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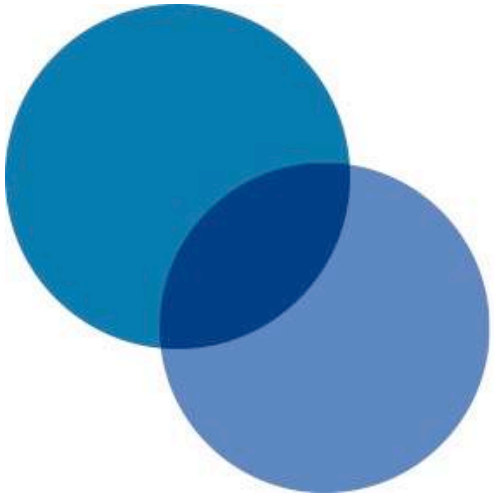

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IMMUNOTHERAPY PATIENT SUMMIT

New York City September 7, 2019

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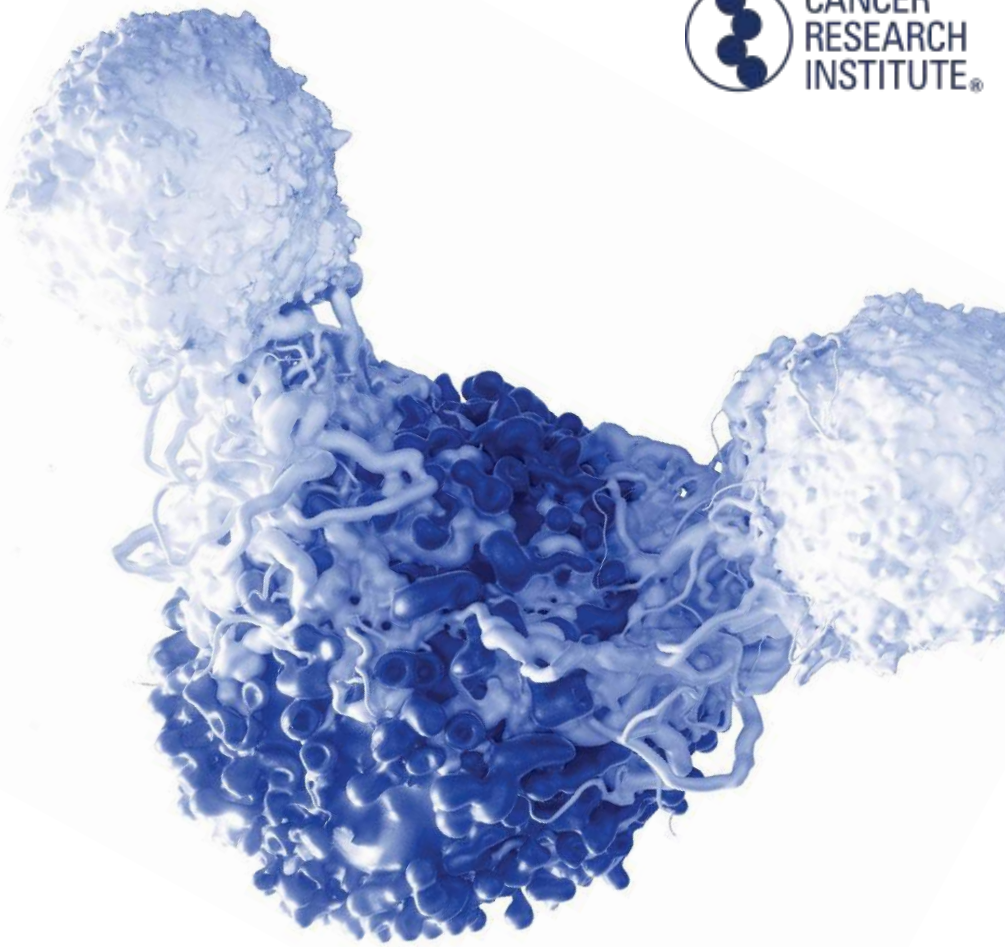

Brian Brewer

Cancer Research Institute

WELCOME

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PATIENT SUMMIT

Speakers

CANCER RESEARCH INSTITUTE IMMUNOTHERAPY PATIENT SUMMIT

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Scientific Experts

Vamsidhar Velcheti, M.D.
NYU Langone's Perlmutter Cancer Center

Sylvia Adams, M.D.
NYU Langone's Perlmutter Cancer Center

Claire Friedman, M.D.
Memorial Sloan Kettering Cancer Center

Gulam A. Manji, M.D., Ph.D.
Columbia University Irving Medical Center

Patient Experts

Dorothy Fabian
Esophageal Cancer

Oswald Peterson
Non-Small Cell Lung Cancer

Tara Ryan
Melanoma

Mary Elizabeth Williams
Melanoma

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Bristol-Myers Squibb

MERCK

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Our Educational Partners

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Thank you to those who helped promote the summit

- American Cancer Society
- Beauty Through the Beast
- Colorectal Cancer Alliance
- Columbia University Irving Medical Center
- Crush It For Curtis Foundation
- Esophageal Cancer Awareness Association
- FORCE
- Gilda's Club NYC
- Go2Foundation For Lung Cancer
- ICLA da Silva Foundation
- Imerman Angels
- Leukemia & Lymphoma Society
- LUNGevity
- Memorial Sloan Kettering Cancer Center
- Pancreatic Cancer Action Network
- Patient Empowerment Network
- Perlmutter Cancer Center at NYU Langone Health
- Ronald McDonald House
- Us TOO
- Young Survival Coalition

Summit Program

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Morning Session	10:00 AM – 12:00 PM
Lunch	12:00 PM – 1:00 PM
Afternoon Session	1:00 PM – 2:15 PM
Breakout Sessions	2:30 PM – 3:15 PM

Clinical Trial Navigator Appointments are available from 9:00 AM to 4:00 PM. Please stop by the check-in desk near registration to learn more.

After the Summit

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You will receive two emails after the summit:

1. **A survey** to share your feedback on the summit as well as insights into future programming.

2. **Information** from the summit day, including this presentation and instructions on how to use our Clinical Trial Finder service.

#CRIsummit

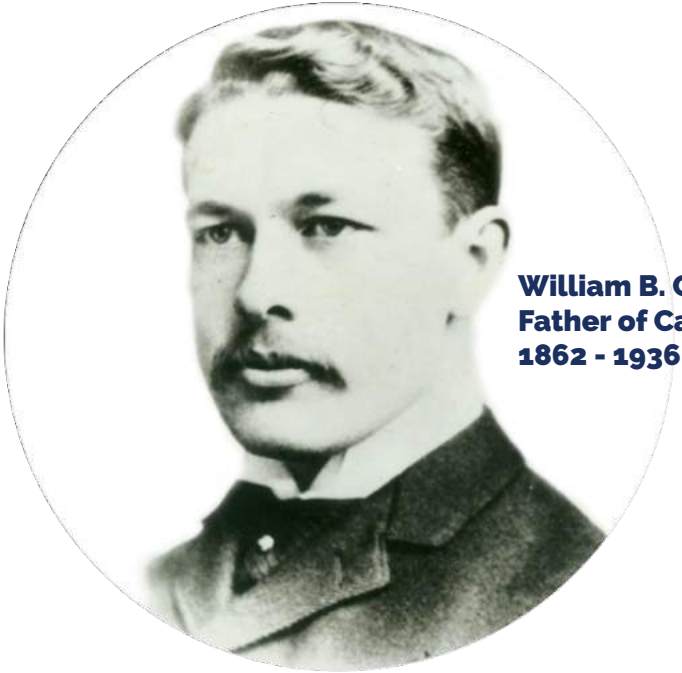
Welcome

Jill O’Donnell-Tormey, Ph.D.

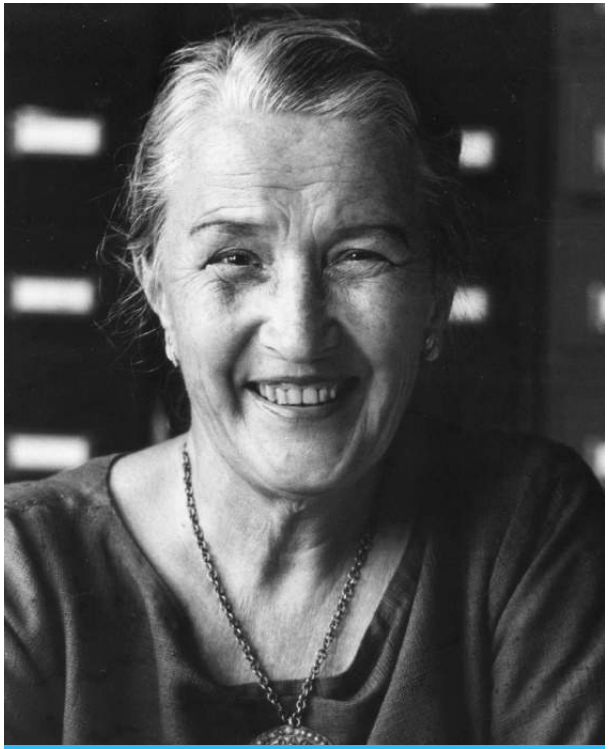
CEO and Director of Scientific Affairs

Cancer Research Institute

Pioneering Immunotherapy



William B. Coley, M.D.
Father of Cancer Immunotherapy
1862 - 1936



Helen Coley Nauts, D.Sc. (Hon.)
Co-Founder, Cancer Research Institute
1907 - 2001

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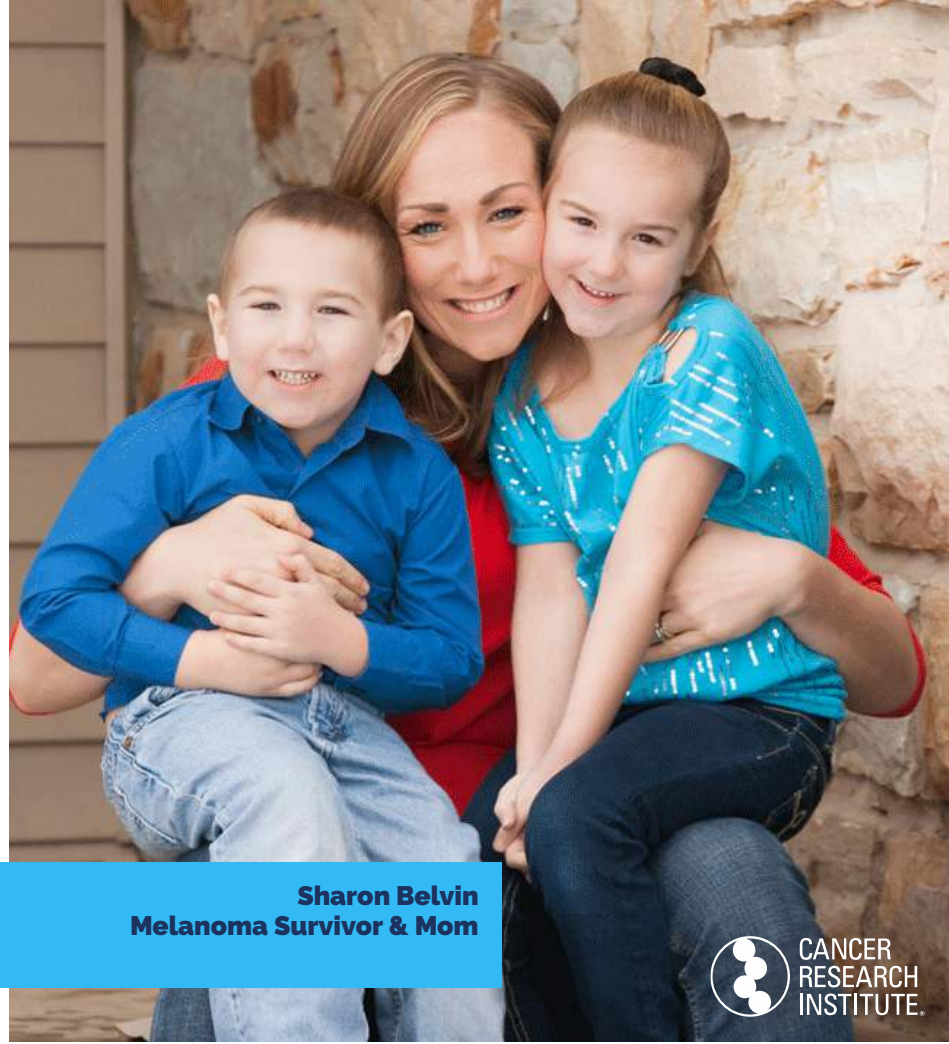
CRI Mission

SAVE MORE LIVES

by fueling the discovery and development of powerful immunotherapies for all types of cancer.



Sharon Belvin
Melanoma Survivor & Mom

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CRI Impact

CANCER RESEARCH INSTITUTE®

FUNDED **3,300** scientists worldwide

INVESTED **$400+** million

TRUSTED **Platinum, A+** charity

#CRIsummit

Welcome

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Benjamin G. Neel, M.D., Ph.D.

Director, Perlmutter Cancer Center at NYU Langone Health

Professor, Department of Medicine, NYU School of Medicine

NYU Langone Health

Perlmutter Cancer Center

Immunotherapy 101

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Vamsi Velcheti, M.D. FACP FCCP

Associate Professor, Department of Medicine
Director, Thoracic Med Oncology Program
NYU Langone's Perlmutter Cancer Center

NYU Langone Health

Perlmutter Cancer Center

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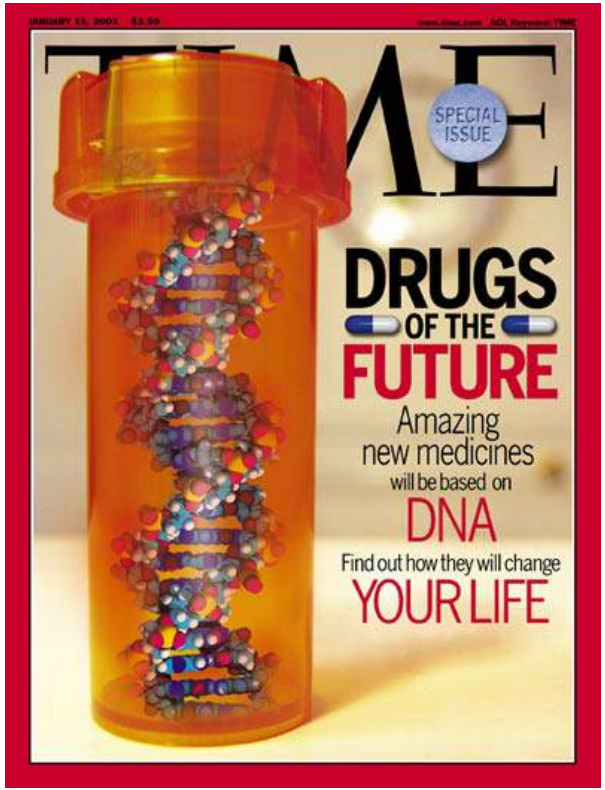

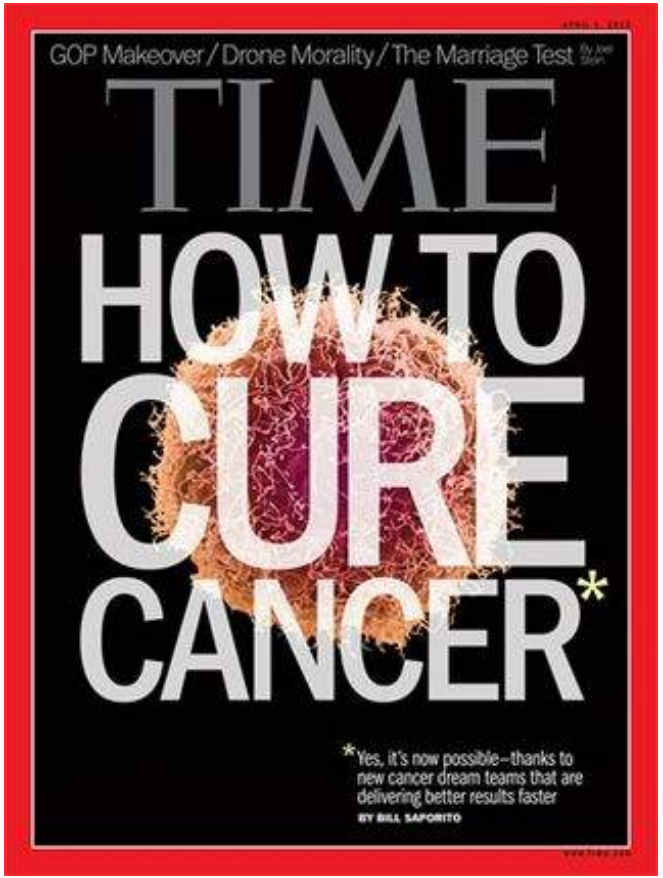

History of targeted therapy: driver discovery

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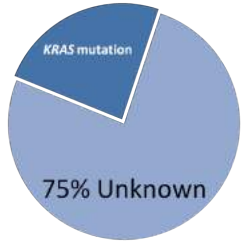
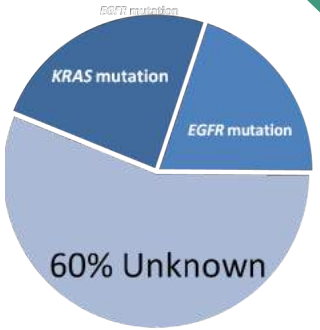
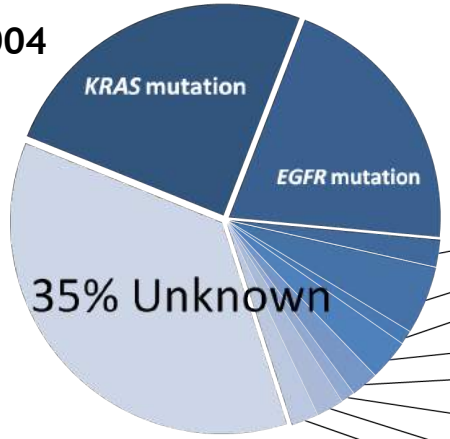


