



# Introduction to Cancer Immunotherapy

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# Ultra-Complete Disclosure

- Consulting:  
Amplimmune, Bristol Myers Squibb, Compugen, Dendreon, NexImmune, ImmunExcite, Janssen, Lilly, Merck, Novartis, Pierre Fabre, Potenza, Roche / Genentech, Vesuvius
- Patents  
Amplimmune, BMS
- Several of the Agents Discussed are NOT FDA-approved for use in cancer treatment

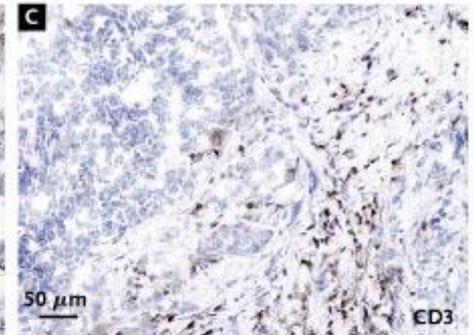
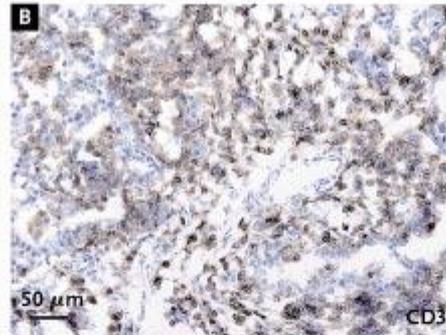
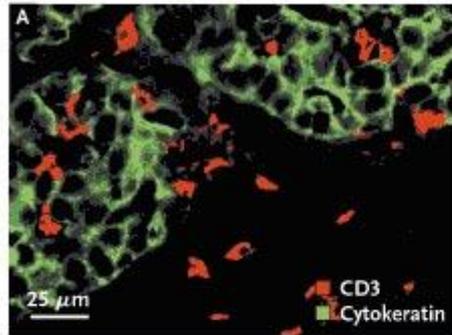
# Learning Objectives

- The immune system can (**sometimes**) eliminate cancer
  - Evidence from pathology studies
  - The immune editing hypothesis
- **Using** the Immune System to Treat Cancer (Immunotherapy)
  - Monoclonal Antibodies (Not covering today)
  - Cancer Vaccines
  - Adoptive Cellular Therapy (ACT)
  - Immune Checkpoint Blockade

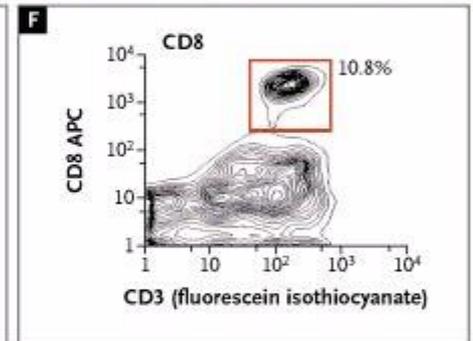
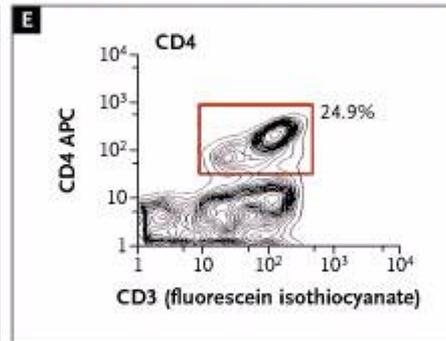
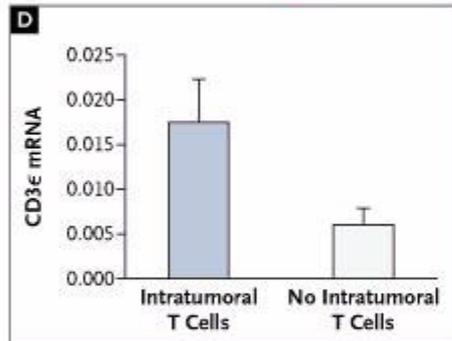
# Endogenous Anti-Tumor Immunity

# Are There Immune Cells in Tumors ?

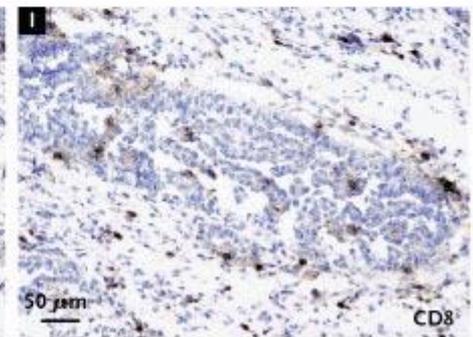
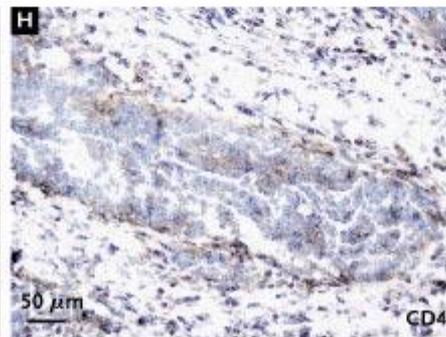
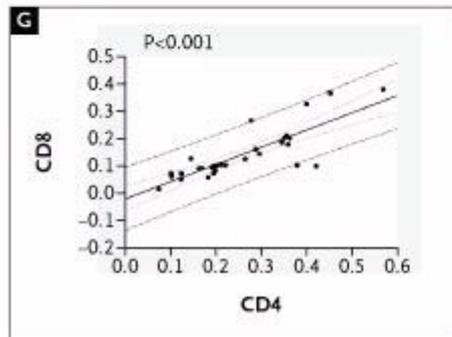
CD3 (all T Cells)



CD4 or CD8  
(By Flow)

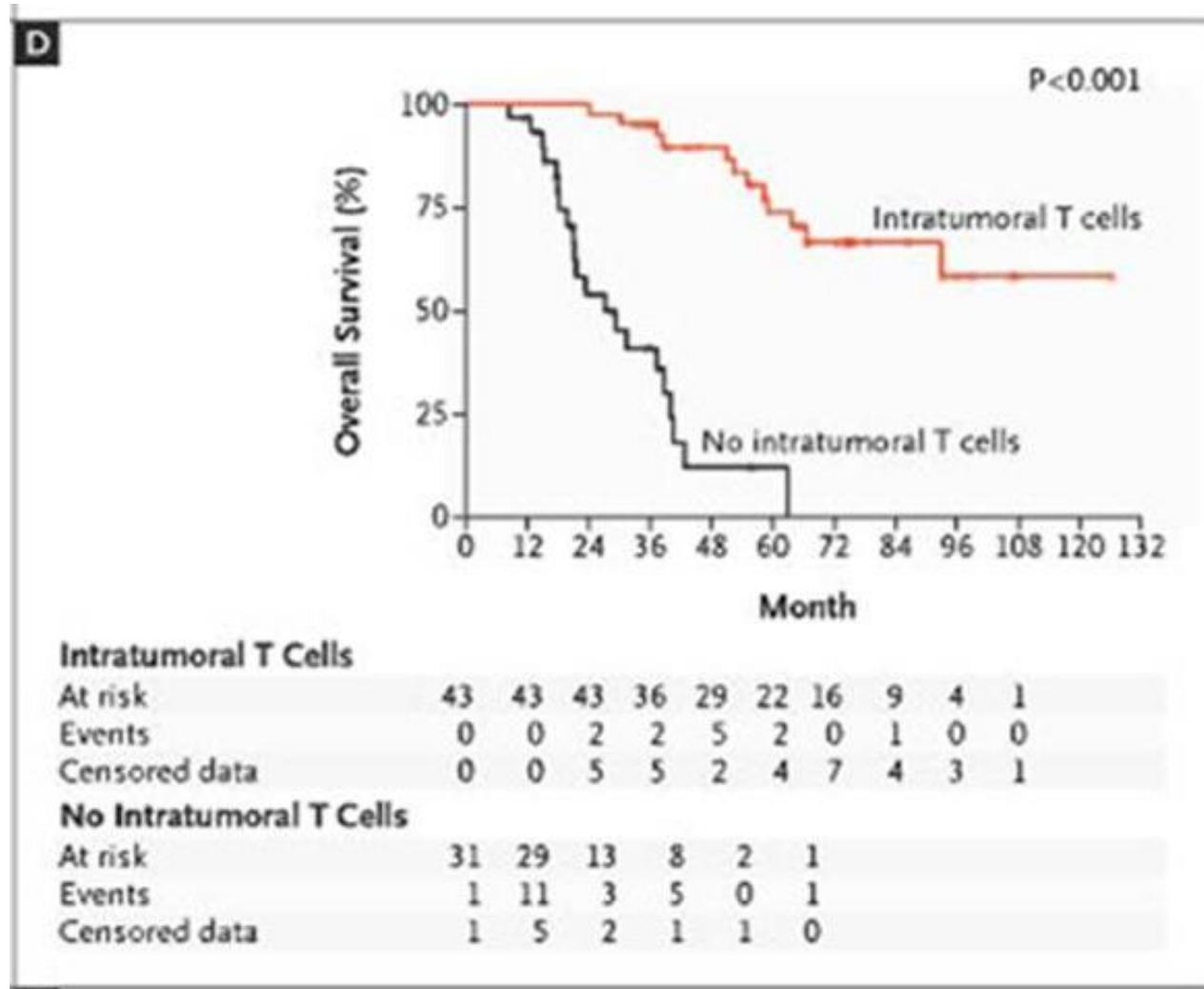


CD4 or CD8  
(By IHC)

