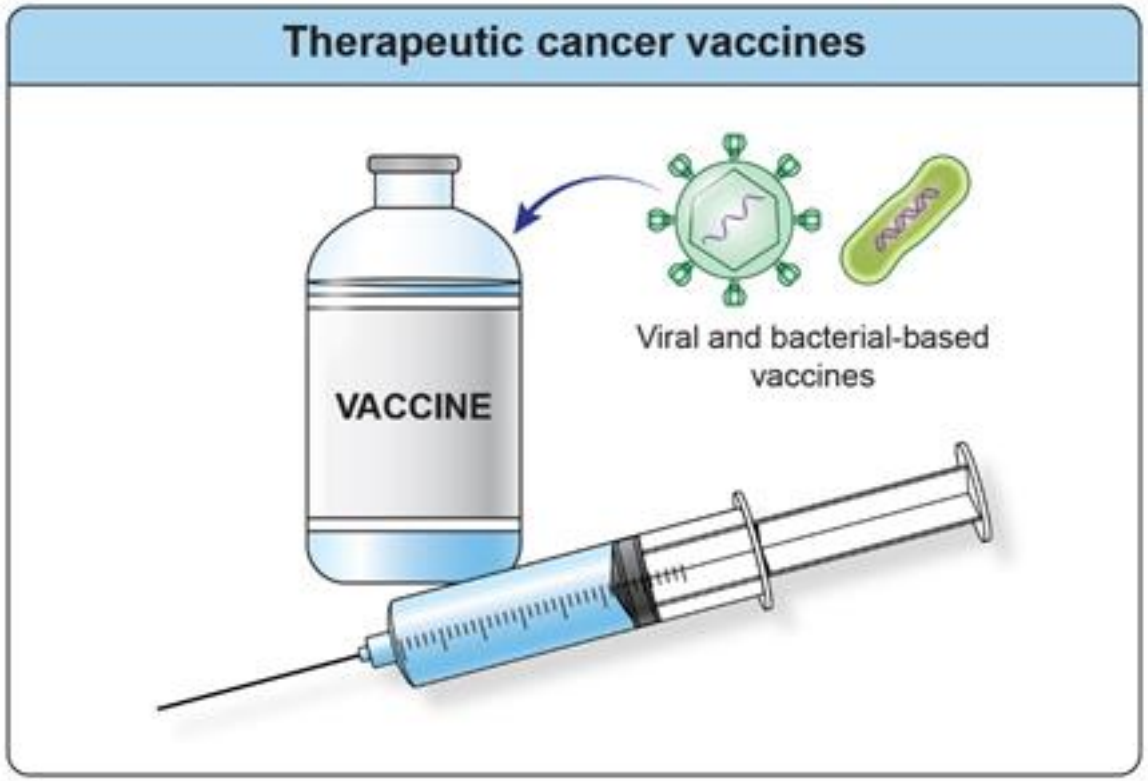
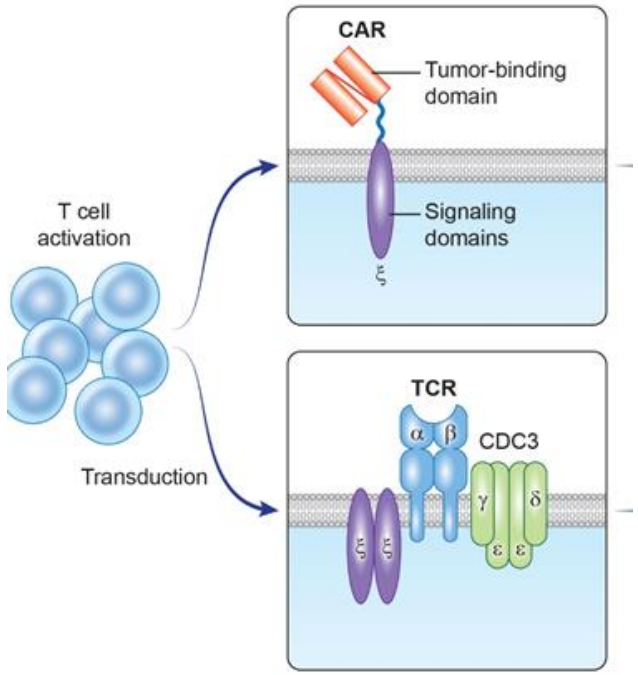