1999



2004

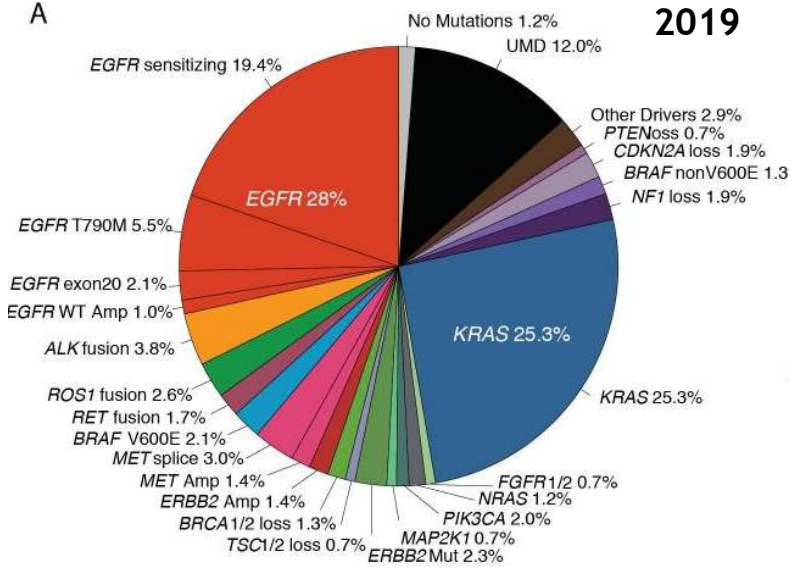


2016

BRAF mutation
ALK rearrangement
MEK mutation
PIK3CA mutation
HER2 mutation
ROS1 fusion
RET translocation
MET amplification

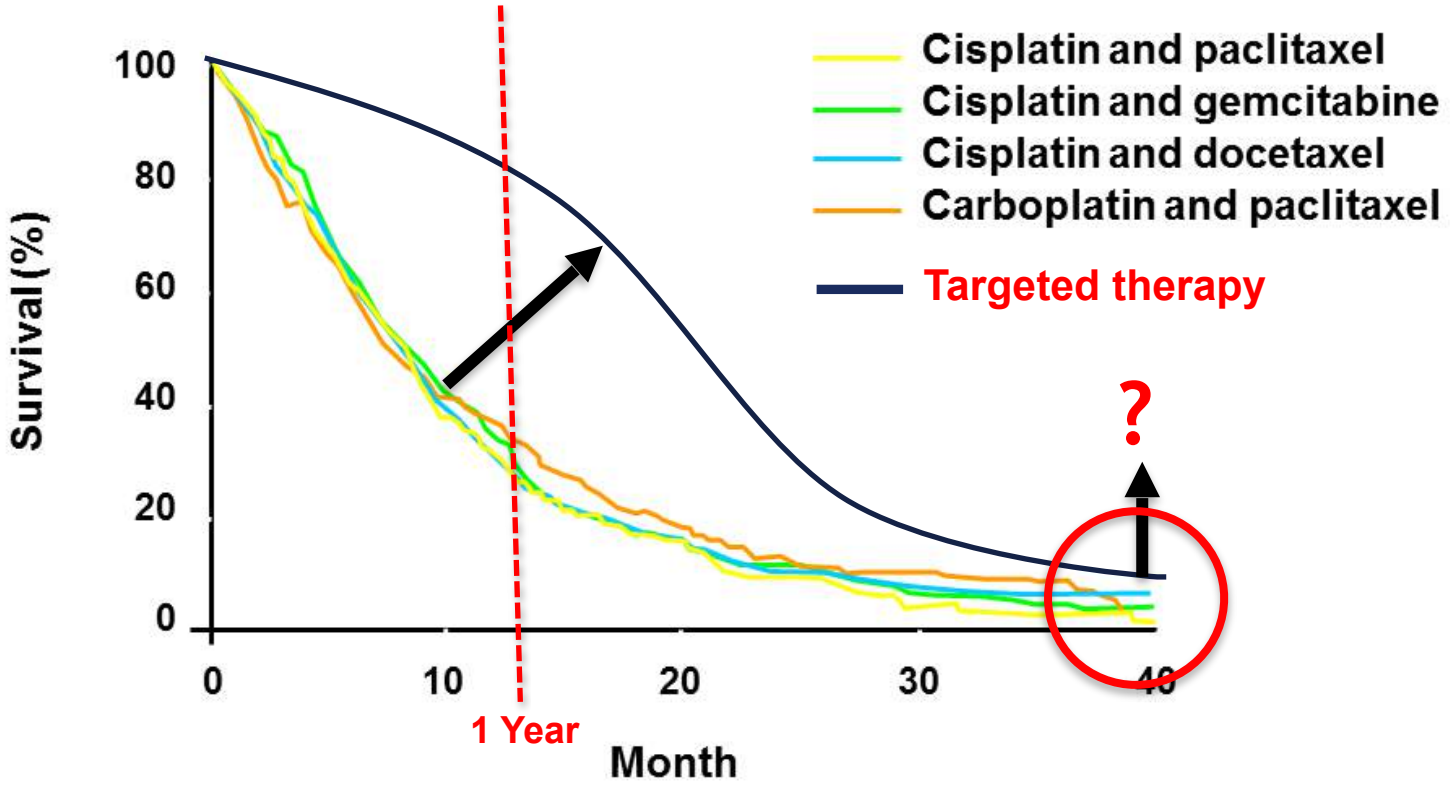
A

2019



Jordan EJ *et al Cancer Discov* 2018

Treatment of Advanced Stage Non-Small Cell Lung Cancer



N Engl J Med. 2002 Jan 10;346(2):92-8.

Oncology as Whack-a-Mole

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Rapid emergence of compensatory mechanisms of resistance

Limitations with Targeted Therapy in Cancer

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- Most solid tumors are genomically very complex.
- Complexity -> inter-tumor heterogeneity, intra-tumor heterogeneity, and evolution of the tumor with treatment stress.
- Resistance is certain and resistance mechanisms are diverse.

Cancer is an Immunological Disorder

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- Immunotherapy can activate immune responses against multiple mutant proteins/neo-antigens.
- The adaptable immune system can keep pace with tumor evolution.

Diversity and Specificity of Anti-Tumor Immune Responses

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Specificity:

Can distinguish minute chemical alterations

Diversity:

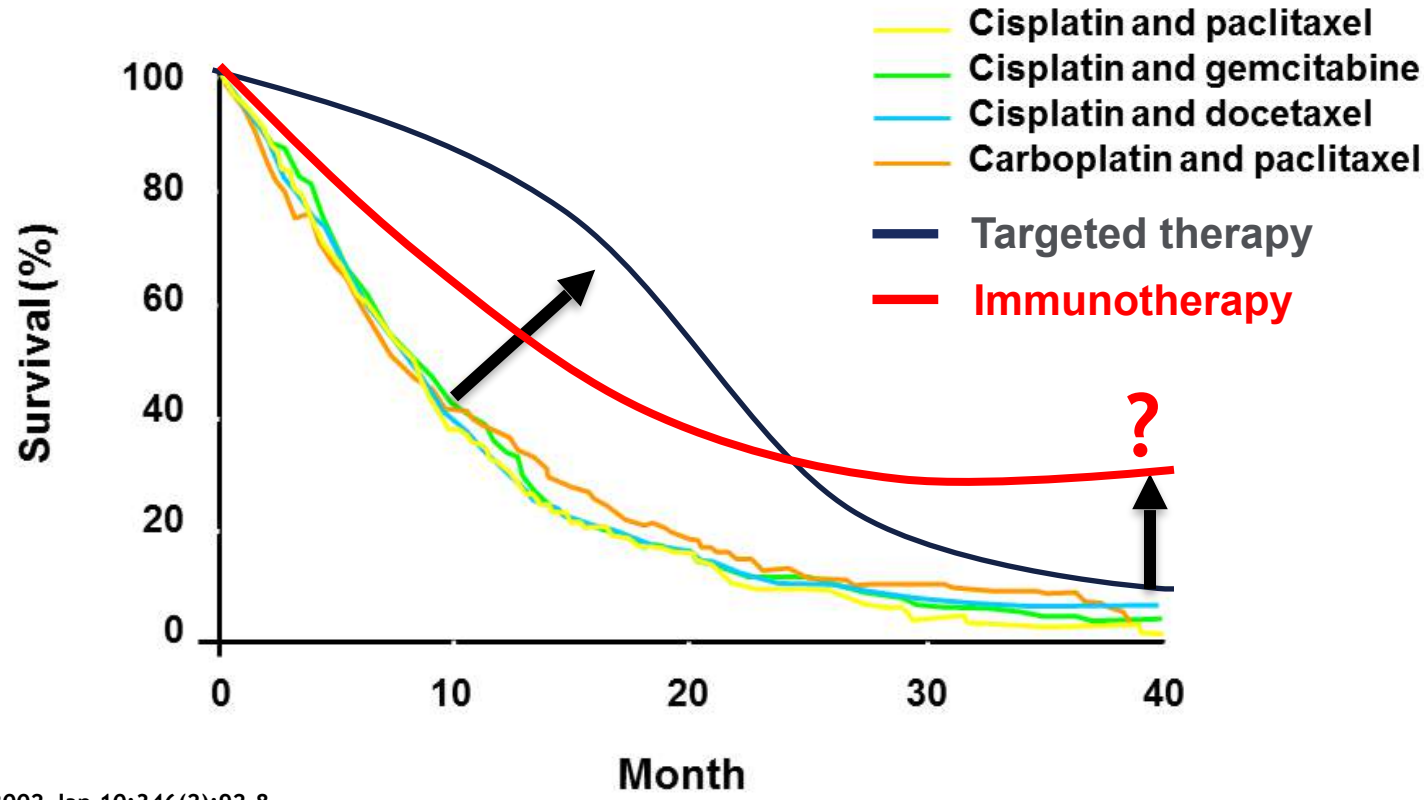
T Cells- 10^{18}

Antibodies- 10^{22}

Memory:

After effective antigen priming, immunity can last for decades.

Treatment of Advanced Stage Non-Small Cell Lung Cancer



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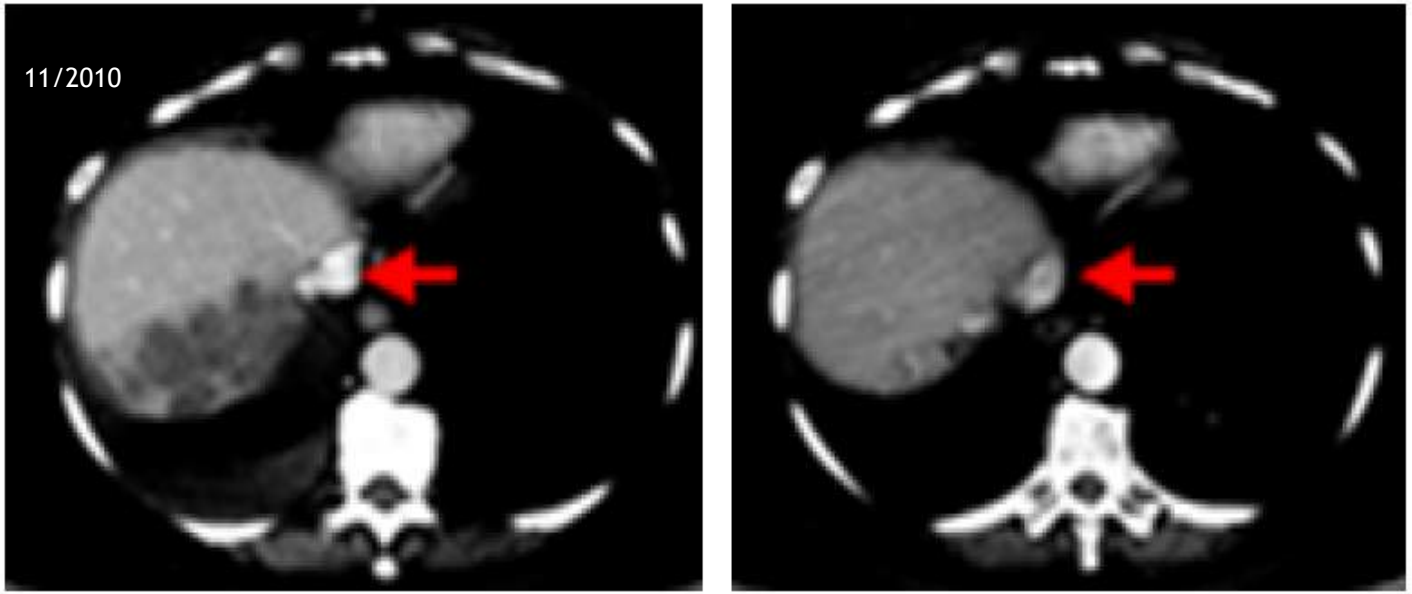

Pre/ Post MDX-1106: 66 y/o ex smoker with KRAS mutant adenocarcinoma of the lung with 3 prior treatments for Stage IV disease; RUQ abdominal pain, anorexia and fatigue resolved within 2 months; **Duration of response: 6 years and ongoing…**

Origin & Revival of Immunotherapy

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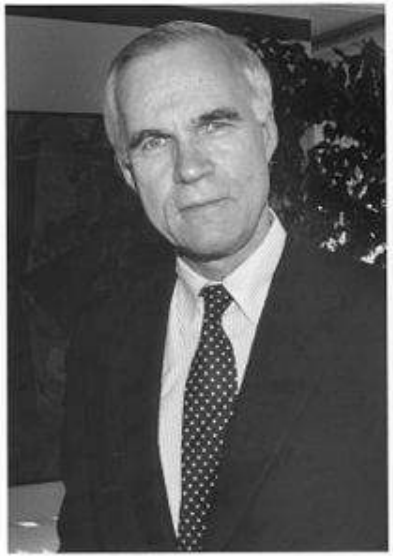
1890s:
William B. Coley

1900s:
Paul Ehrlich



1960s:
Lloyd J. Old

The Immune System at a Glance: Our Natural Defense System

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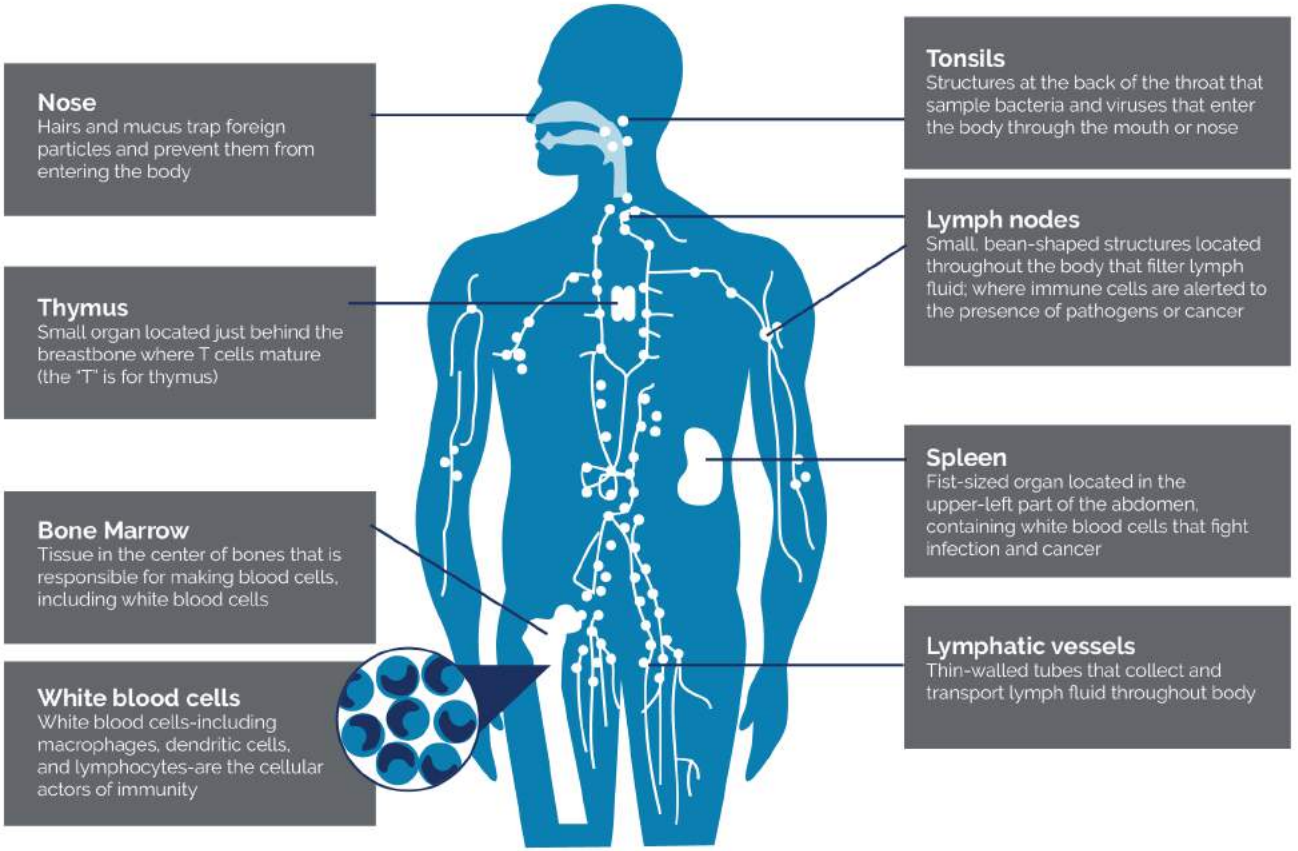