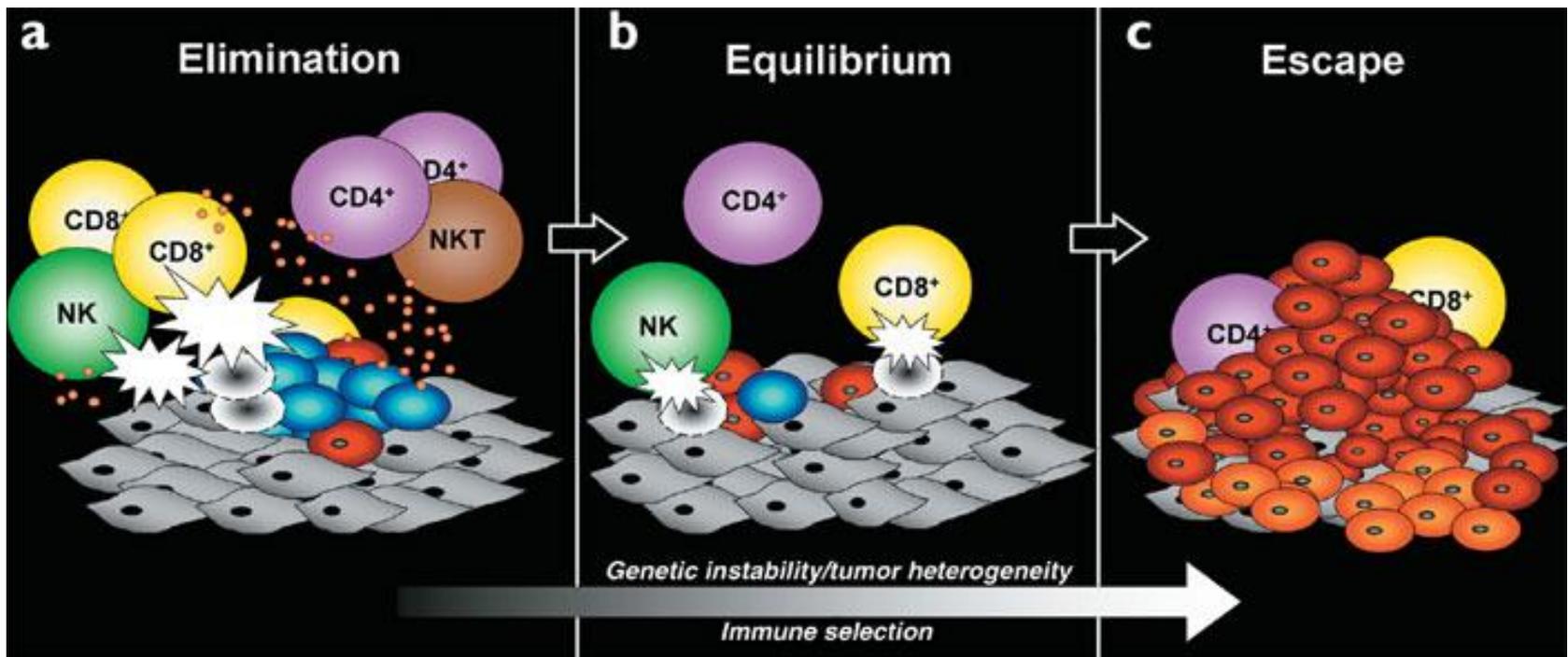


# Do They Matter ?

Stage IV Ovarian Cancer Patients  
With a Complete  
response to  
chemotherapy



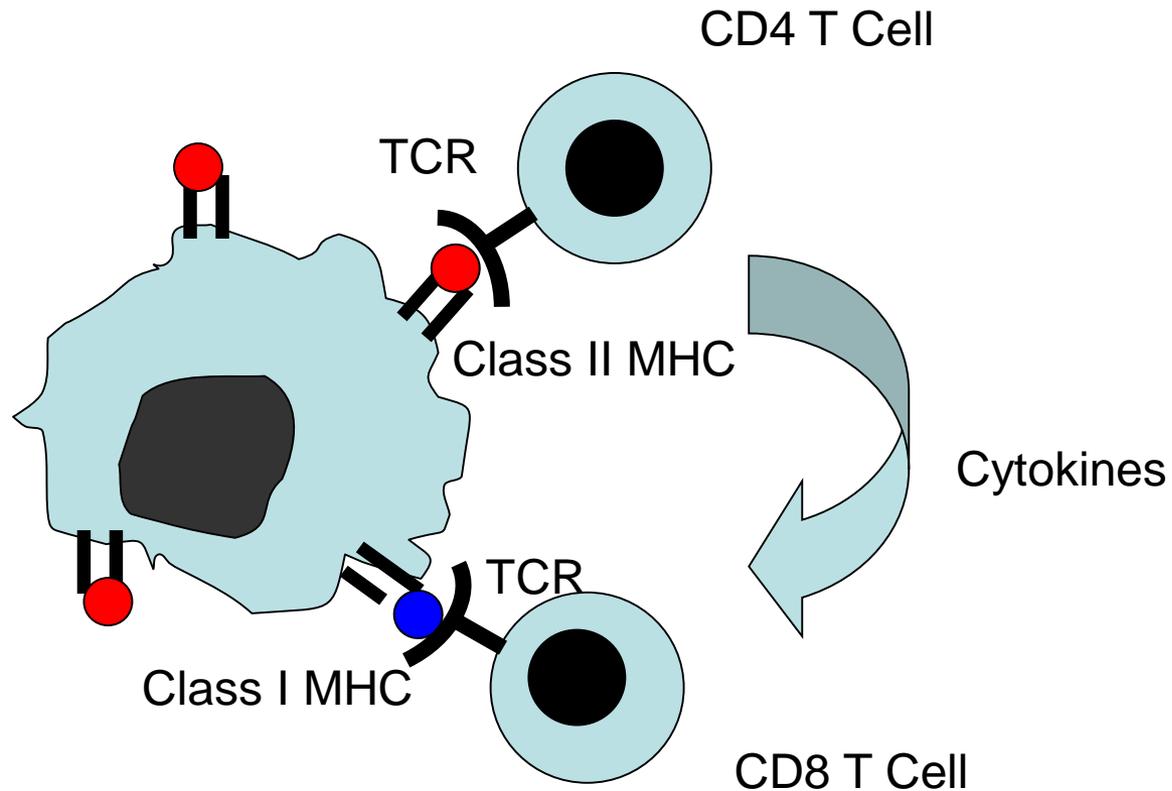
# The Immune Editing Hypothesis (3E's)



