

# Radiation and Immunotherapy

What's it All About?

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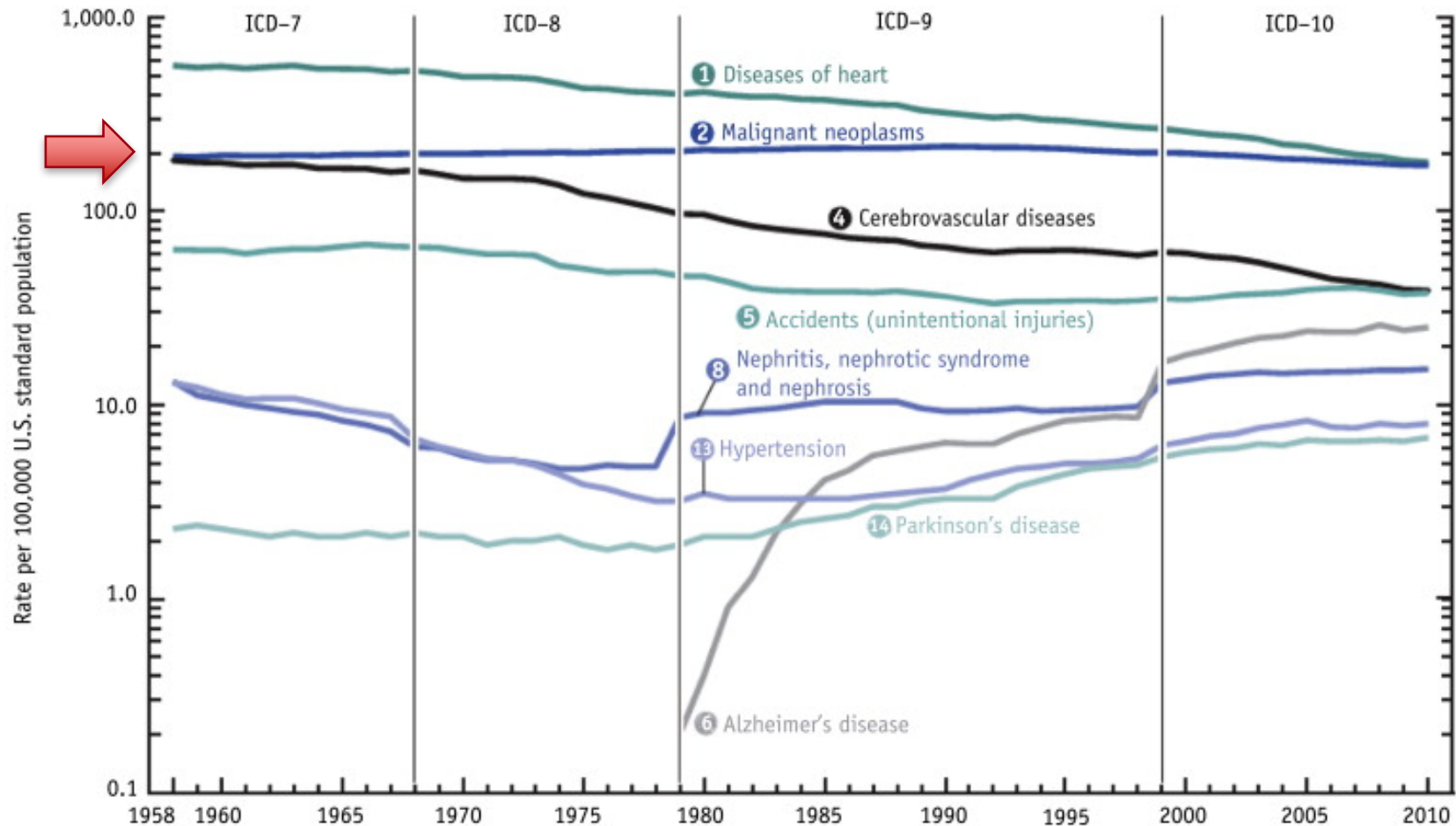


# DISCLAIMER

The information contained in this presentation is not intended as a substitute for professional medical advice, diagnosis or treatment.

It is provided for educational purposes only. You assume full responsibility for how you choose to use this information.