The Cells of the Immune System: The "Soldiers" in our Army

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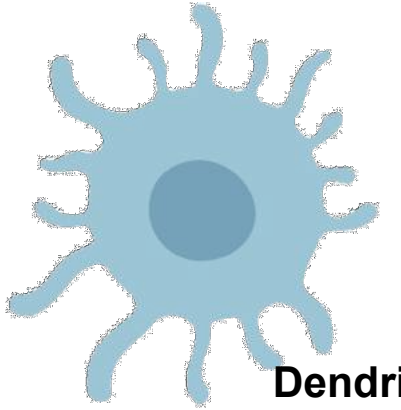
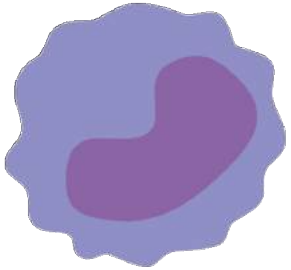
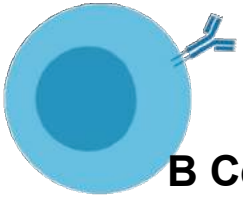


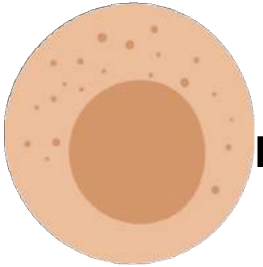
Dendritic Cell



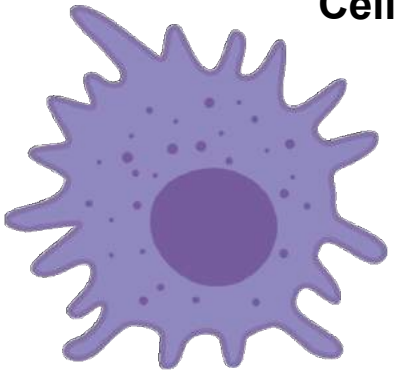
Monocyte



B Cell

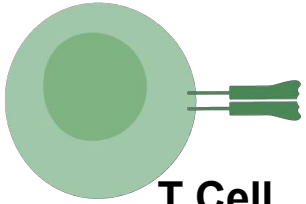


Natural Killer Cell



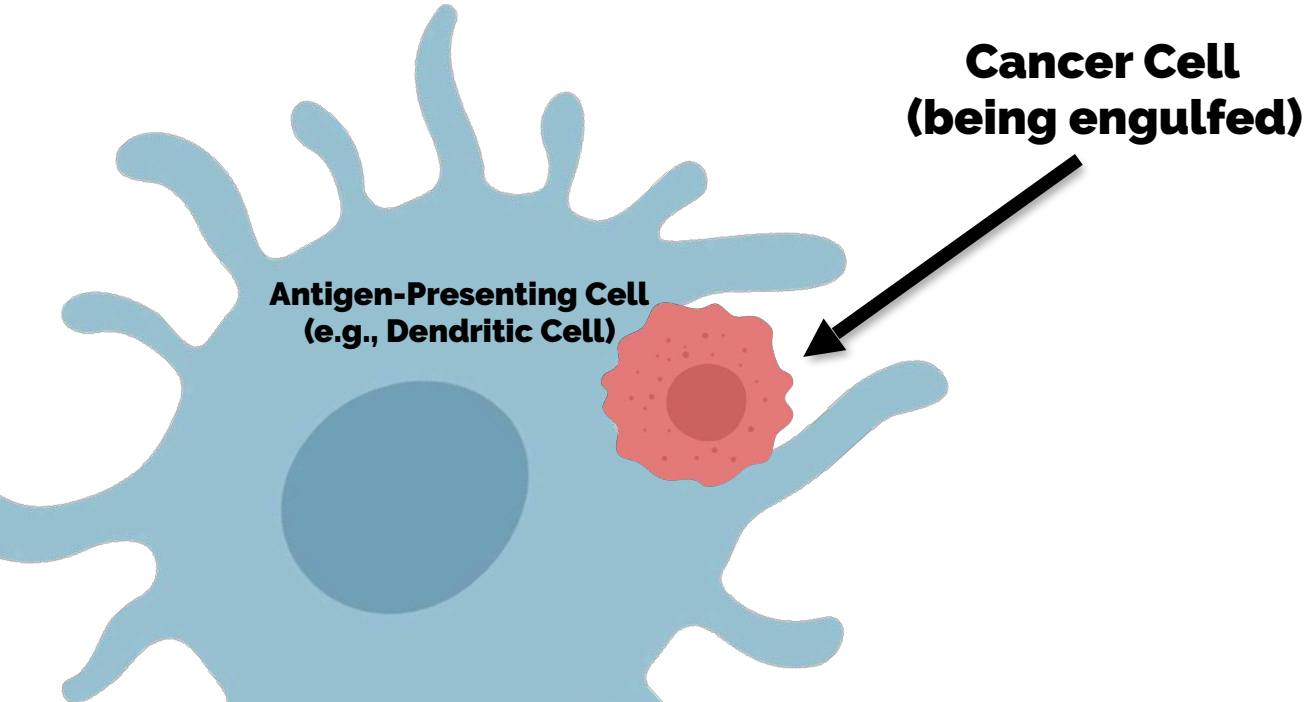
Macrophage

Neutrophil

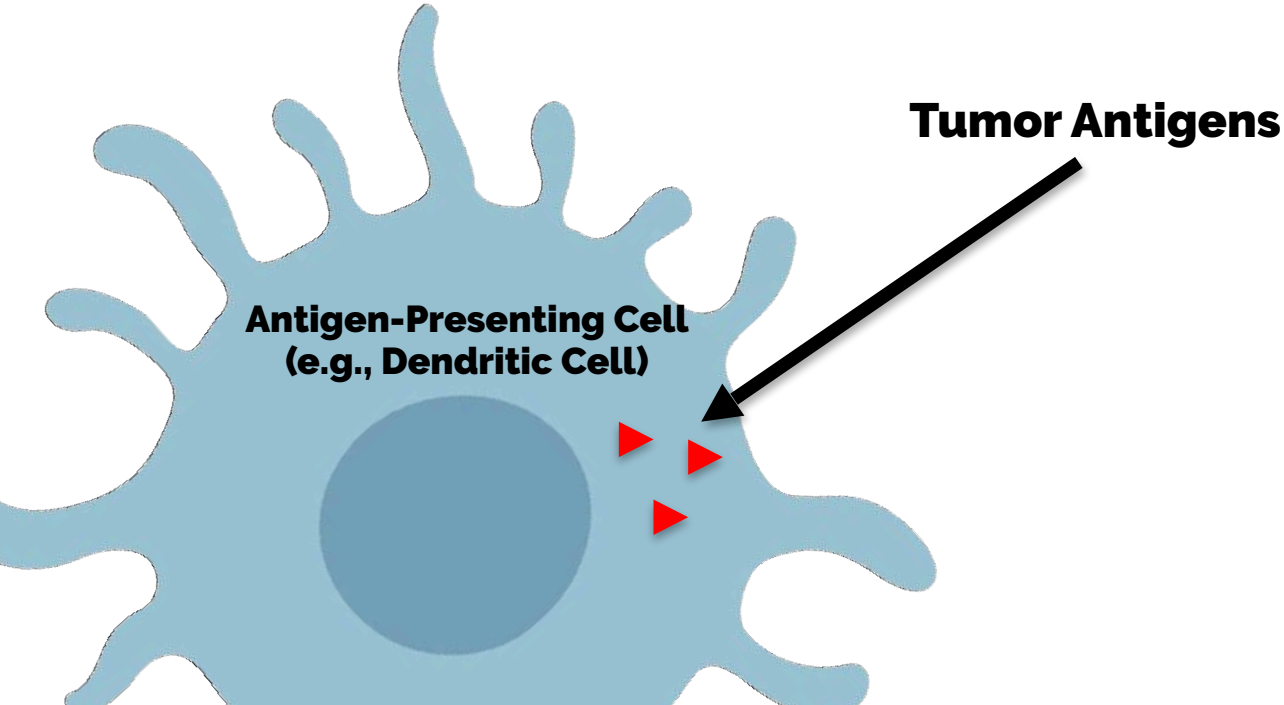


T Cell

Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer



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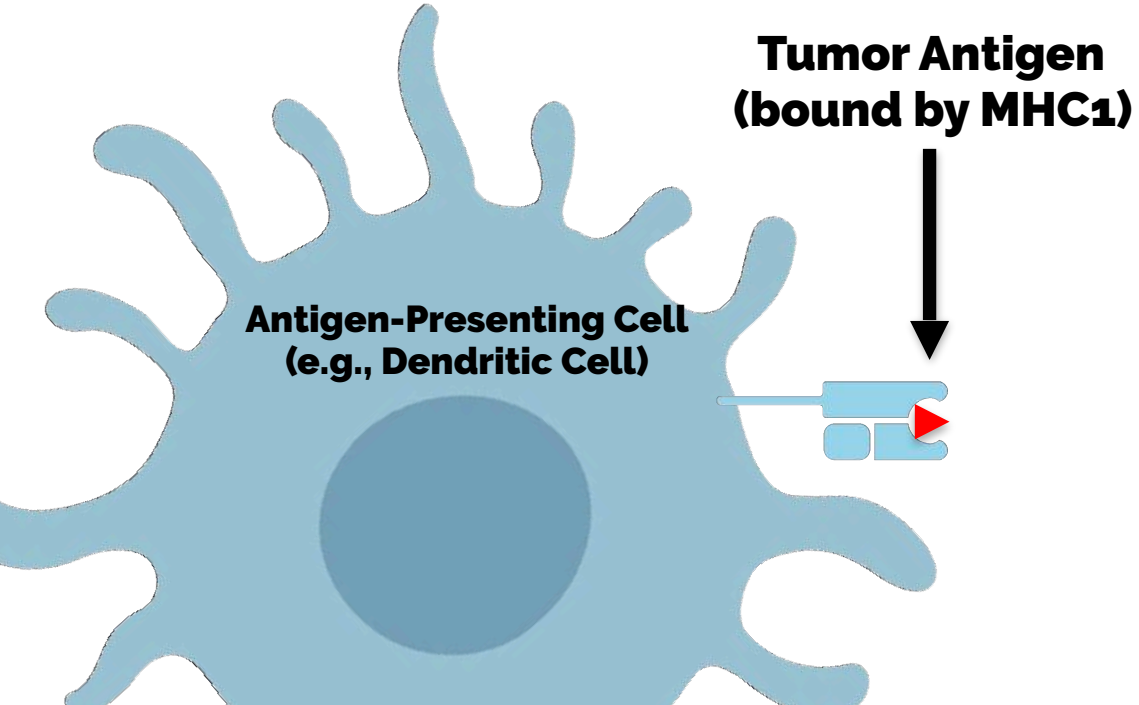