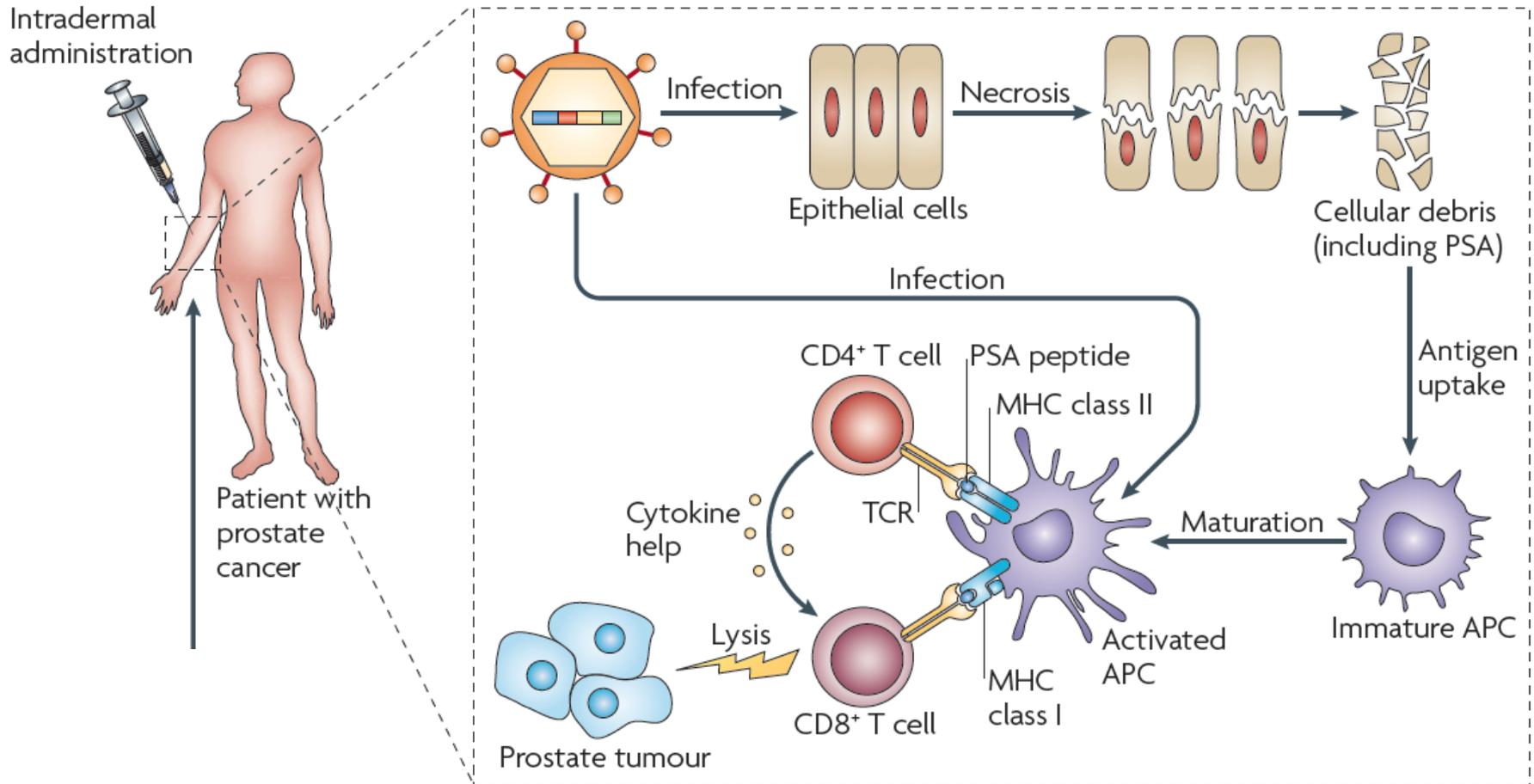
# Cancer Vaccines

# Cancer Vaccine Goal ....

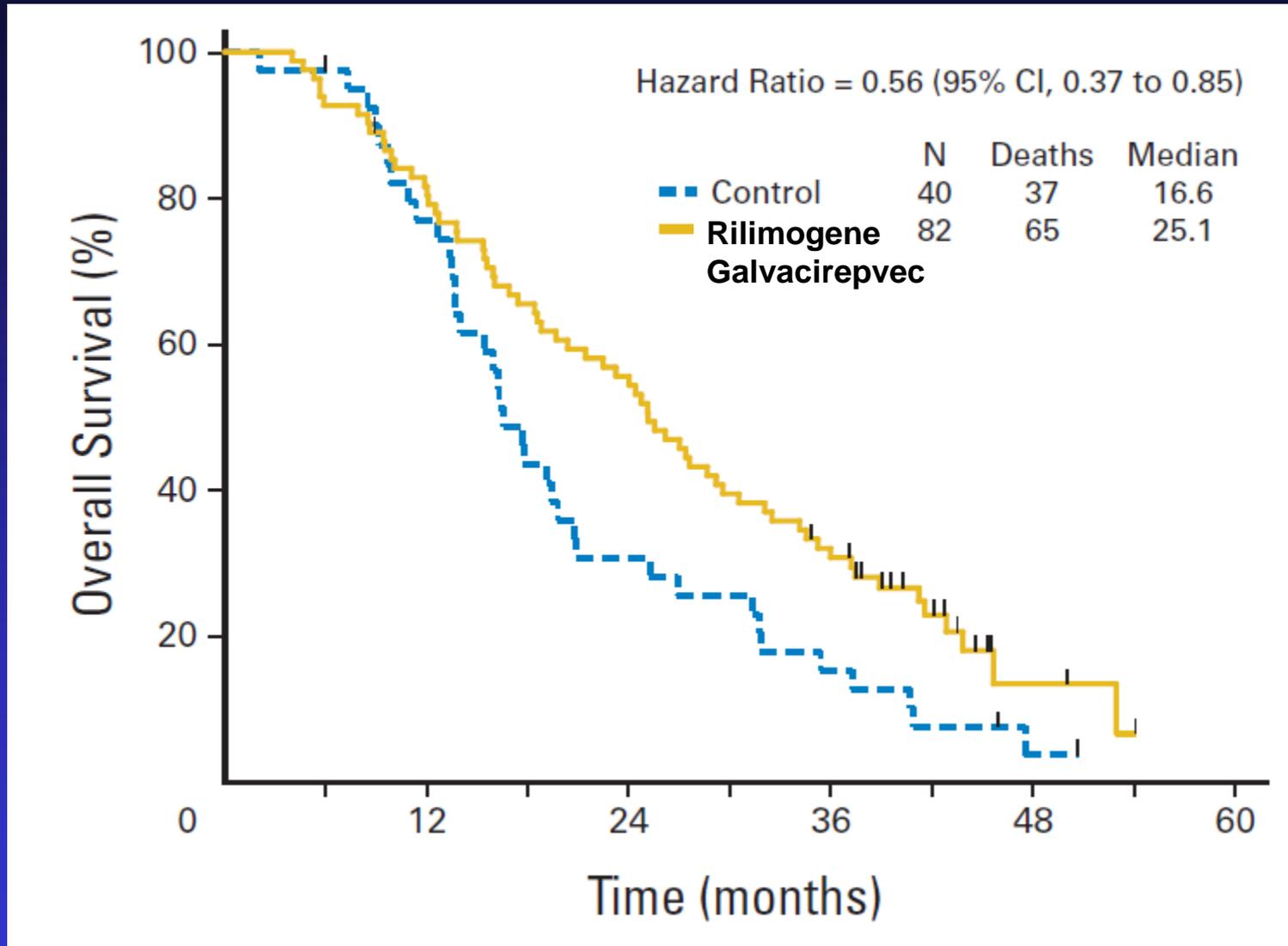
Dendritic Cells Traffic and Present Antigen To Specific CD4 and CD8 T Cells in the Draining Lymph node