# Proportion of U.S. Population Dying of Cancer Has Not Changed Since 1960

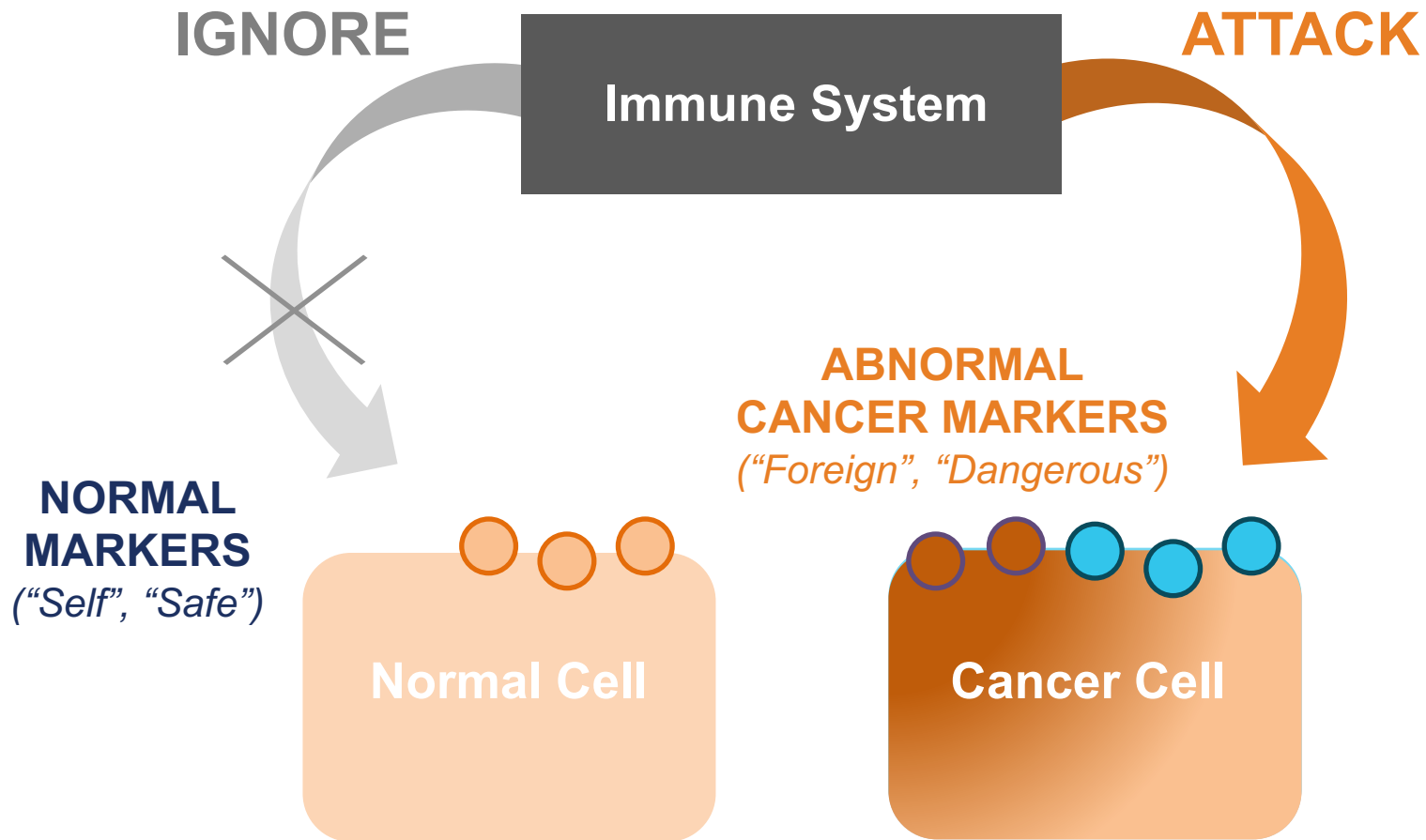


# What Is Cancer Immunotherapy?

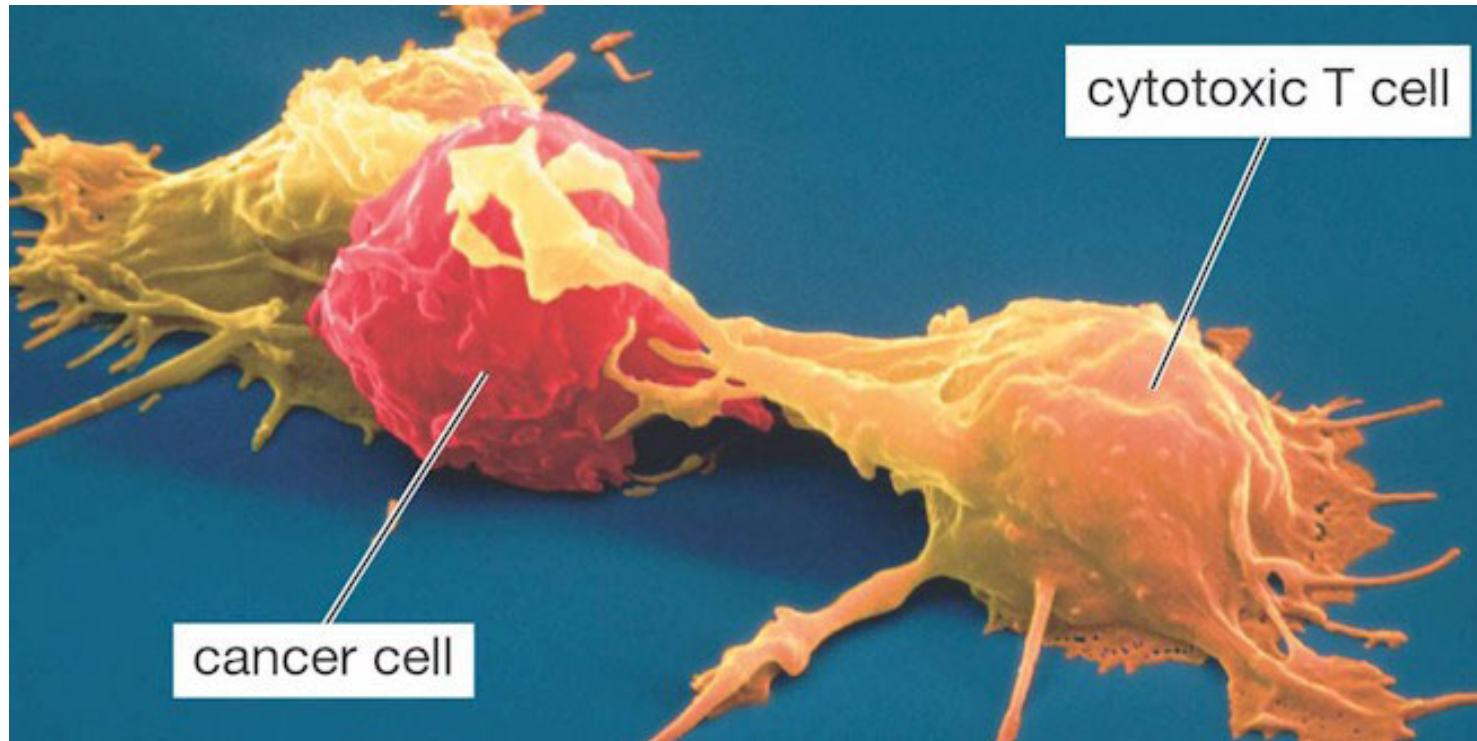
- Standard cancer therapy (chemotherapy, radiation) attacks the tumor cell directly
- Immunotherapy is a treatment that activates the immune system to fight cancer



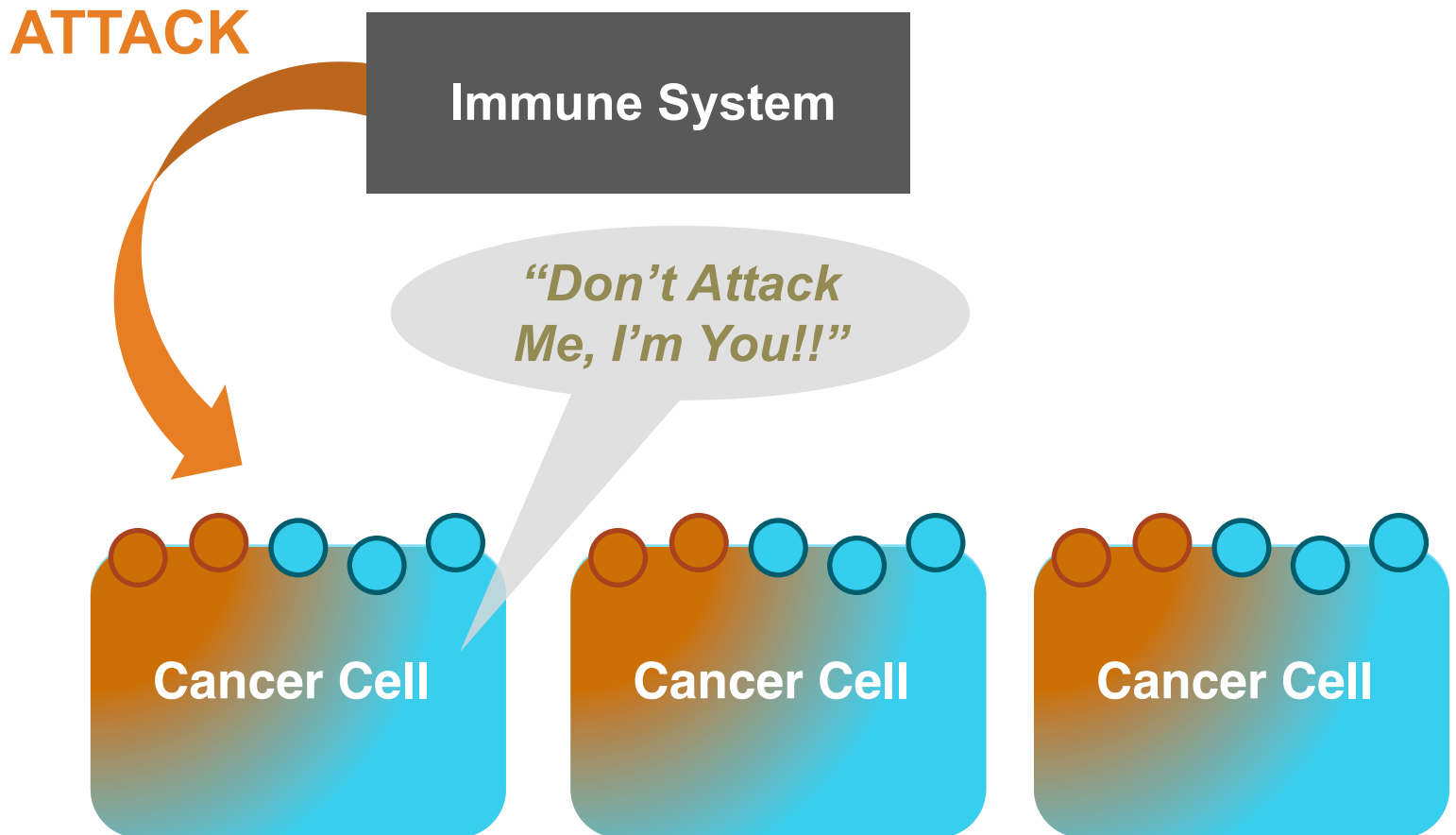
# The Immune System Has a Natural Ability to Recognize and Kill Cancer



# Killer T Cells Attacking a Cancer Cell



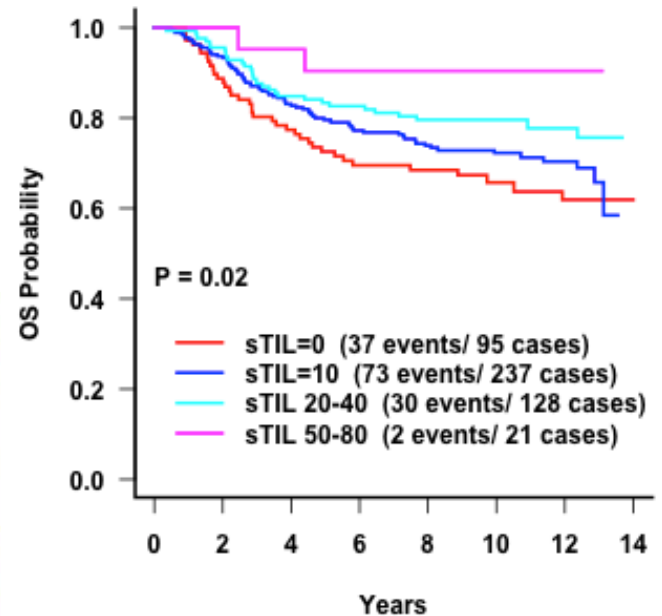
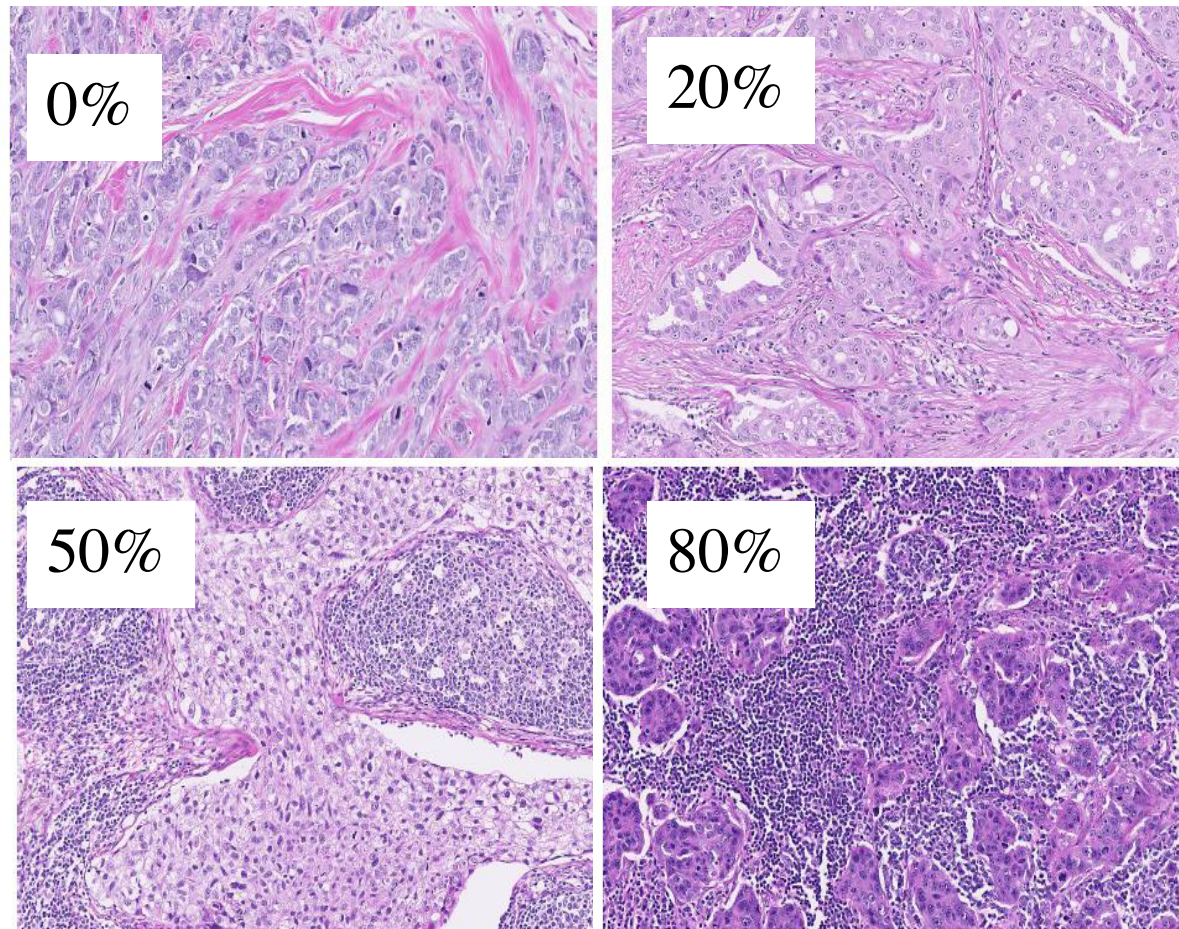
# But Sometimes the Immune System Shuts Down Prematurely or the Attack is Insufficient