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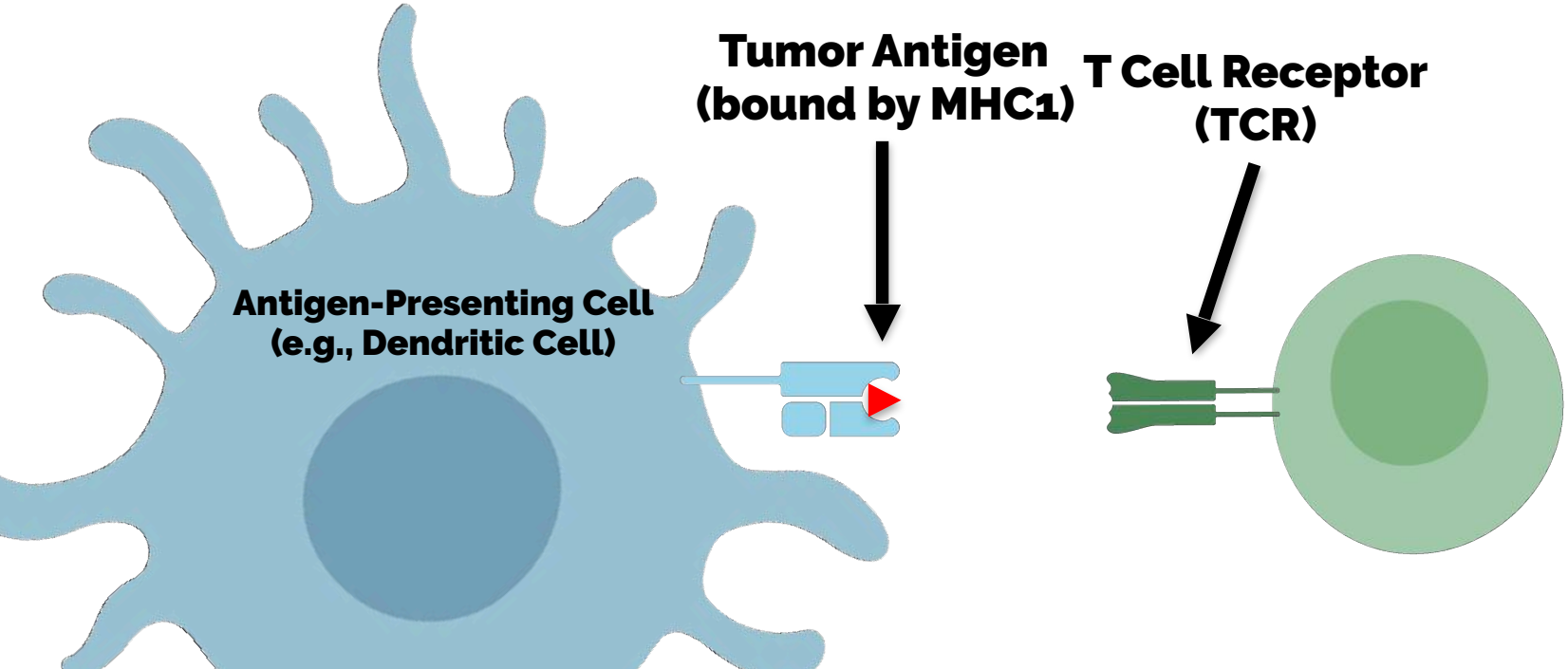
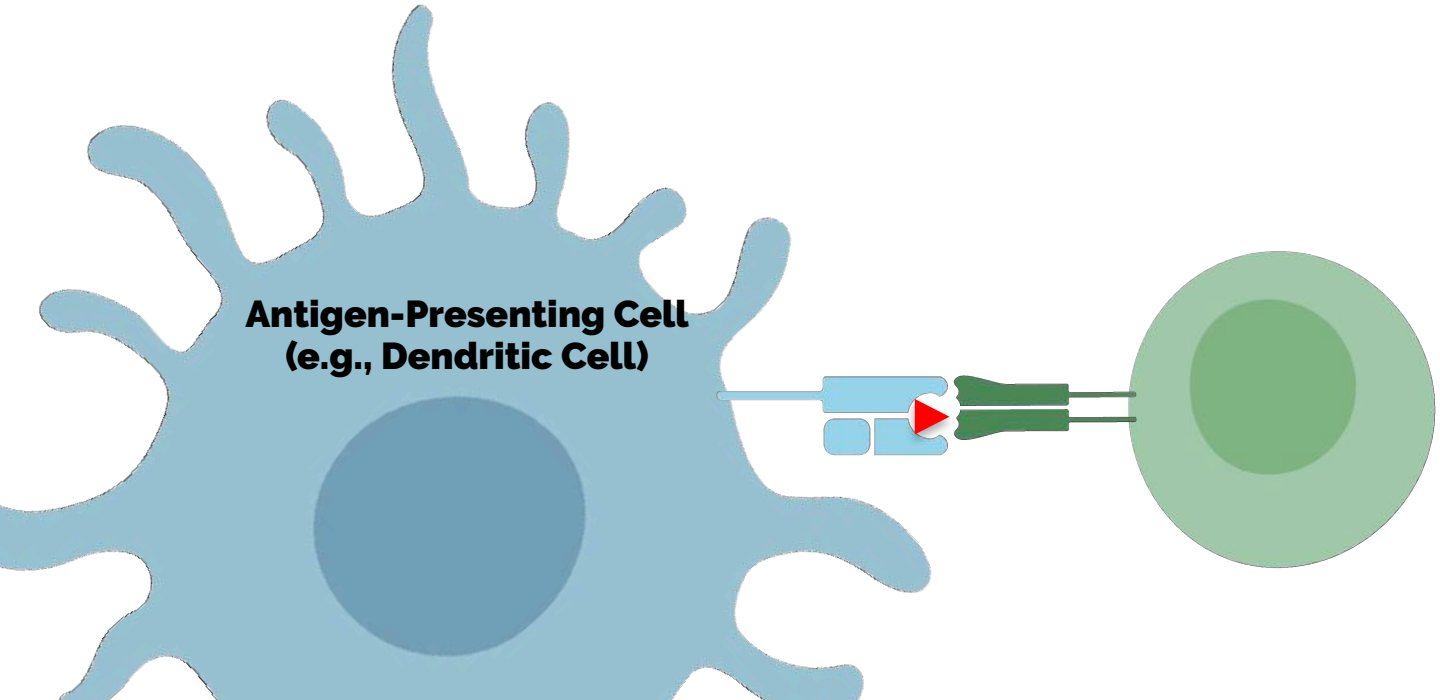
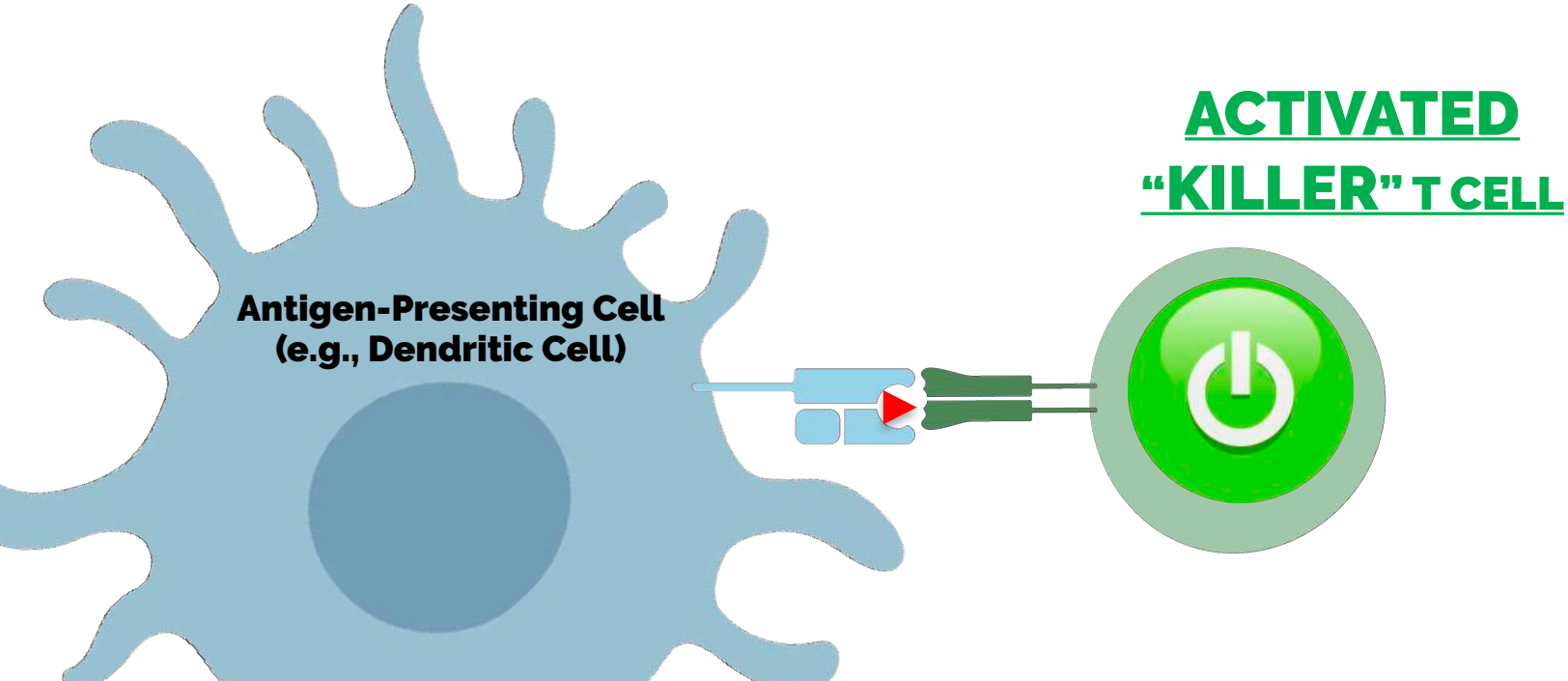


Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer

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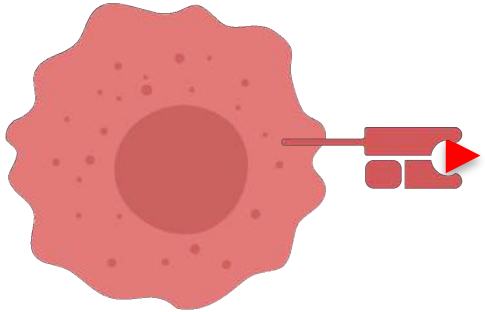
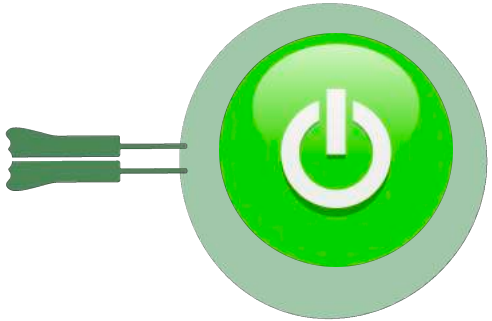
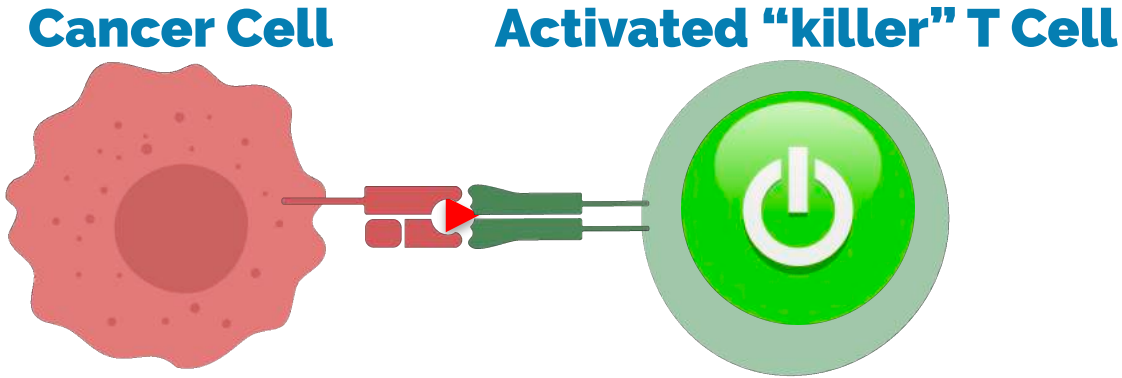
Cancer Cell



Activated “killer” T Cell



Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer

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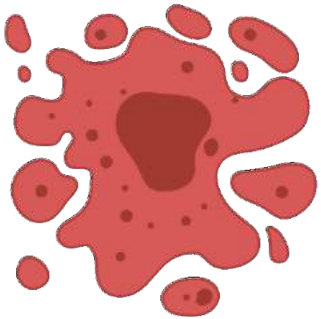
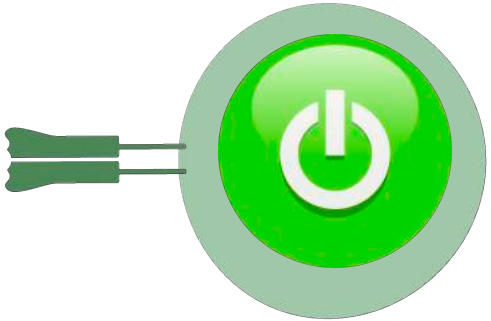
Cancer Cell

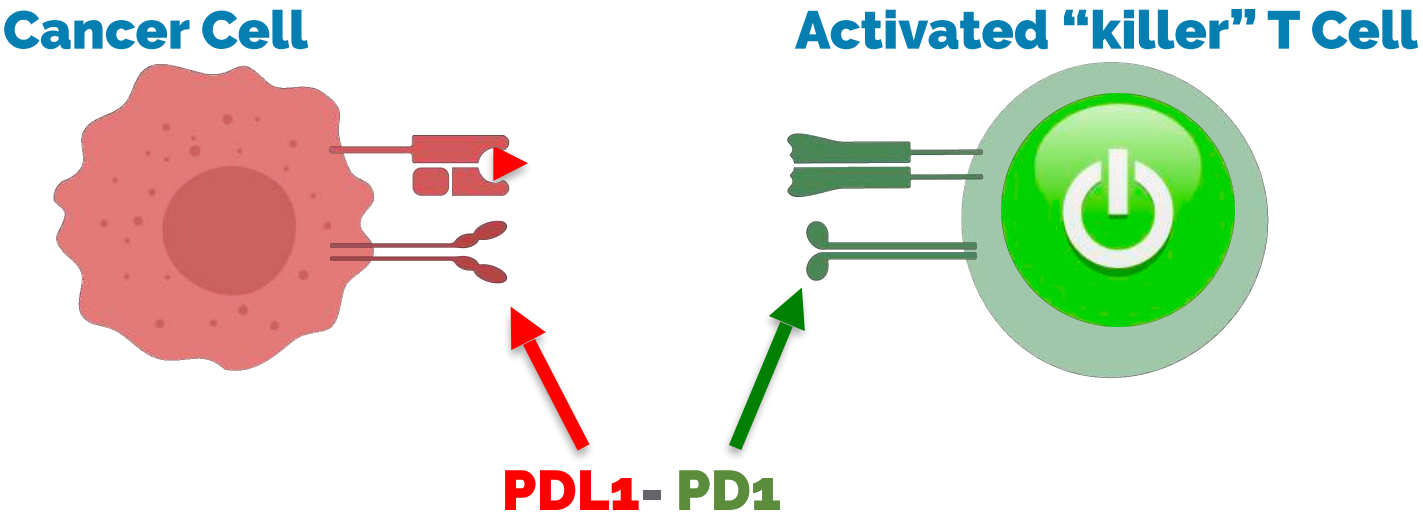


Activated "killer" T Cell

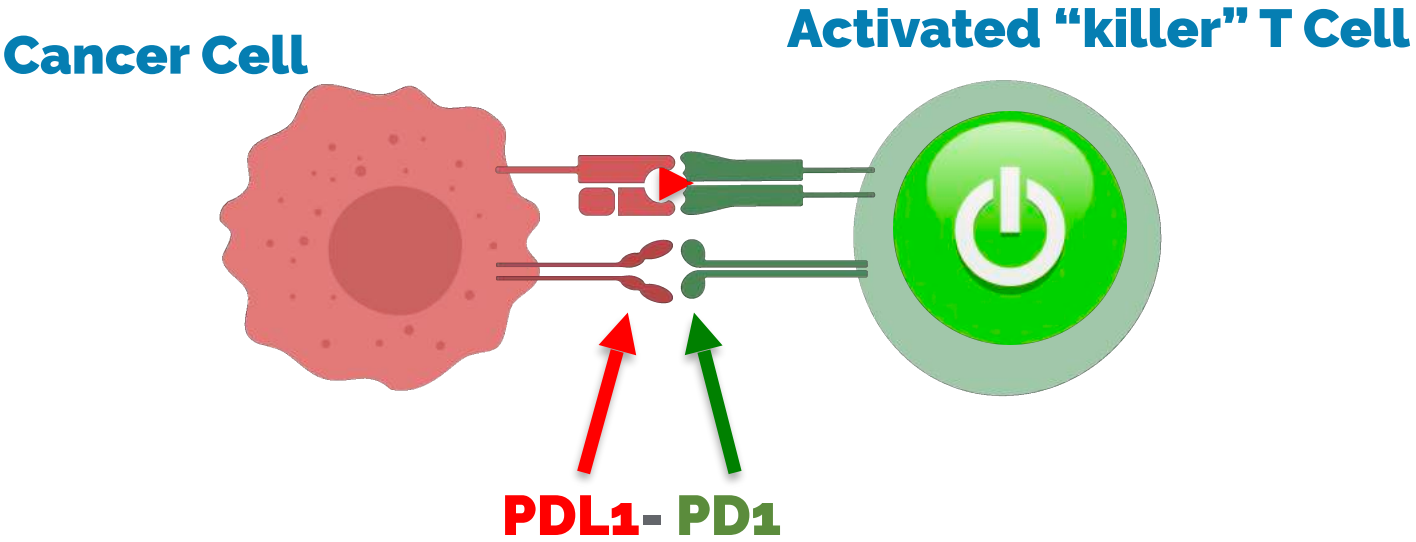


CANCER CELL ELIMINATED!

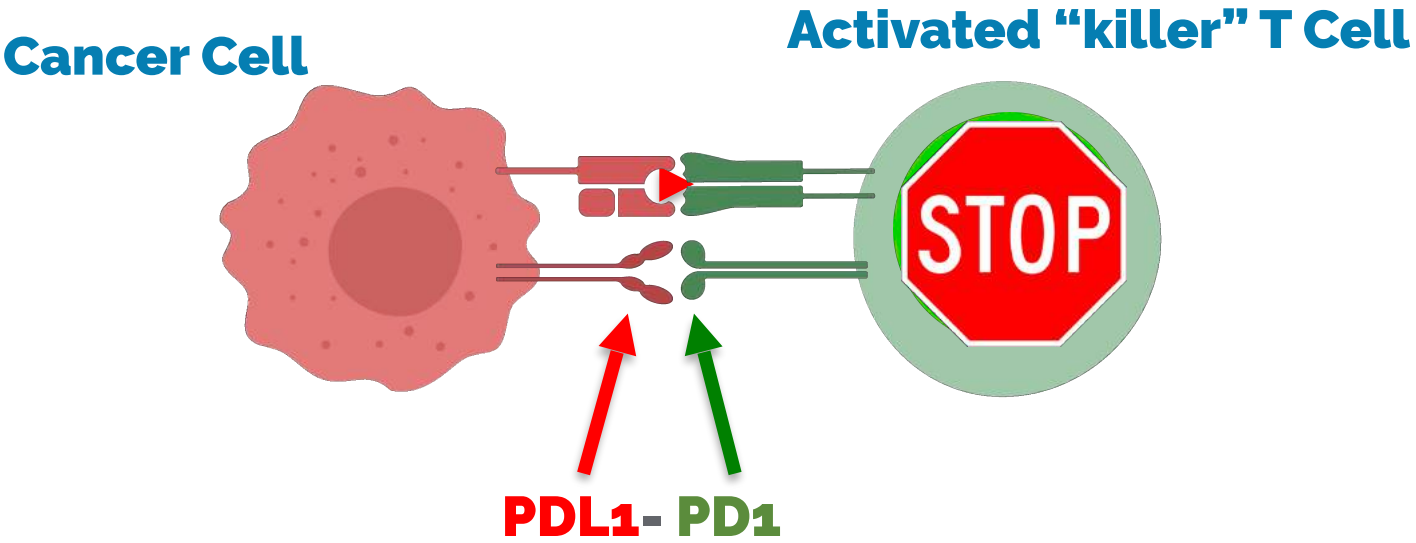
Immune Checkpoints Can Suppress Immune Responses