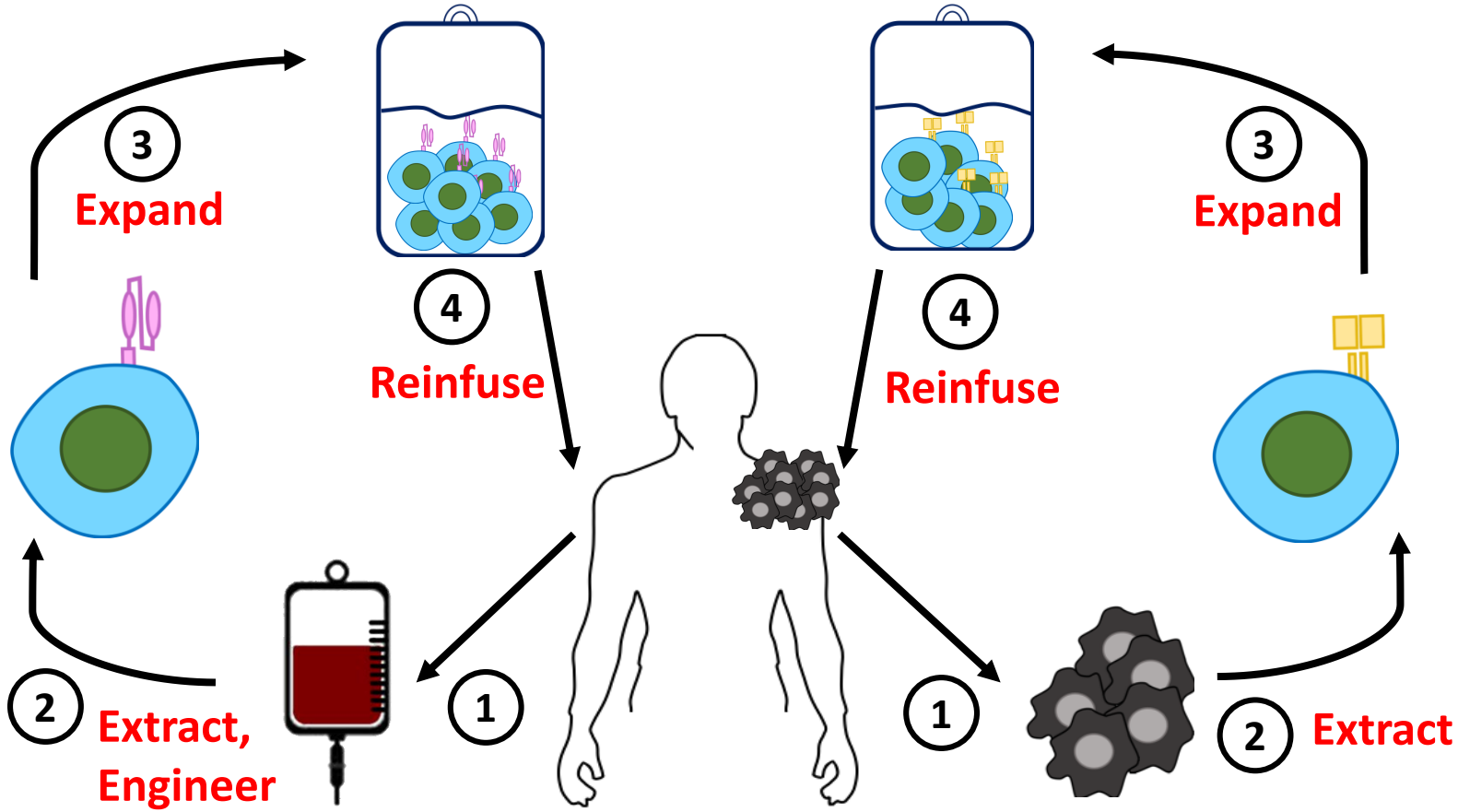

Image courtesy of NCI

# Adoptive T cell transfer (ACT) therapy

Goal:

Overwhelm the tumor with a higher frequency of antigen-specific T cells and/or engineer immune cells to cancer.