# Breast cancer: The Immune System is Present at the Tumor Site But Incapable of Rejecting Cancer

Immunologic phenotypes of tumor/host in 481 TNBC patients from ECOG trials E2197/E1199



for every 10% increase in TILs, a 14% reduction of risk of recurrence or death

Adams et al JCO 2014 Sep 20;32(27):2959-66.

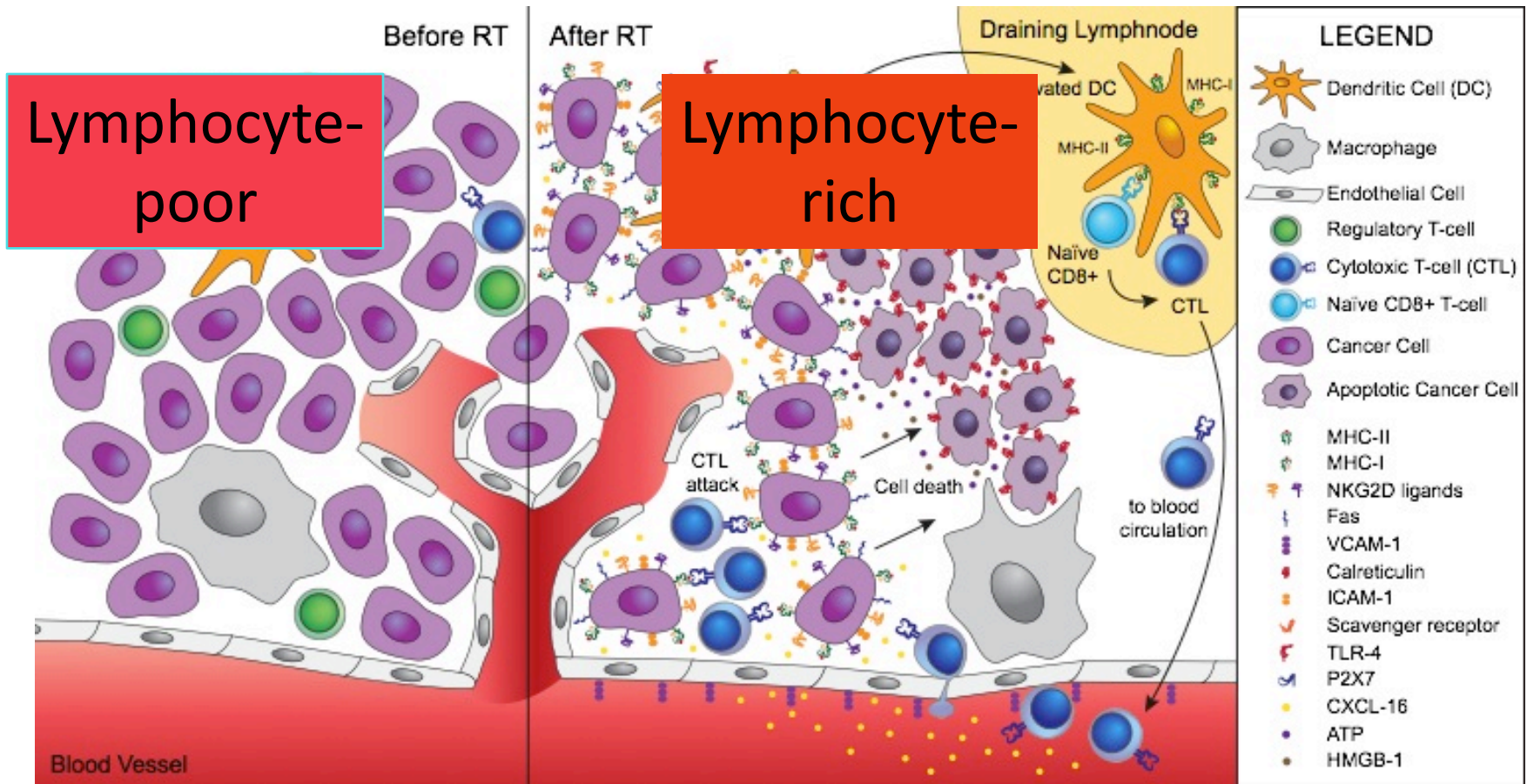
# Breast Cancer

- The immune system is present at the tumor site but incapable of rejecting cancer; immunosuppression dominates in established tumors
- For every 10% increase in tumor infiltrating immune cells, a 14% reduction of risk of recurrence or death