Immune Checkpoints Can Suppress Immune Responses

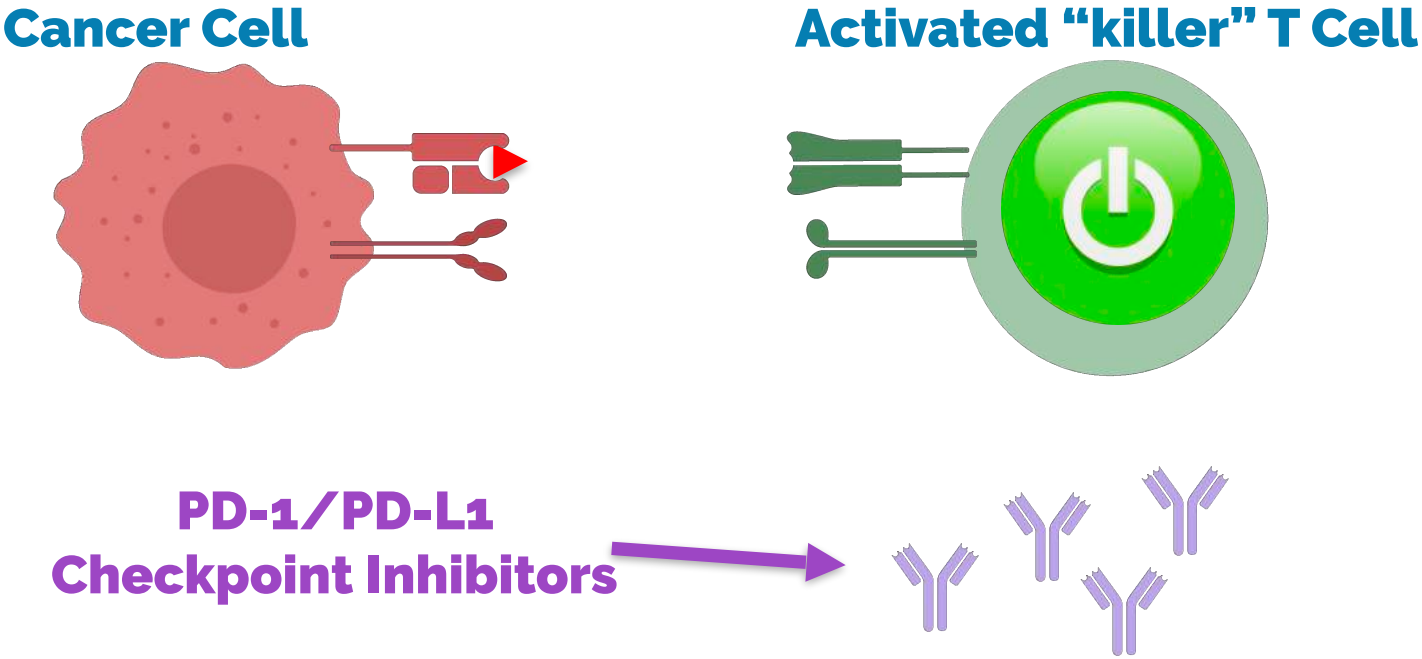


Immune Checkpoints Can Suppress Immune Responses



Normally, PDL1-PD1 leads to T cell "exhaustion"

Checkpoint Immunotherapy Can Promote Anti-Cancer Activity



Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

65 YEARS IN IMMUNOTHERAPY

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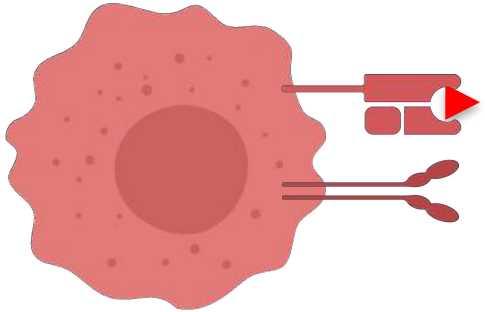
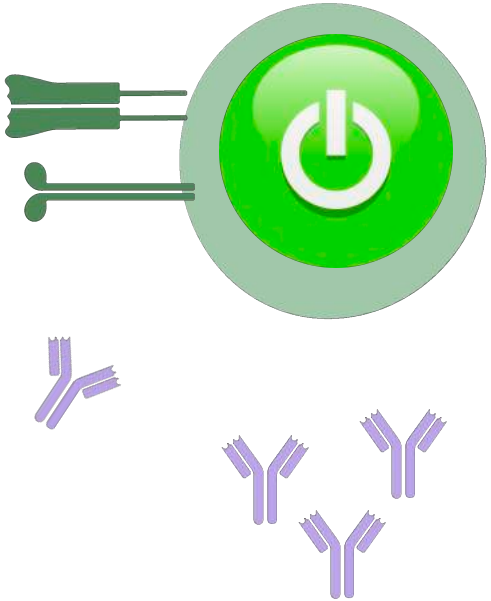
Cancer Cell



Activated “killer” T Cell



Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

65 YEARS IN IMMUNOTHERAPY

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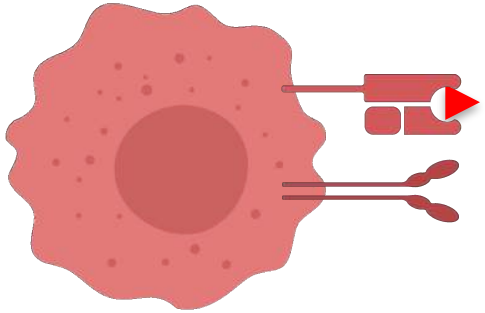
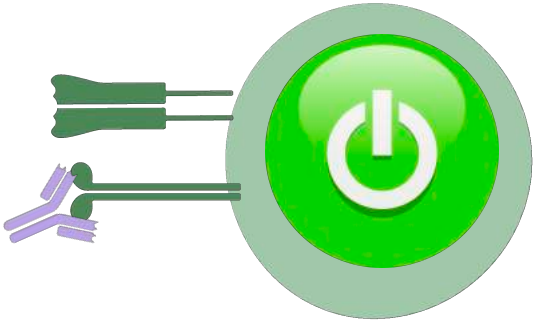
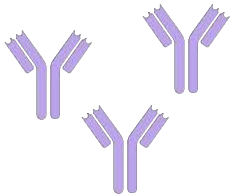
Cancer Cell

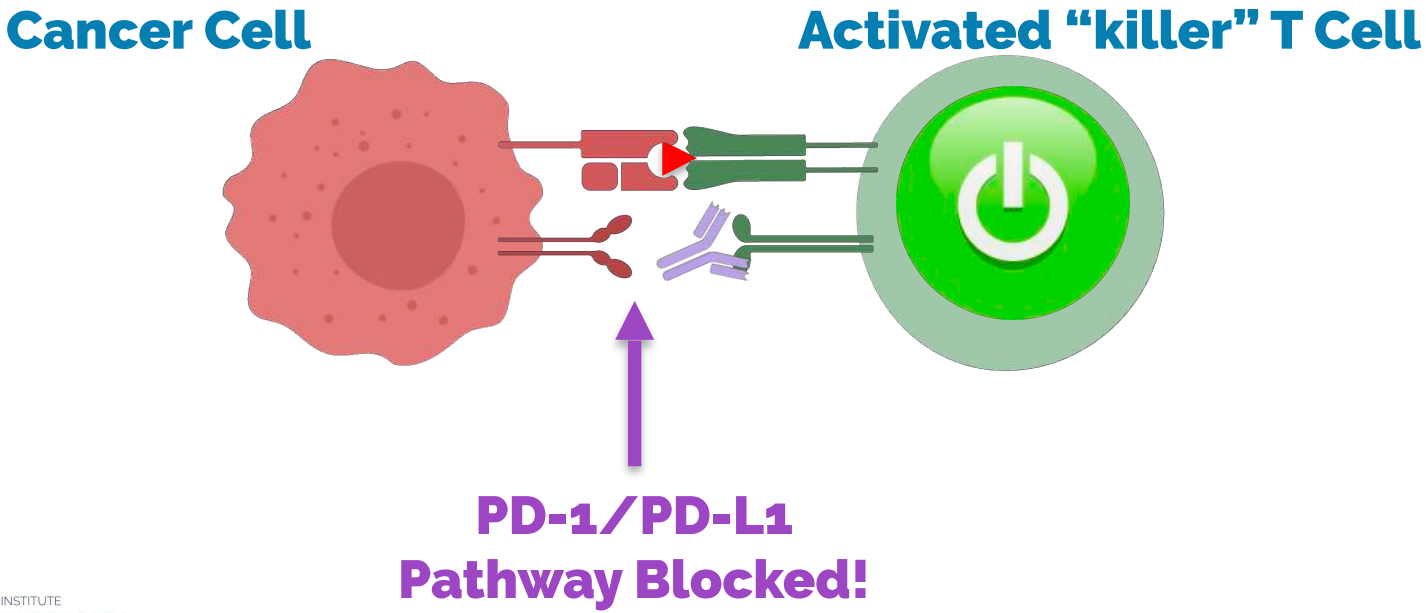


Activated “killer” T Cell





Checkpoint Immunotherapy Can Promote Anti-Cancer Activity



Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

65 YEARS IN IMMUNOTHERAPY

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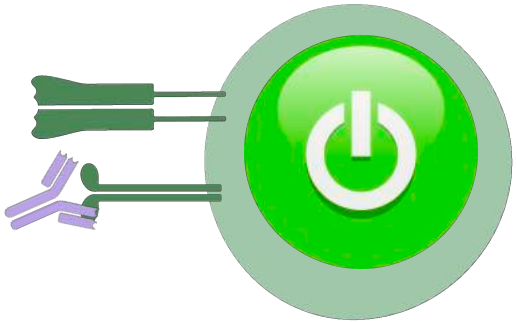
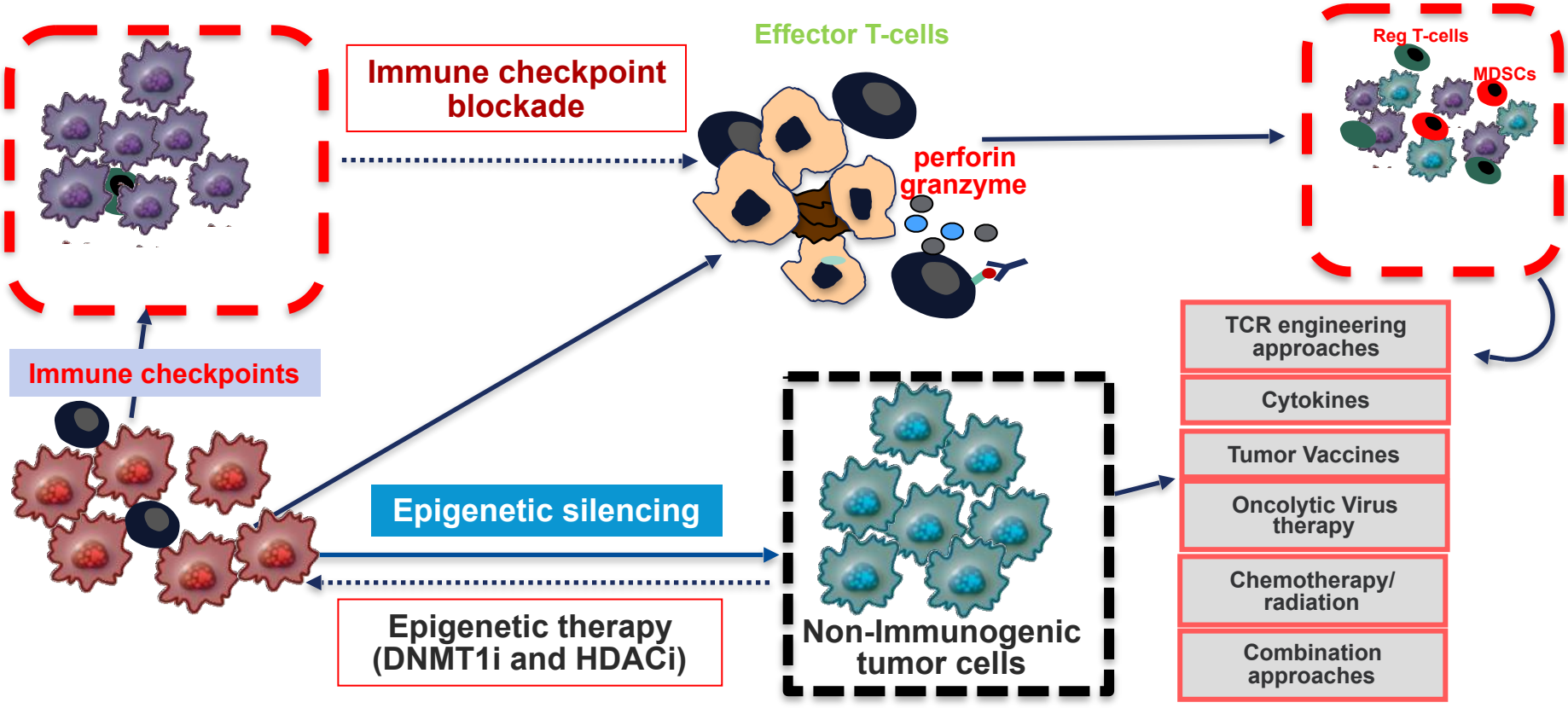
Cancer Cell

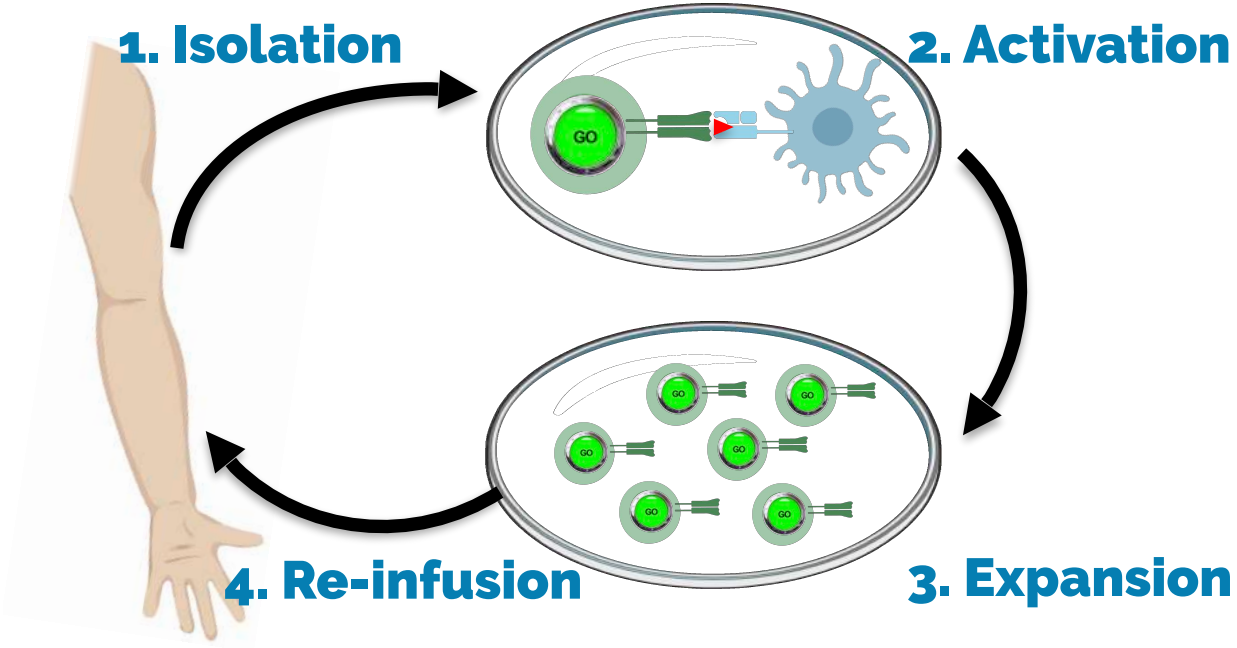
Activated "killer" T Cell



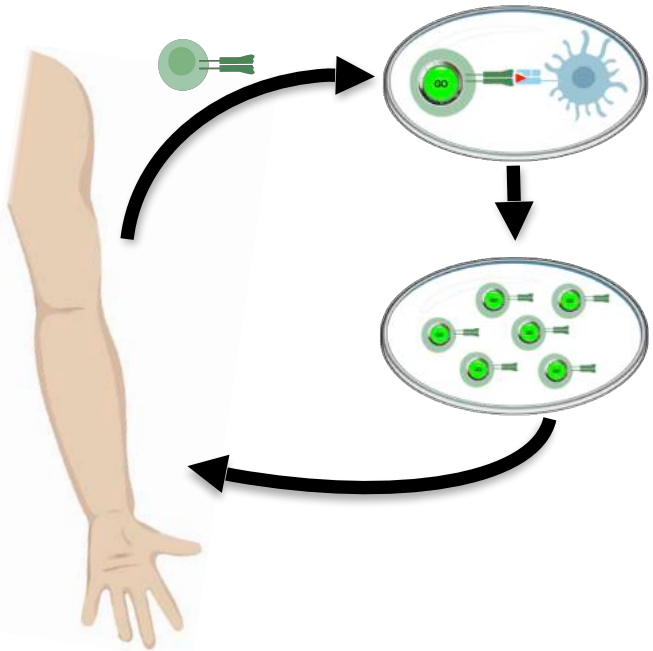
CANCER CELL ELIMINATED!