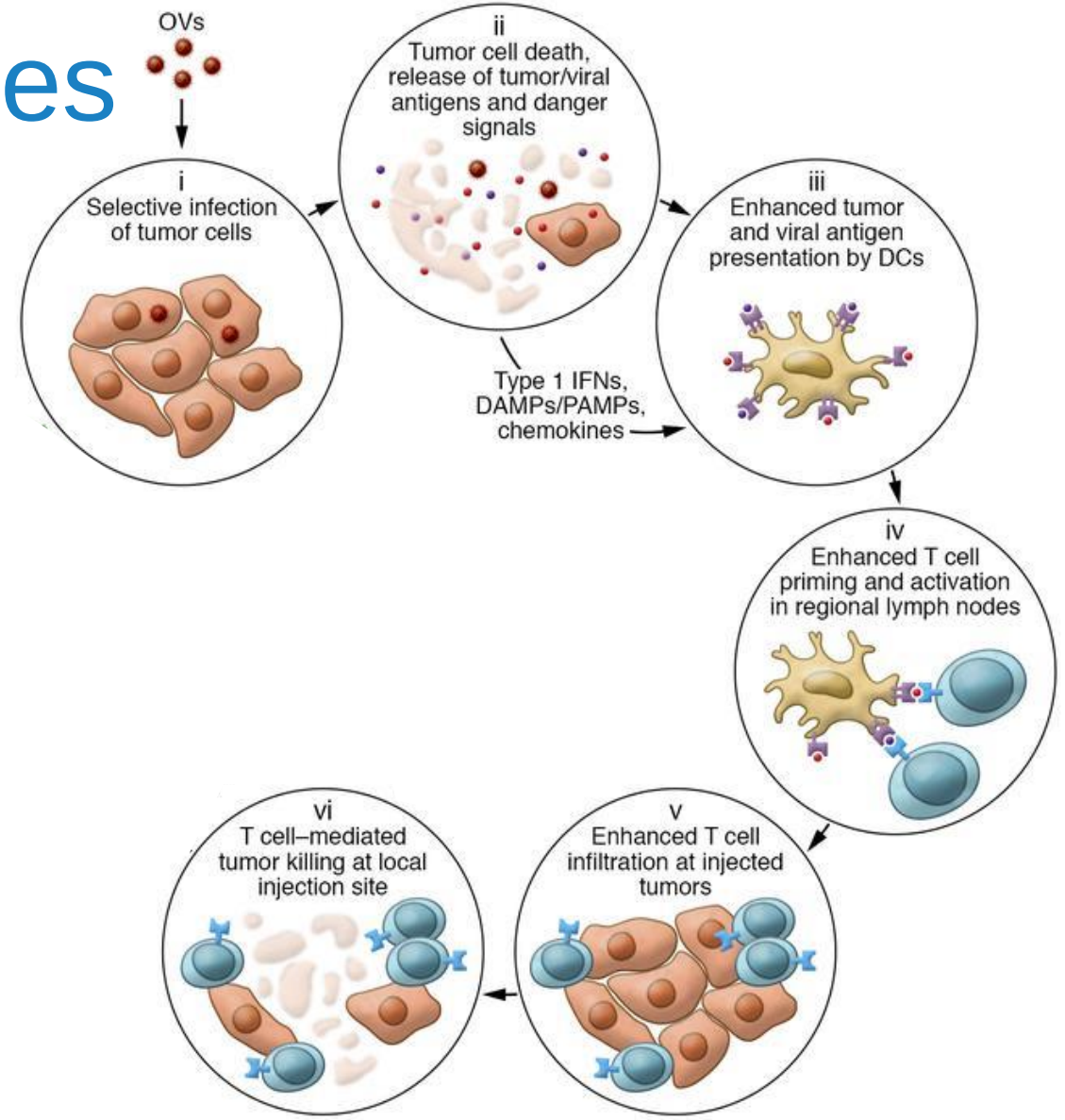

Made by Aubrey Smith, Senior Grad Student in Paulos Lab

Image courtesy of NCI

# Oncolytic Viruses

Goal:

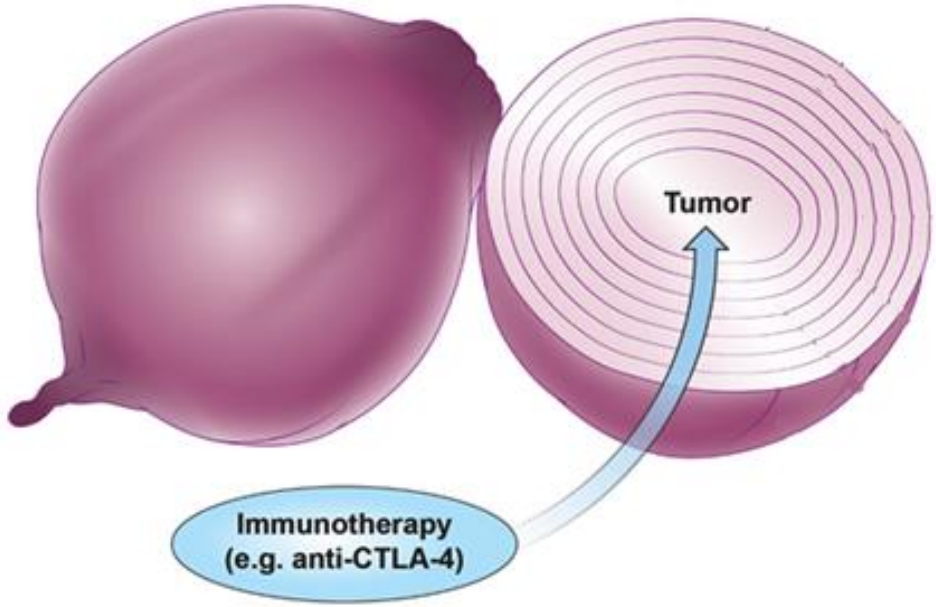
Specifically target and kill tumor cells through viral replication AND release innate immune activators and tumor antigens