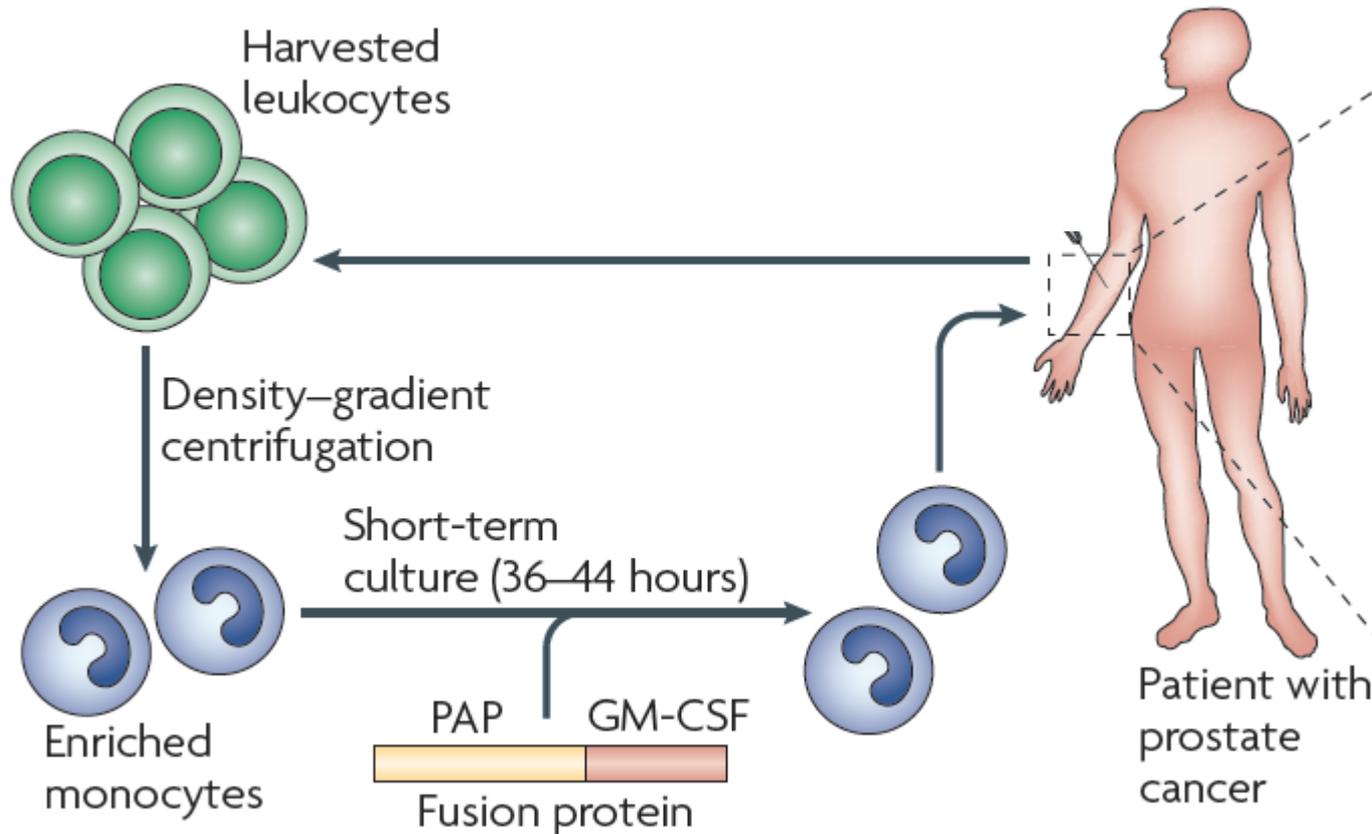
# A Viral-Based Vaccine For Prostate Cancer



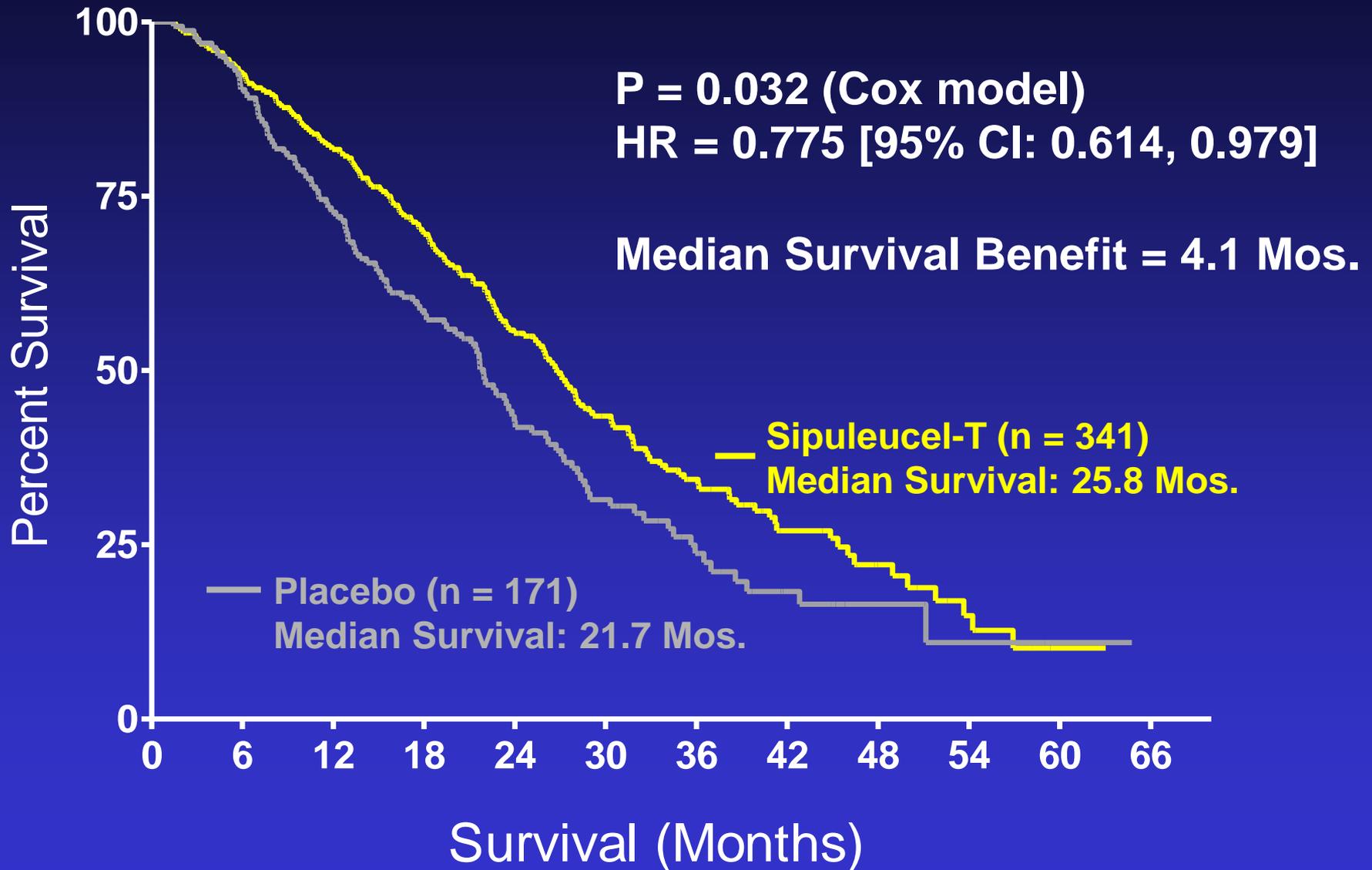
# Evidence for Activity



# A “Dendritic Cell” Vaccine: Sipuleucel T



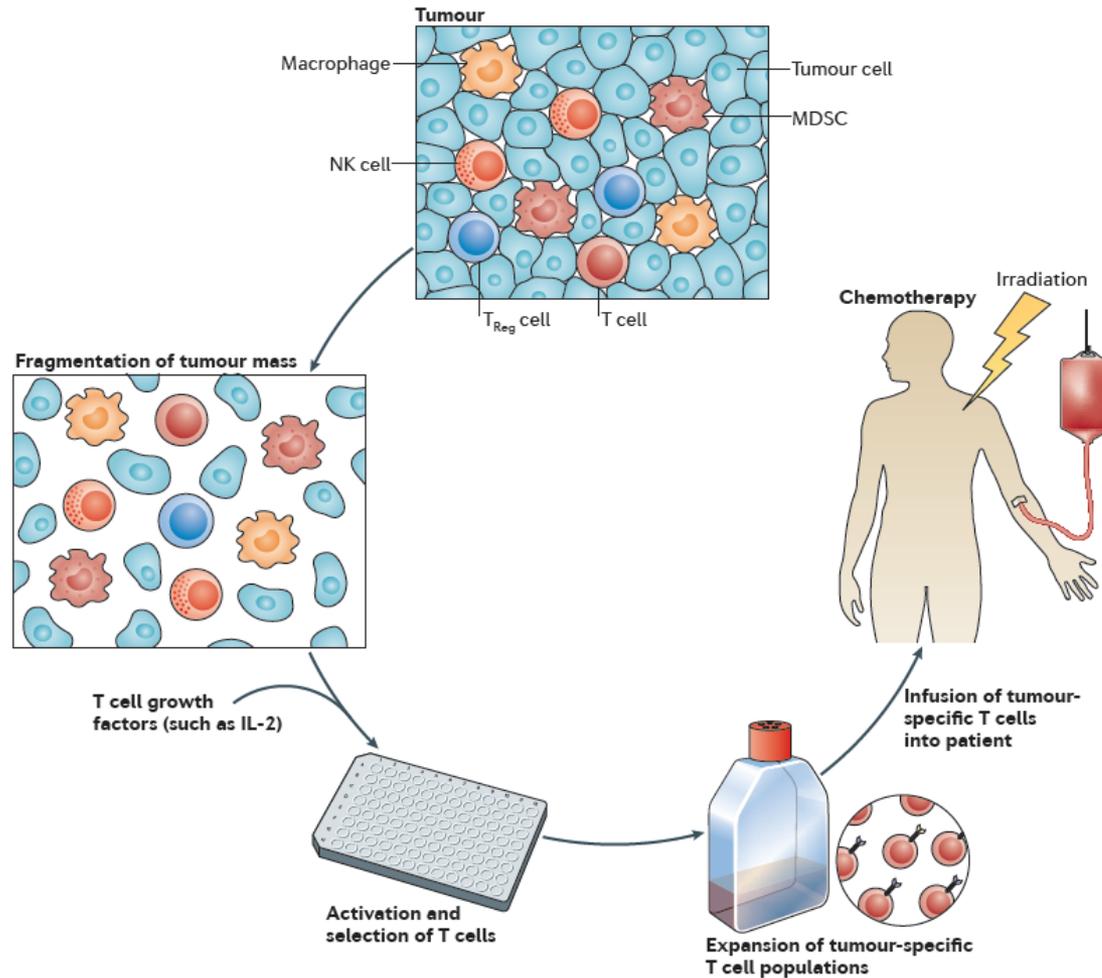
# IMPACT Overall Survival: Primary Endpoint Intent-to-Treat Population