*Adams et al JCO 2014 Sep 20;32(27):2959-66.*

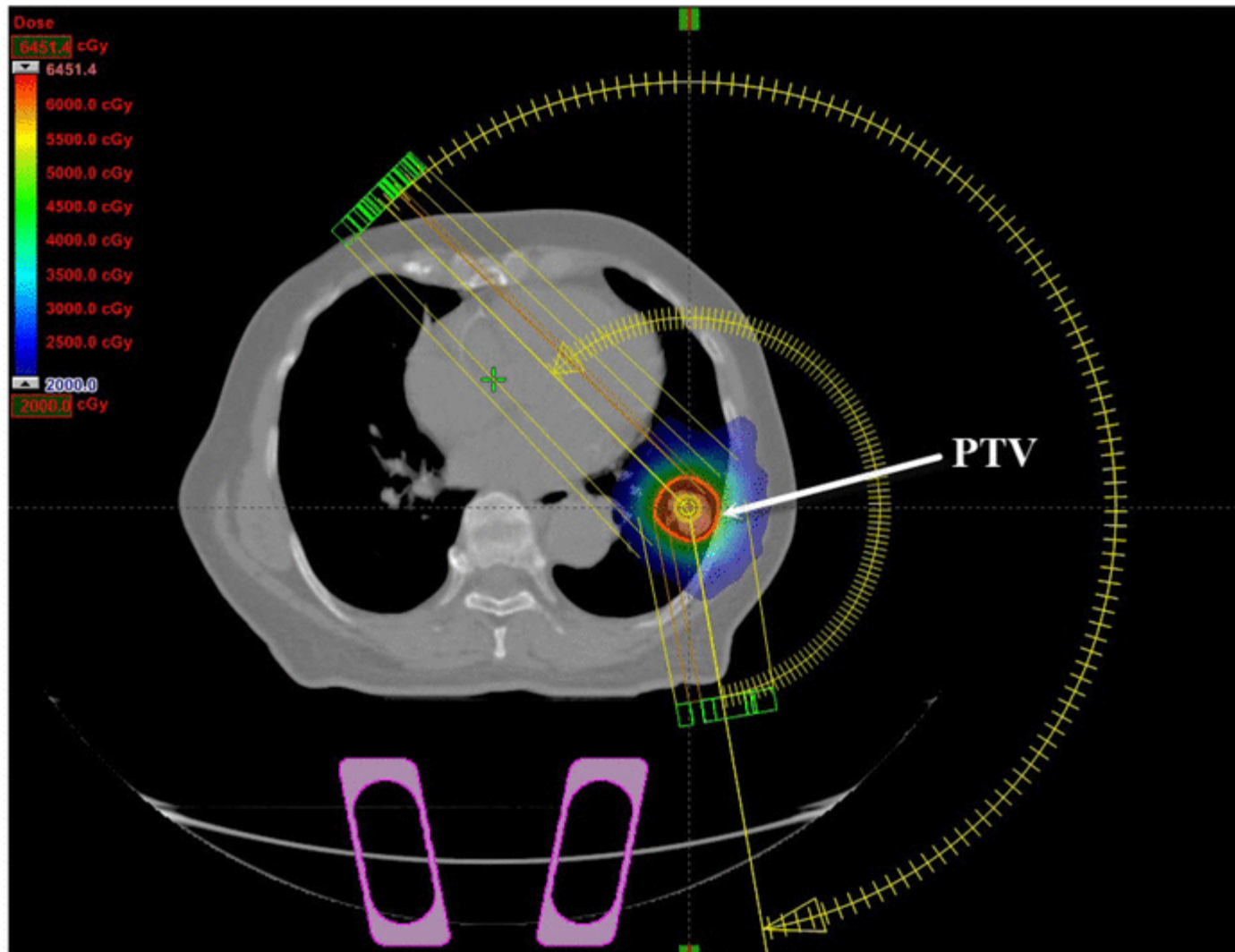


# CAN RADIOTHERAPY RESET THE IMMUNOLOGIC PHENOTYPES OF A TUMOR?



*IJROBP 2004, Lancet Oncology 2009, JNCI 2012*

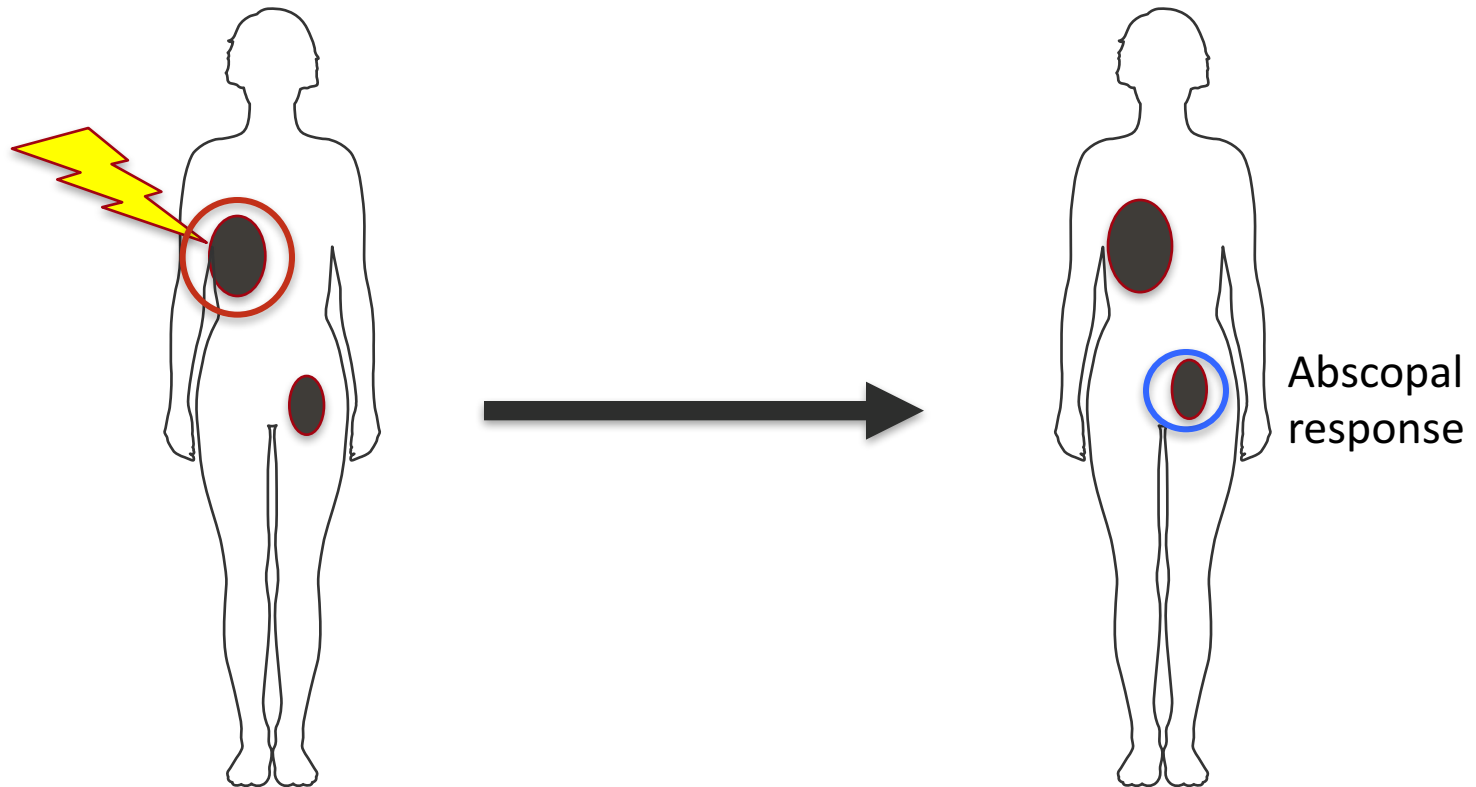
# How is Radiotherapy Delivered in the Modern Era?



