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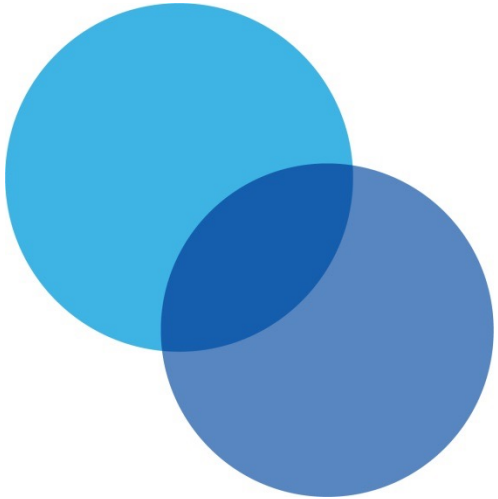

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IMMUNOTHERAPY PATIENT SUMMIT

Boston July 29, 2019

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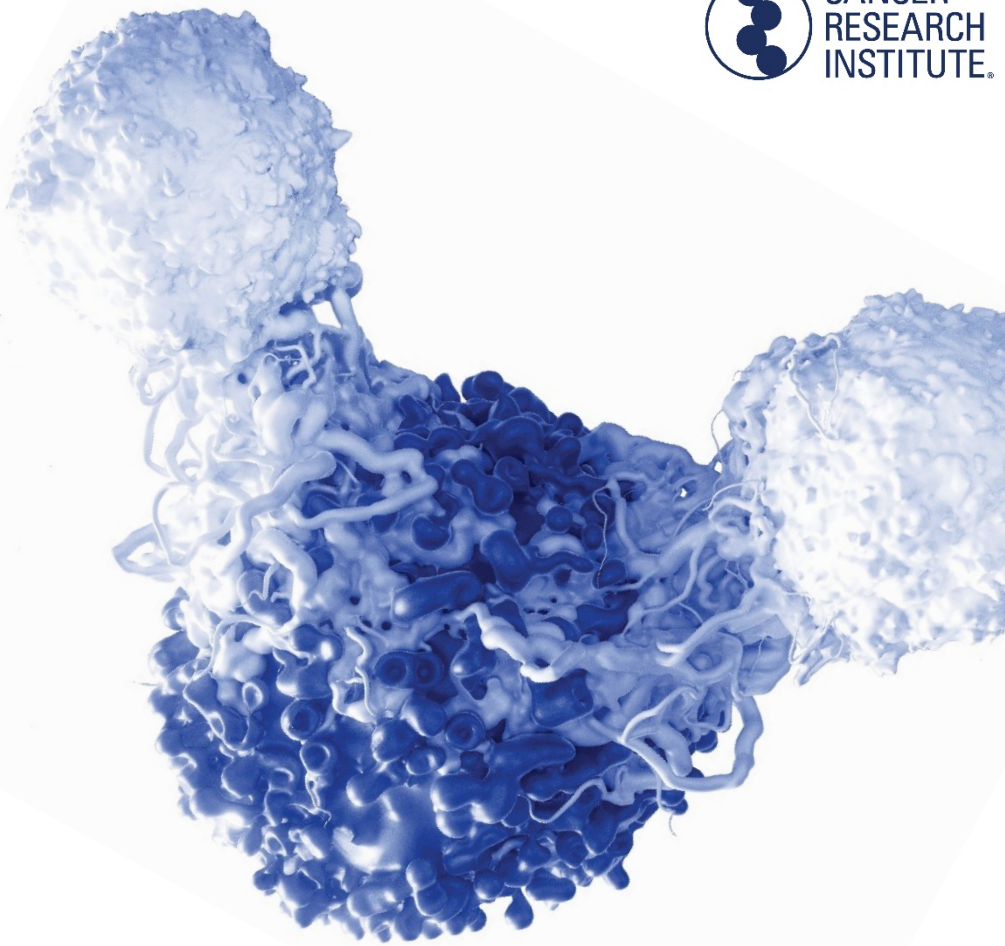

Brian Brewer

Cancer Research Institute

WELCOME

CANCER RESEARCH INSTITUTE
IMMUNOTHERAPY
PATIENT SUMMIT

Speakers

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Scientific Experts

David A. Reardon, M.D.
Dana-Farber Cancer Institute

Susanne Baumeister, M.D.
Boston Children's Hospital

Justin F. Gainor, M.D.
Massachusetts General Hospital

Kimmie Ng, M.D.
Dana-Farber Cancer Institute

Patient Experts

Ernestina Dos Reis
Glioblastoma

Ariella Chivil
Hodgkin Lymphoma

Cole Malone
Acute Lymphoblastic Leukemia

Denise Malone
Cole's mother and caregiver

John White
Prostate Cancer

Our Sponsors

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Thank you to those who helped promote the summit

- American Cancer Society
- Blum Resource Center
- Colorectal Cancer Alliance
- Crush It for Curtis Foundation
- Dana-Farber Cancer Institute
- Esophageal Cancer Awareness Association
- FORCE
- Go2Foundation
- Healing Garden Cancer Support
- Imerman Angels
- Leukemia & Lymphoma Society
- LUNGevity
- Pancreatic Cancer Action Network
- Patient Empowerment Network
- The Jimmy Fund
- Us TOO
- Wellness Warriors Boston
- Young Survival Coalition

SCHEDULE OF EVENTS

9:00 am	Registration and networking
10:00 am	Program commences
	WELCOME Brian Brewer
10:15 am	**HEAR FROM THE EXPERTS** Immunotherapy Basics David A. Reardon, M.D.
	PANEL: RESEARCH UPDATES Moderator David A. Reardon, M.D. Panelists Susanne Baumeister, M.D. Justin F. Gainor, M.D. Kimmie Ng, M.D., M.P.H
11:30 am	**PATIENT PERSPECTIVE** A message from Ariella Chivil, Hodgkin lymphoma survivor
12:00 pm	Lunch and networking
1:00 pm	**LEARN ABOUT CLINICAL TRIALS** Brian Brewer
1:15 pm	**IMMUNOTHERAPY PATIENT PANEL** Moderator Brian Brewer Panelists Ernestina Dos Reis Cole Malone Denise Malone John White
2:00 pm	Transitional Break
2:15 pm	**BREAKOUT SESSIONS** Your choice of moderated, deeper-dive Q&A with our experts **General Immunotherapy** David A. Reardon, M.D. **Childhood Cancer** Susanne Baumeister, M.D. **Gastrointestinal Cancer** Kimmie Ng, M.D., M.P.H. **Lung and Esophageal Cancers** Justin F. Gainor, M.D.
3:15 pm	Program closes
9:00 am – 4:00 pm	**CLINICAL TRIAL NAVIGATOR APPOINTMENTS** Appointments are available all day. If you didn't pre-register, but you are interested in scheduling an appointment, please visit the Clinical Trial Navigator desk for more information.

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.

Welcome

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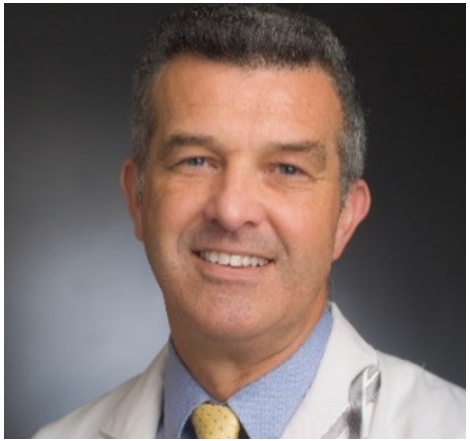
Laurie H. Glimcher, M.D.

President and CEO, Dana-Farber Cancer Institute
Richard and Susan Smith Professor of Medicine,
Harvard Medical School

DANA-FARBER CANCER INSTITUTE

Immunotherapy 101



David A. Reardon, M.D.
Professor of Medicine, Harvard Medical School
Clinical Director, Center for Neuro-Oncology
Dana-Farber Cancer Institute
david_reardon@dfci.harvard.edu

Immunotherapy 101

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Overview

A. Background

B. Basics: How our immune system works
- Immune checkpoint therapy
- Adoptive cellular therapies, CARS
- Oncolytic viruses
- Vaccines

C. Challenges

Origin & Revival of Immunotherapy

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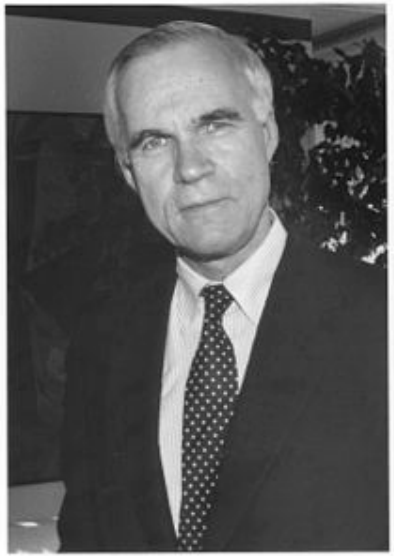
1890s:
William B. Coley

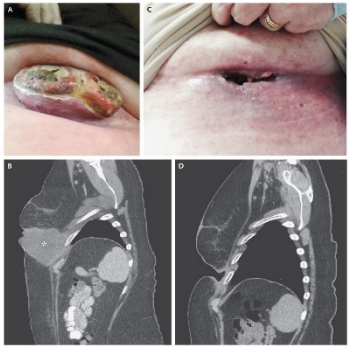
1900s:
Paul Ehrlich



1960s:
Lloyd J. Old

Attributes of our Immune System

1. Highly potent, coordinated attack



1 dose immunoRx
NEJM 2015

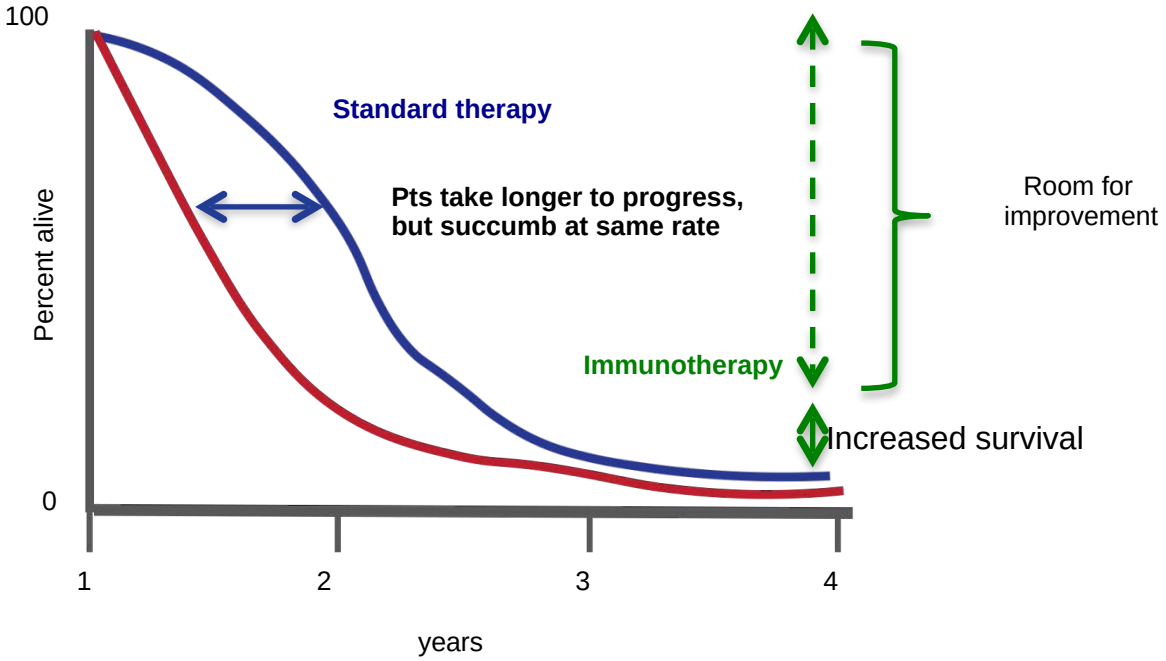
2. Exquisite specificity: designed to avoid cross-reactivity and damage to normal cells

3. Memory

Faroe Islands
- 1781: measles outbreak
- 1846: 2nd outbreak

No one infected in 1st outbreak got measles with 2nd outbreak

Immunotherapy: A Potential Cure?



