

The Immune System in Cancer: Impact on Cancer Immunotherapy, The Most Successful Approach to Cancer Treatment Ever

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Depts. of Medicine, and Microbiology, Immunology & Molecular Genetics

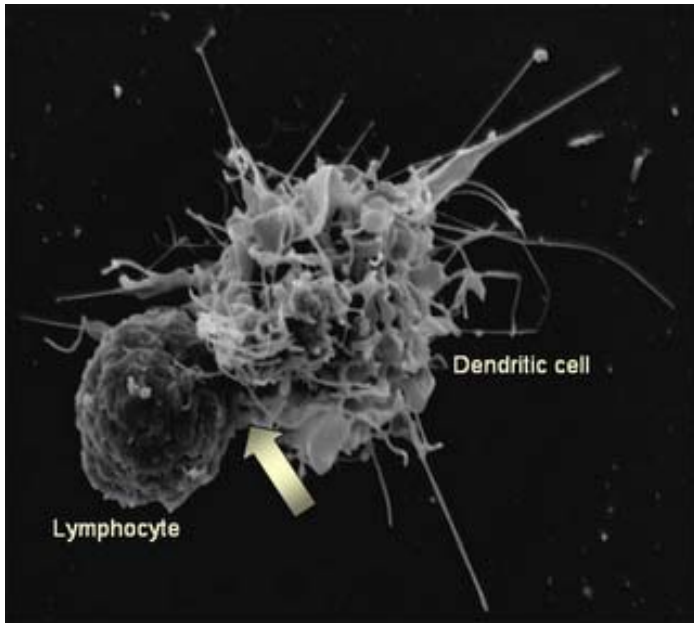
UT Health Cancer Center

University of Texas Health, San Antonio, TX USA

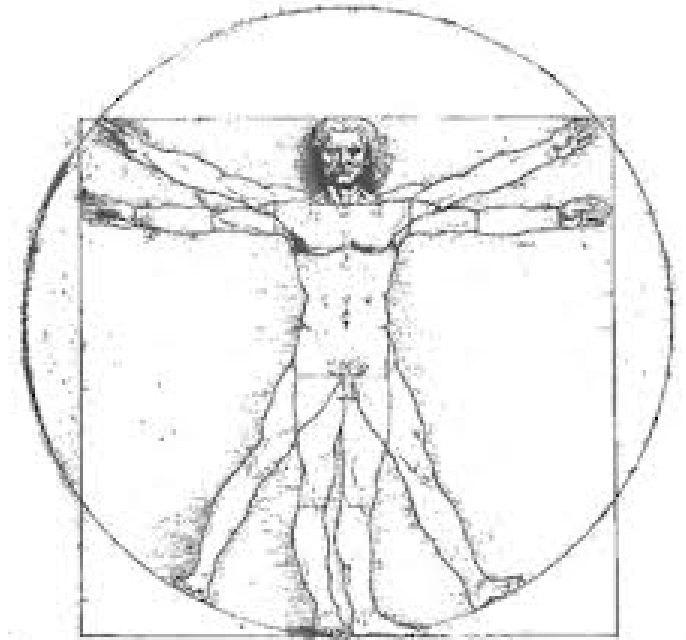
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South Texas Research Facility