# Can Radiation Therapy Help the Immune System to Reject Cancer?

## Abscopal effects

*(ab-scopus = away from the target)*





## Systematic review of case reports on the abscopal effect

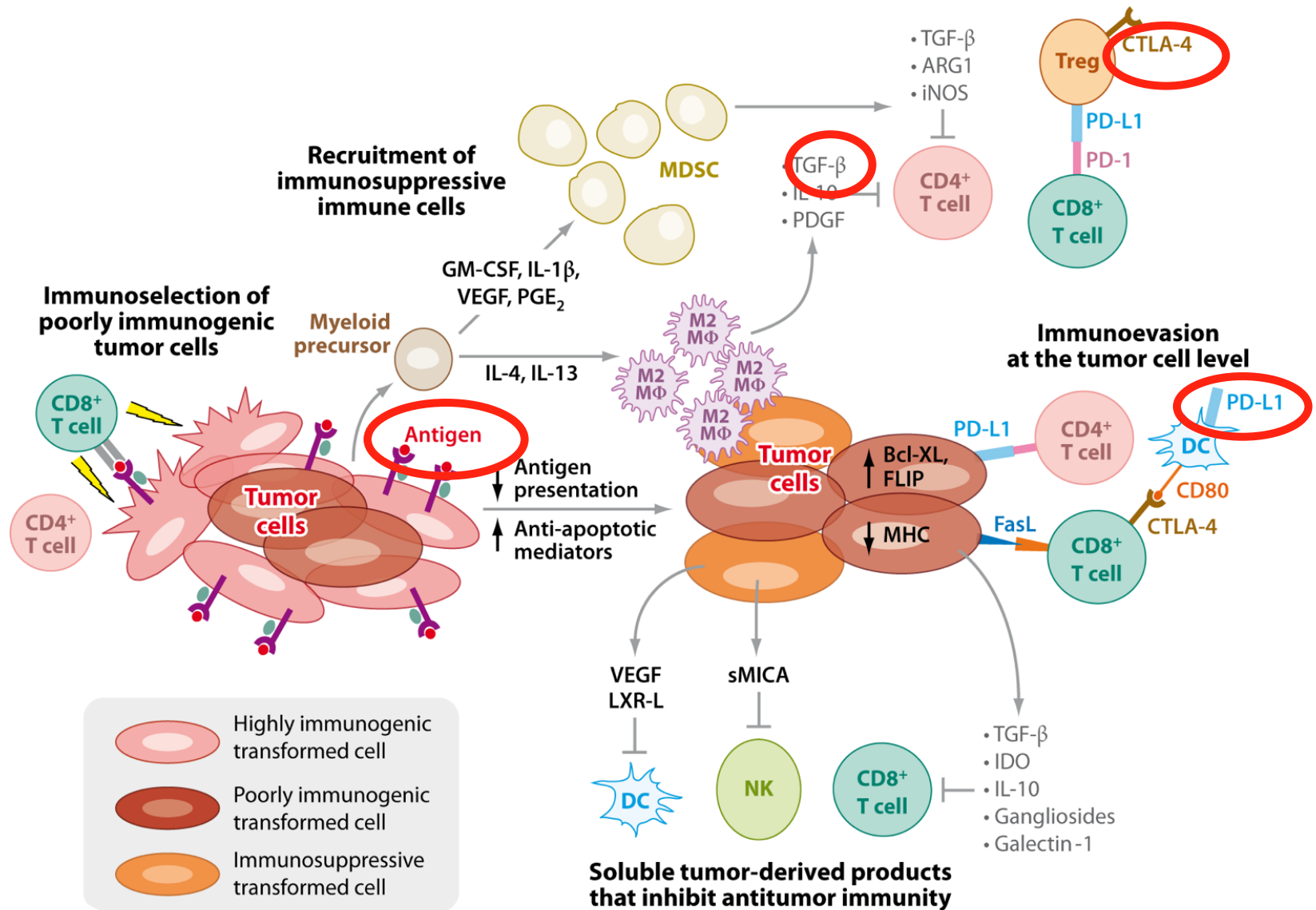


Yazan Abuodeh, MD, Puja Venkat, MD,  
Sungjune Kim, MD, PhD

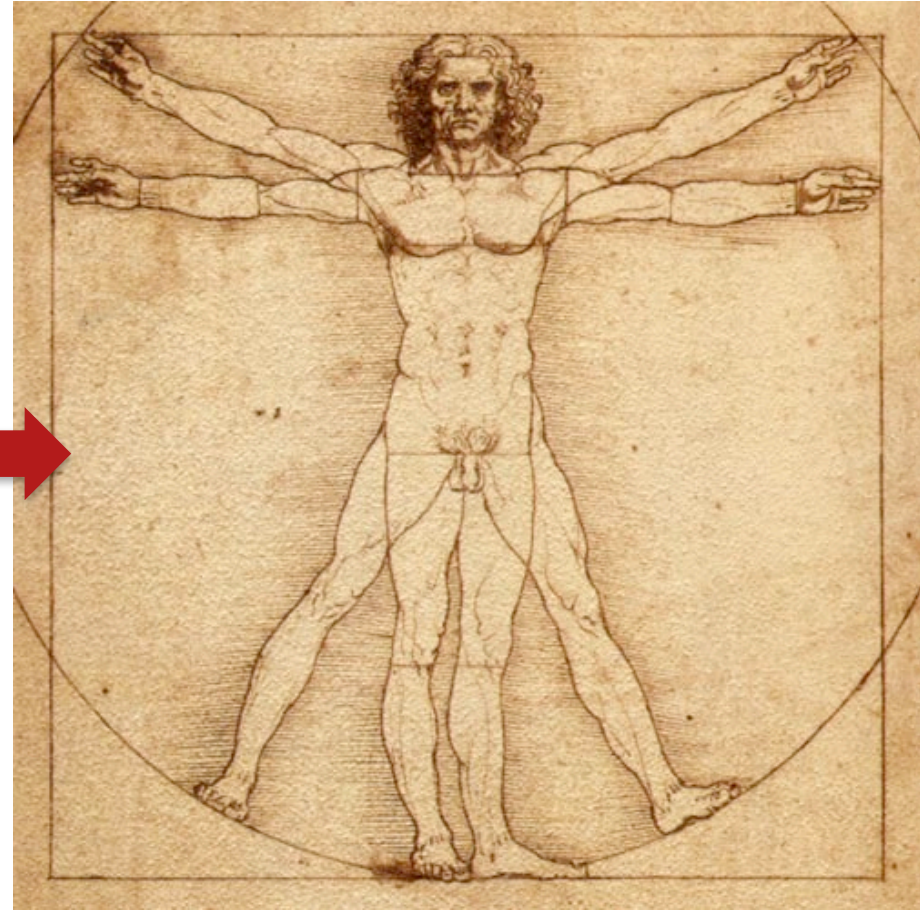
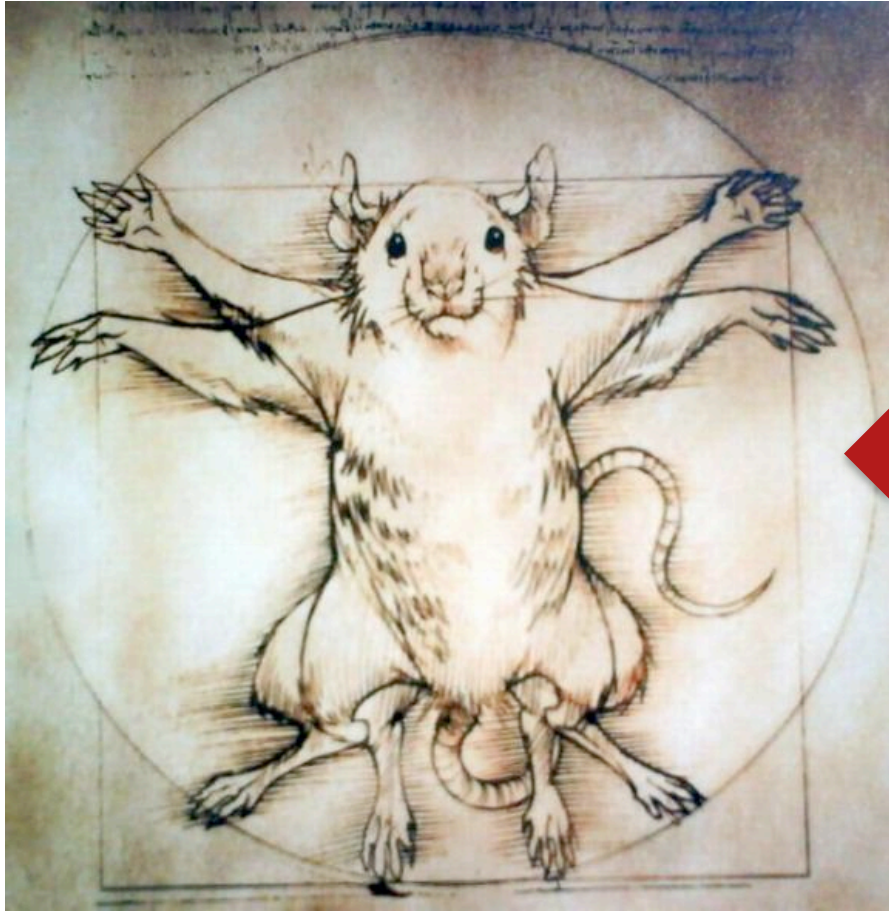
- 1969-2014: only 46 abscopal cases

# WHY ARE ABSCOPAL EFFECTS SO RARE?

# IMMUNOSUPPRESSION DOMINATES IN ESTABLISHED TUMORS



# Of Mice and Men





# Pioneers in Translating Radiation and Immunotherapy from the Lab to the Clinic



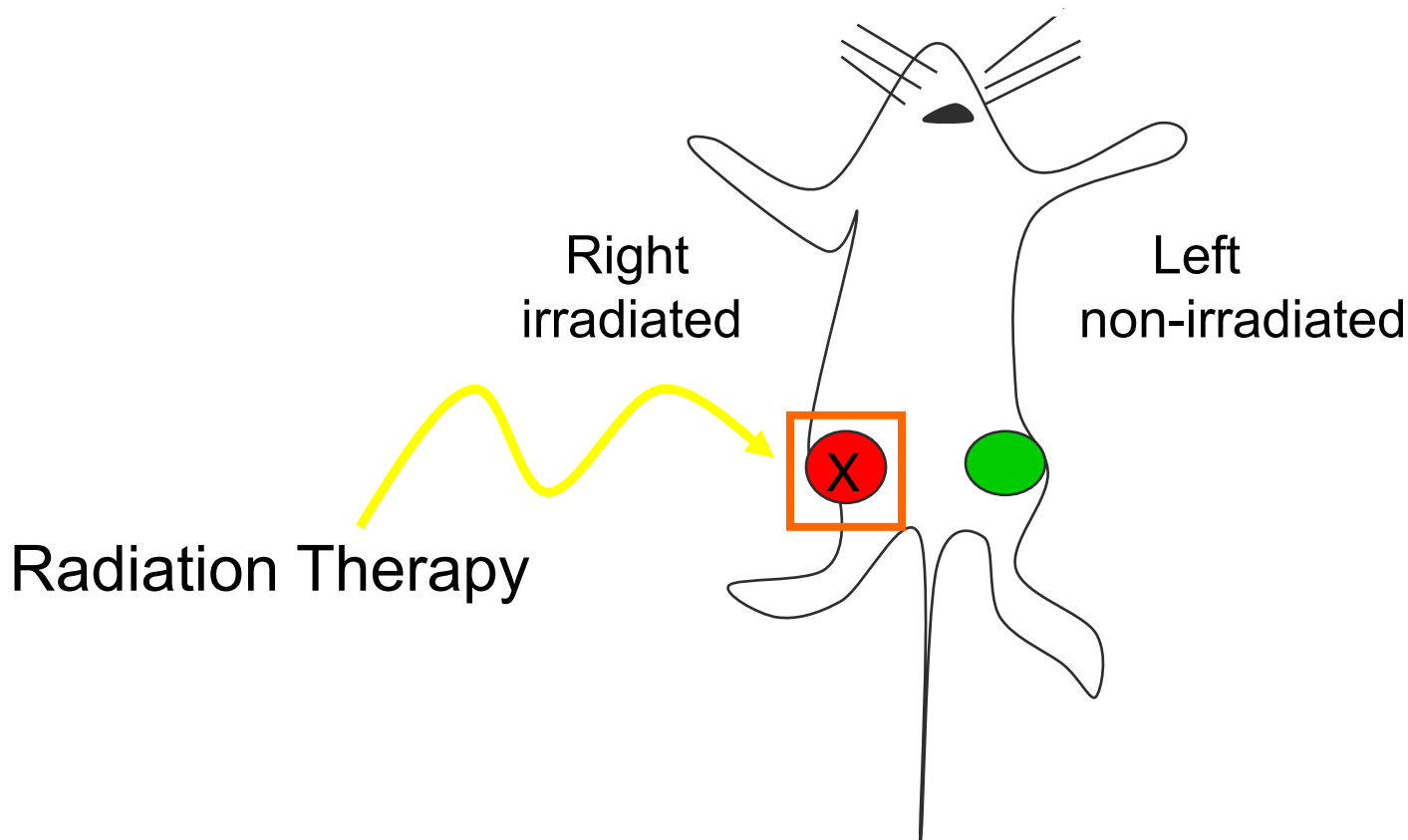
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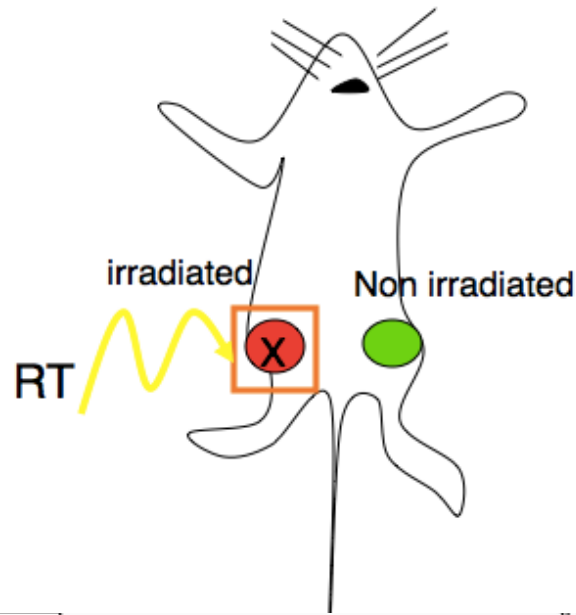