The Immune System at a Glance: Our Natural Defense System

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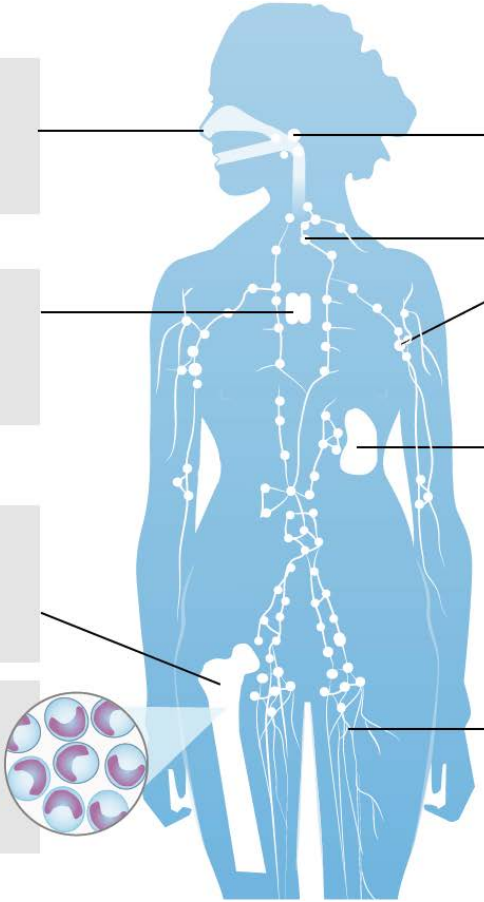
Nose
Hairs and mucus trap foreign particles and prevent them from entering the body

Thymus
Small organ located just behind the breastbone where T cells mature (the "T" is for thymus)

Bone marrow
Tissue in the center of bones that is responsible for making blood cells, including white blood cells

White blood cells
White blood cells—including macrophages, dendritic cells, and lymphocytes—are the cellular actors of immunity



Tonsils
Structures at the back of the throat that sample bacteria and viruses that enter the body through the mouth or nose

Lymph nodes
Small, bean-shaped structures located throughout the body that filter lymph fluid; where immune cells are alerted to the presence of pathogens or cancer

Spleen
Fist-sized organ located in the upper-left part of the abdomen, containing white blood cells that fight infection and cancer

Lymphatic vessels
Thin-walled tubes that collect and transport lymph fluid throughout body

The Cells of the Immune System: The “Soldiers” in our Army

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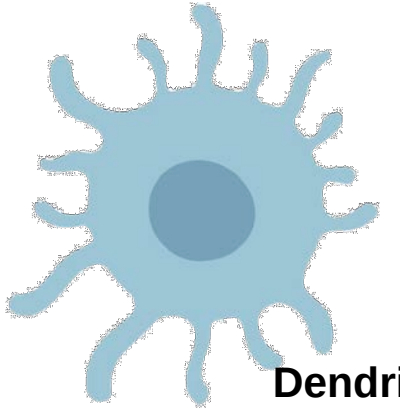
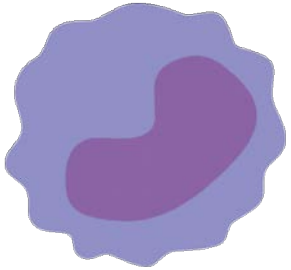
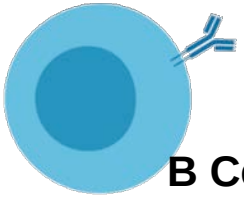


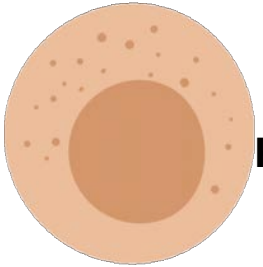
Dendritic Cell



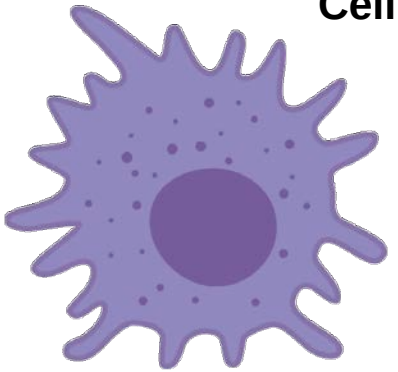
Monocyte



B Cell

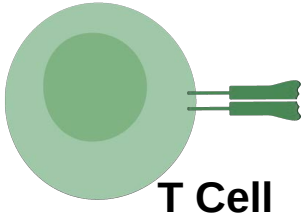


Natural Killer Cell



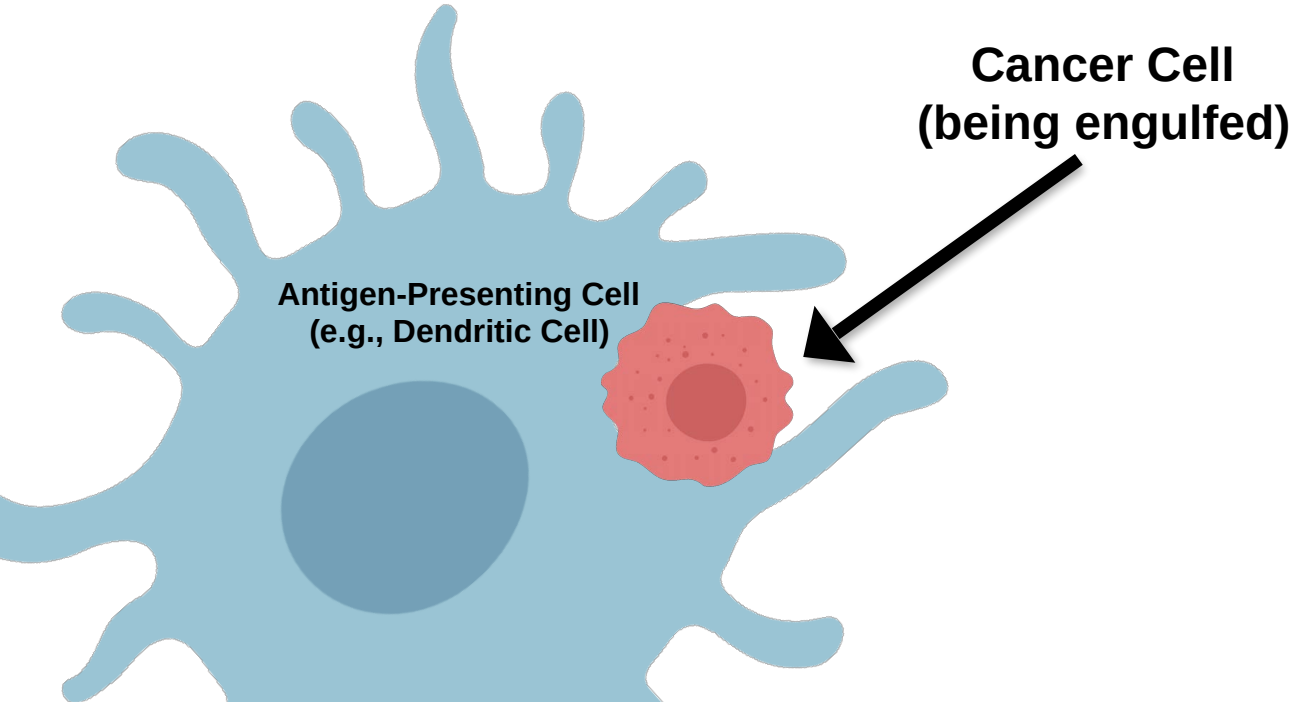
Macrophage

Neutrophil

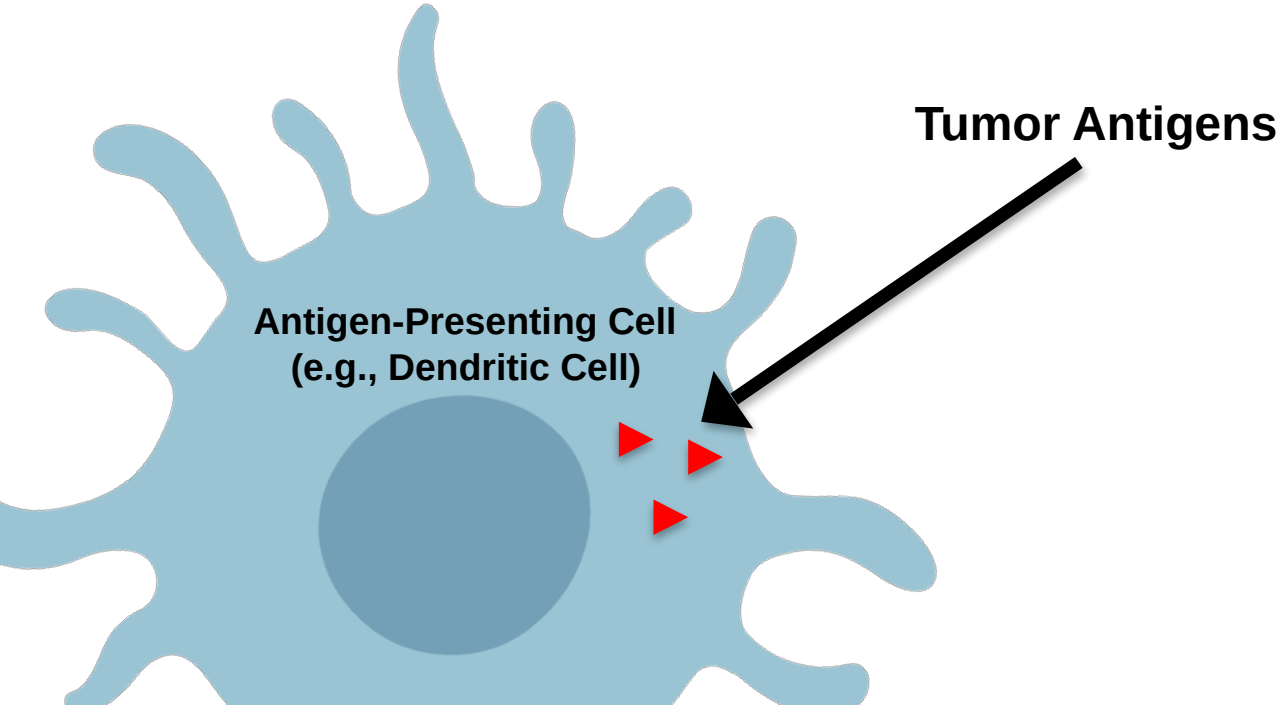


T Cell

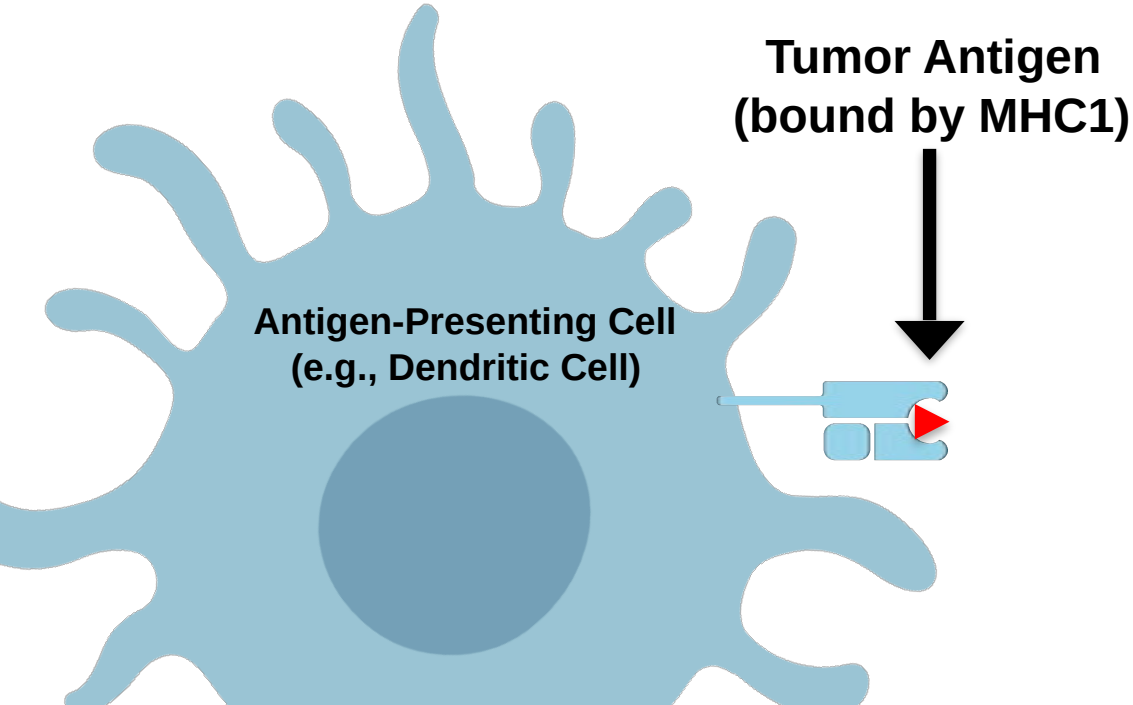
Adaptive Immune Responses Against Cancer