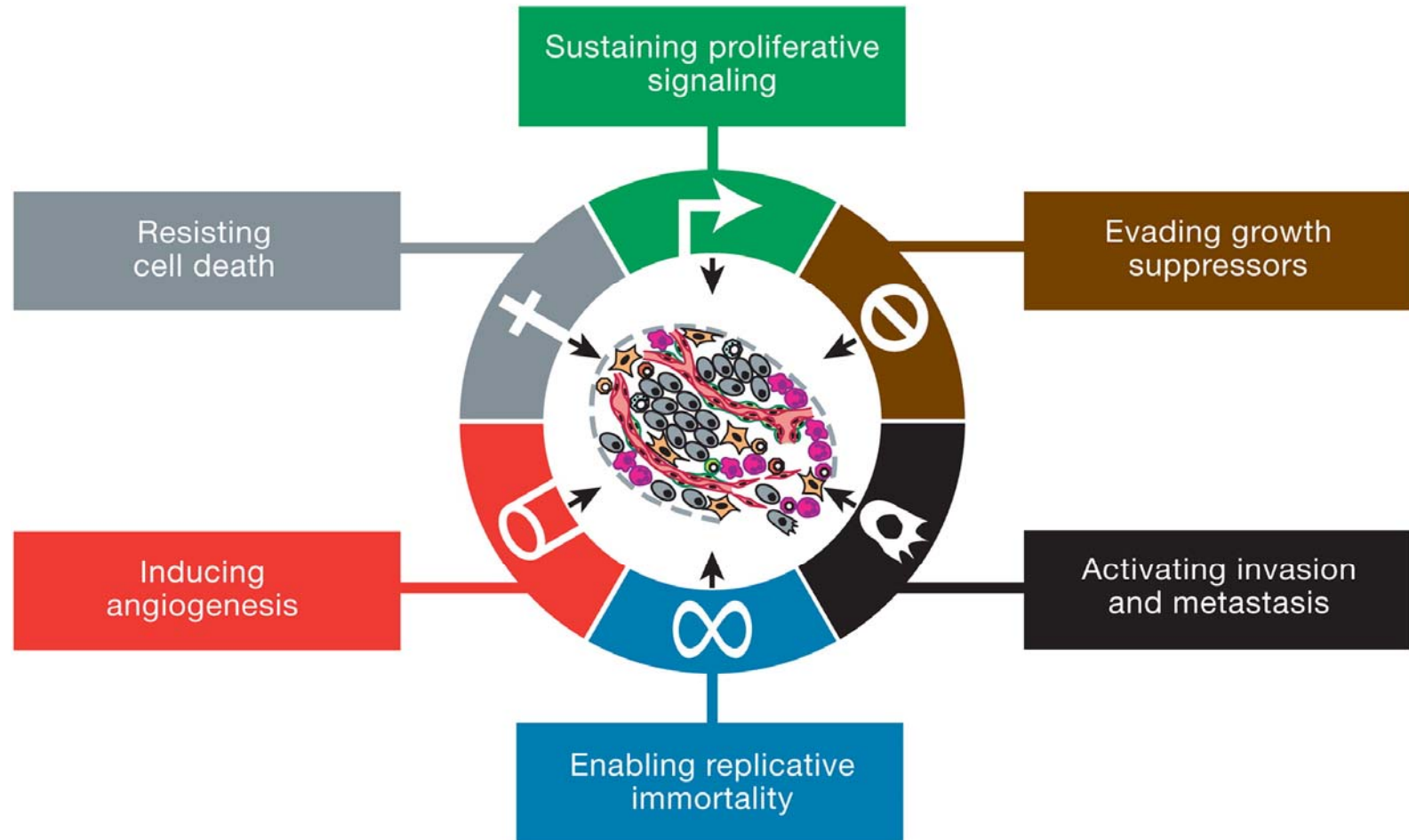
Overview



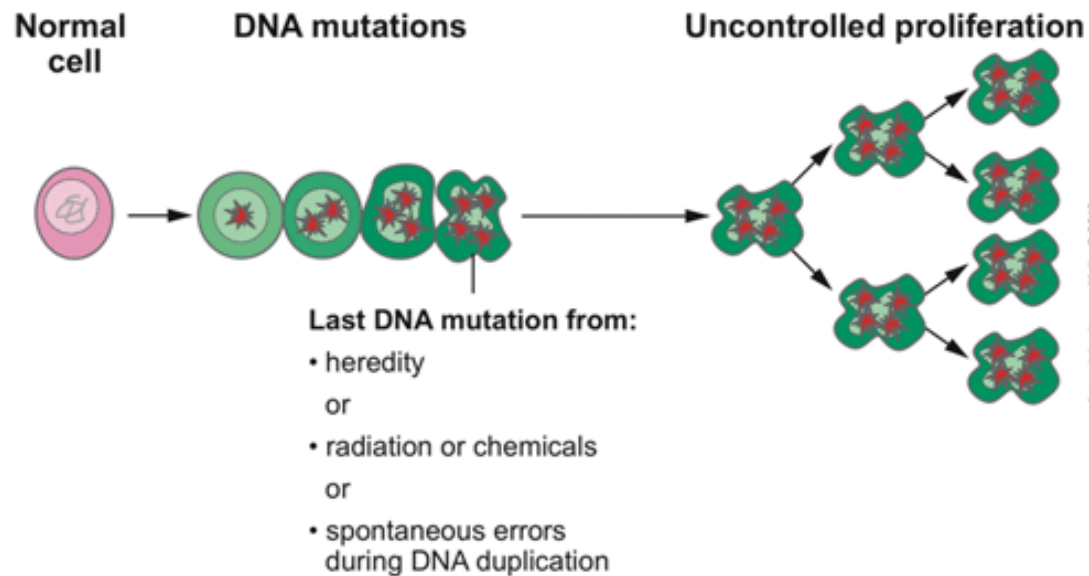
- Tumor immunology and immunotherapy
- Excellent approved cancer immunotherapy agents
- Some of our trial data
- New immunotherapy trials in 2019 at Mays Cancer Center