# Radiation Stimulates the Immune System to Attack and Shrink a Distant Tumor

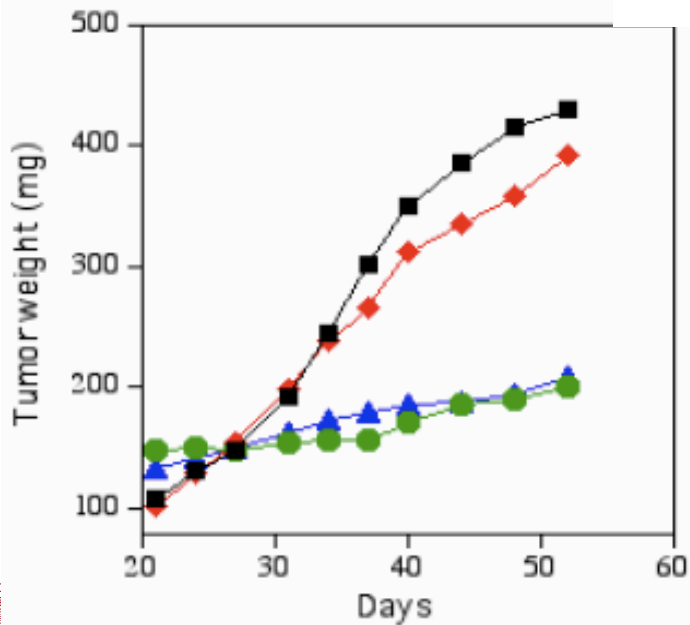


TSA Breast cancer mouse model

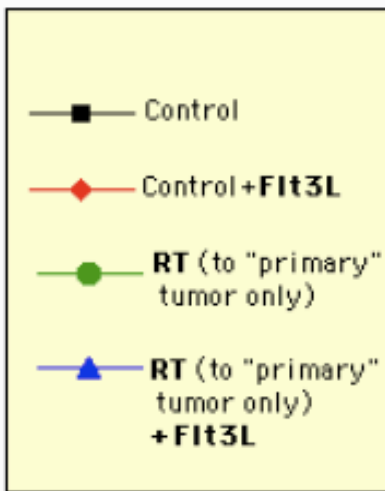
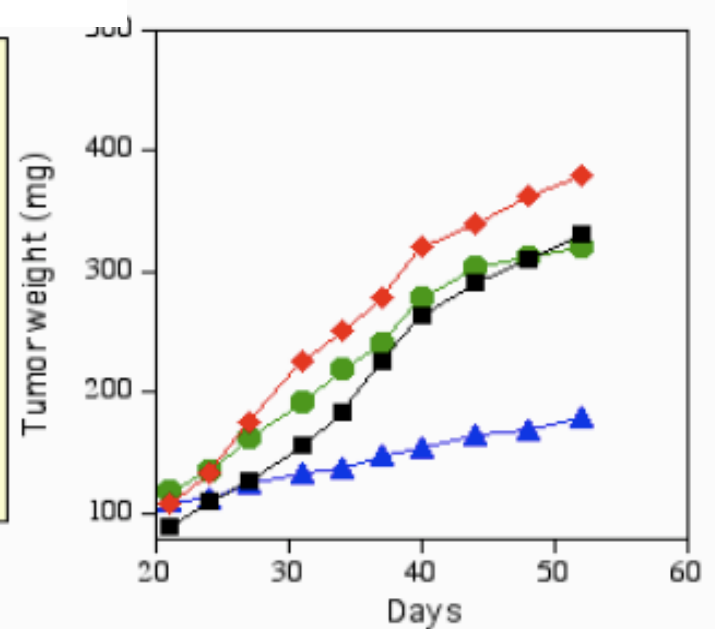
# RADIATION AND FLT-3L INDUCE AN ABSCOPAL EFFECT



## Irradiated



## Non-irradiated



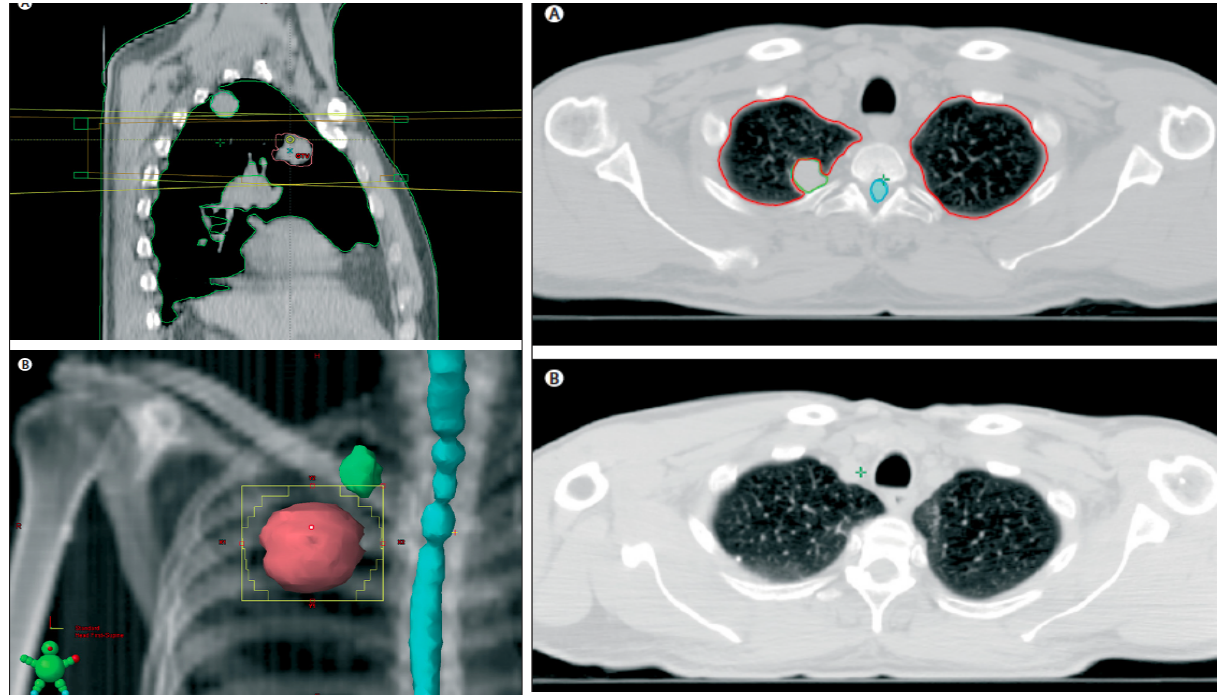
# Radiation with Immunotherapy, can stimulate the Immune System to Attack and Shrink a Distant Tumor

- A proof-of-principle trial: Local radiotherapy and GM-CSF—an immunotherapy—to generate abscopal responses in patients with metastatic solid tumors
- 26.8% abscopal responses
- Median overall survival: 20.98 months versus 8.33 months