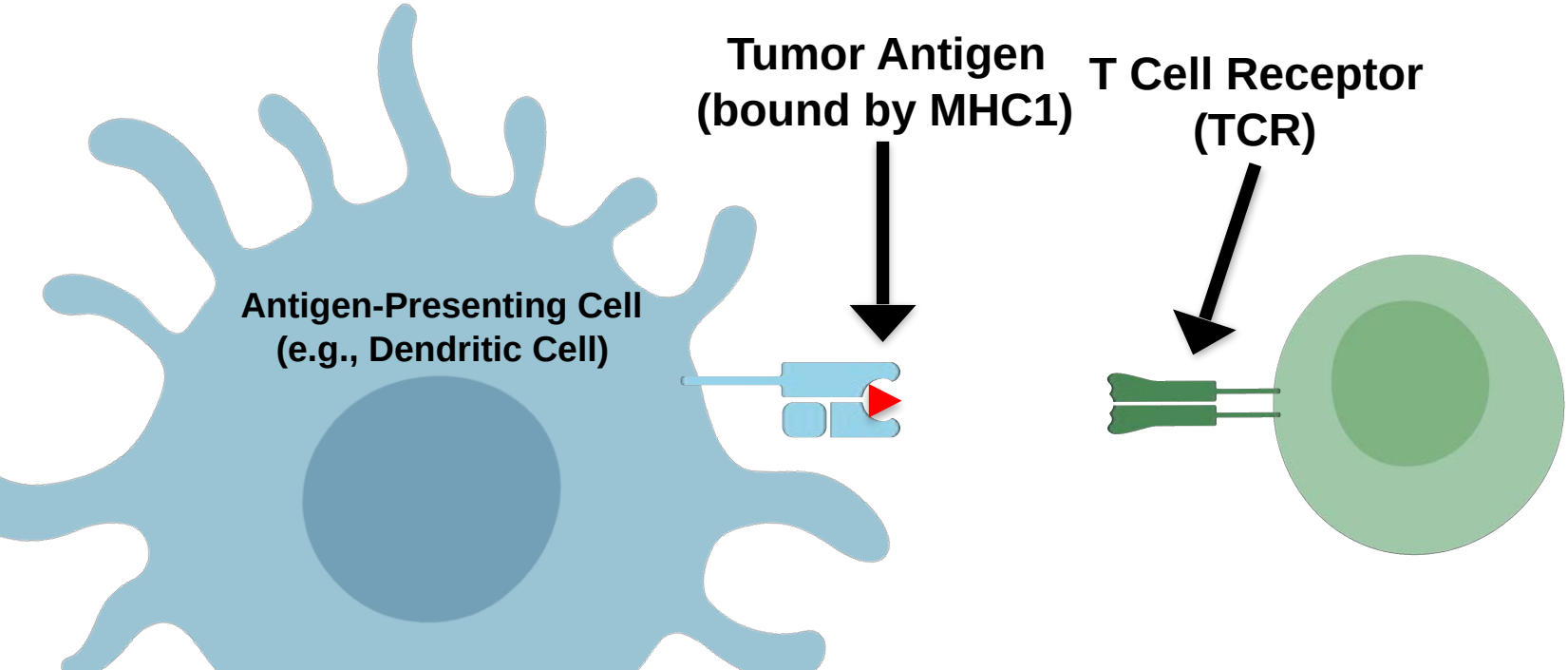
Adaptive Immune Responses Against Cancer



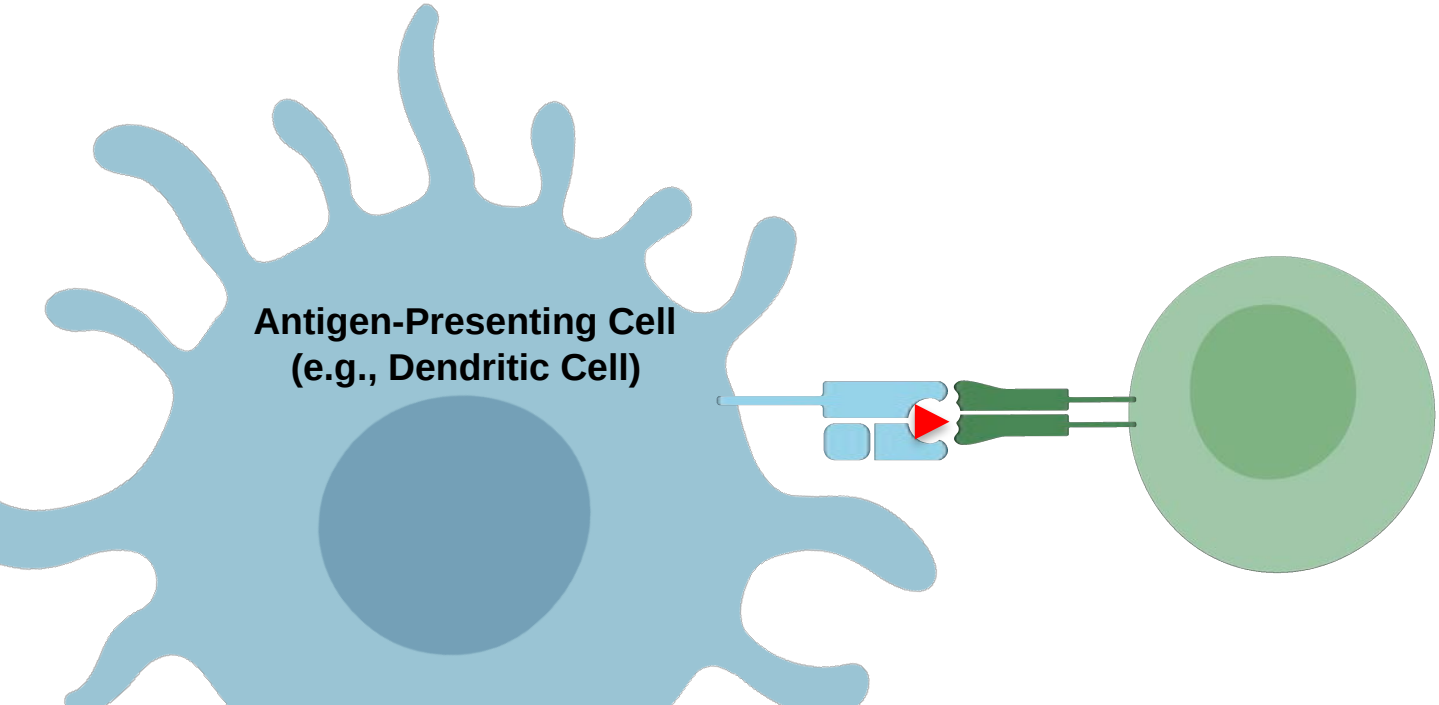
Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer

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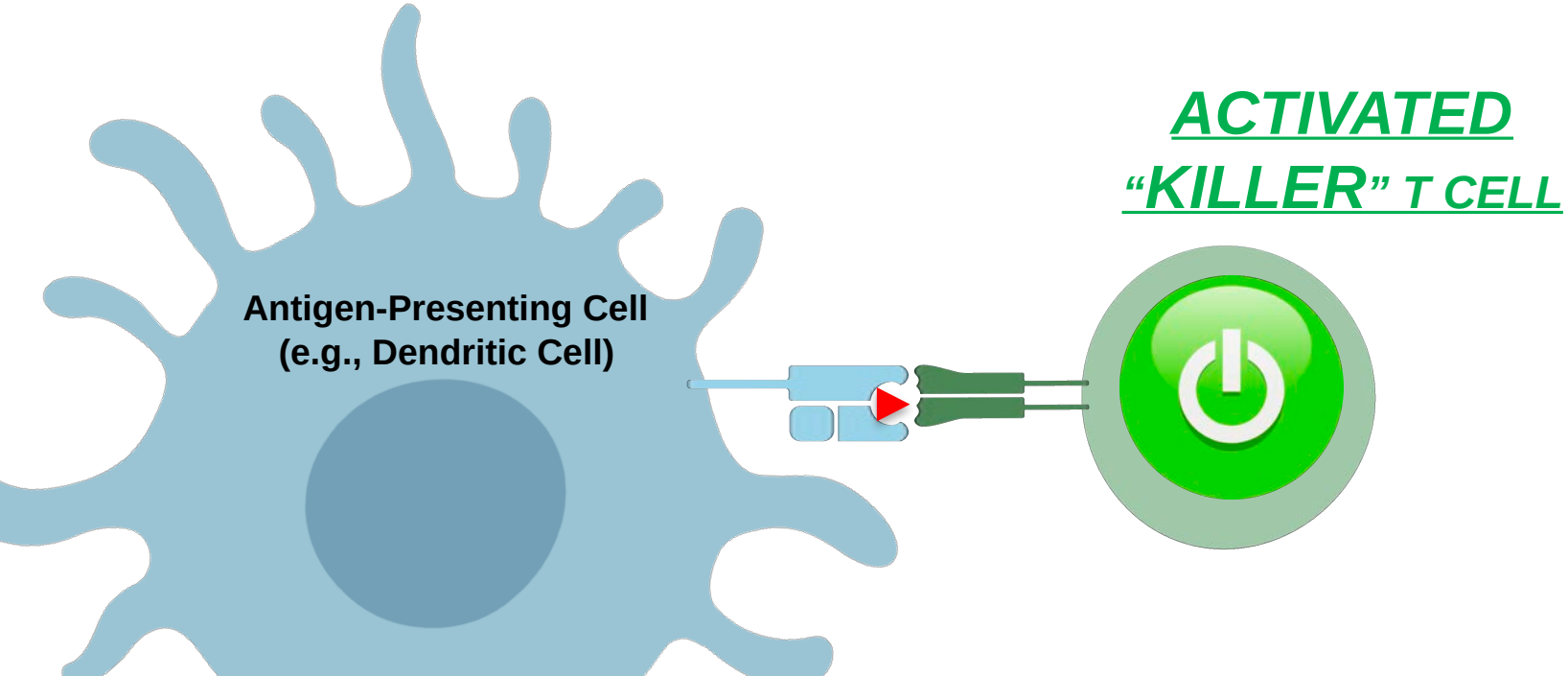

Adaptive Immune Responses Against Cancer

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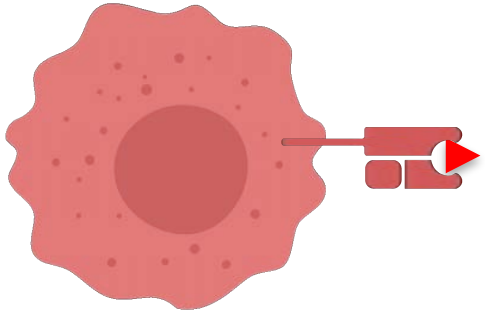
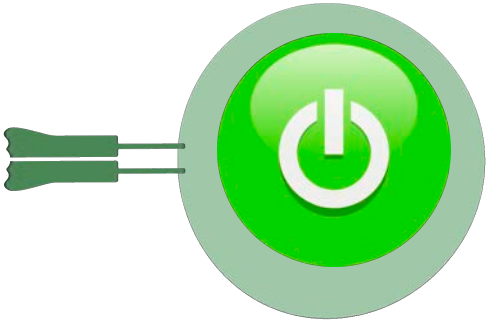
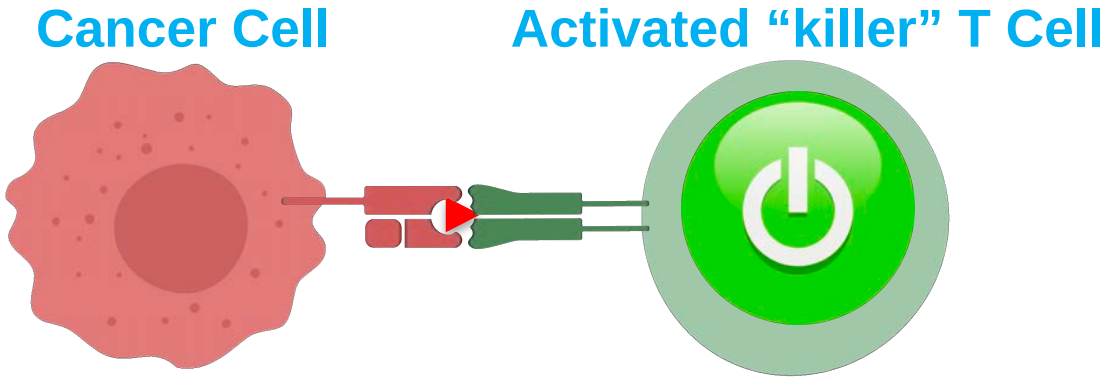
Cancer Cell



Activated “killer” T Cell



Adaptive Immune Responses Against Cancer



Adaptive Immune Responses Against Cancer

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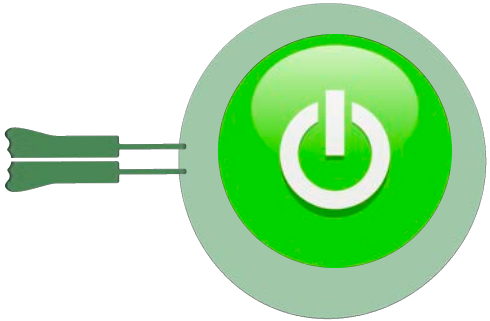
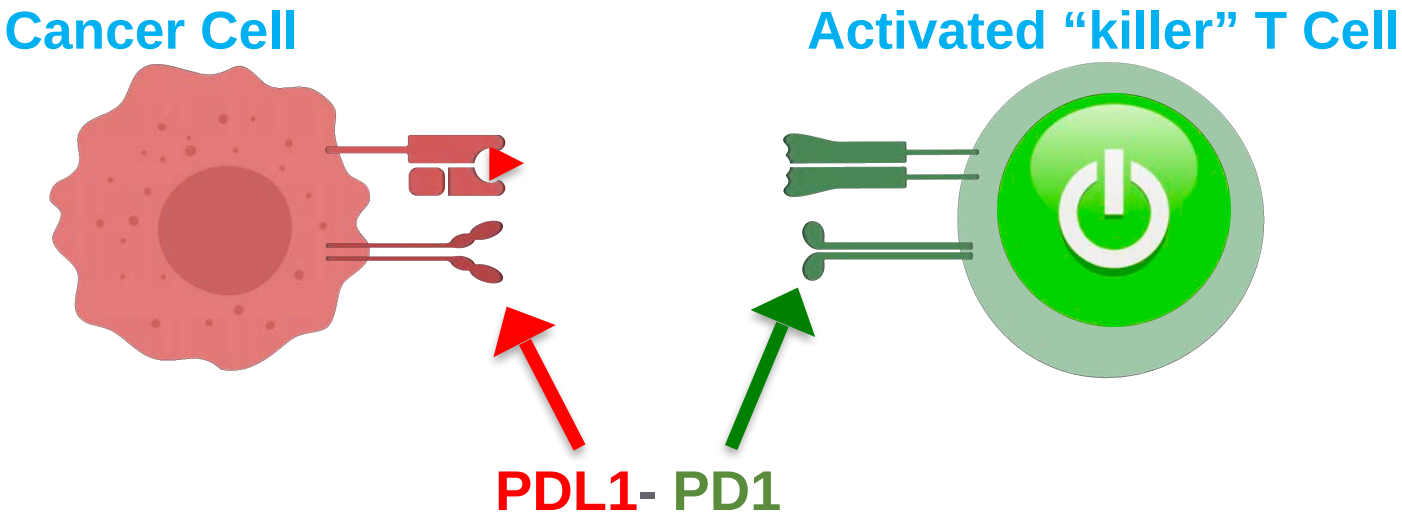
Cancer Cell