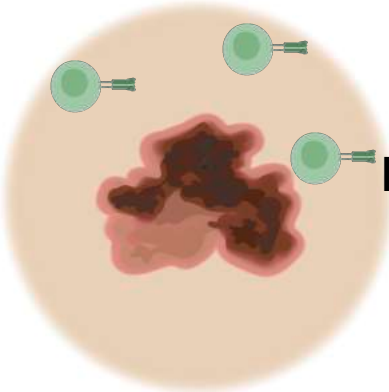


Adoptive T Cell Immunotherapy

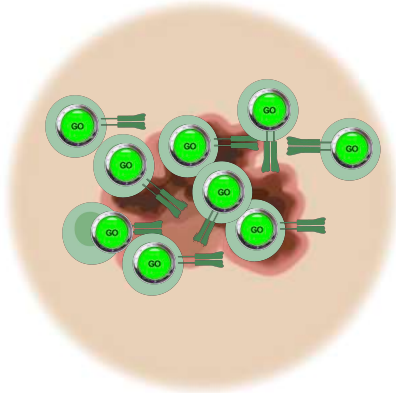


Adoptive T Cells In Action (Against Melanoma)





Melanoma (Before)



Melanoma (After)

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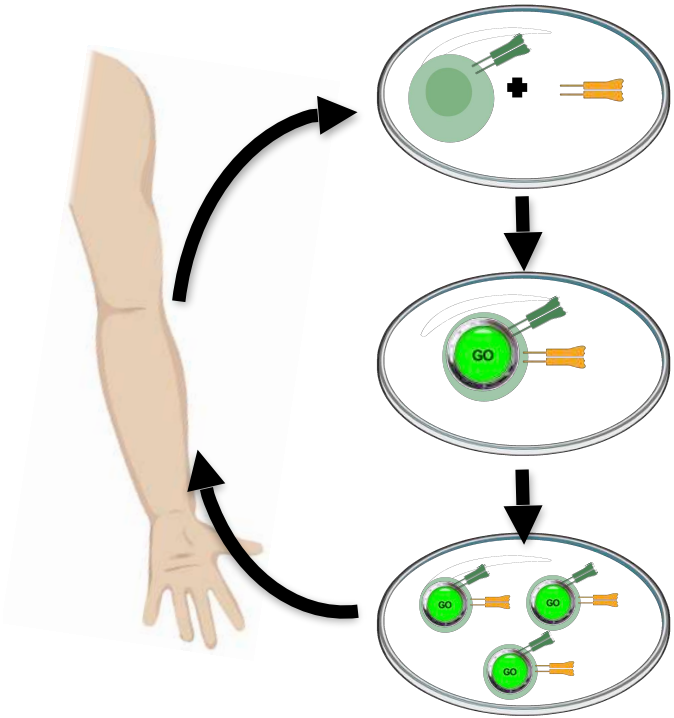
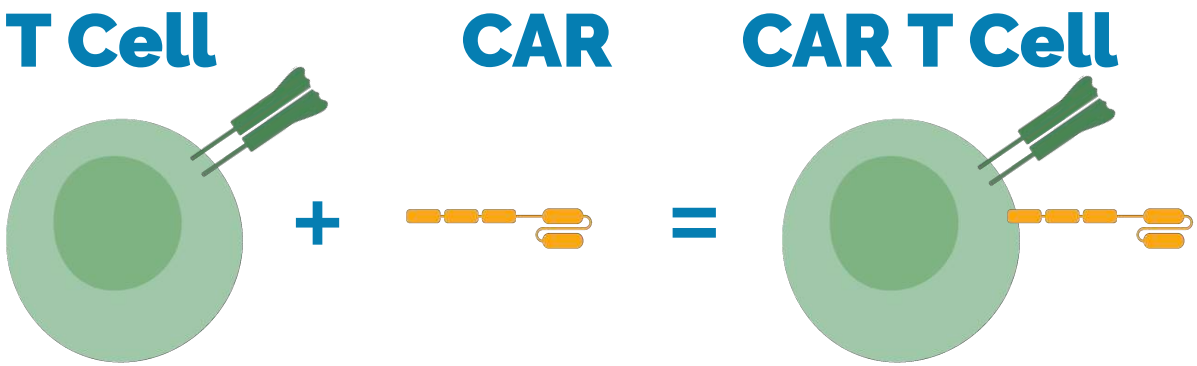
T Cell Receptor Engineering

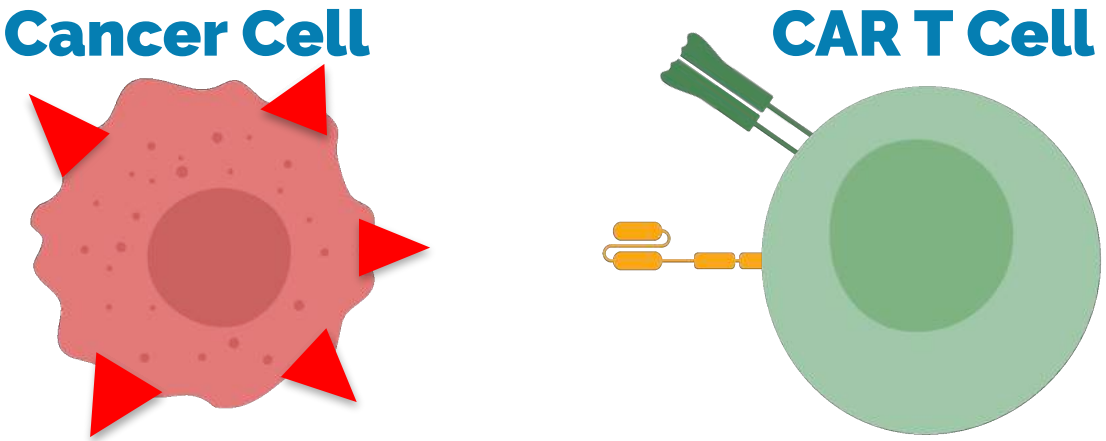


Equip T cells with new, cancer-targeting TCR

CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

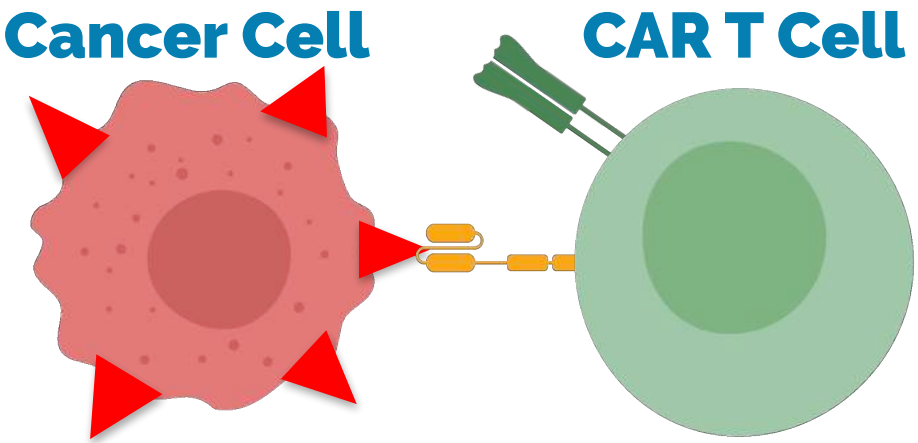


CAR T Cell Immunotherapy (Chimeric Antigen Receptor)



CARs enable MHC-independent targeting & killing!

CAR T Cell Immunotherapy (Chimeric Antigen Receptor)



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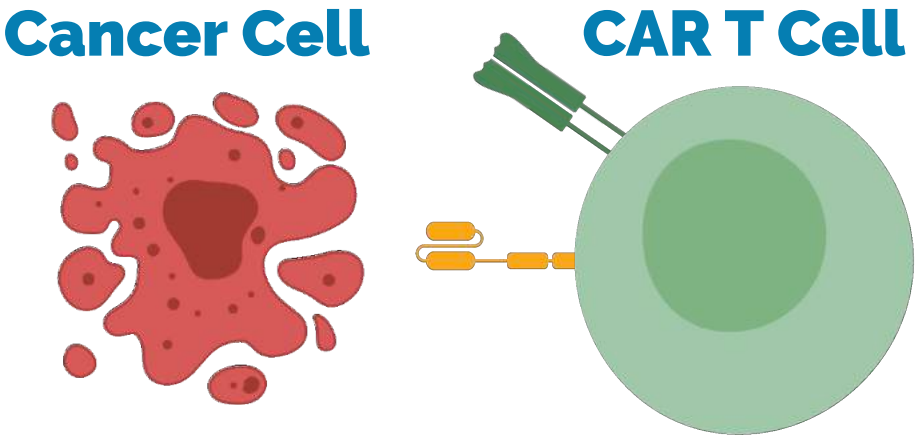
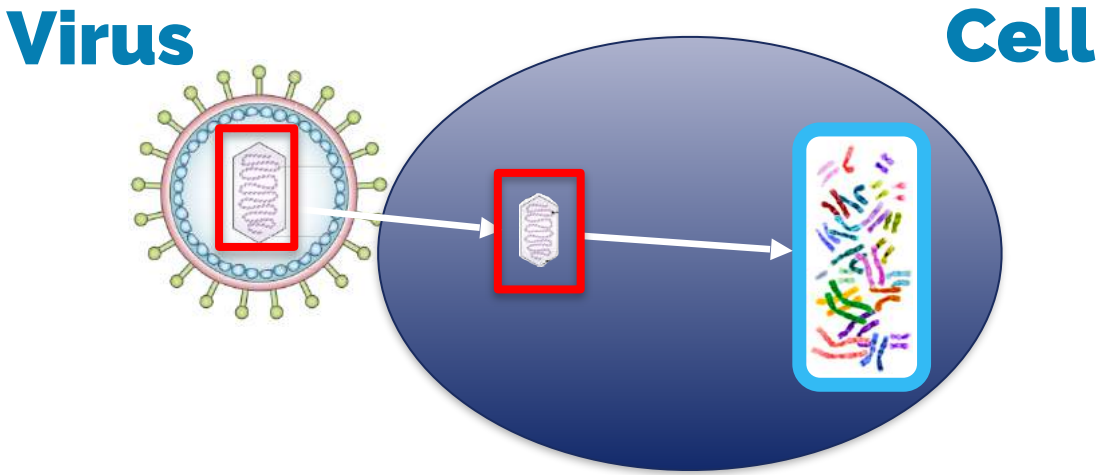
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)



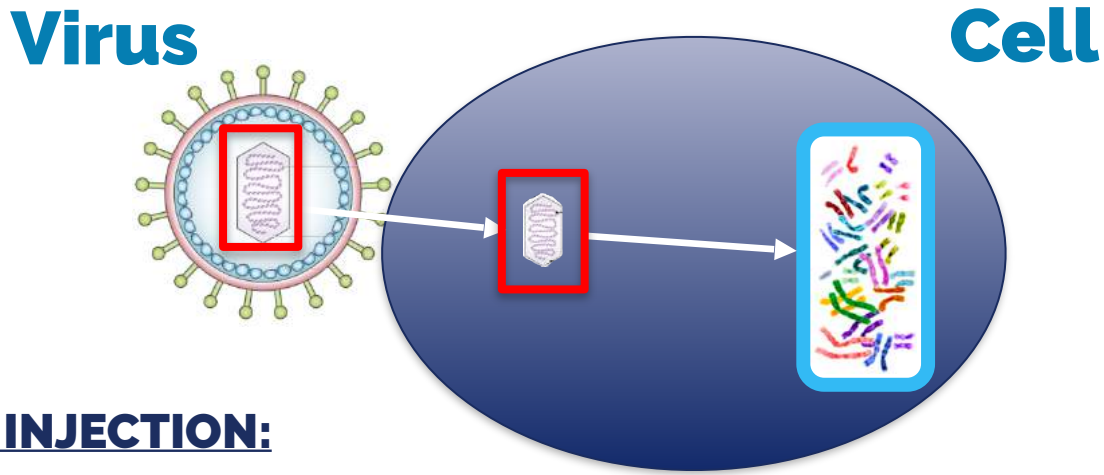
CARs enable MHC-independent targeting & killing!

Oncolytic Virus Immunotherapy



- **Viruses can alter our cells' DNA, by inserting their own genetic material**
- **Impaired defenses make tumor cells more susceptible to infection**

Oncolytic Virus Immunotherapy



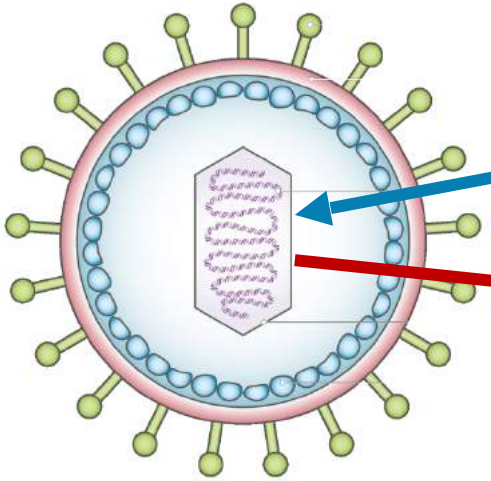
AFTER INJECTION:

1) Viruses cause tumor cells to “burst” & release antigens

2) Immune cells uptake & present tumor antigens

3) Stimulates adaptive, and potentially systemic, immune responses

Reprogramming Oncolytic Viruses To Enhance Anti-Tumor Activity



(+) INSERT
Immune-stimulating genes

(—) REMOVE
Disease-causing genes (selective targeting of tumors)

Cancer Vaccines

Tumor Antigens
(provided by vaccine)

Cancer Vaccines

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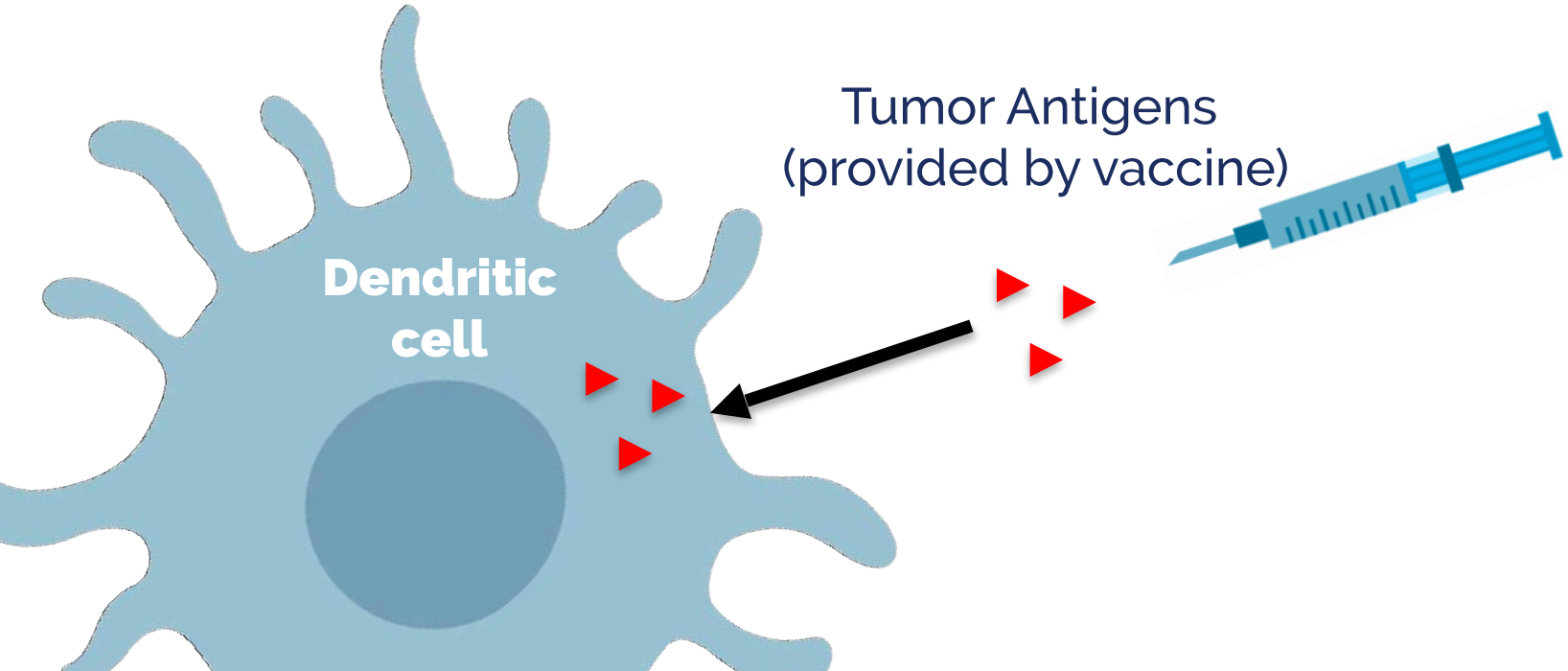