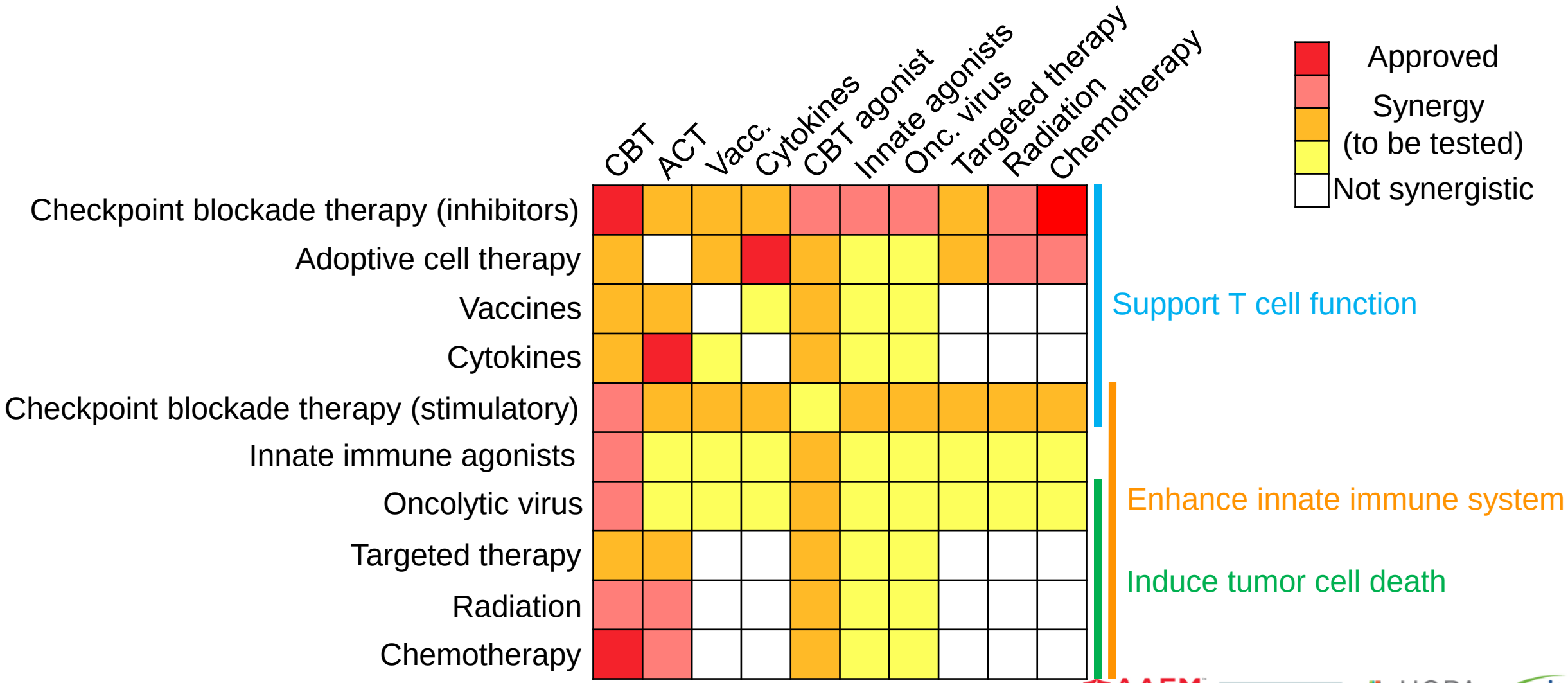

Modified from Bommereddy et al. JCI 2018

# Multi-layered Immunosuppression

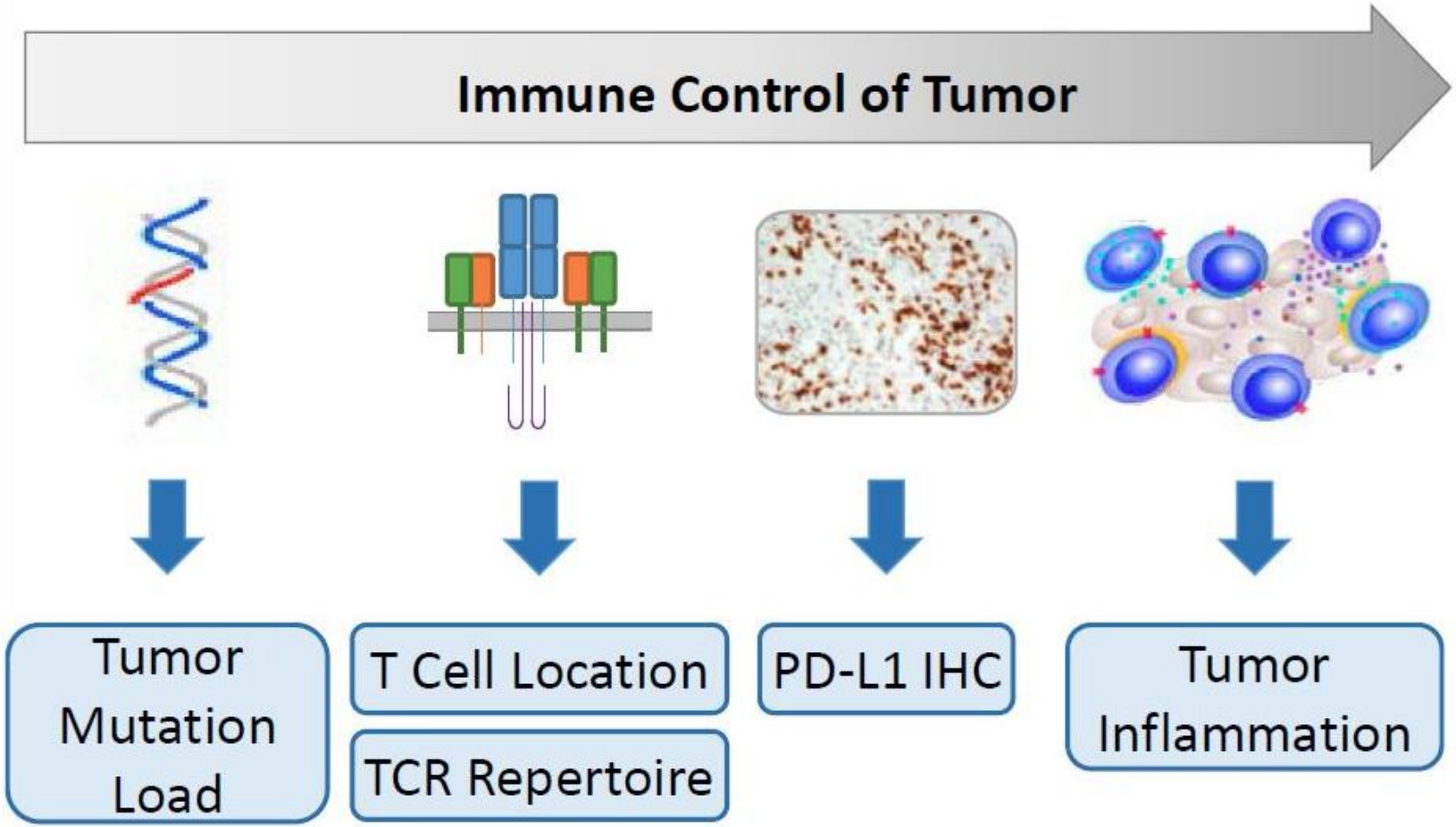
- Tumors insulate themselves
- Overcoming suppression in the tumor is a daunting challenge for T cells
- Immunotherapy can “peel back” layers
- Combination therapy might be needed