Activated “killer” T Cell

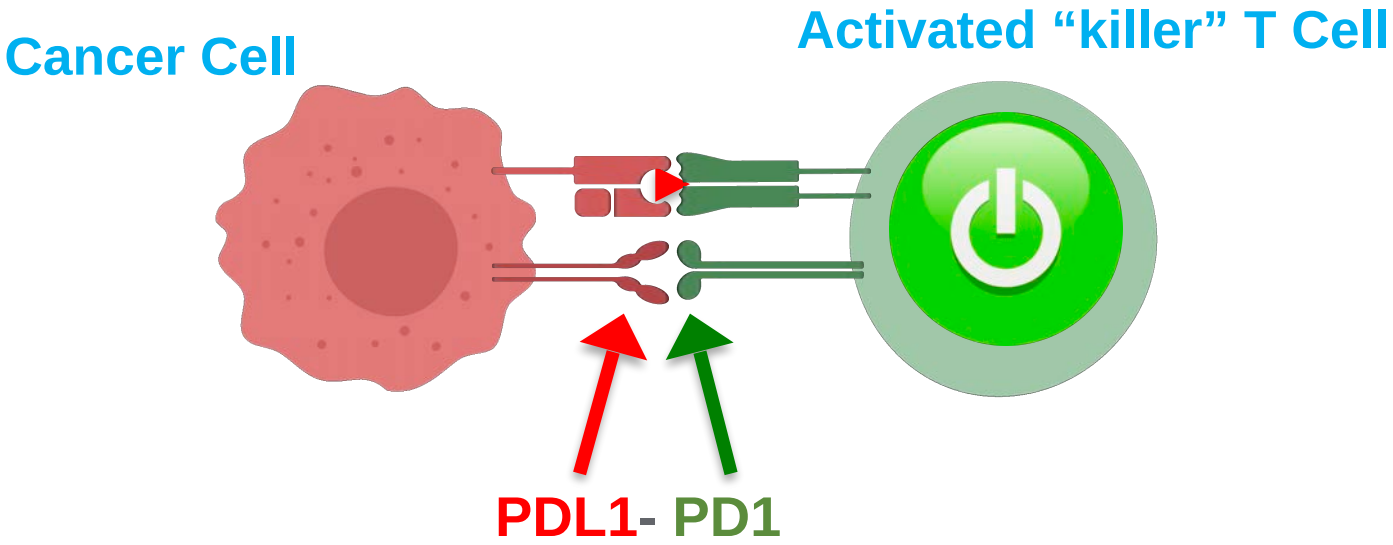


CANCER CELL ELIMINATED!

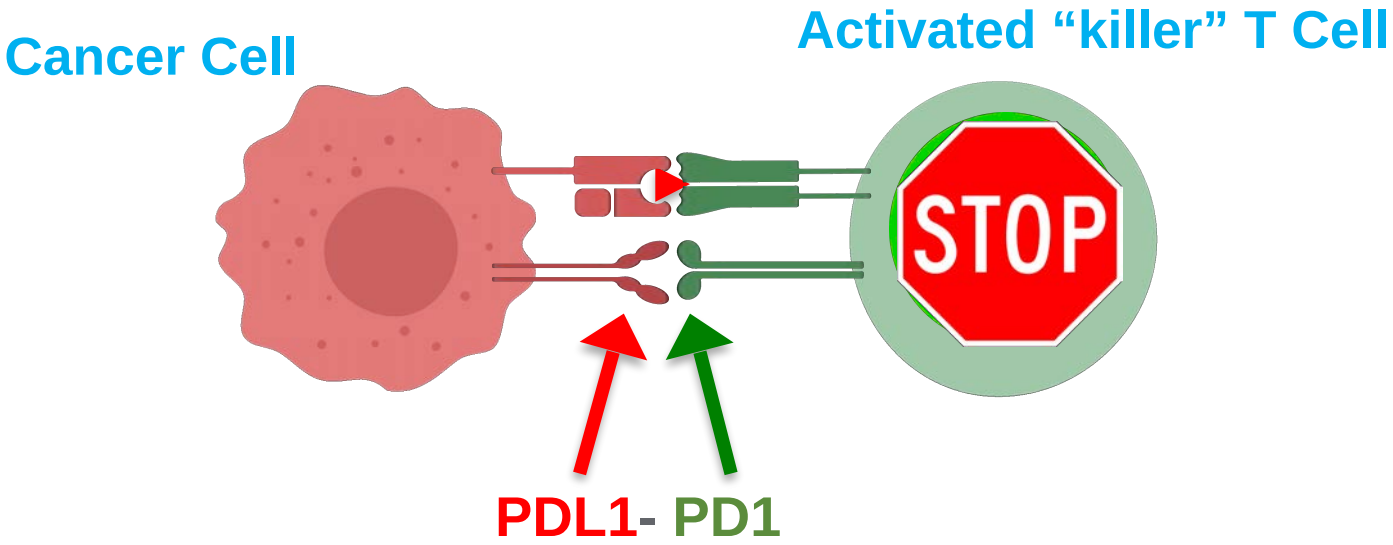
Immune Checkpoints Can Suppress Immune Responses



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

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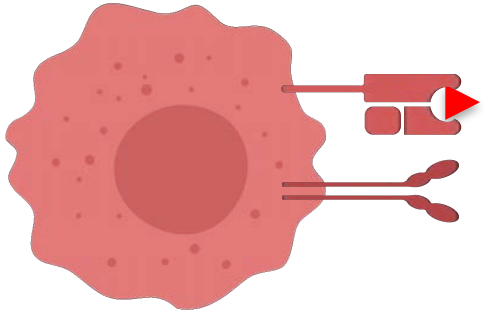
Cancer Cell



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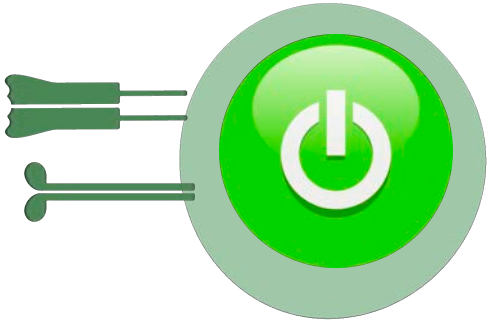
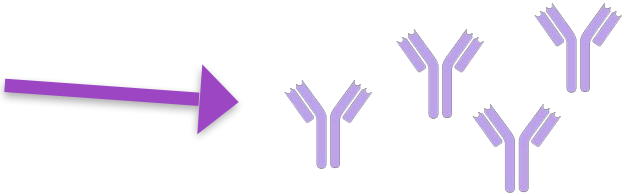


PD-1/PD-L1
Checkpoint Inhibitors



Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

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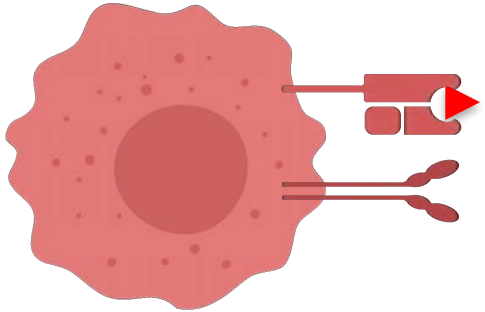
Cancer Cell



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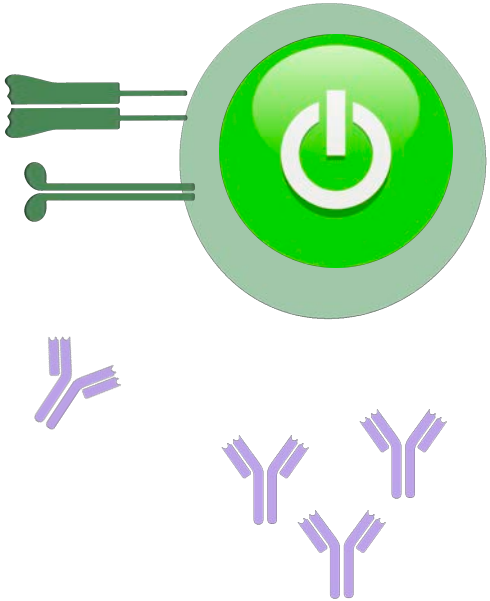

Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

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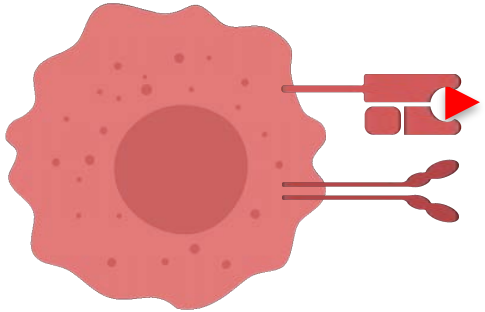
Cancer Cell



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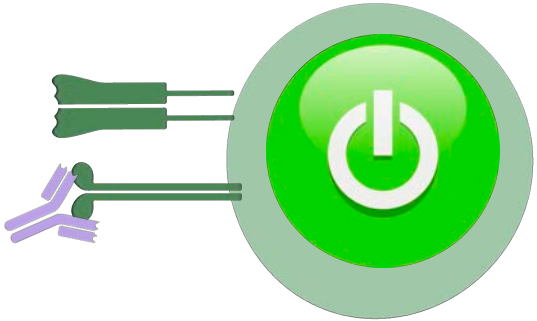

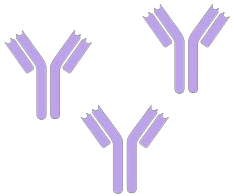

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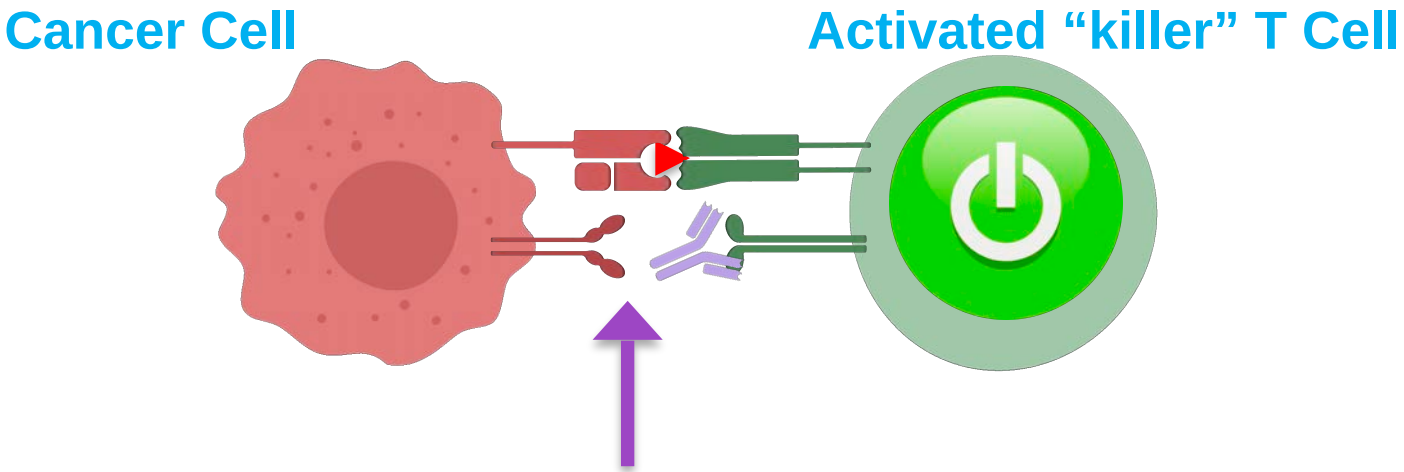

Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

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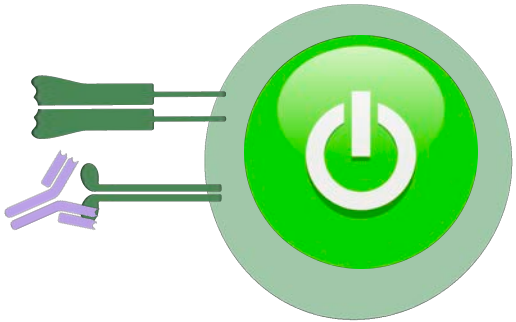
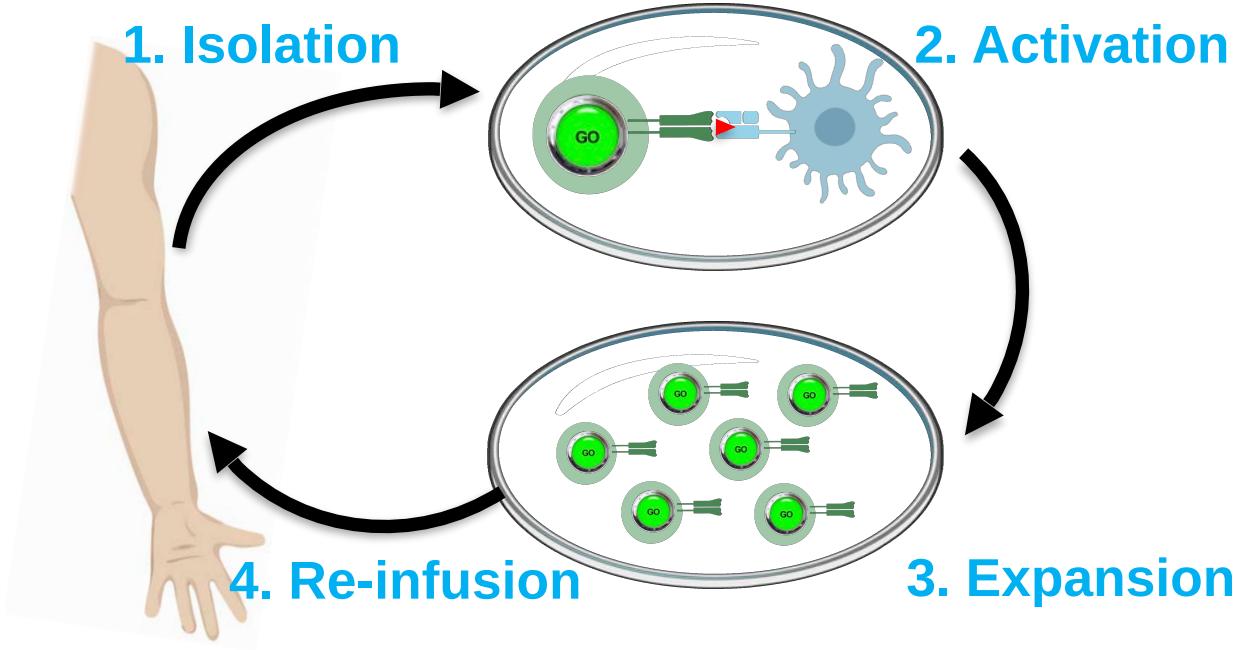
Cancer Cell

Activated “killer” T Cell

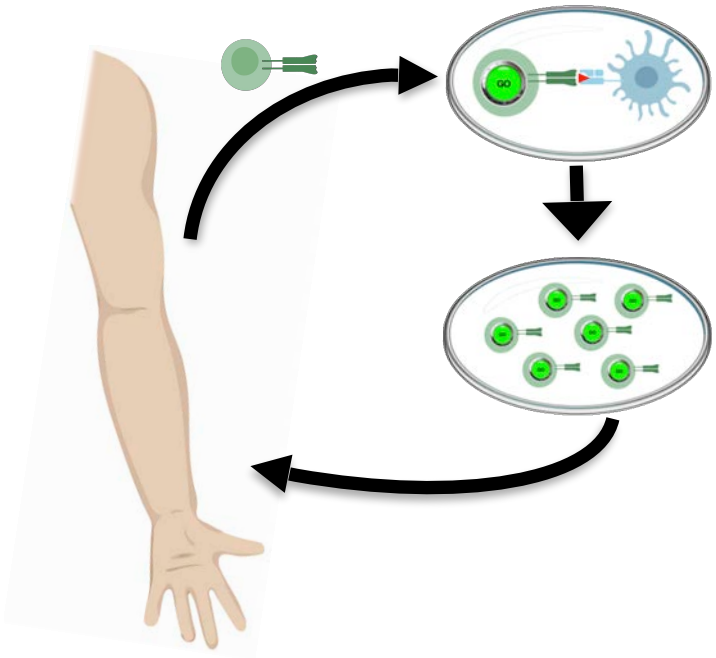


CANCER CELL ELIMINATED!

Adoptive T Cell Immunotherapy



Adoptive T Cells In Action (Against Melanoma)



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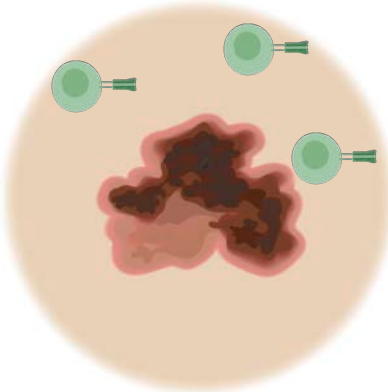
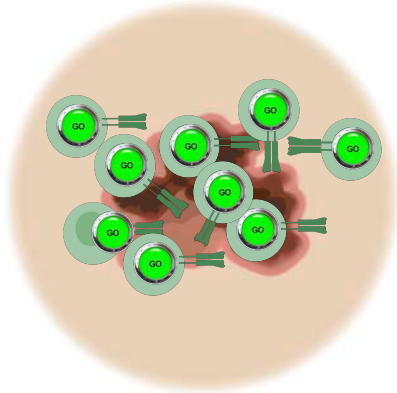
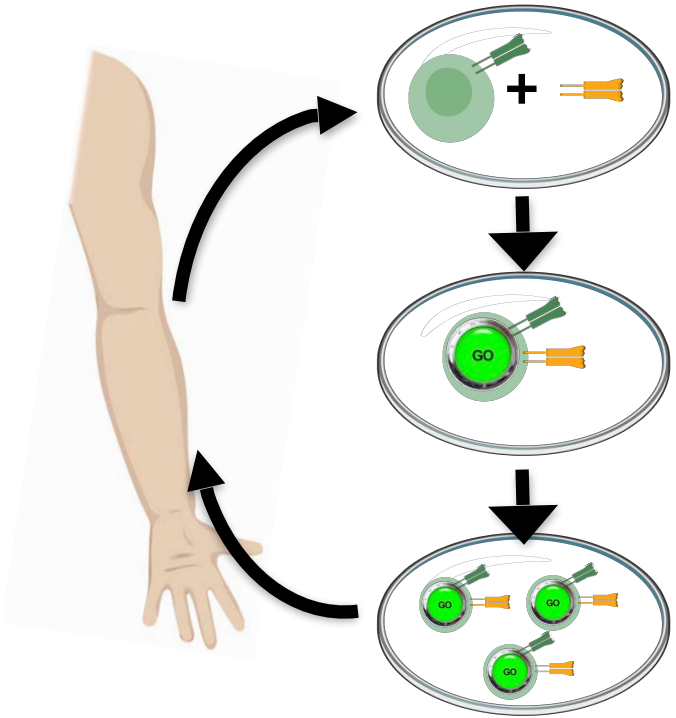


Melanoma (Before)



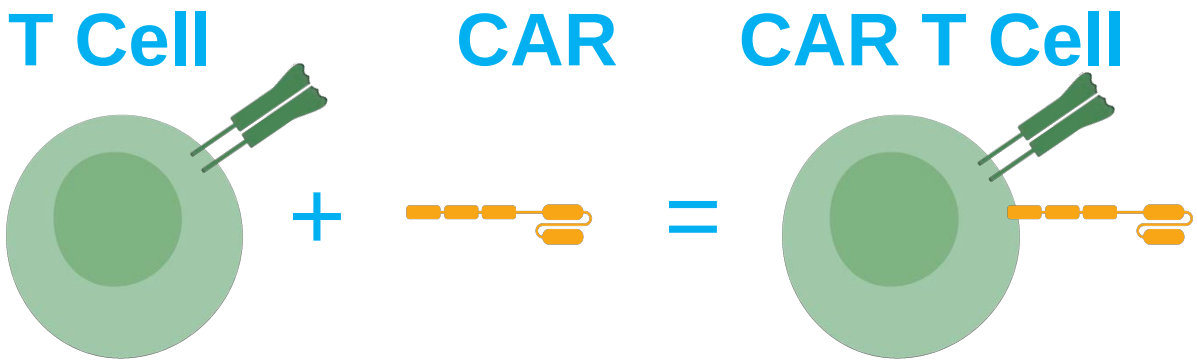
Melanoma (After)

T Cell Receptor Engineering

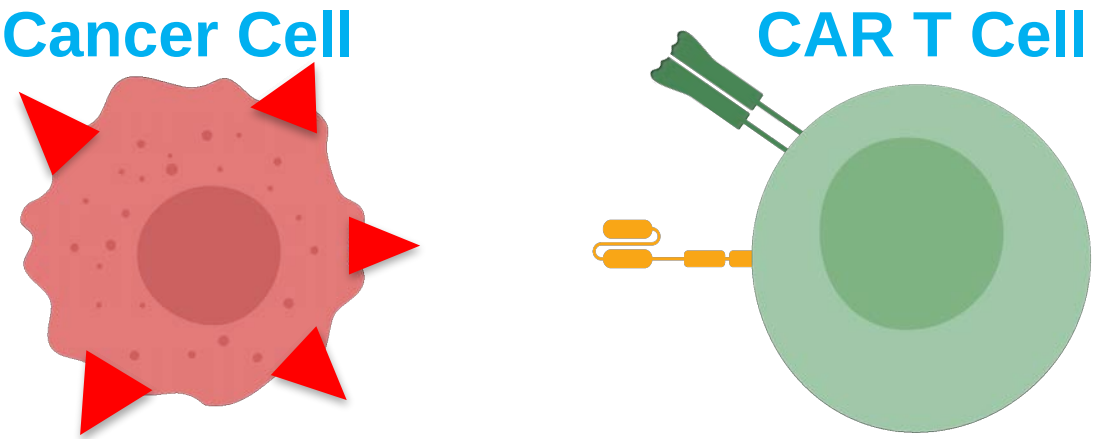


Equip T cells with new, cancer-targeting TCR

CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

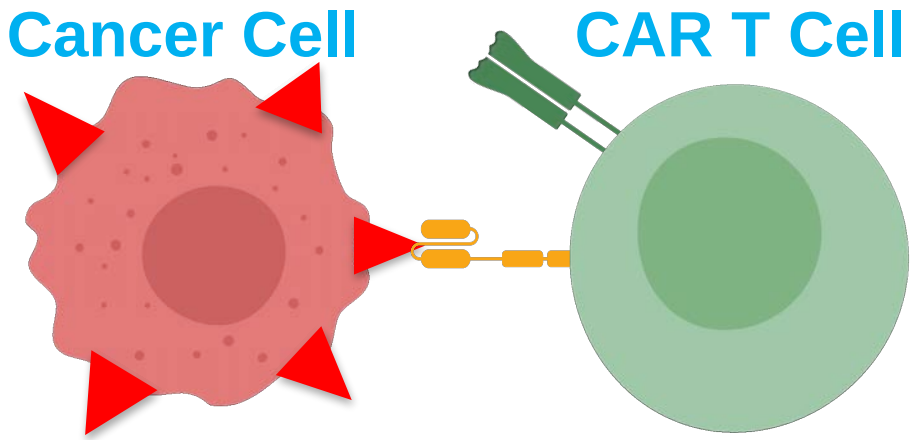


CAR T Cell Immunotherapy (Chimeric Antigen Receptor)



CARs enable MHC-independent targeting & killing!

CAR T Cell Immunotherapy (Chimeric Antigen Receptor)



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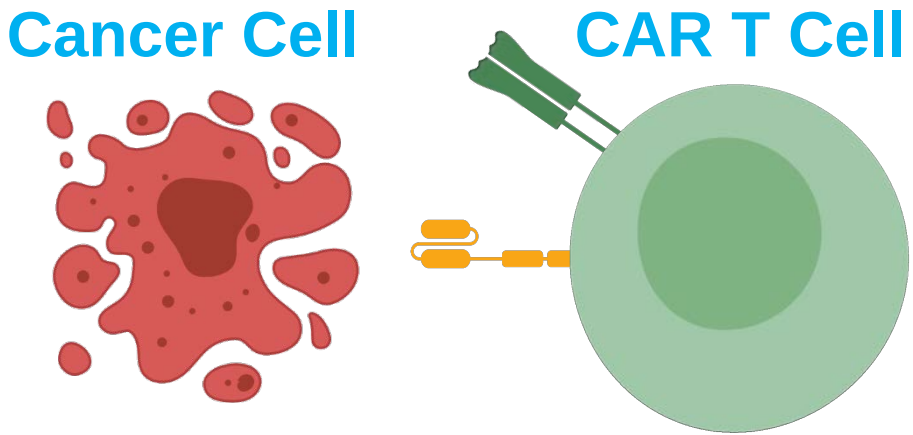
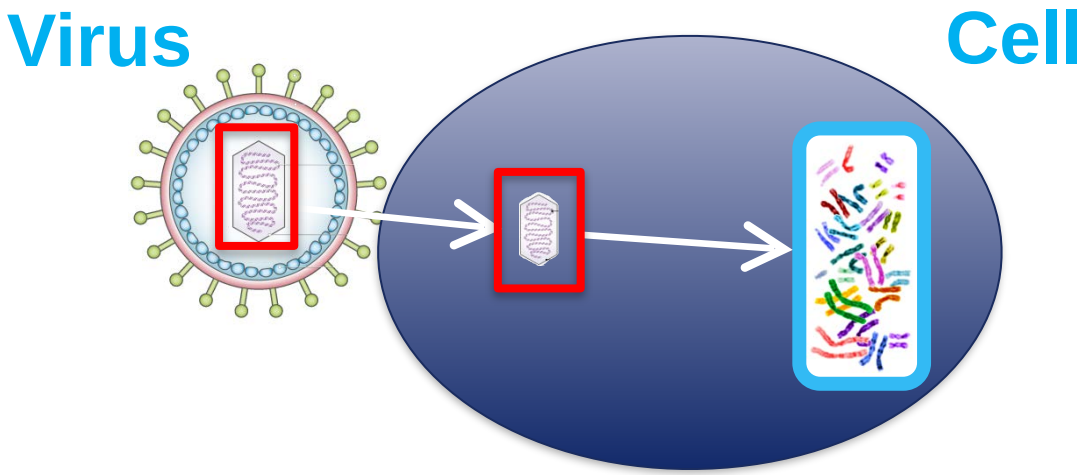
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)



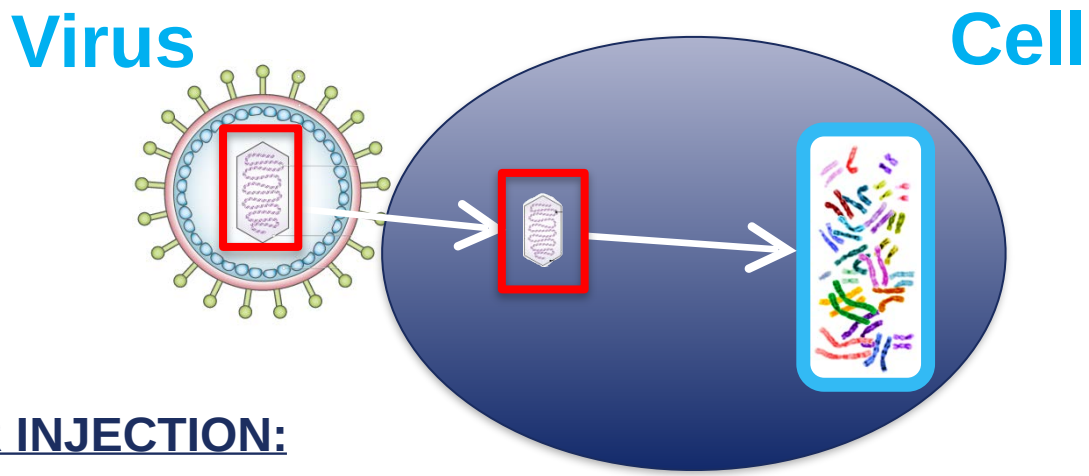
CARs enable MHC-independent targeting & killing!