6 Hallmarks of Cancer

Hannahan and Weinberg *Cell* 2000



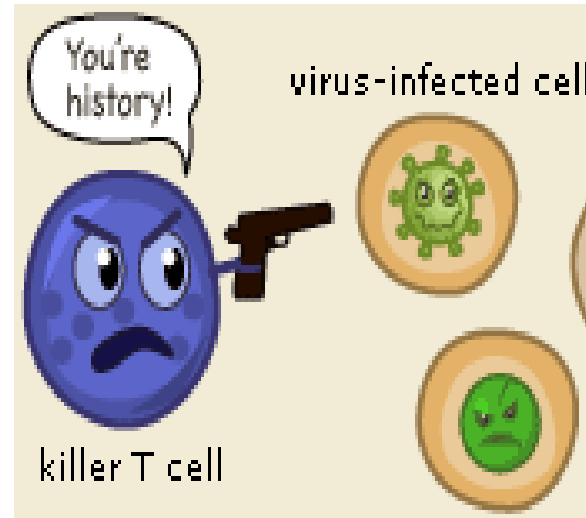
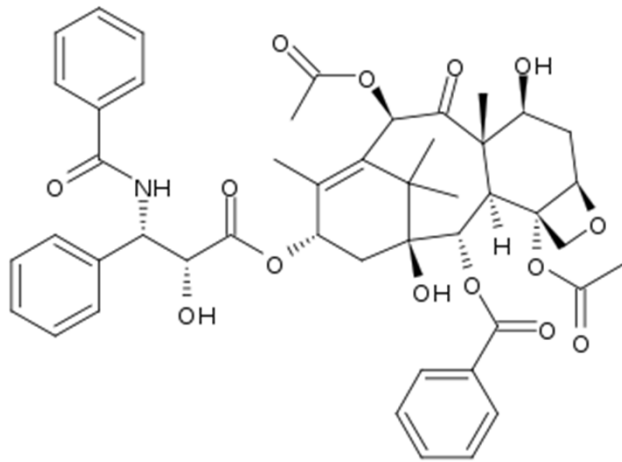
Cancer Arises From DNA Mutations in Cells



Artwork by Jeanne Kelly, © 2010.