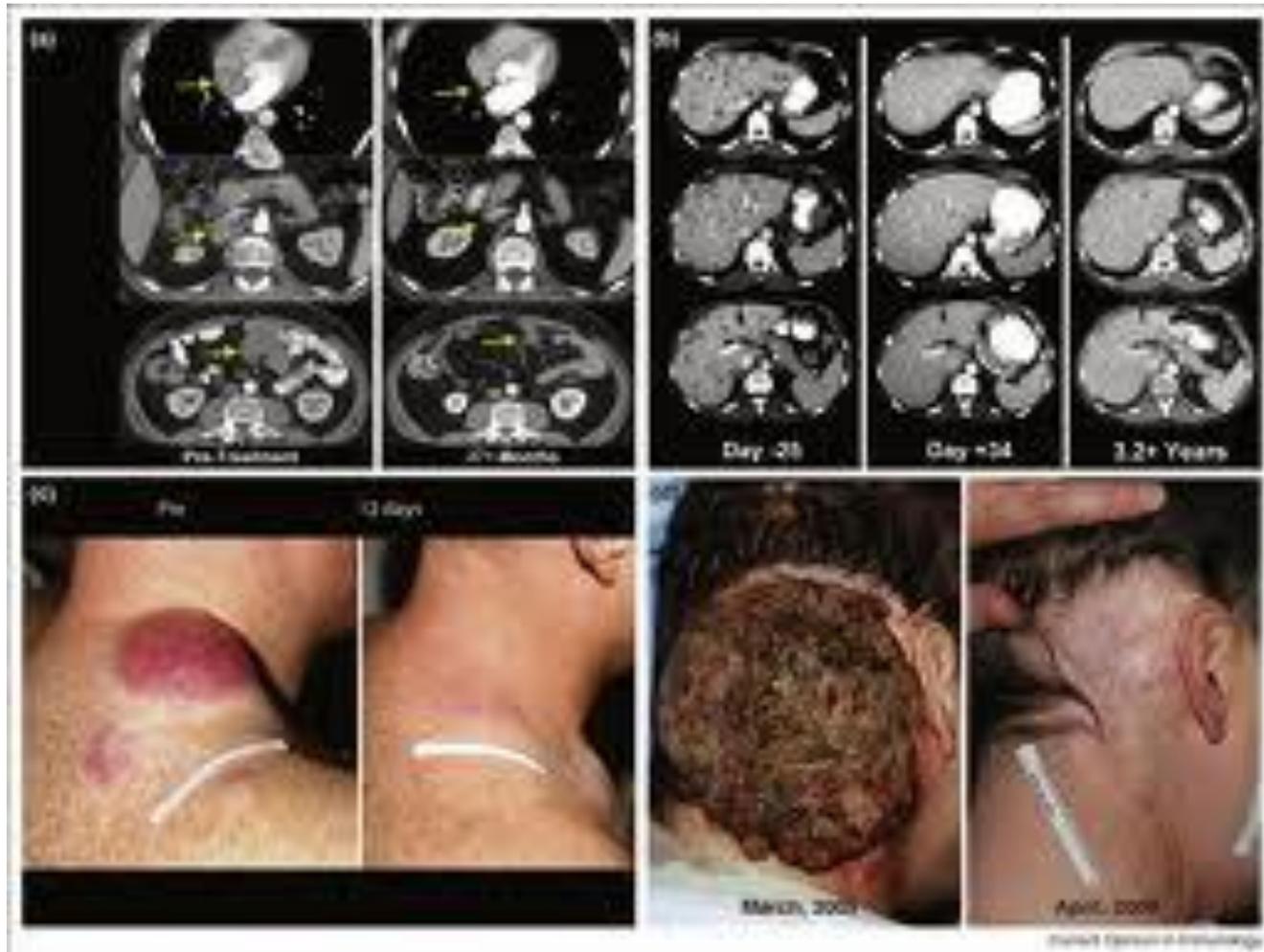
# Adoptive Cellular Therapy (ACT)

# Getting the Lymphocytes From The TUMOR itself

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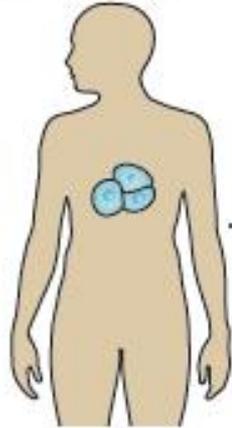