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



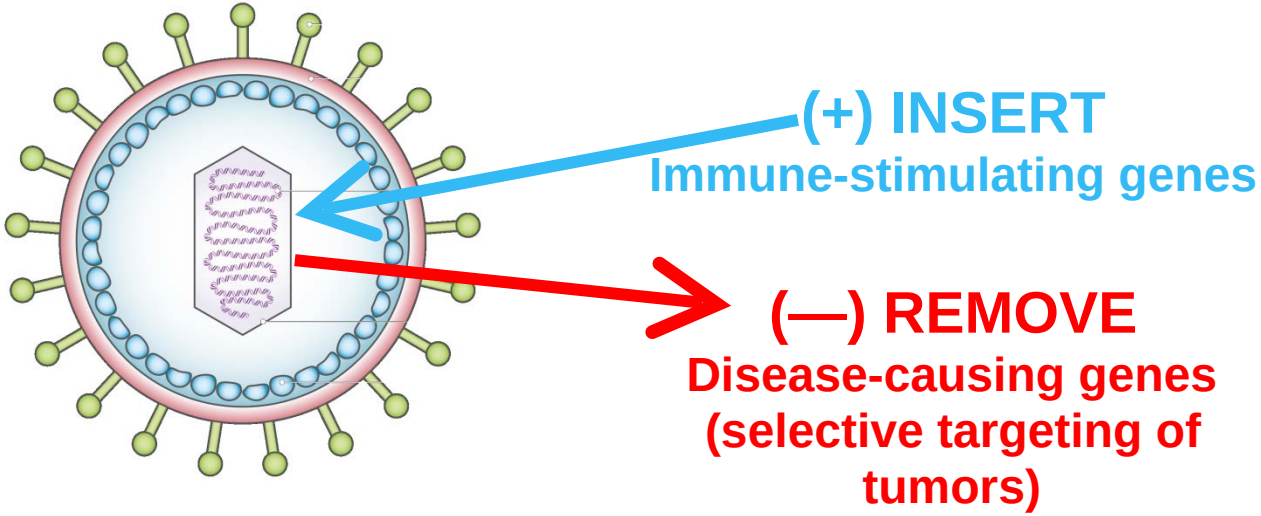
AFTER INJECTION:

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

2) Immune cells uptake & present tumor antigens

3) Stimulates adaptive, and potentially systemic, immune responses

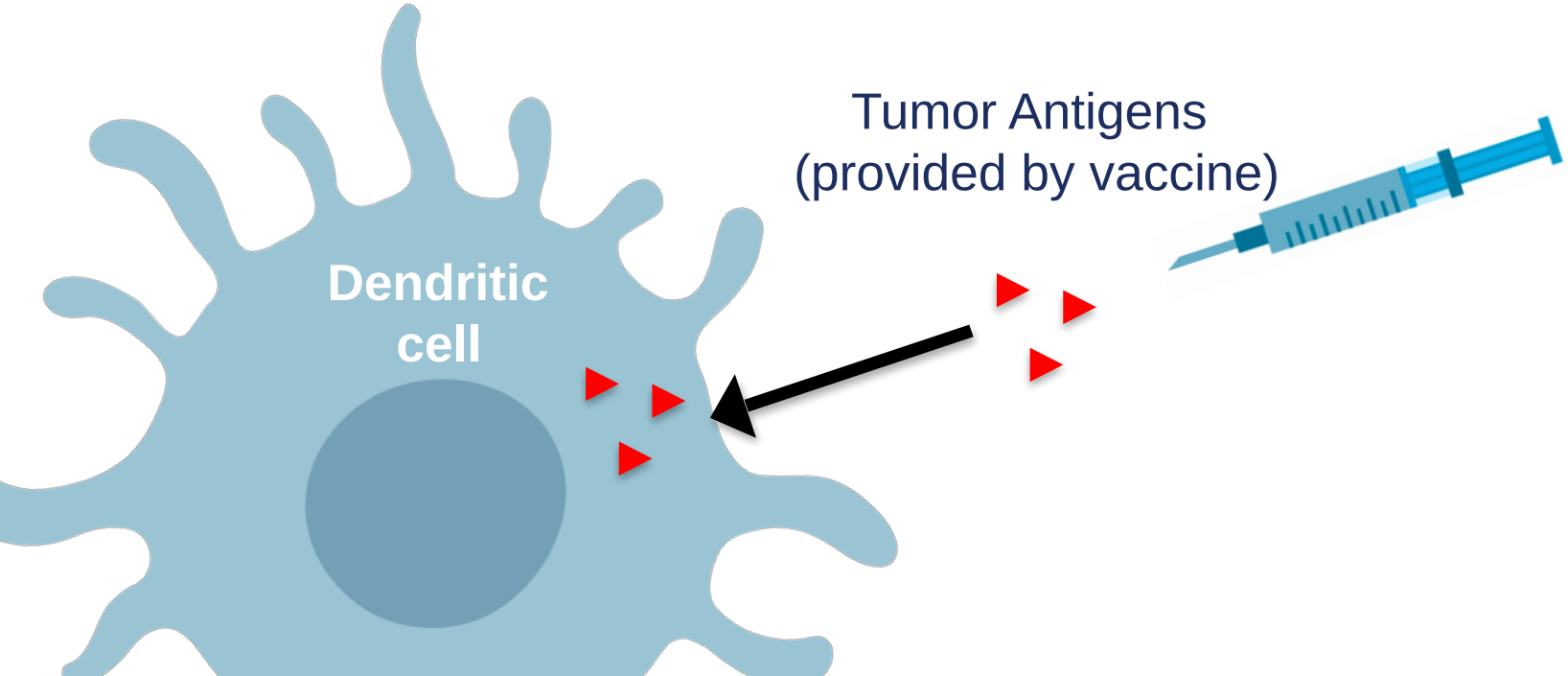
Reprogramming Oncolytic Viruses To Enhance Anti-Tumor Activity



Cancer Vaccines

Tumor Antigens
(provided by vaccine)

Cancer Vaccines



Cancer Vaccines

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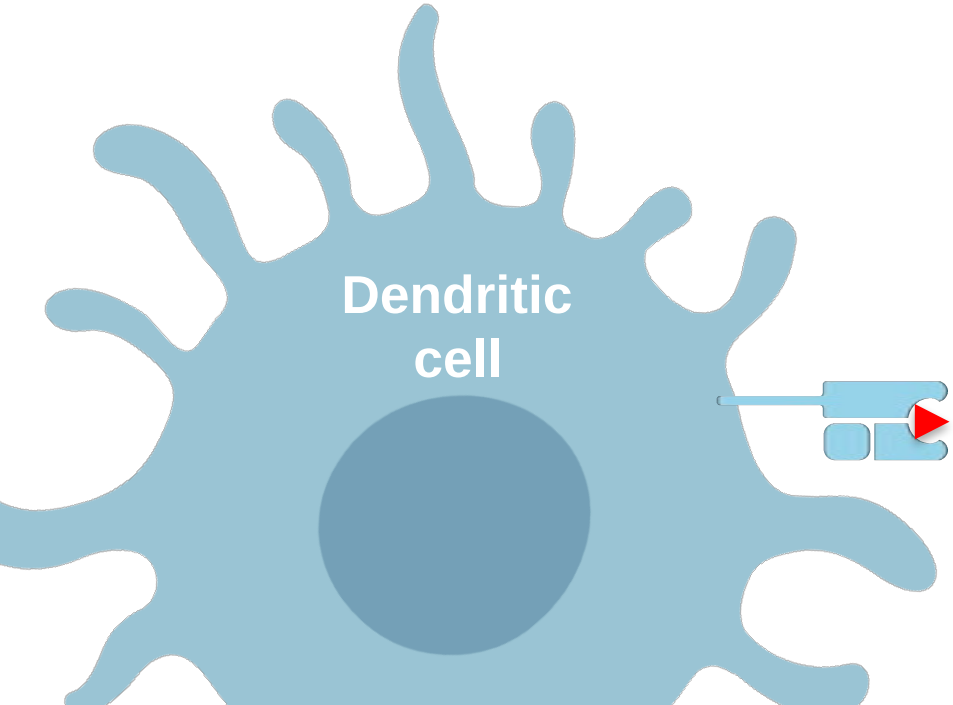
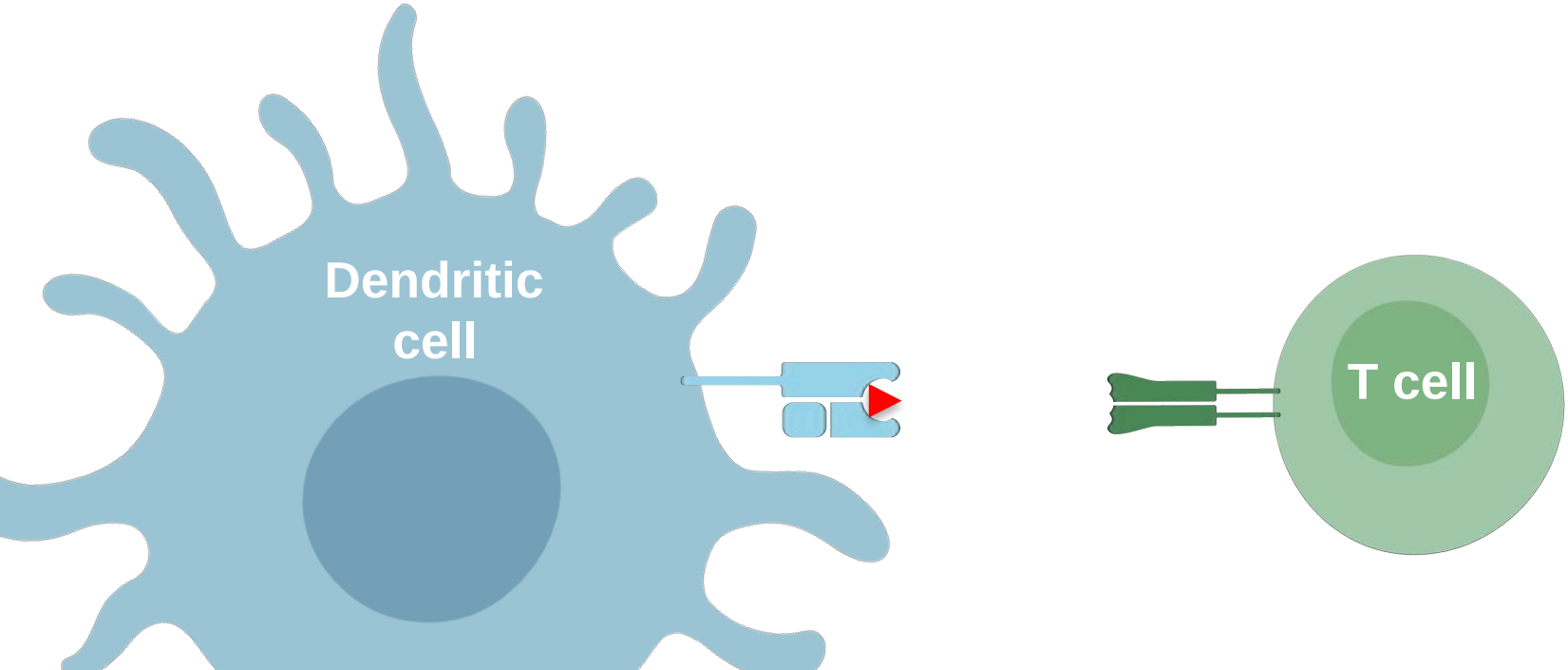