Cancer Vaccines

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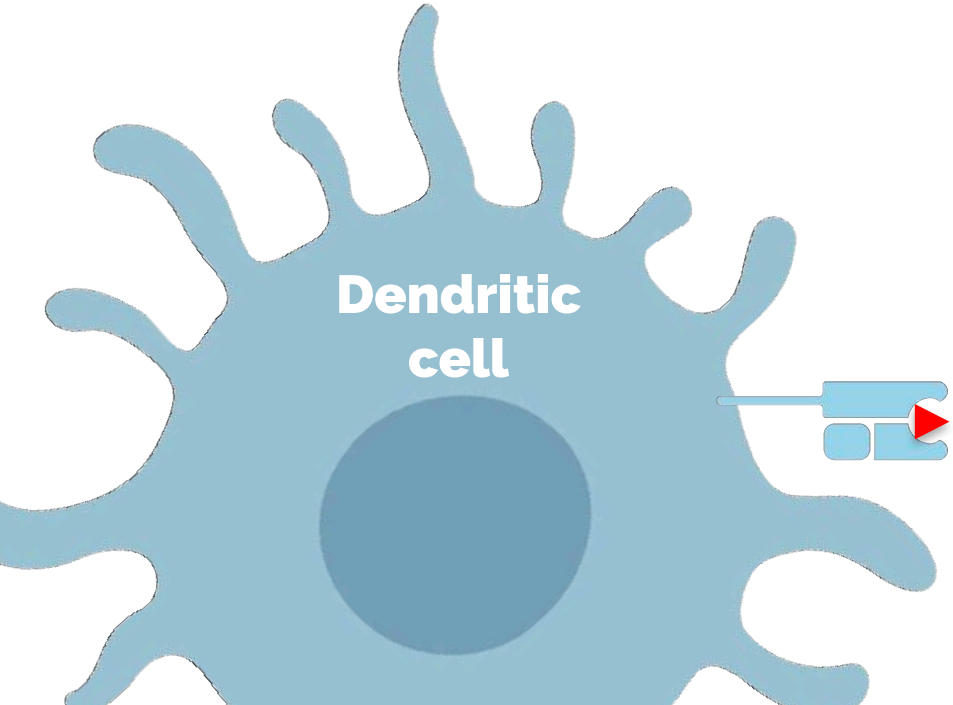

Cancer Vaccines

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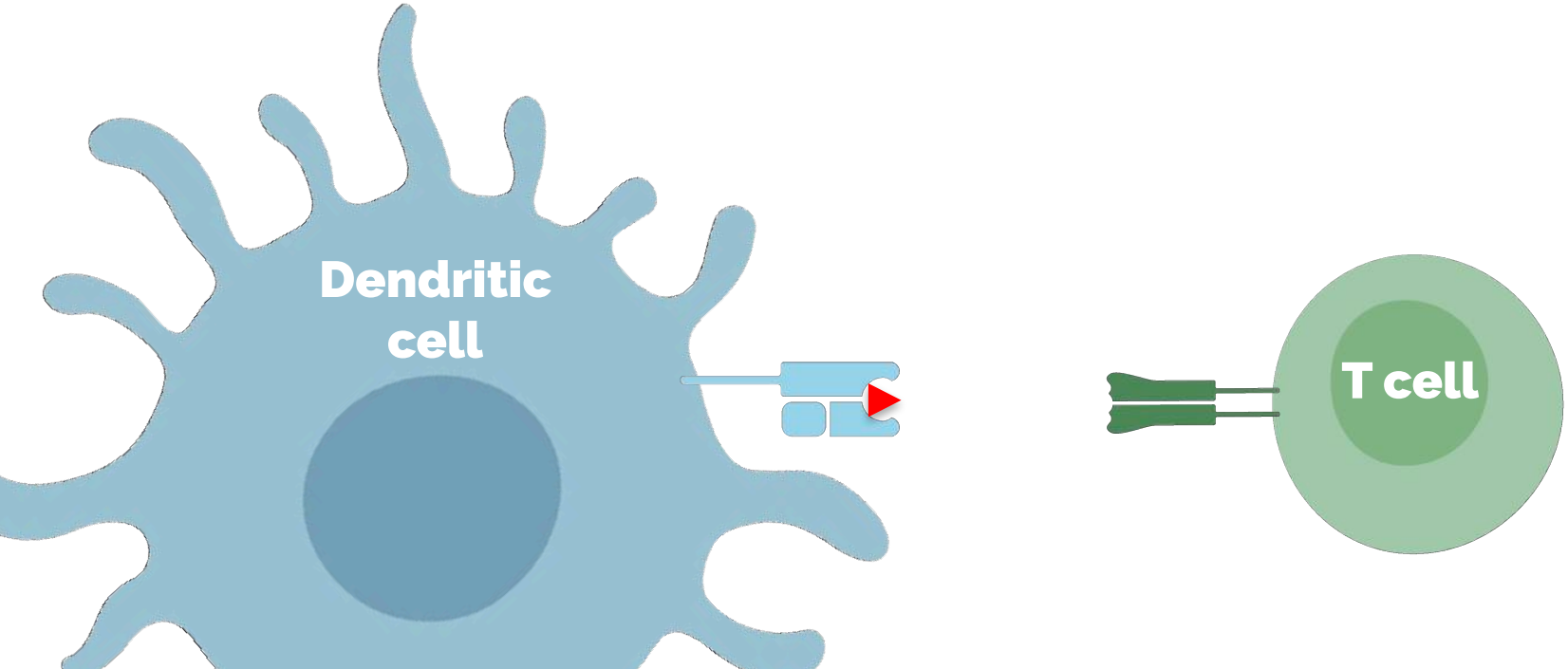

Cancer Vaccines

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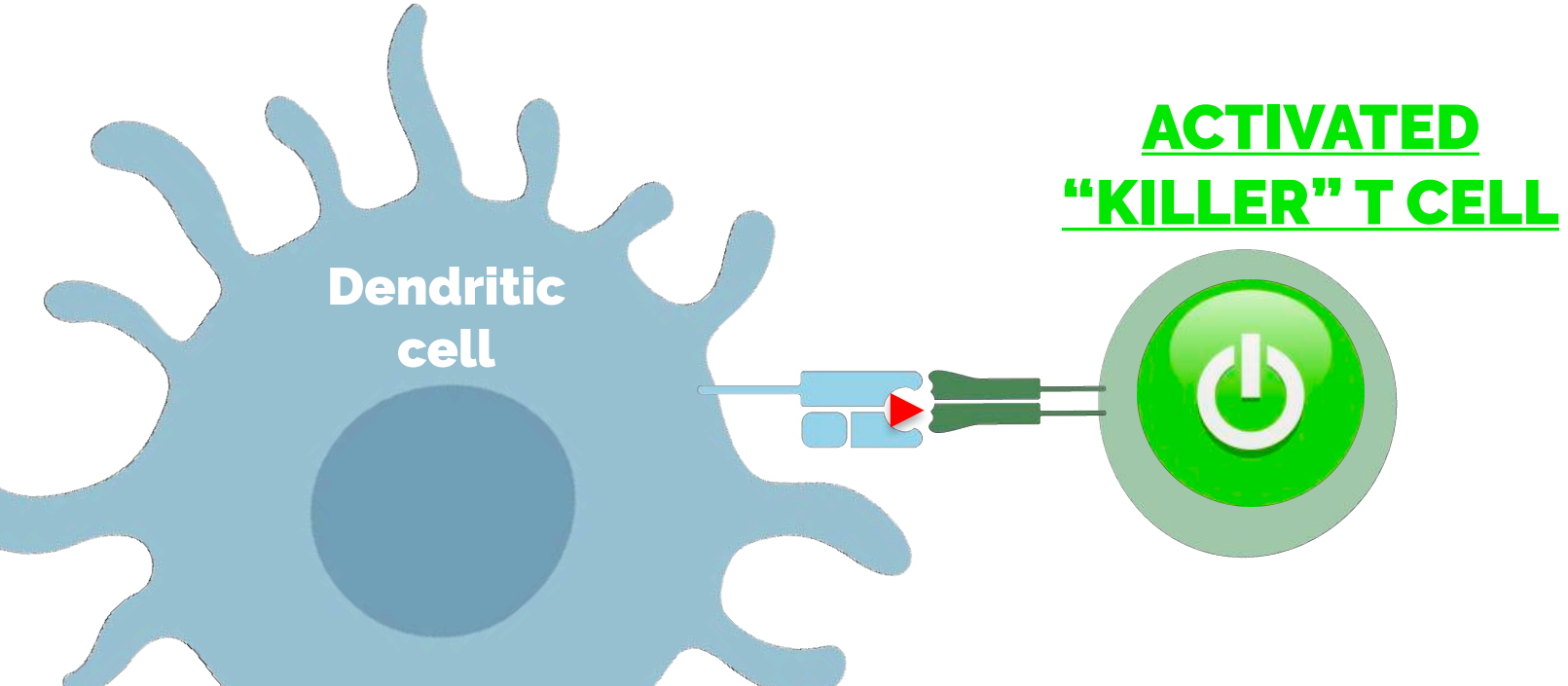

Vaccine-Induced Elimination of Cancer Cells

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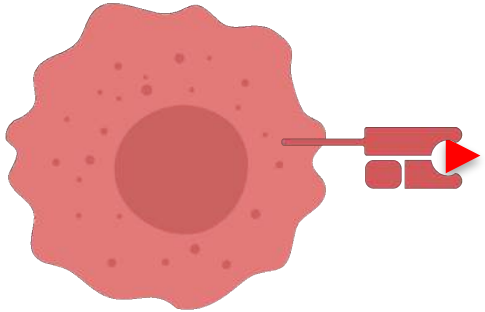
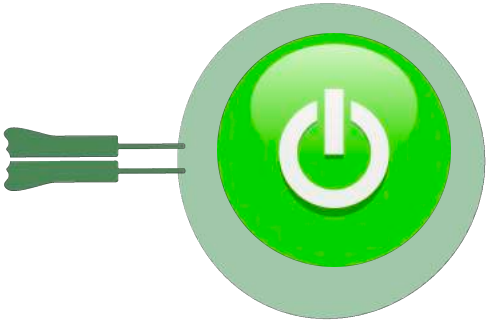
Cancer Cell



Activated “killer” T Cell



Vaccine-Induced Elimination of Cancer Cells

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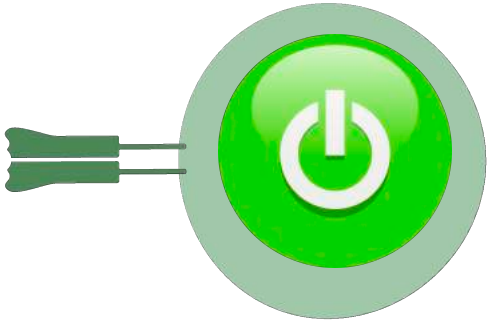
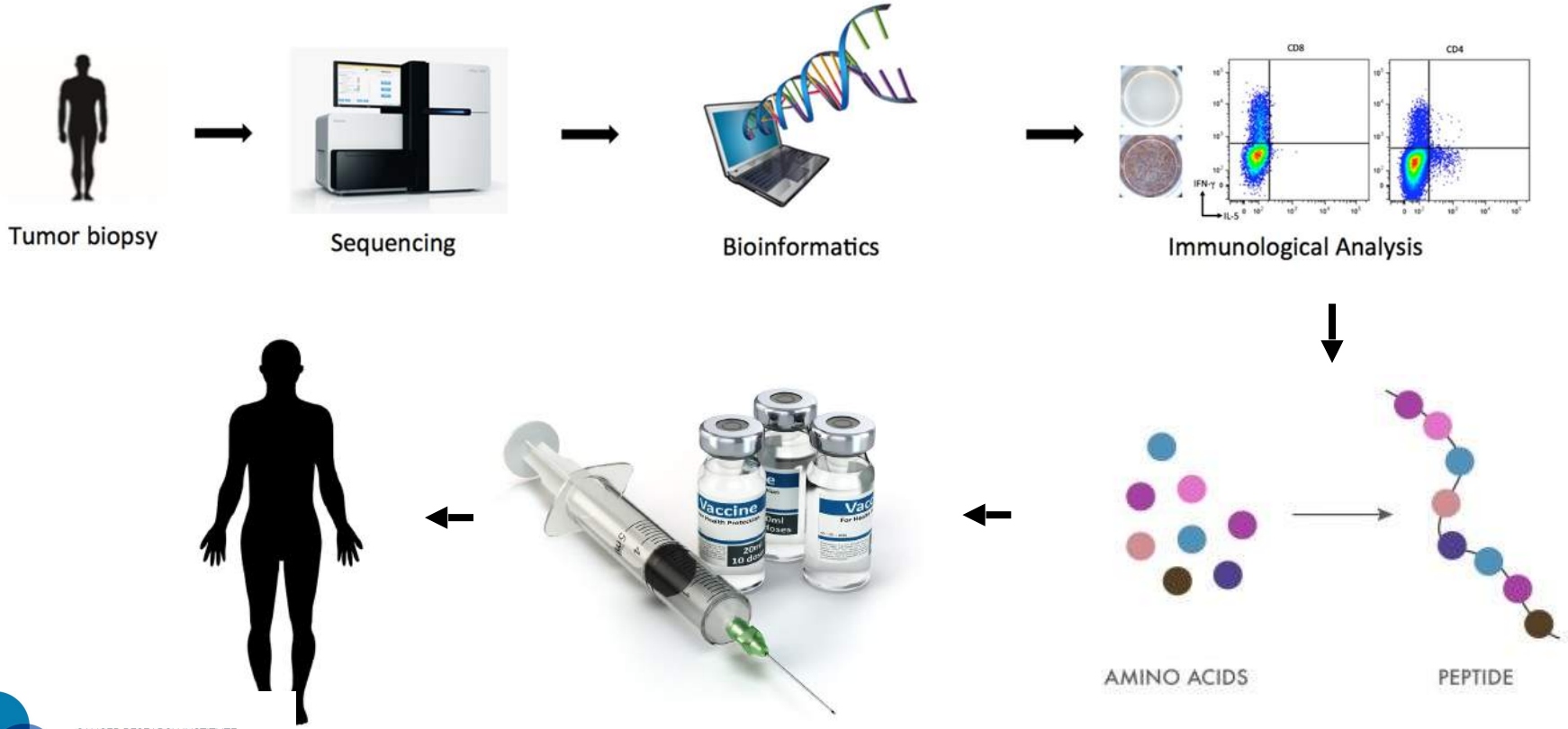
Cancer Cell

Activated "killer" T Cell



Personalized Neoantigen Vaccine Trial



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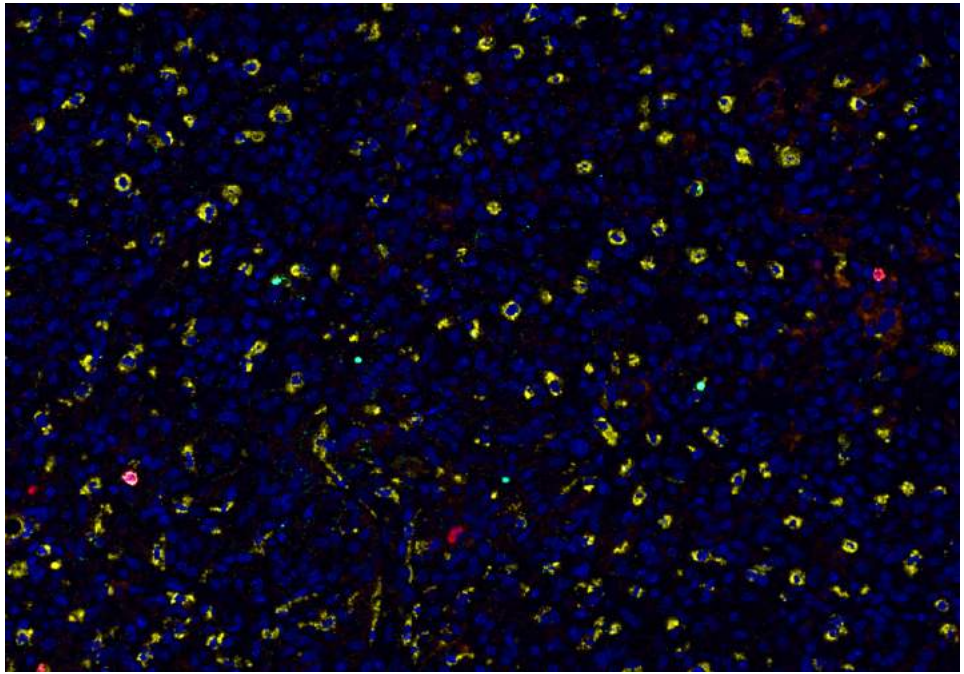
Why have most responses been modest and why are some cancers refractory to immunotherapy?