# Seems to Work



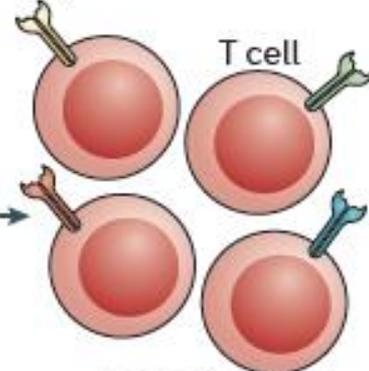
# Re-Engineering A Patient's T Cells

Tumour sample from patient



TCR

T cell

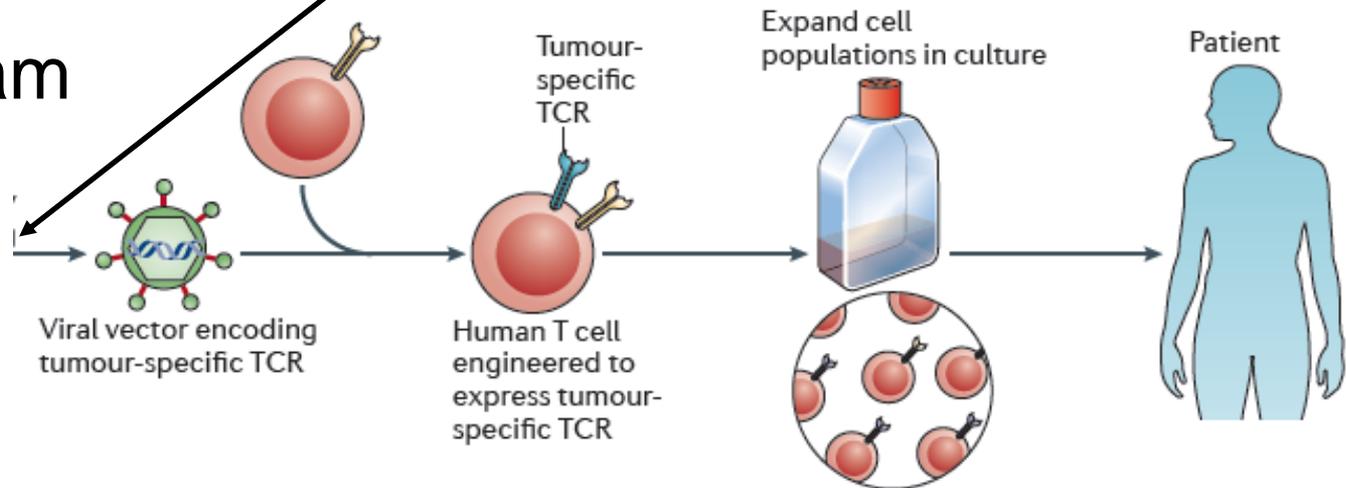


T cells isolated from tumour

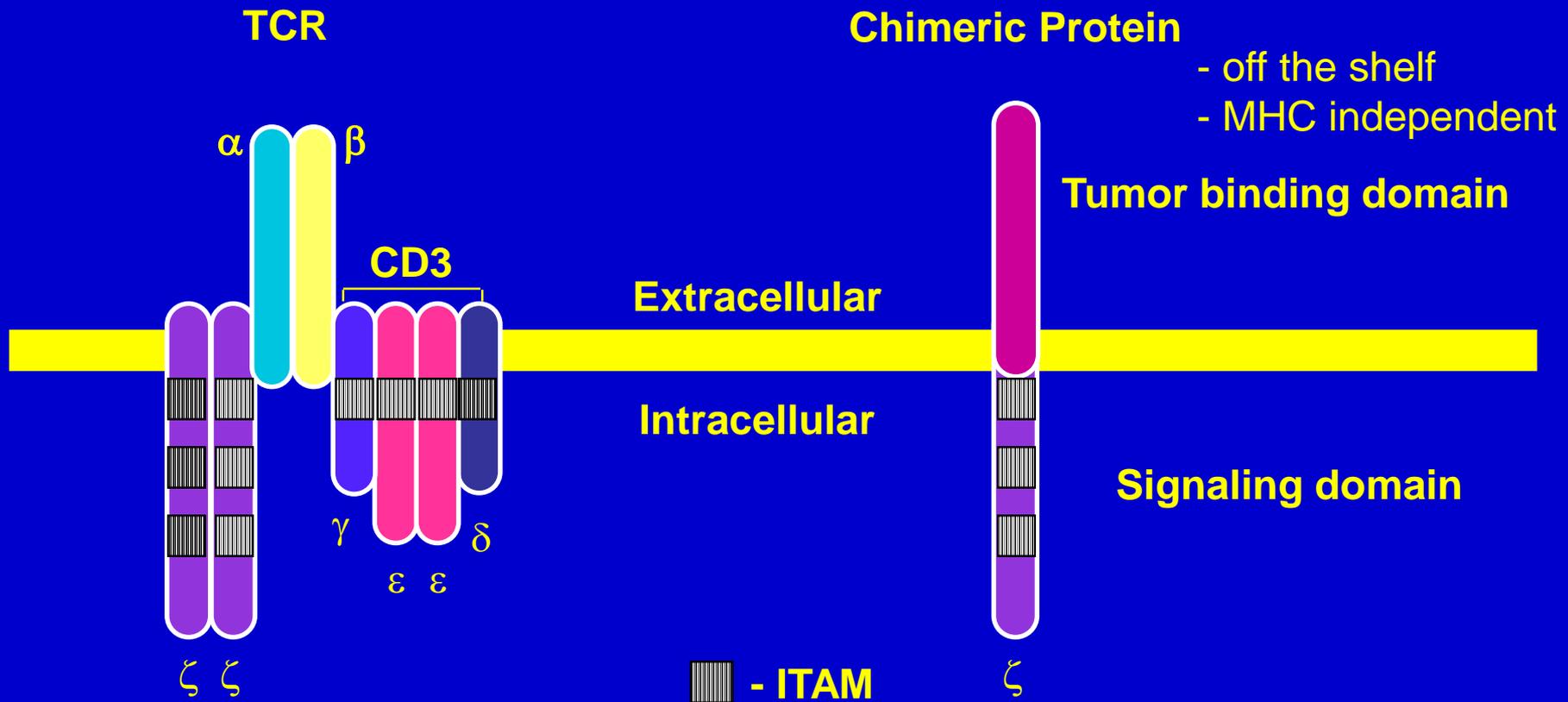
Avidity testing

1. Pick a winner

2. Re-program T cells