Cancer Vaccines



Cancer Vaccines

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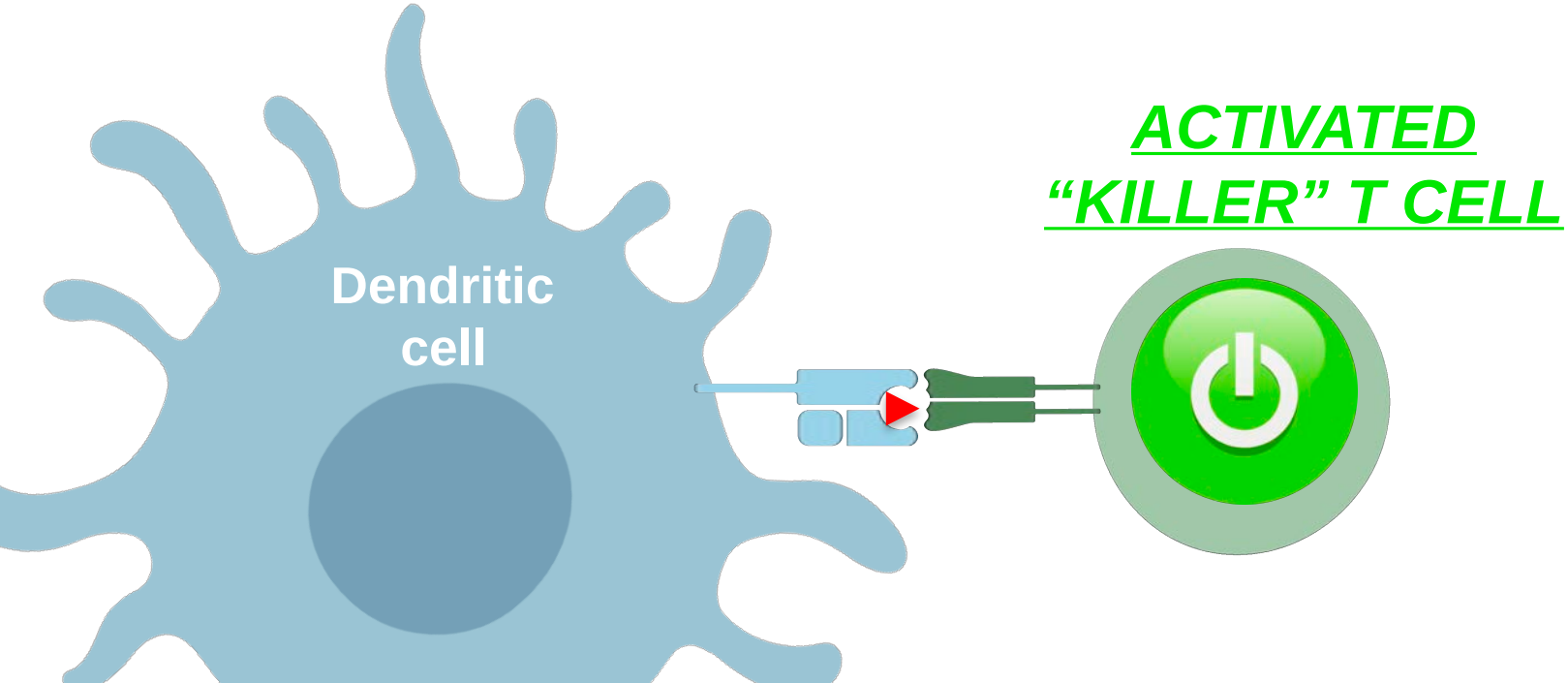

Vaccine-Induced Elimination of Cancer Cells

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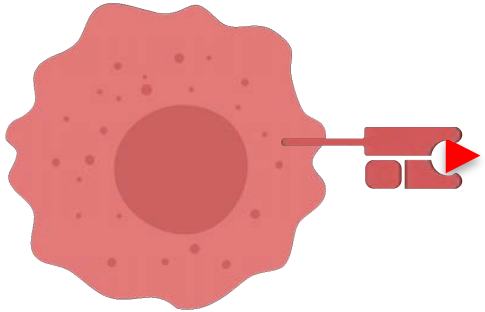
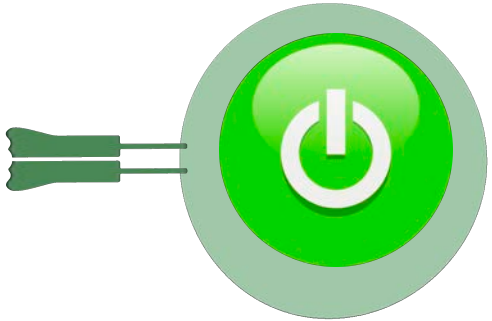
Cancer Cell



Activated “killer” T Cell



Vaccine-Induced Elimination of Cancer Cells

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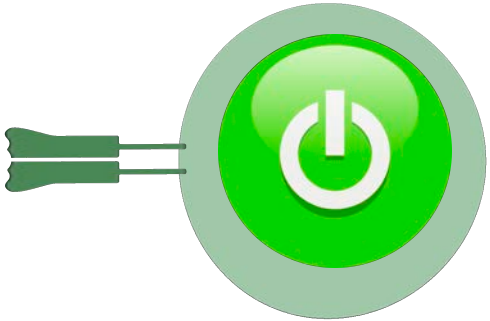
Cancer Cell

Activated “killer” T Cell



Personalized Neoantigen Vaccine Trial

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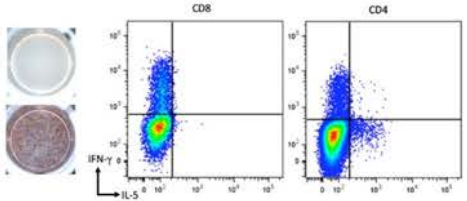
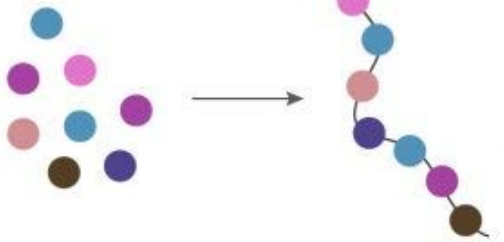
Tumor biopsy

Sequencing

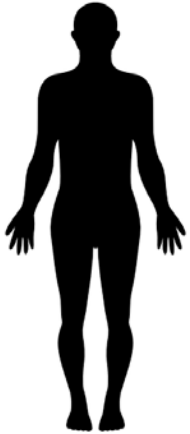
Bioinformatics



Immunological Analysis



AMINO ACIDS PEPTIDE



Challenges in Cancer Immunotherapy

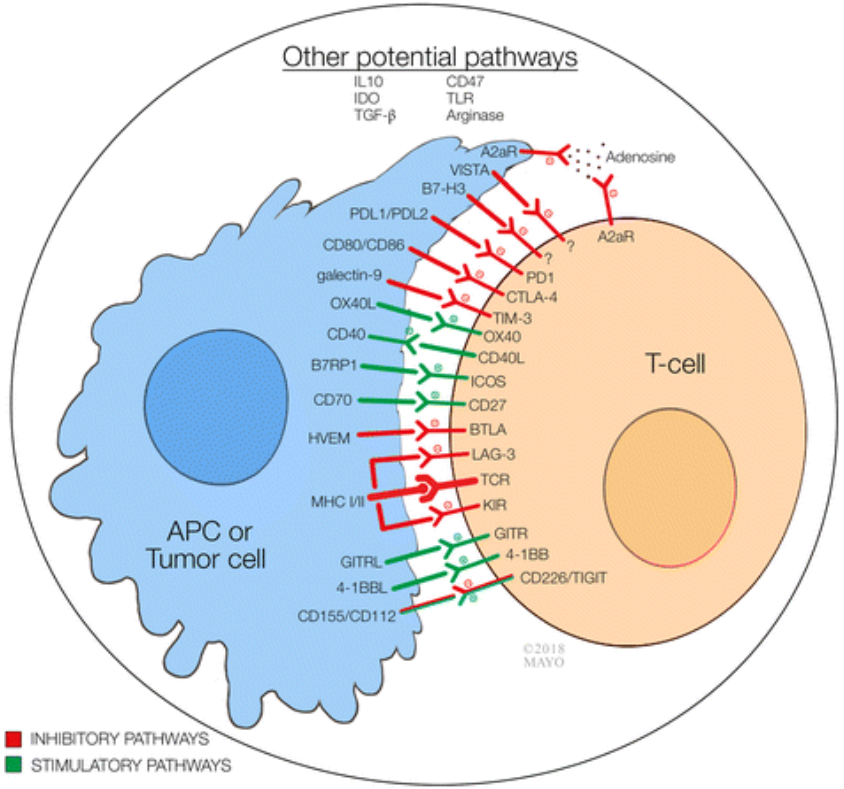
- Discovering and validating new biomarkers to help doctors predict which patients will respond to which immunotherapies

- Determining the best way to combine immunotherapies with each other as well other treatments to extend immunotherapy's benefits for more patients

- Learning how to decouple side effects of immunotherapy from benefit

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

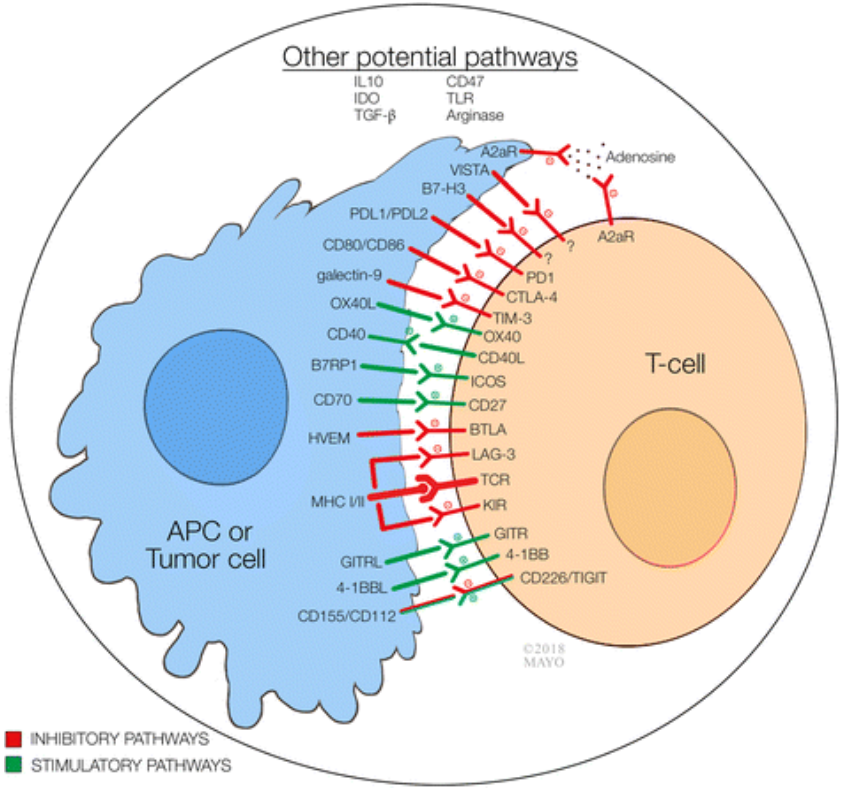
1. Cancers upregulate molecules to turn off immune cells



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

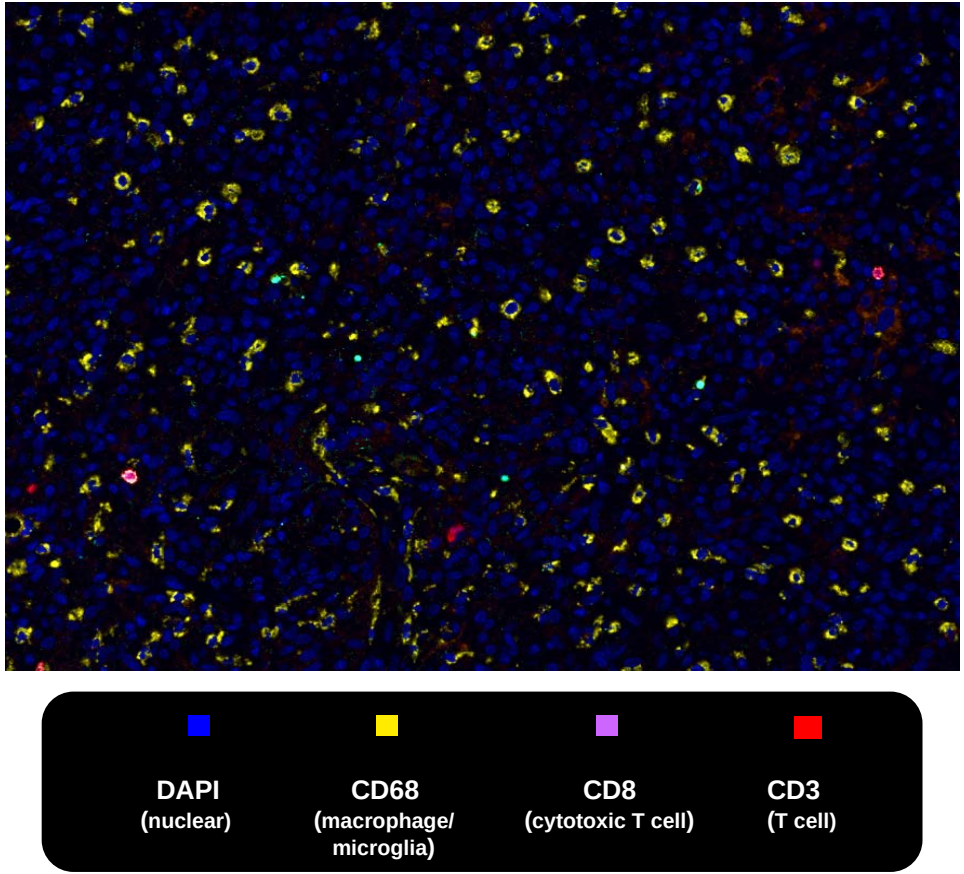


Why have most responses been modest and why are some cancers refractory to immunotherapy?