Immunity is extremely sensitive and specific

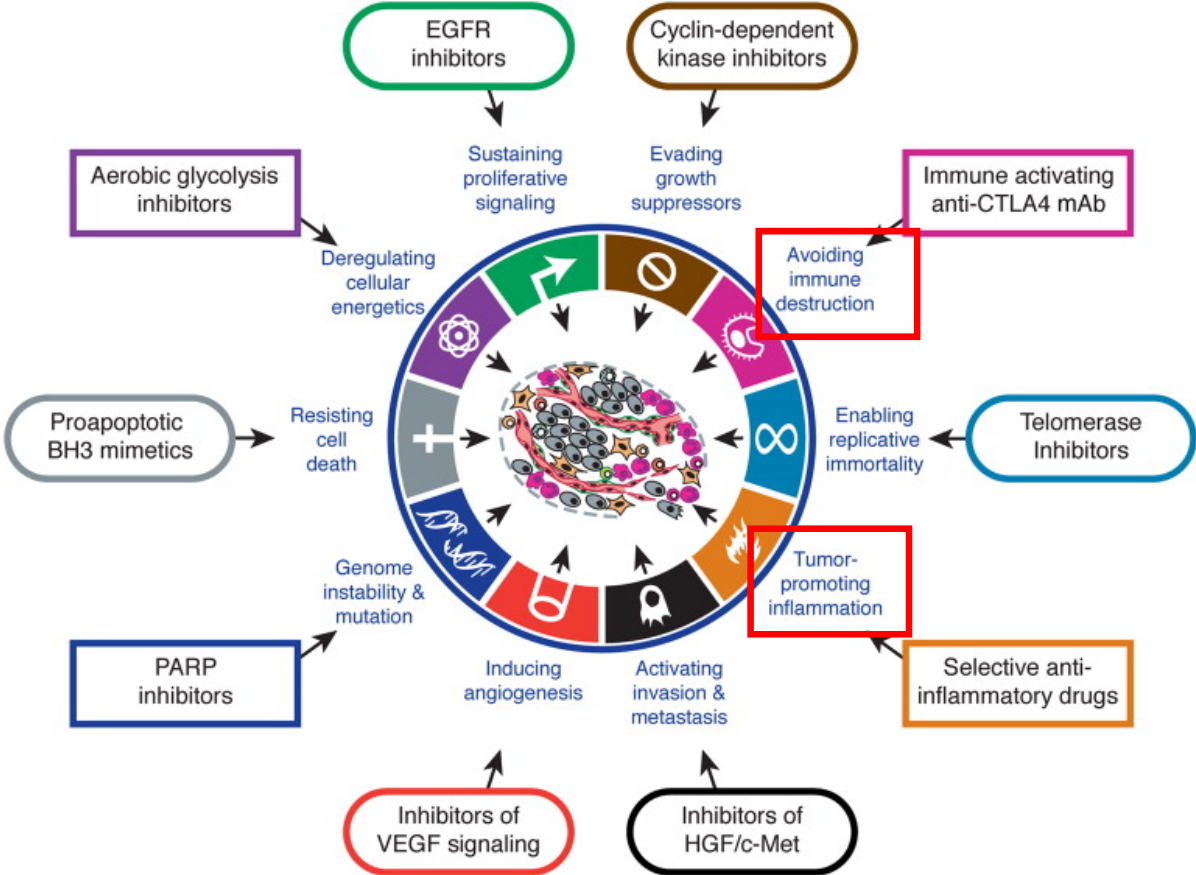
Paclitaxel (Taxol) is one of the most effective anti-cancer drugs ever developed. It can reduce selected cancers by a factor of 100 with limited specificity.



Immune defense can effect a one trillion-fold reduction in viral burden with 100% specificity.