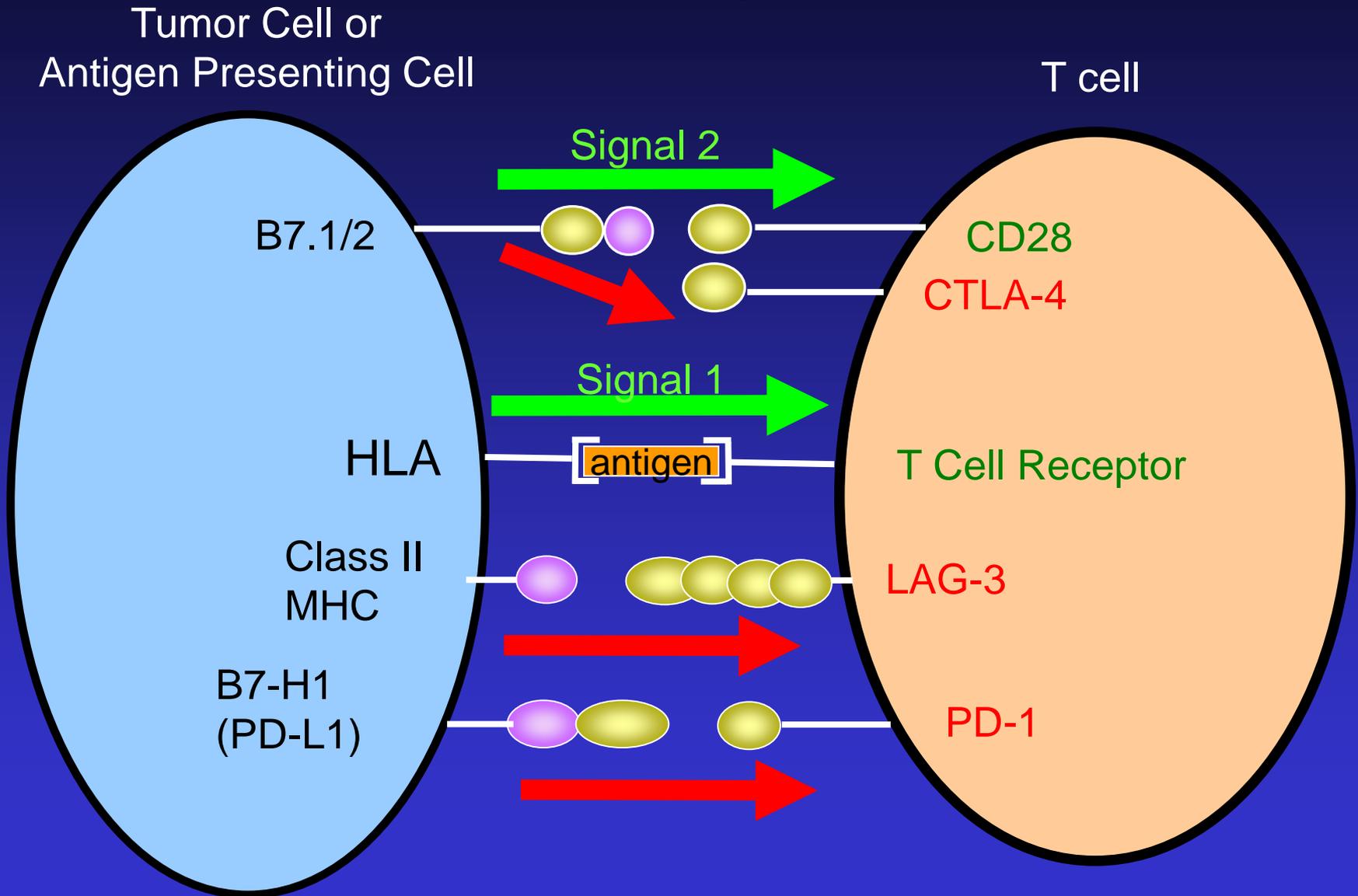


# A "Chimeric" Antigen Receptor (CAR)

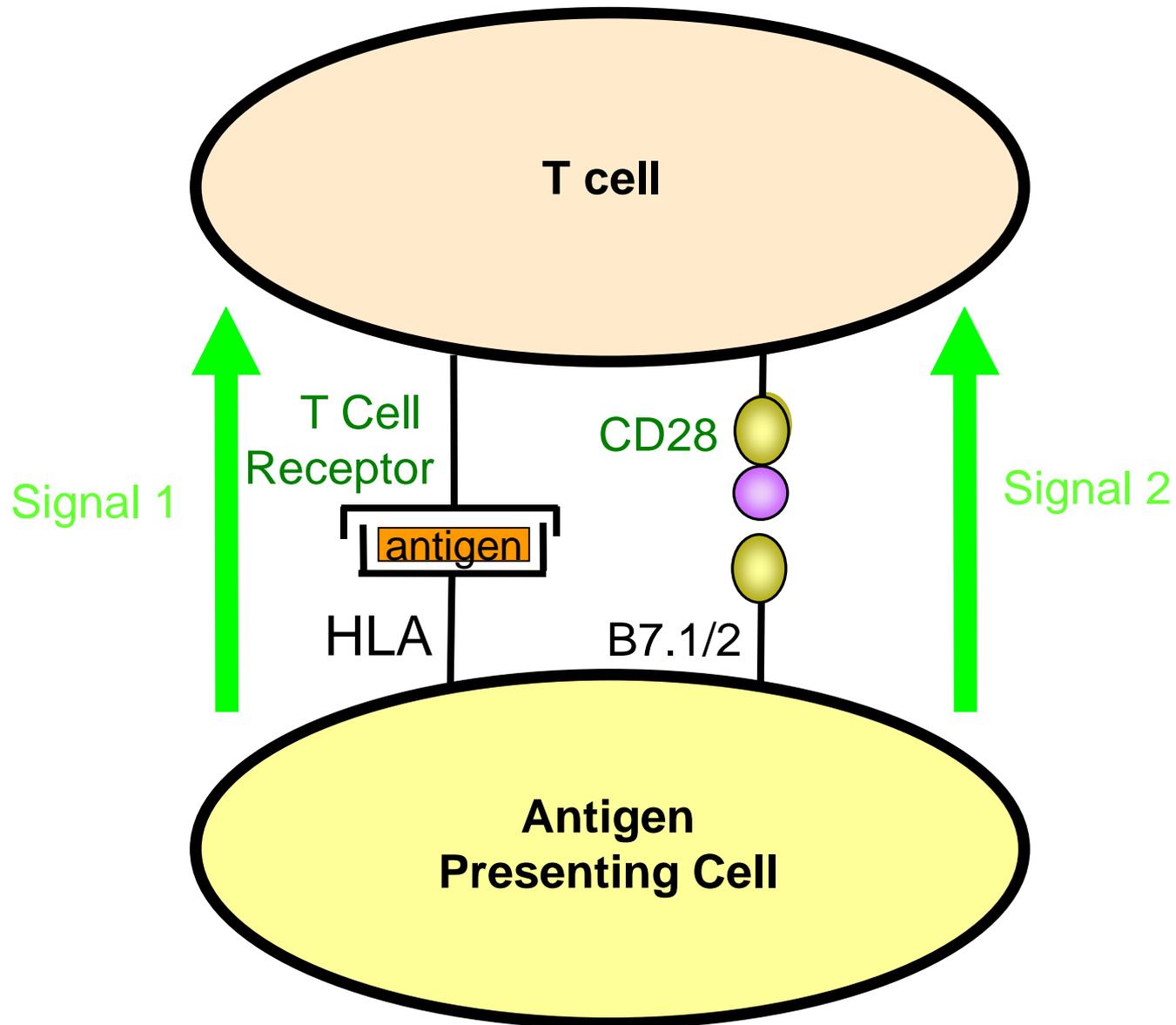


# Immune Checkpoints

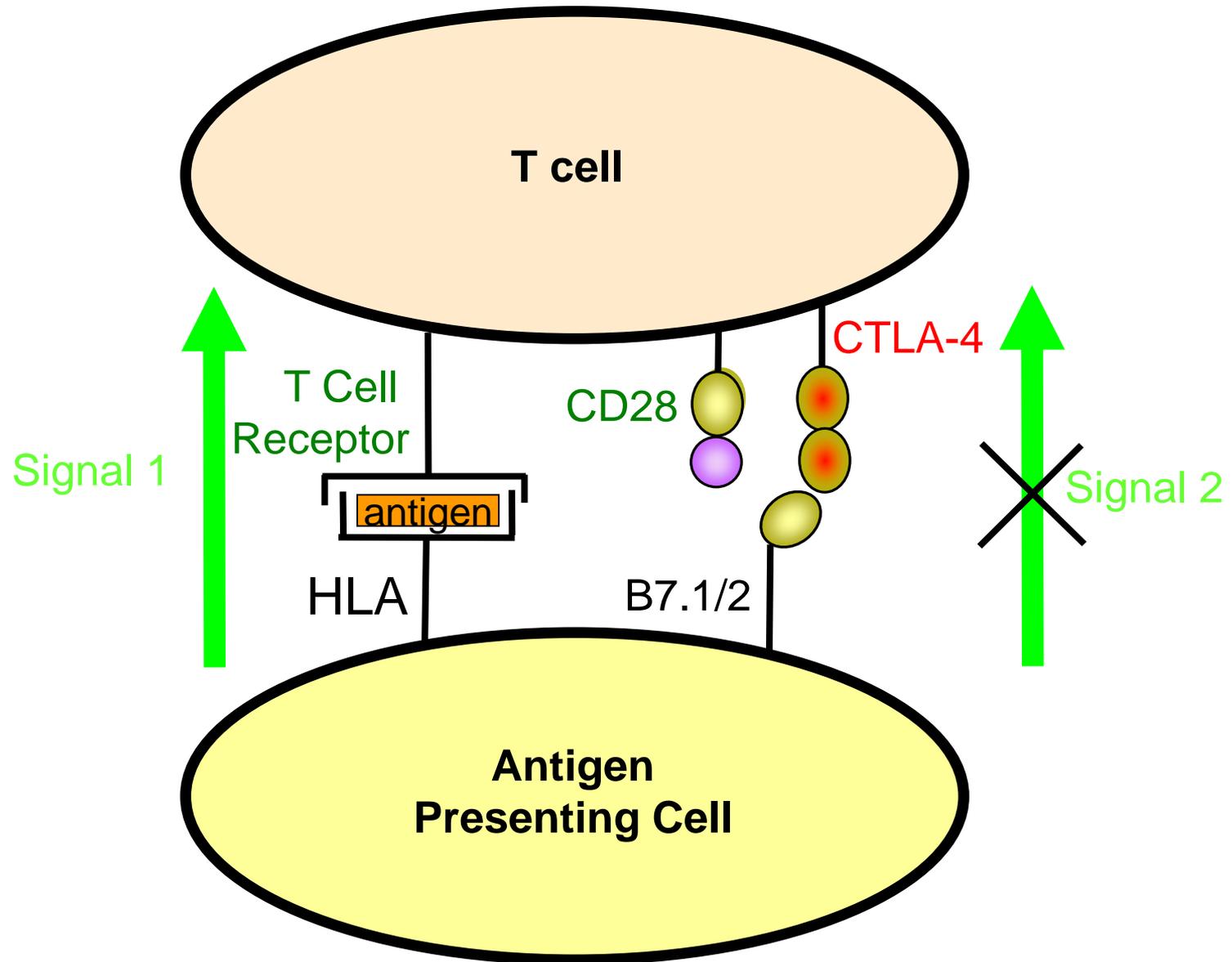
# Immune Checkpoint Molecules Attenuate a T Cell Response



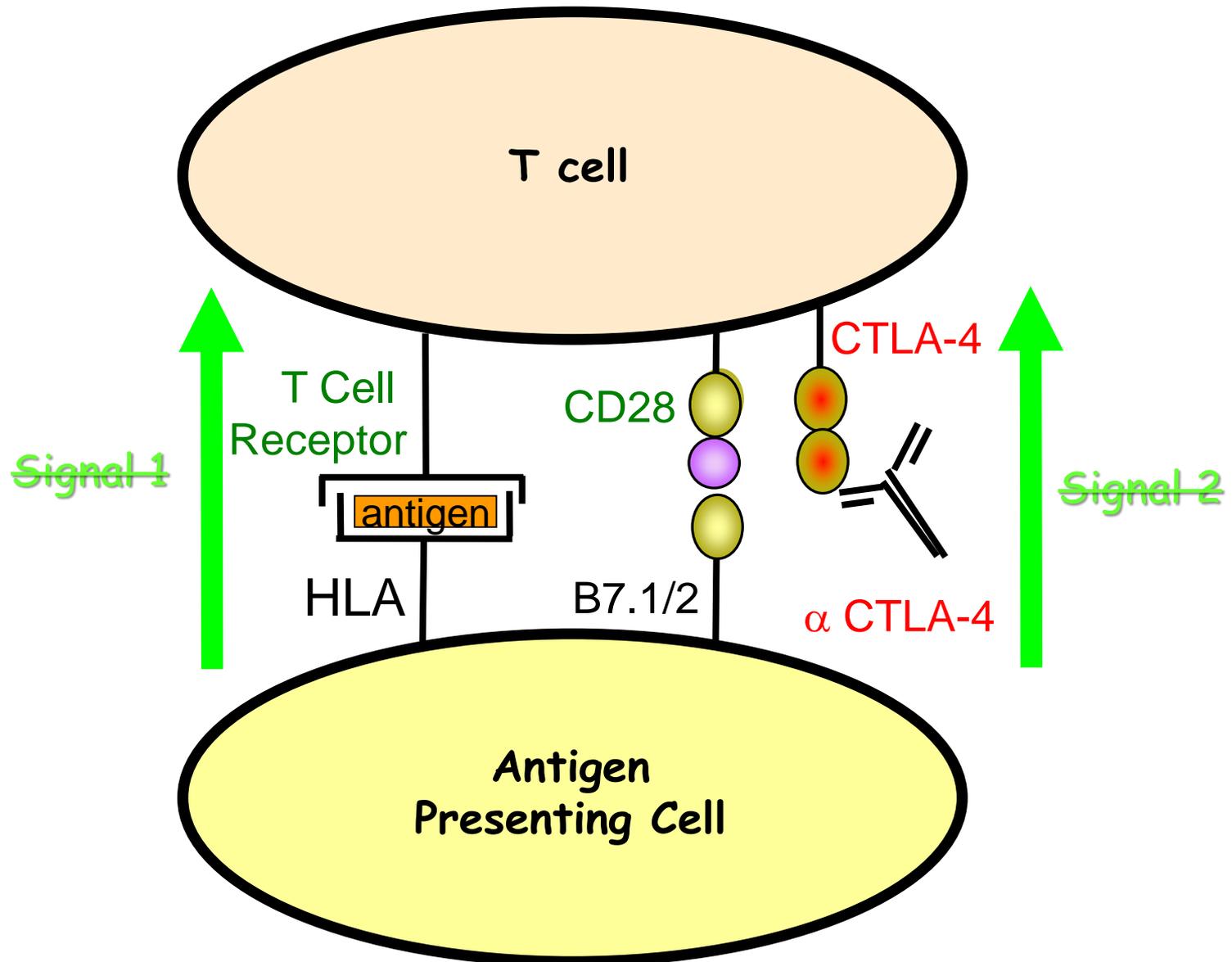
# T Cell Activation Requires TWO Signals