*Golden et al Lancet Oncology 2015*



# ABSCOPAL RESPONSE AFTER RADIATION AND GM-CSF



RT: 3.5 GyX10

GM-CSF: 125  $\mu\text{g}/\text{m}^2$   
Daily X 14 days

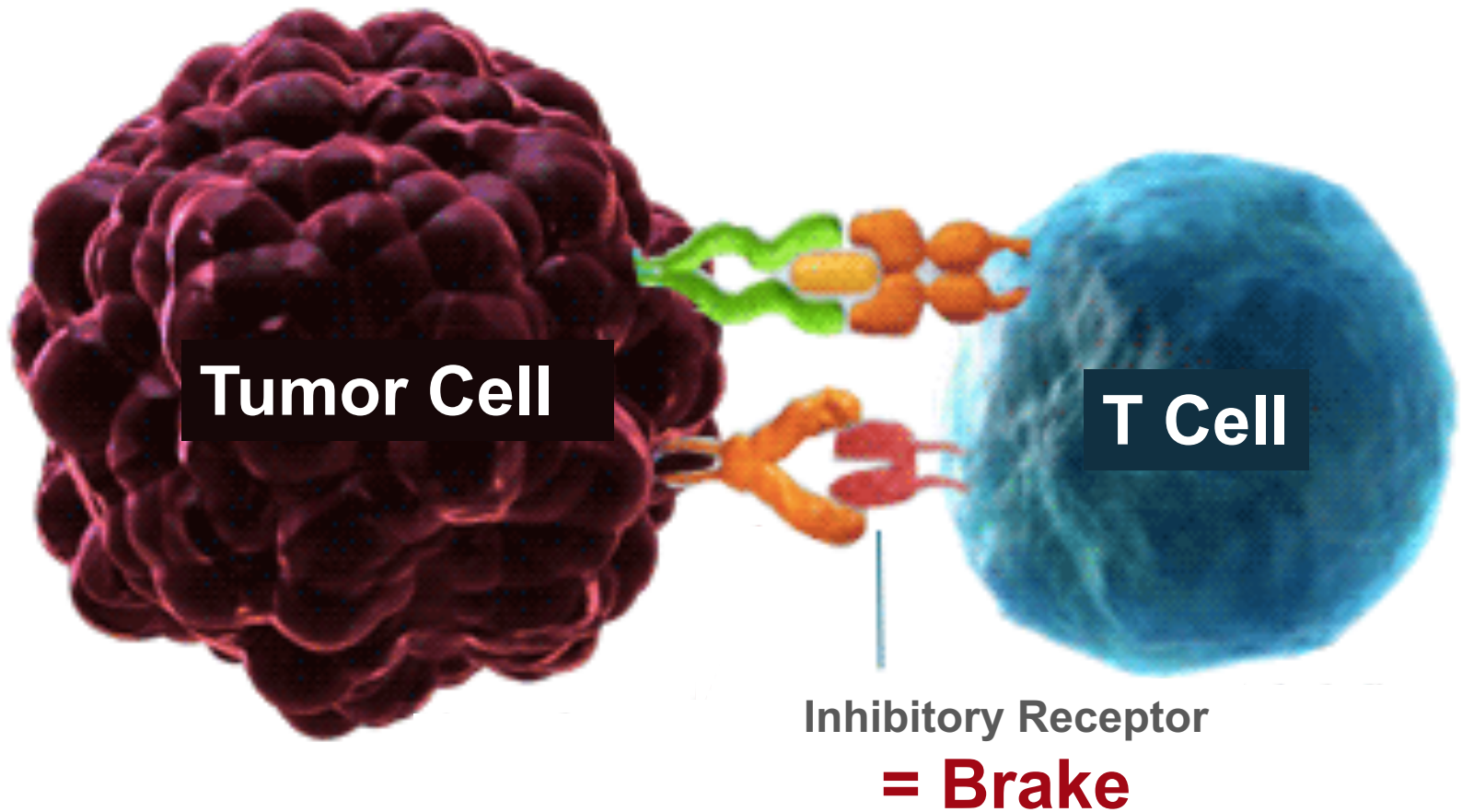
# Unleashing the Immune System to Fight Cancer

**James P. Allison, Ph.D.**

2015 Lasker-DeBakey Clinical  
Medical Research Award



# Instead of Pressing on the Accelerator, Release the Brakes



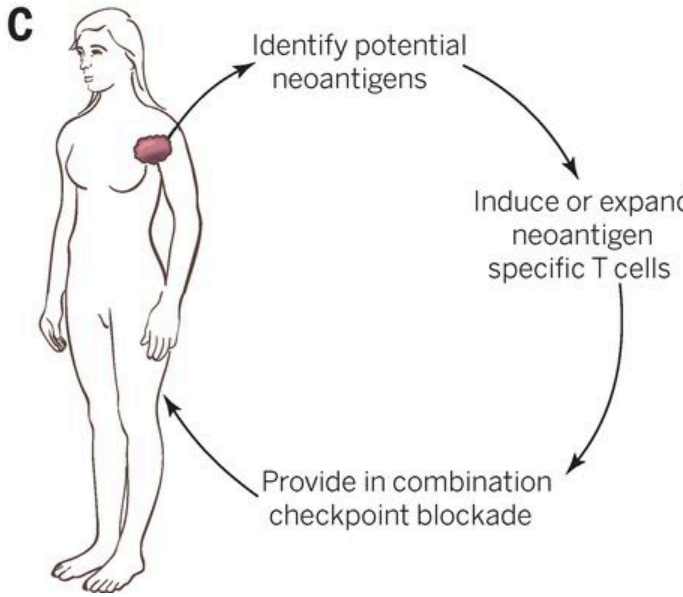
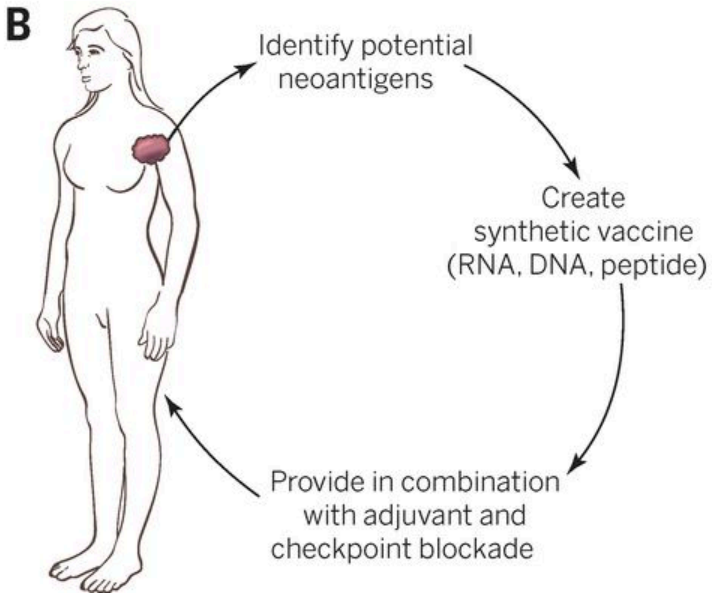
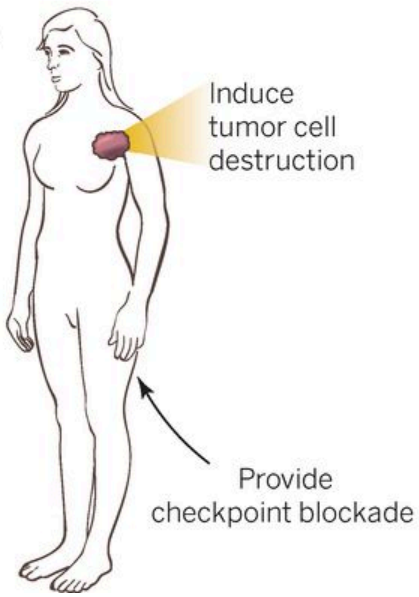
# Immune Checkpoint Blockade + Radiotherapy

- Immune checkpoint blockade is a type of immunotherapy that uses antibodies against the brakes in T cells, activating them and killing cancer cells
- We have shown that radiotherapy and immune checkpoint blockade complement each other
- Only with the combination of the two did we see improved survival, due to T cell-mediated control of the irradiated tumor and metastases