# Combination Immunotherapies

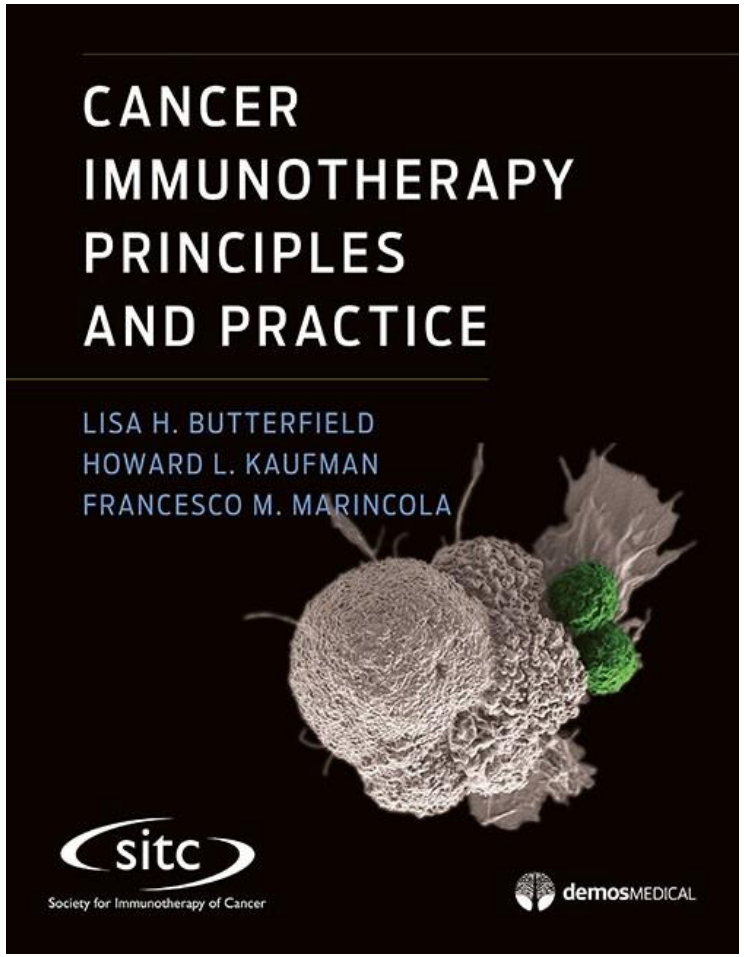


# Immunotherapy Biomarkers




Cesano et al. Biomedicines 2018

# Further Resources

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Cancer Immunotherapy CONNECT