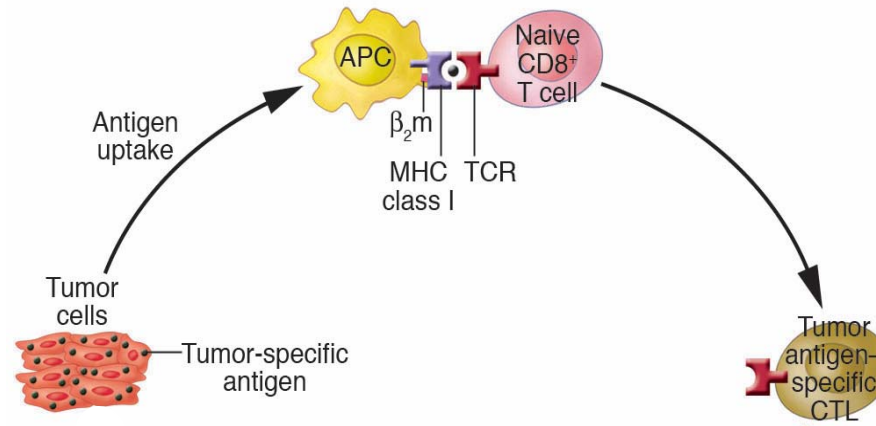
10 Hallmarks of cancer

Hannanhan and Weinberg. *Cell* 2011 144(5):646-74



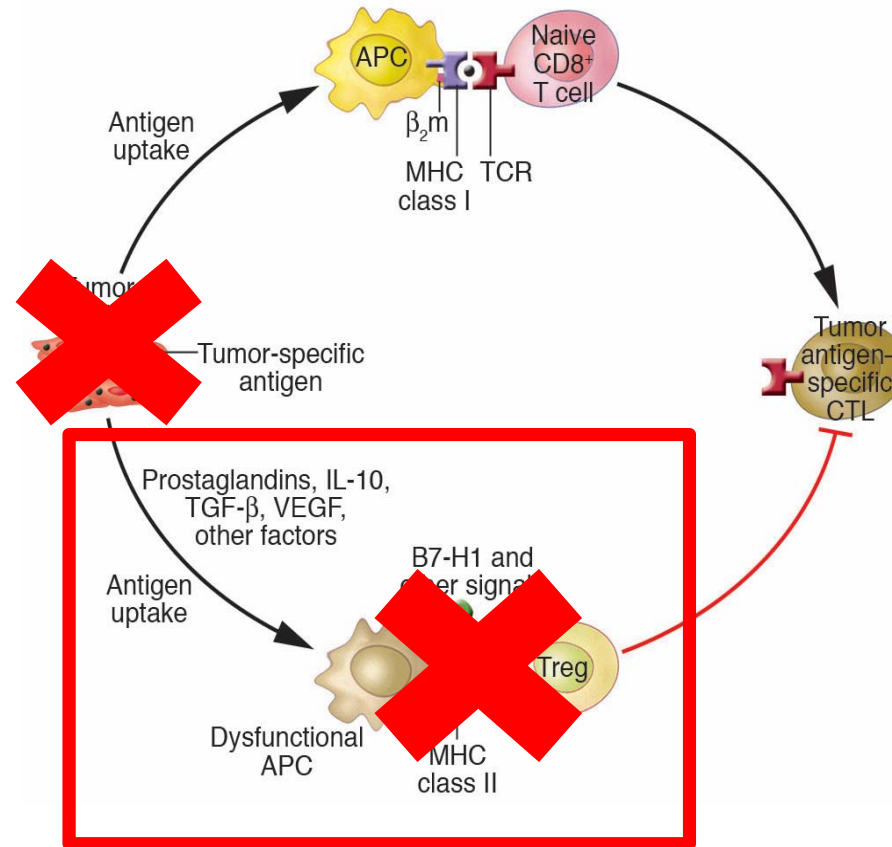
How tumor cells produce an immune response