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



Immunotherapy 101

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Conclusion

A. Background

B. Basics: How our immune system works
- Immune checkpoint therapy
- Adoptive cellular therapies, CARS
- Oncolytic viruses
- Vaccines

C. Challenges

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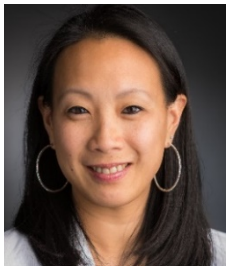
The Leader in Immunotherapy

LATEST RESEARCH UPDATES

Moderator
David A. Reardon, M.D.
Neurological cancer

Panelist
Susanne Baumeister, M.D.
Childhood cancer

Panelist
Justin Gainor, M.D.
Esophageal and lung cancers



Panelist
Kimmie Ng, M.D., M.P.H.
Gastrointestinal cancer

Patient Perspective

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Ariella Chivil

Surviving Hodgkin Lymphoma

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Lunch and Networking

Lavine Family Dining Pavilion

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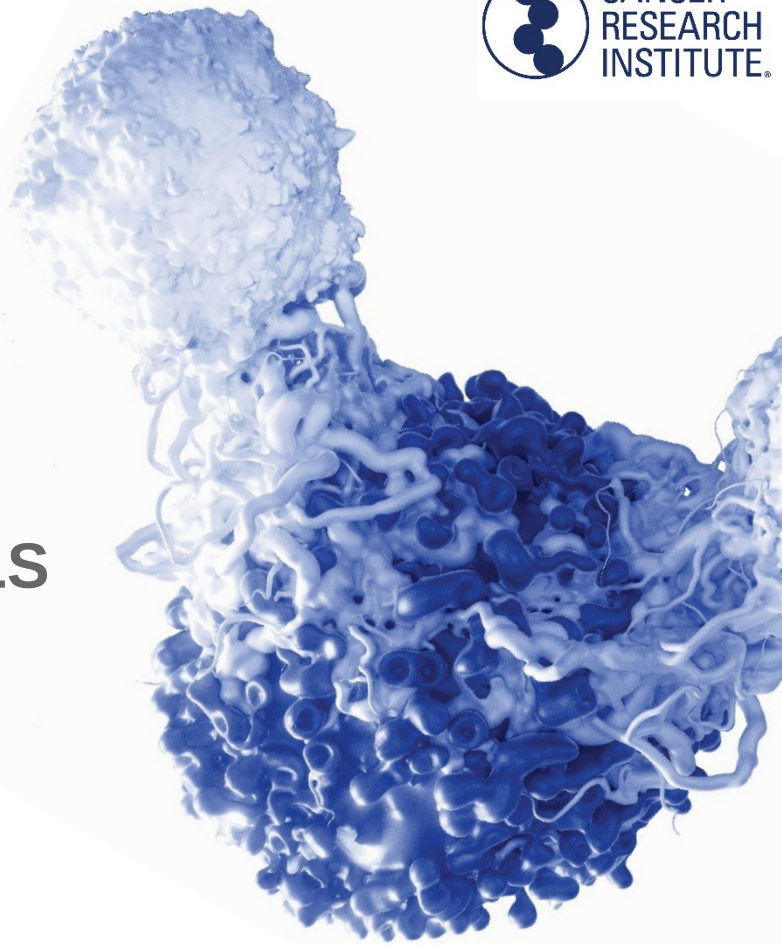

Brian Brewer

Cancer Research Institute

LEARN ABOUT CLINICAL TRIALS

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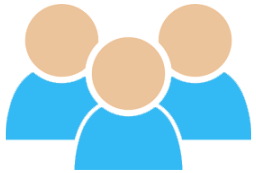
What Are Clinical Trials?



- 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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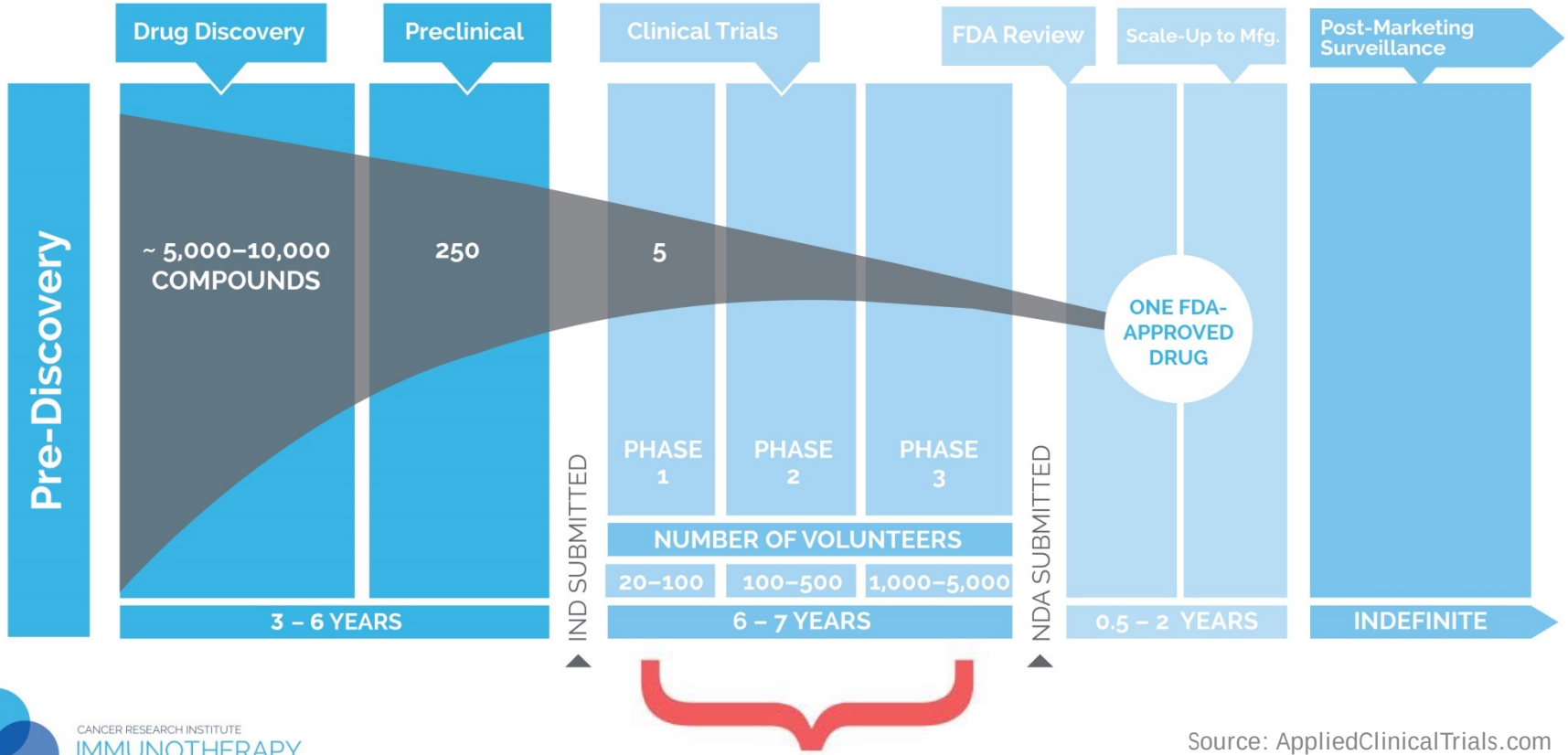

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Source: AppliedClinicalTrials.com

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

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

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

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.

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

Clinical Trials: Myth versus Fact

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

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.

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

Clinical Trials: Myth versus Fact

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?

- 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	**Ernestina Dos Reis** Glioblastoma
	Cole Malone Acute Lymphoblastic Leukemia
	Denise Malone Cole’s mom
	John White Prostate Cancer

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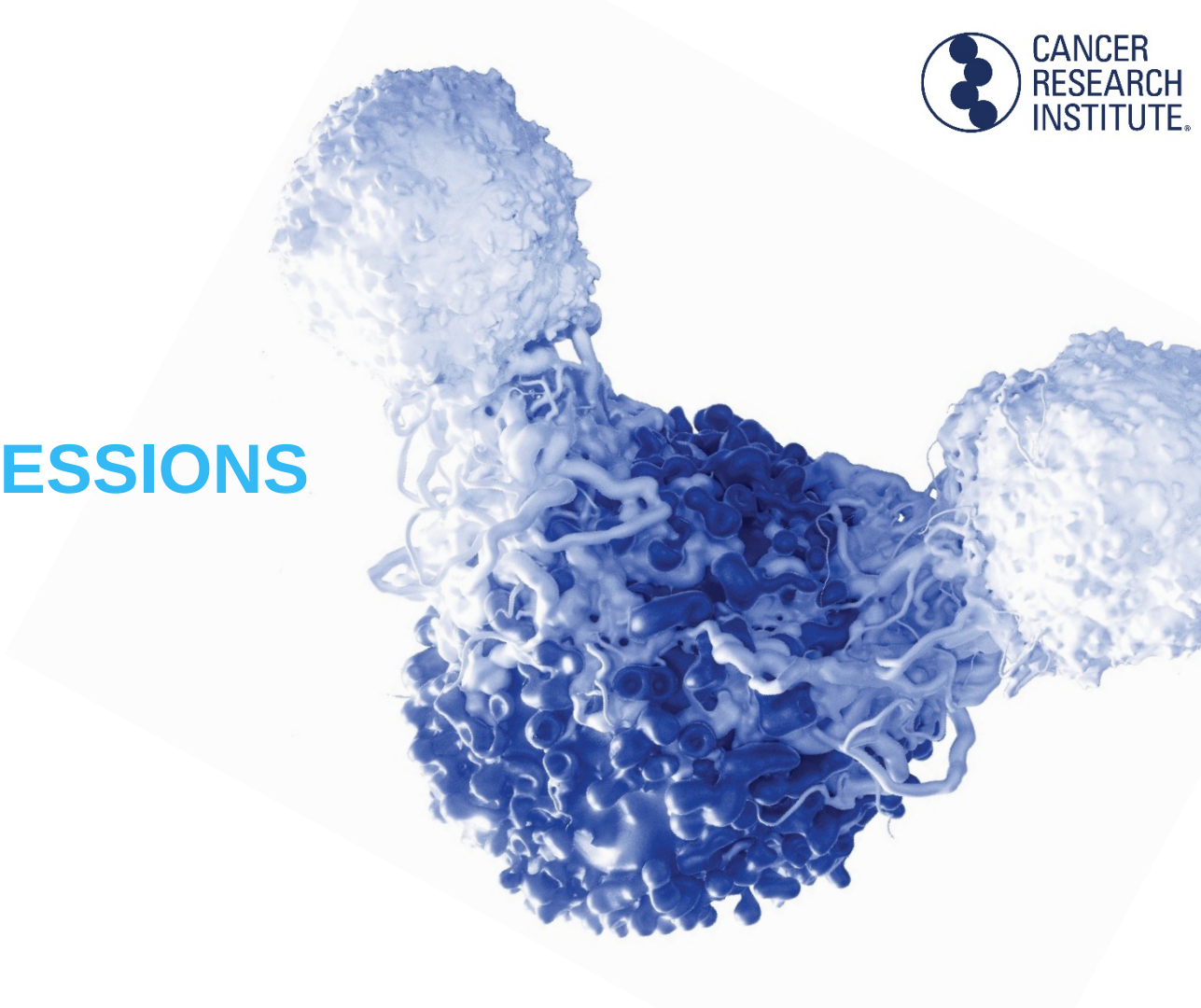
BREAKOUT SESSIONS



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Breakout Session Rooms

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General Immunotherapy David A. Reardon, M.D.	Dining Pavilion
Childhood Cancer Susanne Baumeister, M.D.	Room 308
Gastrointestinal Cancer Kimmie Ng, M.D., MPH	Room 307
Lung and Esophageal Cancers Justin F. Gainor, M.D.	Room 306

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Thank you to those who helped promote the summit

- American Cancer Society
- Blum Resource Center
- Colorectal Cancer Alliance
- Crush it for Curtis Foundation
- Dana-Farber Cancer Institute
- Esophageal Cancer Awareness Association
- FORCE
- Go2Foundation
- Healing Garden Cancer Support
- Imerman Angels
- Leukemia & Lymphoma Society
- LUNGevity
- Pancreatic Cancer Action Network
- Patient Empowerment Network
- The Jimmy Fund
- Us TOO
- Wellness Warriors Boston
- 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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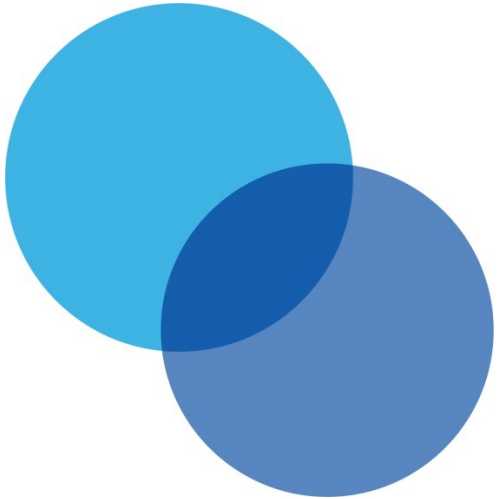

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Boston July 29, 2019