# Strategies to Establish Patient-Specific Anti-tumor Immunity

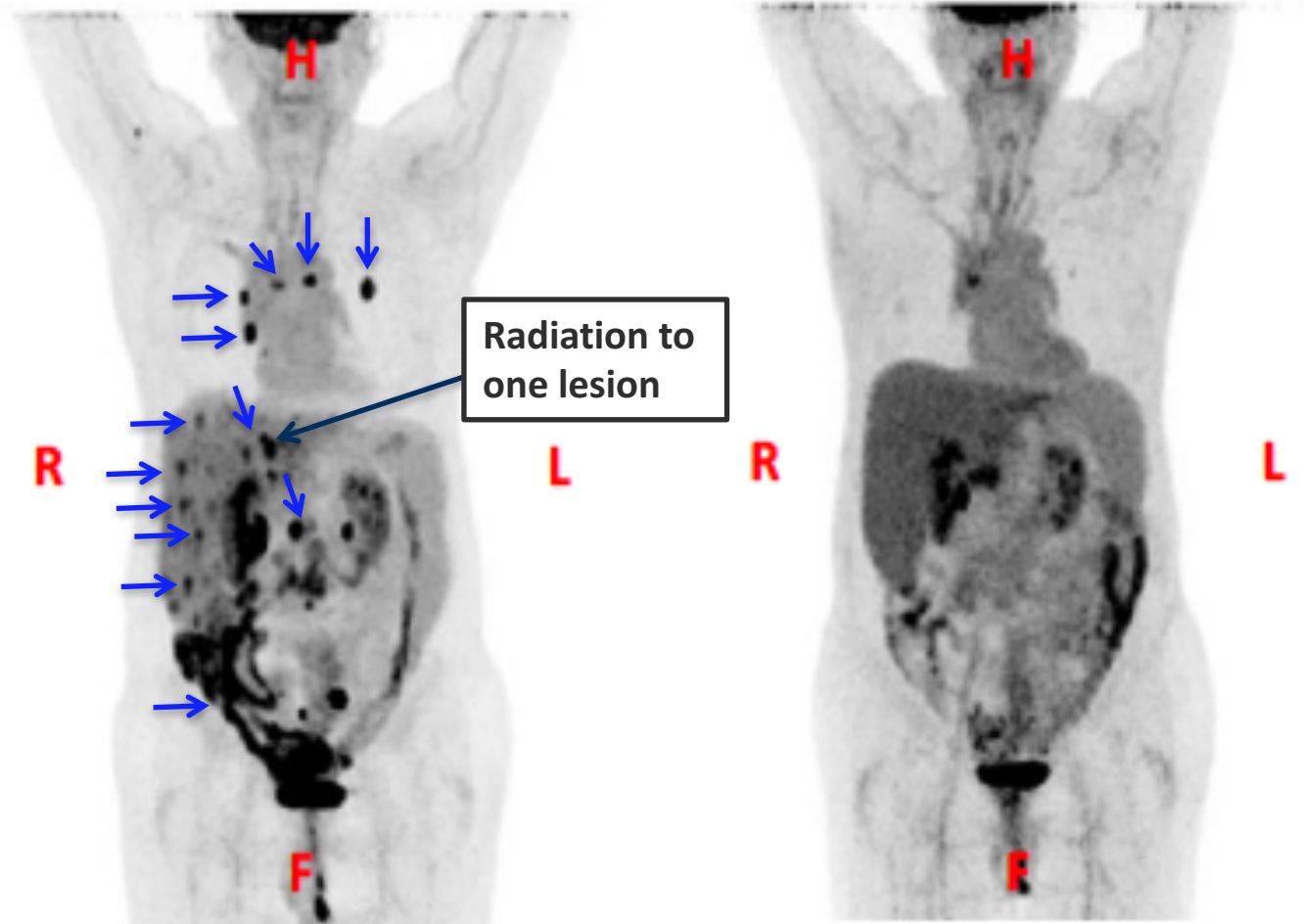


Ton N. Schumacher, and Robert D. Schreiber *Science* 2015;348:69-74



# Mr. P: Patient with Lung Cancer Metastasized To Liver, Lung and Bone achieves a complete response

Treated with **Radiation Plus Checkpoint Blockade**



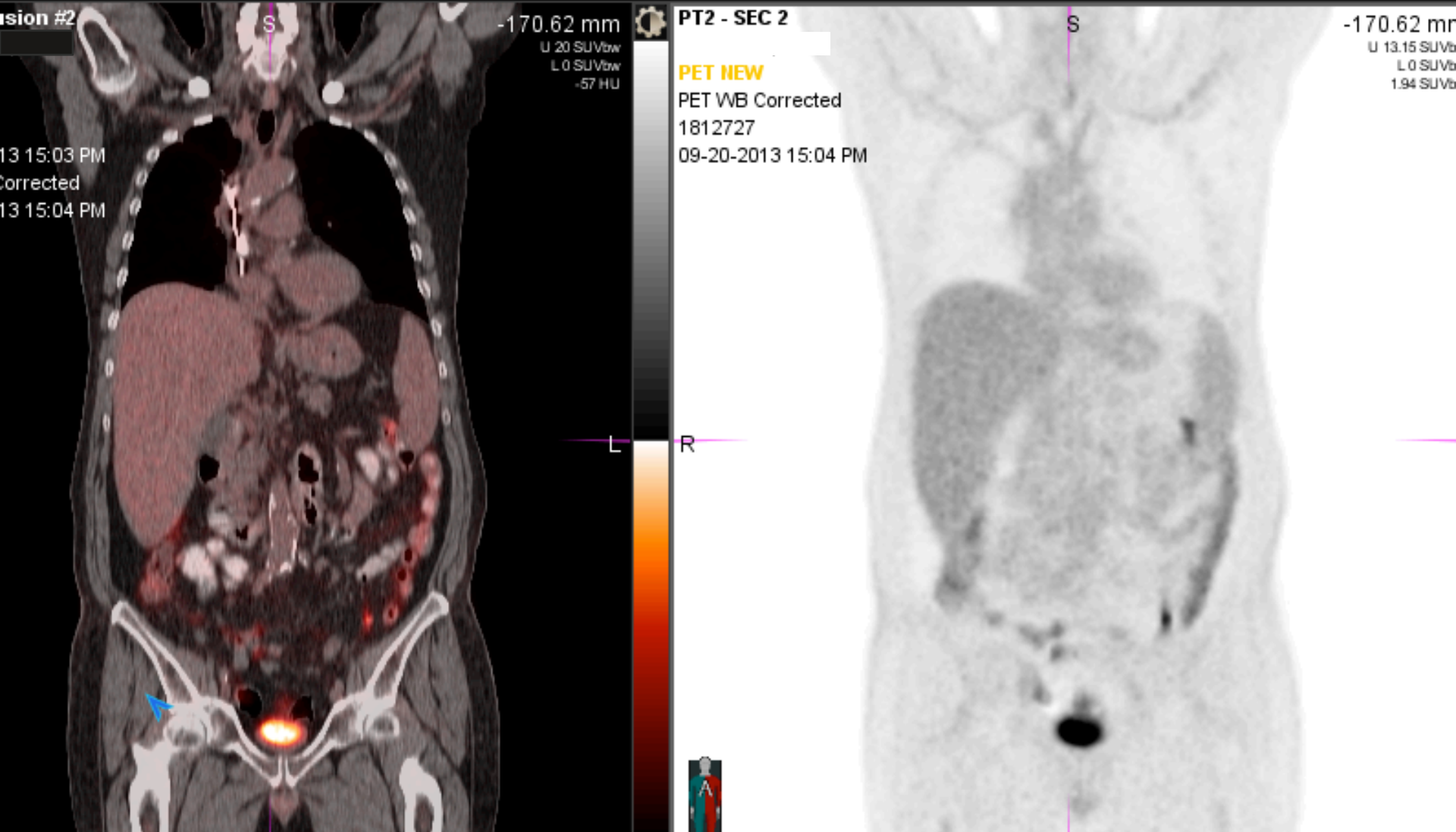
August 2012

January 2013

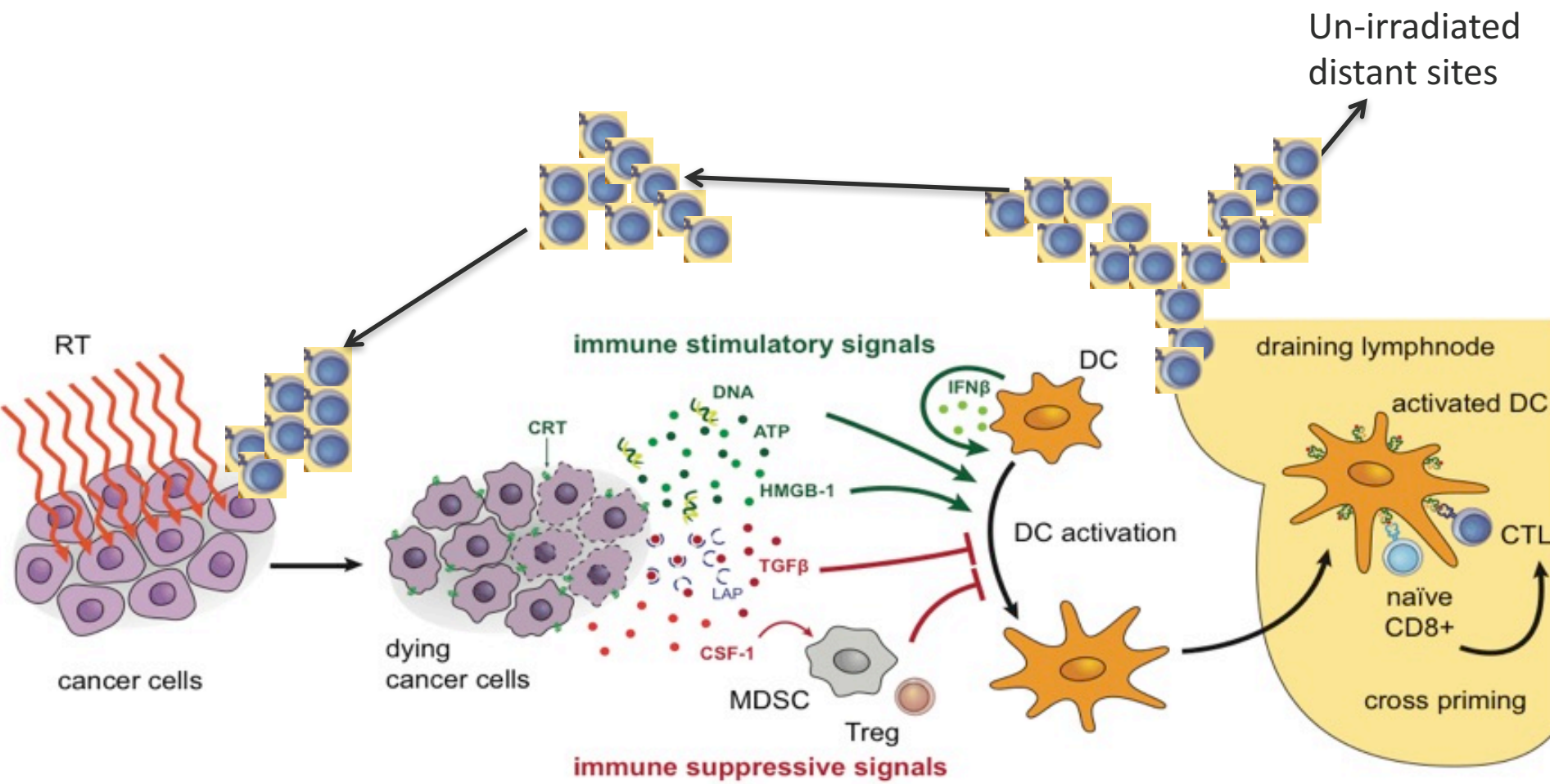
Golden et al. *New York Presbyterian*



# Mr. P: Four Years After Treatment



*Currently at 4 years without any other therapy  
and with no evidence of disease*



# Key Points

- Cancer kills by metastatic spread
- Cancer is the result of a failure of the immune system to reject it
- Cancer often “blinds” the immune system
- Radiation therapy can un-blind the immune system and restore an immune response
- Radiation and checkpoint blockade or other immunotherapies can lead to tumor rejection in patients with metastatic disease
- Radiation is a new class of immunotherapy

> 80 Clinical Trials are Now Testing the  
Combination of Radiotherapy and  
Immunotherapy



# Thank You!