# CTLA-4 Prevents Normal T Cell Activation

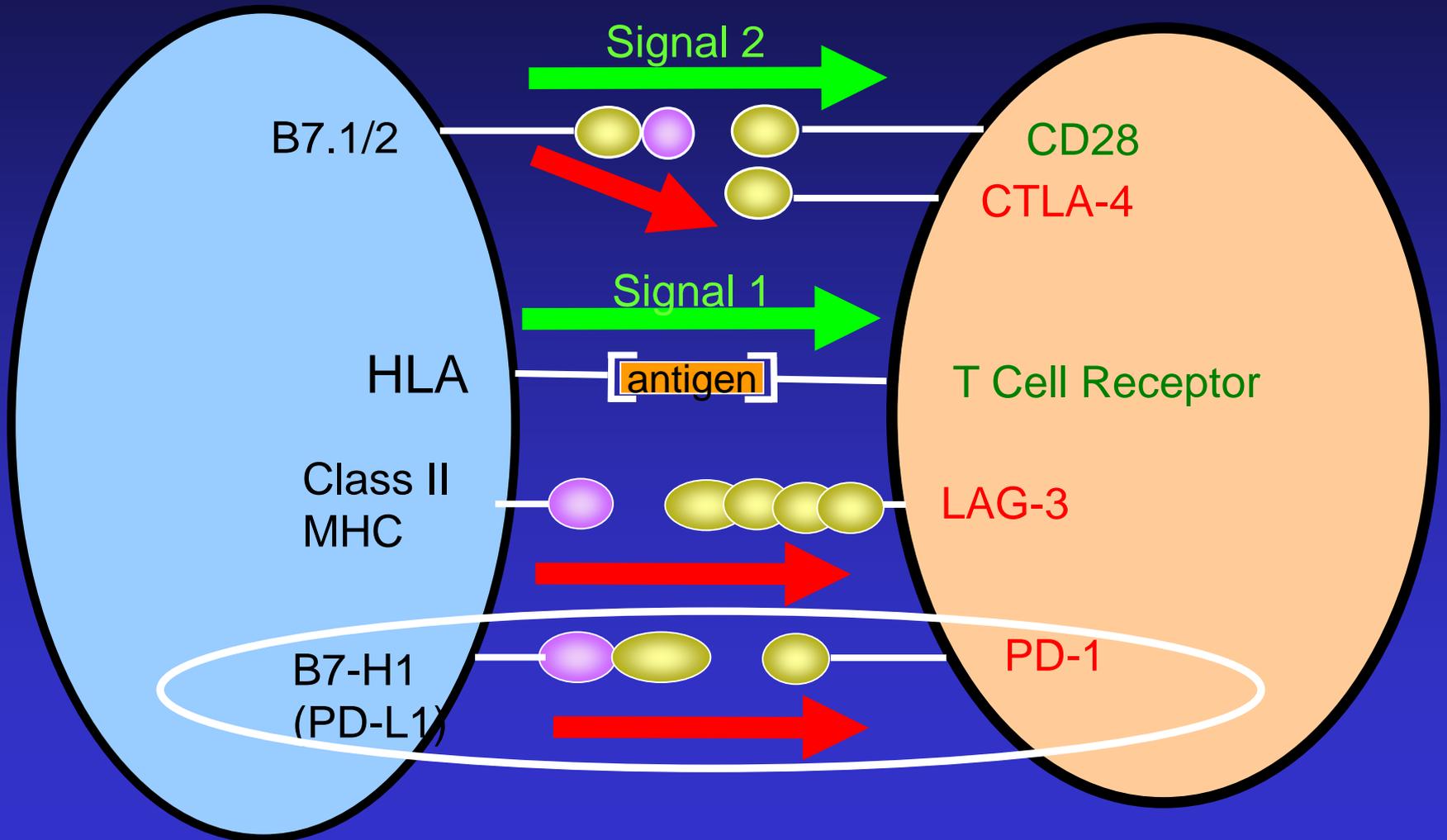


# Anti-CTLA-4 Blocks the CTLA-4 Checkpoint and Restores T Cell Activation



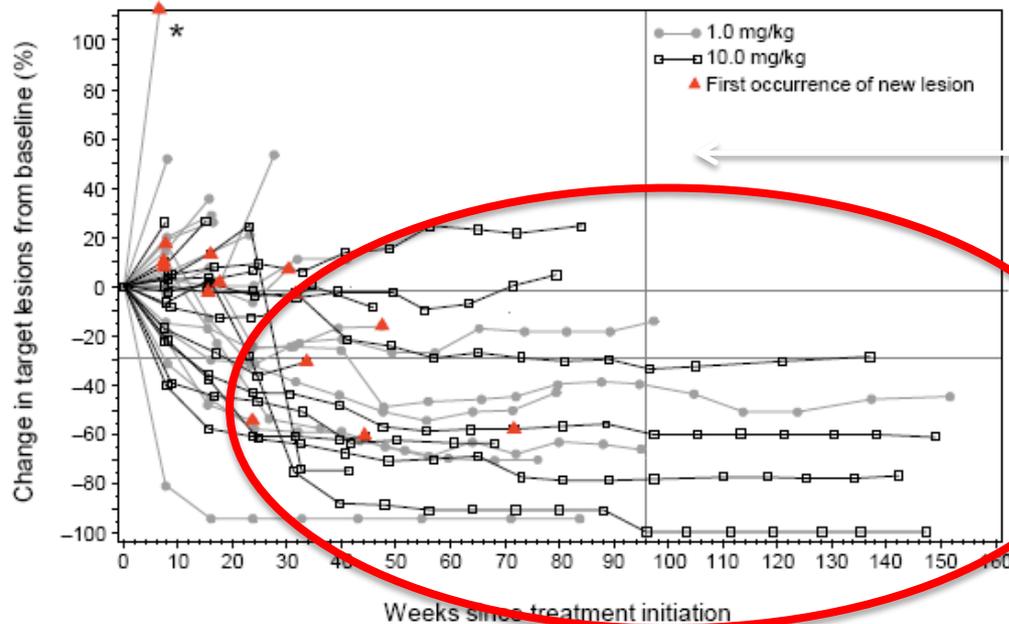
Tumor Cell or  
Antigen Presenting Cell

T cell



# A Second Trial of Anti-PD-1 – Higher / More Frequent Dosing - Results in Kidney Cancer Patients

- Generally tolerable: fatigue, rash, pruritus, diarrhea
  - 3 deaths: pneumonitis (non-RCC)
- Preliminary efficacy in heavily pre-treated patients:
  - 29% objective responses
  - Median PFS 7.3 months



All stopped therapy

**Durability of  
Response  
Even Off Drug**

# Summary

- Cancer Vaccines:
  - Sipuleucel – T = FDA approved
  - Intra-Tumoral Vaccination in Melanoma
- Chimeric Antigen Receptor Expressing T Cells (CAR-T)
  - Promising early results in hematological malignancies
  - Being commercialized by many companies
- Immune Checkpoint Blockade
  - Anti-CTLA-4 (Ipilimumab) is FDA-approved to treat melanoma
  - Anti-PD-1 antibodies FDA-approved to treat melanoma, NSCLC
  - NINE anti-PD-1 antibodies are in clinical trials