1. Cancers upregulate molecules to turn off immune cells
2. Cancers secrete chemicals to turn off the immune system
3. Cancers recruit suppressive cells to inactivate/block the immune response



DAPI (nuclear)
CD68 (macrophage/ microglia)
CD8 (cytotoxic T cell)
CD3 (T cell)

•**Panel Discussion**

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LATEST RESEARCH UPDATES

Moderator
Vamsidhar Velcheti, M.D.
NYU Langone's Perlmutter Cancer Center

Panelist
Silvia Adams, M.D.
Breast cancer

Panelist
Claire Friedman, M.D.
Gynecologic cancer

Panelist
Gulam A. Manji, M.D., Ph.D.
Gastrointestinal cancer

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Immunotherapy Patient Perspective

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Mary Elizabeth Williams

Journalist and Melanoma Veteran

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#CRIsummit

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Lunch and Networking

Alumni Hall B Breezeway, MSB Large Conference Room, and Smilow Cafe

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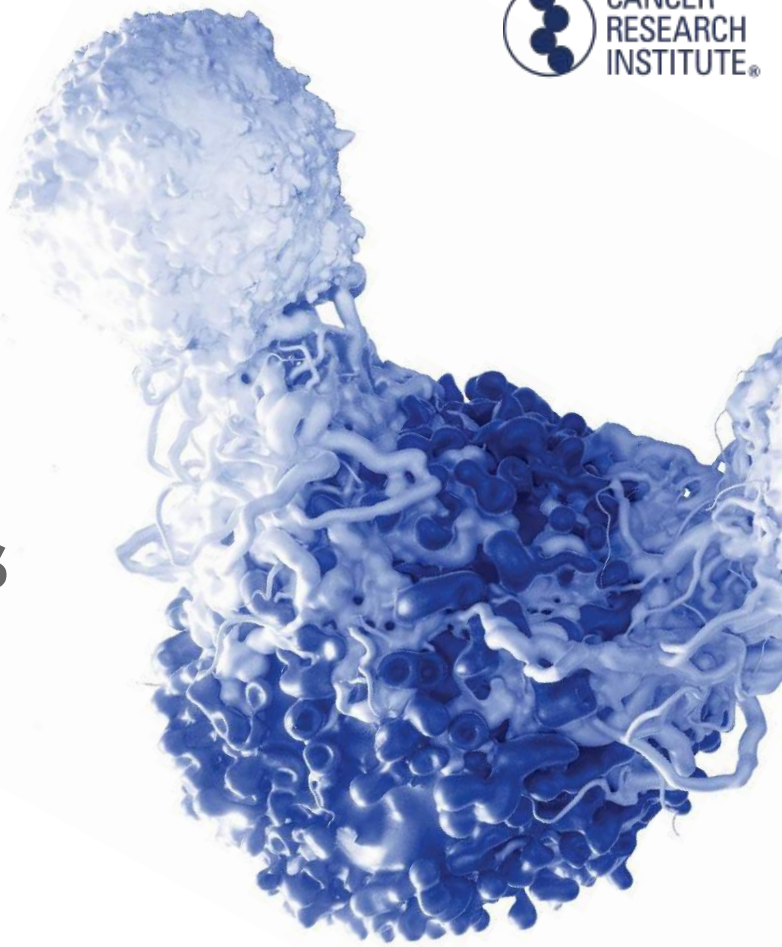

Brian Brewer

Cancer Research Institute

LEARN ABOUT CLINICAL TRIALS

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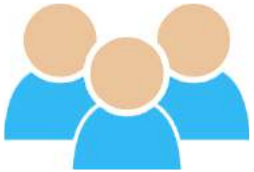
What Are Clinical Trials?



- Research studies that involve people
- Designed to answer specific questions about new and existing treatments
- Aim to improve treatments and the quality of life for people with disease

Getting from Discovery to Approval

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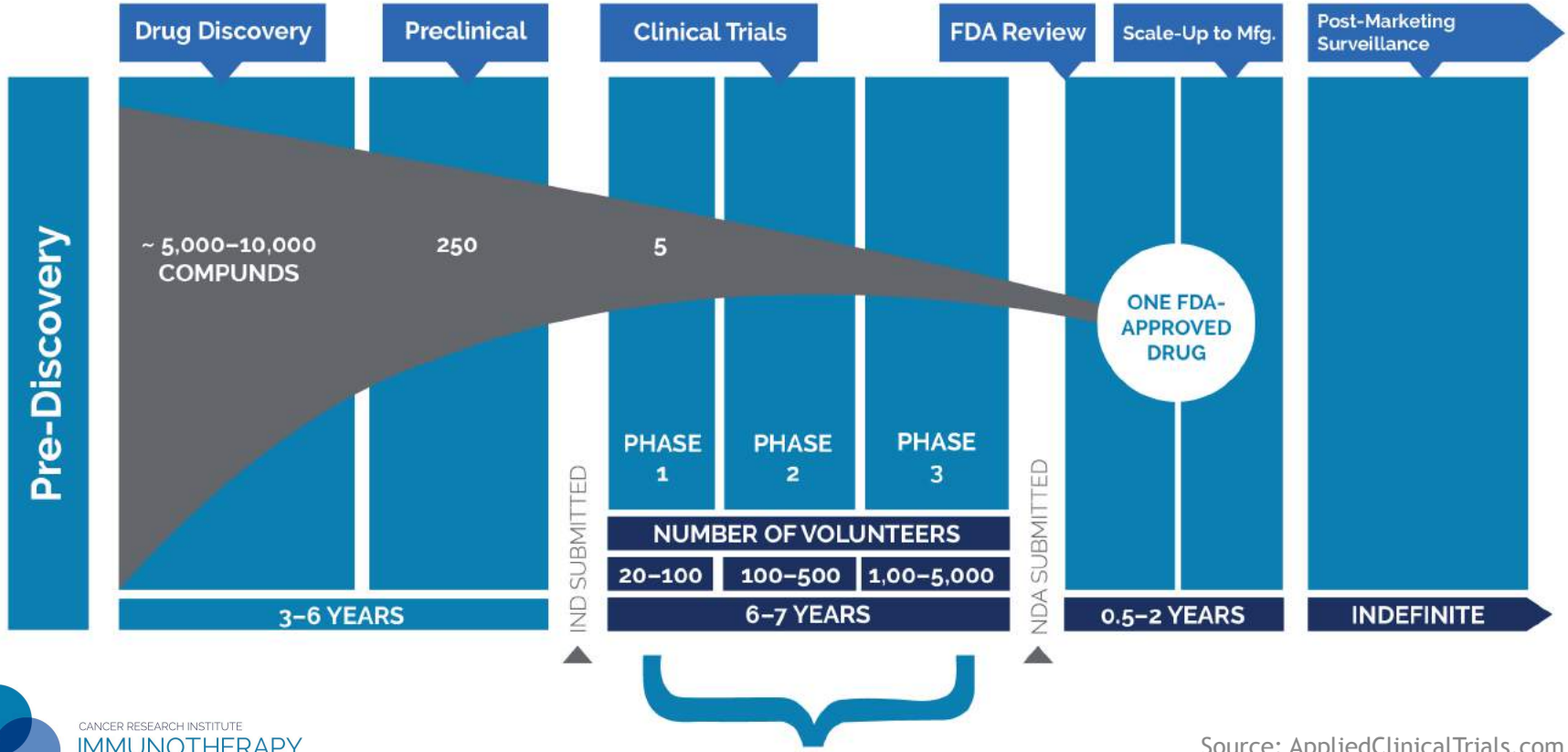

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Source: AppliedClinicalTrials.com

What Are Clinical Trial Phases?

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Phase 1

Is the treatment safe?

Purpose:

- First study in humans
- Find best dose, delivery method, and schedule
- Monitor for side effects
- Determine safety

Number of people: 20-100

Phase 2

Does it work?

Purpose:

- Look for effect on specific type(s) of cancer
- Continue monitoring for side effects and safety

Number of people: 100-500

Phase 3

Does it work better?

Purpose:

- Compare new treatment (or new use of a treatment) with current standard treatment
- Determine risk vs. benefit

Number of people: 1,000-5k+

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Pros and Cons of Clinical Trials

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Potential Advantages	Potential Disadvantages
Access to best possible care	Unknown side effects or risks
Receiving new drugs before they're widely available	Unknown benefits—drugs may not work as intended
Close monitoring by medical team	Not all patients may benefit
Chance to play active role in healthcare and research	Frequent tests and clinic visits
Help future generations	Possible need to travel to trial sites

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Questions to Ask Before Volunteering

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- Why is this trial being done?
- Why is it believed that the treatment being studied may be better than the standard treatment?
- What are my other options (standard treatments, other trials)?
- How did patients do in any previous studies of this treatment?
- How will the doctor know if treatment is working?
- How long will the trial last?

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Questions to Ask Before Volunteering

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- Can I continue to receive this treatment after the trial ends?
- What kinds of procedures or tests are involved?
- What impact with the trial have on my daily life?
- Will I have to travel for treatment? Will I be compensated?
- How often will I need to travel to receive treatment?
- Will I be hospitalized as part of the trial?
- What costs (if any) will be my responsibility to pay?

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Getting into a Clinical Trial Isn't Always a Given

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Trials are designed to ask specific questions, and must adhere strictly to entry criteria to ensure data is accurate and meaningful.

This also helps ensure patients who could be made worse by treatment are not exposed to the risk.

Common criteria include:

- **cancer type or stage**
- **treatment history**
- **genetic factors**
- **age**
- **medical history**
- **current health status**

Clinical Trials: Myth versus Fact

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I might only get placebo
("sugar pill") instead of treatment.

Placebos are rarely used and never given in the absence of some form of treatment.

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Clinical Trials: Myth versus Fact

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Trials are only for people who have run out of treatment options (a “last resort”).

Clinical trials are designed for people with cancer of all types and stages.

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Patient Resource, “Understanding Clinical Trials: A Guide for Patients and Their Families”

Clinical Trials: Myth versus Fact

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I need to travel to a large hospital or cancer center to participate in a clinical trial.

Trials take place at local hospitals, cancer centers, and doctors' offices in all parts of the country, in both urban and rural areas.

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Clinical Trials: Myth versus Fact

My health insurance doesn't cover the cost of care in a clinical trial.

Doctor visits, hospital stays, and certain testing procedures may be covered by insurance. Research costs are typically covered by the trial sponsor.

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Clinical Trials: Myth versus Fact

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Signing a consent form “locks” me into staying in a trial.

Fact: You are free to change your mind for any reason about participating in a trial anytime before or during a trial.

Patient Resource, “Understanding Clinical Trials: A Guide for Patients and Their Families”

Clinical Trials: Myth versus Fact

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I will be made to feel like a "guinea pig" experiment.

Fact: The overwhelming majority of trial participants say they were treated with dignity and respect, and report having had a positive experience in a trial.

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Clinical Trials: Myth versus Fact

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Clinical trials aren't safe.

Fact: Safeguards including an Institutional Review Board, Data and Safety Monitoring Board, and an ongoing informed consent process ensure patients' rights and safety are protected.

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

A Word About Informed Consent

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Informed consent = having all the facts before and during a trial

- Study purpose
- Length of time of the study
- Predictable risks
- Possible benefits
- Expectations
- Patient's rights

- Treatment alternatives
- Patient health monitoring
- Safeguards in place
- How to withdraw from study

Be bold in asking for details.
It's YOUR treatment plan.

How Can I Find a Clinical Trial?

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- Ask your doctor
- Ask another doctor if necessary…
- Contact a patient advocacy organization
  - Seek assistance from a clinical trial navigator, if offered
  - CRI Clinical Trial Finder: 1 (855) 216-0127
- Search online
  - https://www.cancerresearch.org/patients/clinical-trials
  - https://clinicaltrials.gov/

Immunotherapy Patient Panel

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Moderator	Panel
Brian Brewer	**Dorothy Fabian** Esophageal Cancer
	Oswald Peterson Lung Cancer
	Tara Ryan Melanoma

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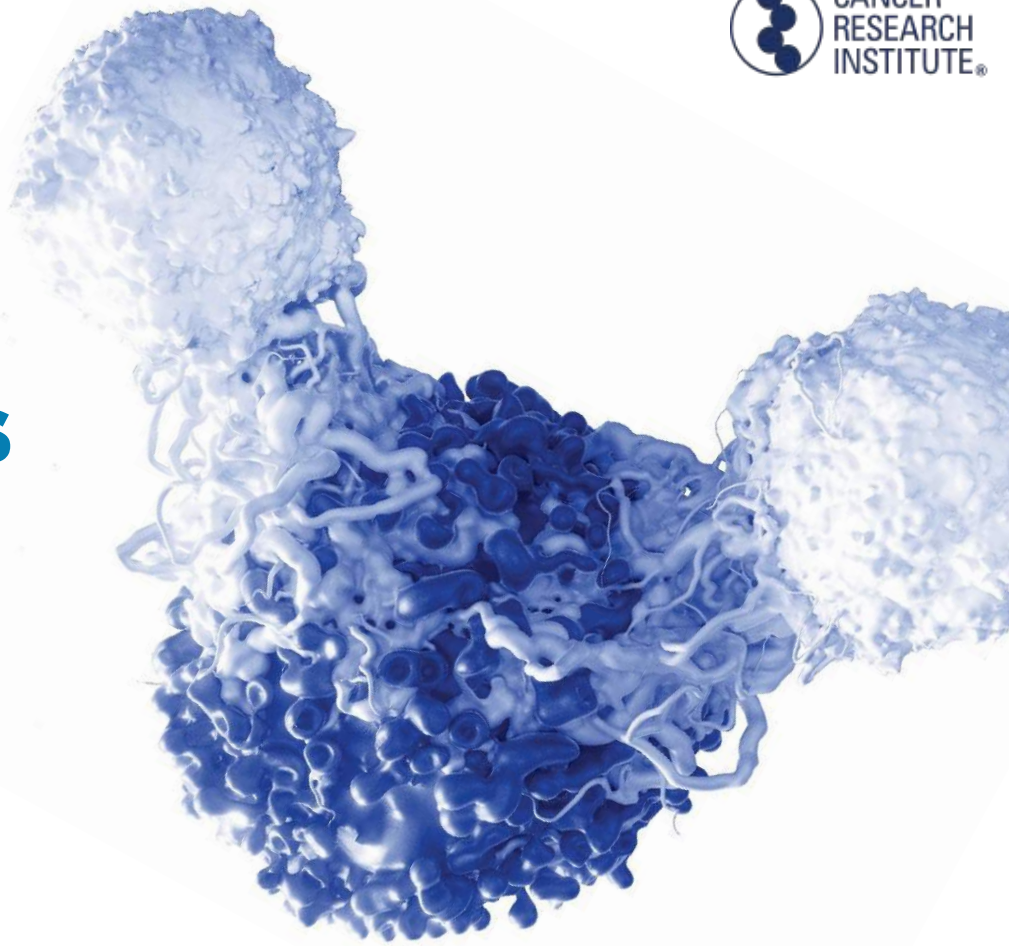
BREAKOUT SESSIONS



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Breakout Session Rooms

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General Immunotherapy **Vamsidhar Velcheti, M.D.**	**Farkas**
Breast Cancer **Sylvia Adams, M.D.**	**Alumni Hall B**
Gastrointestinal Cancer **Gulam A. Manji, M.D., Ph.D.**	**Murphy**
Gynecologic Cancer **Claire Friedman, M.D.**	**MSB 193**

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Thank you to those who helped promote the summit

- American Cancer Society
- Beauty Through the Beast
- Colorectal Cancer Alliance
- Columbia University Irving Medical Center
- Crush It for Curtis Foundation
- Esophageal Cancer Awareness Association
- FORCE
- Gilda's Club NYC
- Go2Foundation for Lung Cancer
- ICLA da Silva Foundation
- Imerman Angels
- Leukemia & Lymphoma Society
- LUNGevity
- Memorial Sloan Kettering Cancer Center
- Pancreatic Cancer Action Network
- Patient Empowerment Network
- Perlmutter Cancer Center at NYU Langone Health
- Ronald McDonald House
- Us TOO
- Young Survival Coalition

After the Summit

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You will receive two emails after the summit:

1. **A survey** to share your feedback on the summit as well as insights into future programming.

2. **Information** from the summit day, including this presentation and instructions on how to use our Clinical Trial Finder service.

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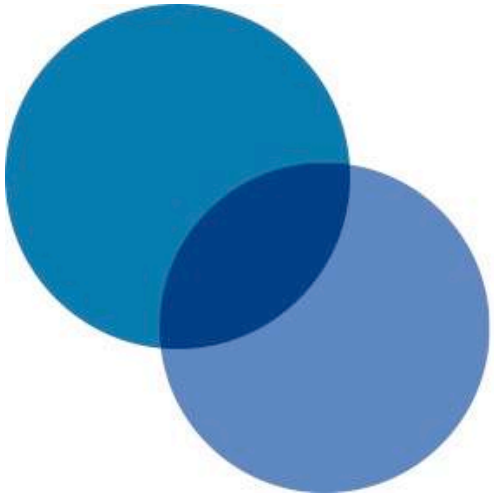

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New York City September 7, 2019