T. J. Curiel 2007 *J Clin Invest* 117(5):1167-1174

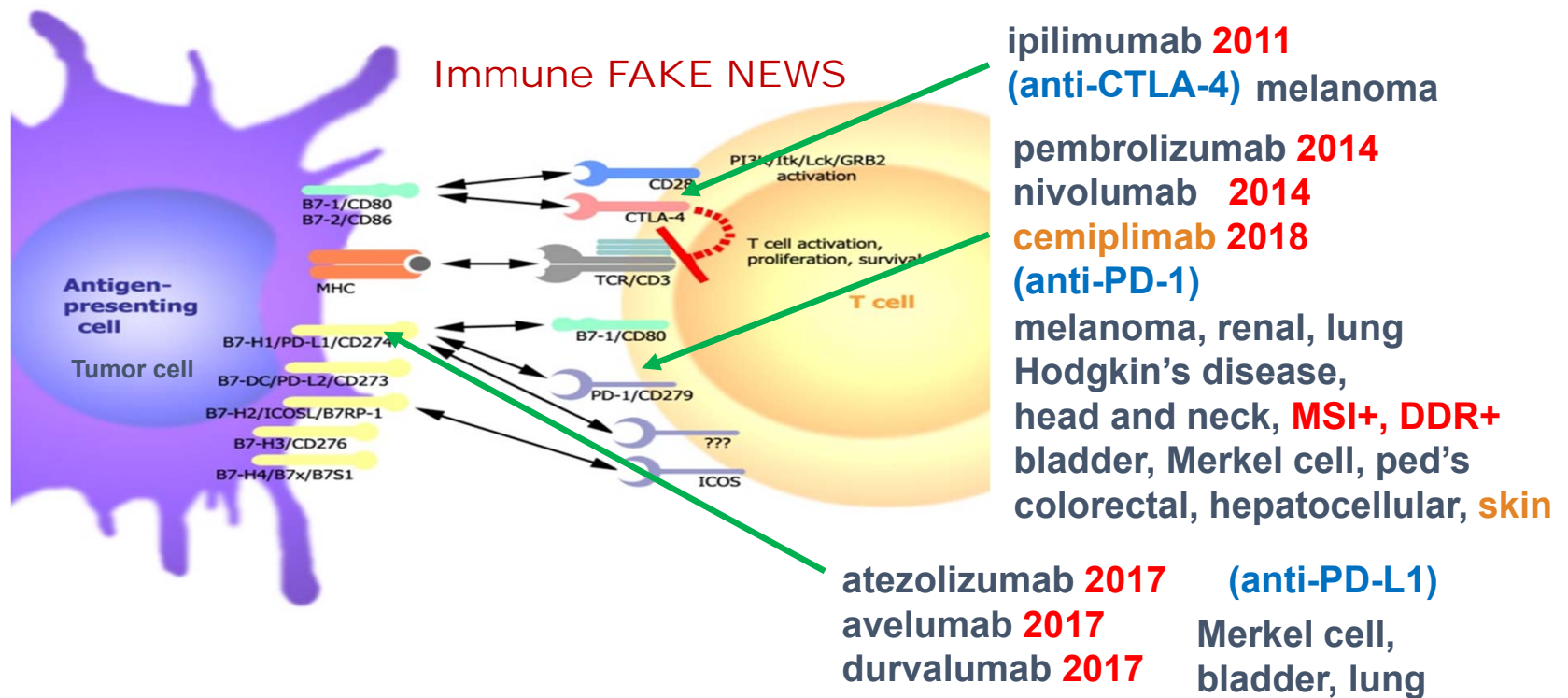


In tumors, many pathways inhibit tumor immunity

T. J. Curiel 2007 *J Clin Invest* 117(5):1167-1174

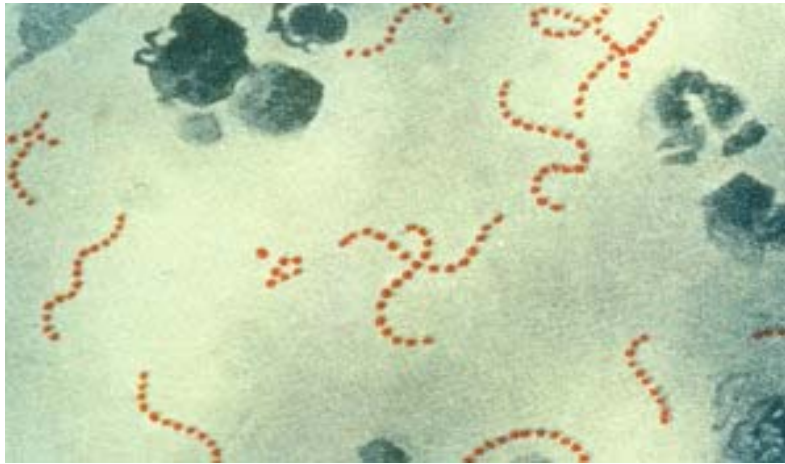


Immune checkpoints and their inhibition



When was the first cancer immunotherapy FDA approved?

Coley's Toxins: the first FDA-approved cancer immunotherapy **1923**



- Heat killed *Streptococcus pyogenes* and *Serratia marcescens*
- CpG motifs in bacterial DNA probably induced endogenous TNF- α and other cytokines
- CpGs in human cancer trials to date have not been successful

Coley's Toxins marketed by Parke-Davis
from 1923-1962 to treat sarcoma

Ipilimumab (Yervoy) anti-CTLA-4 antibody blocks suppressive signals and gets FDA approval March 2011 for melanoma

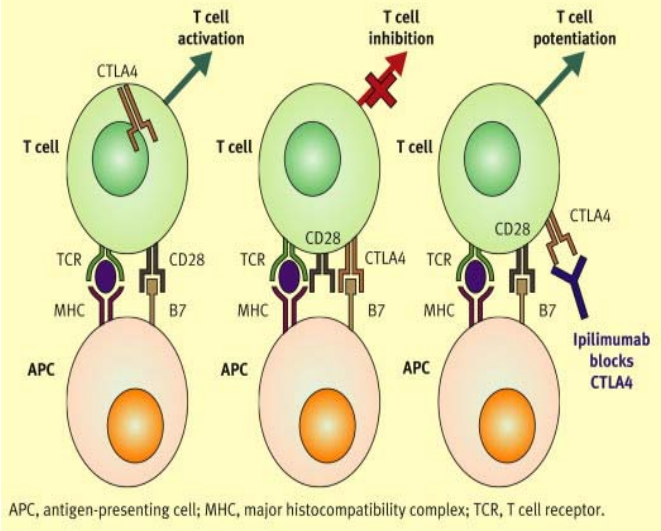
Unique Kinetics of Response in Patients Treated With Ipilimumab



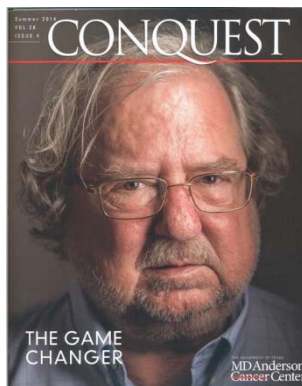
Hodi, et al., *N Engl J Med* 2010; 363:711-723

Expensive: \$85,000 and up
 Extend life several weeks to several months
 Significant side effects

Ipilimumab mechanism of action. Note the blockade of the checkpoint molecule CTLA-4 leading to T cell potentiation

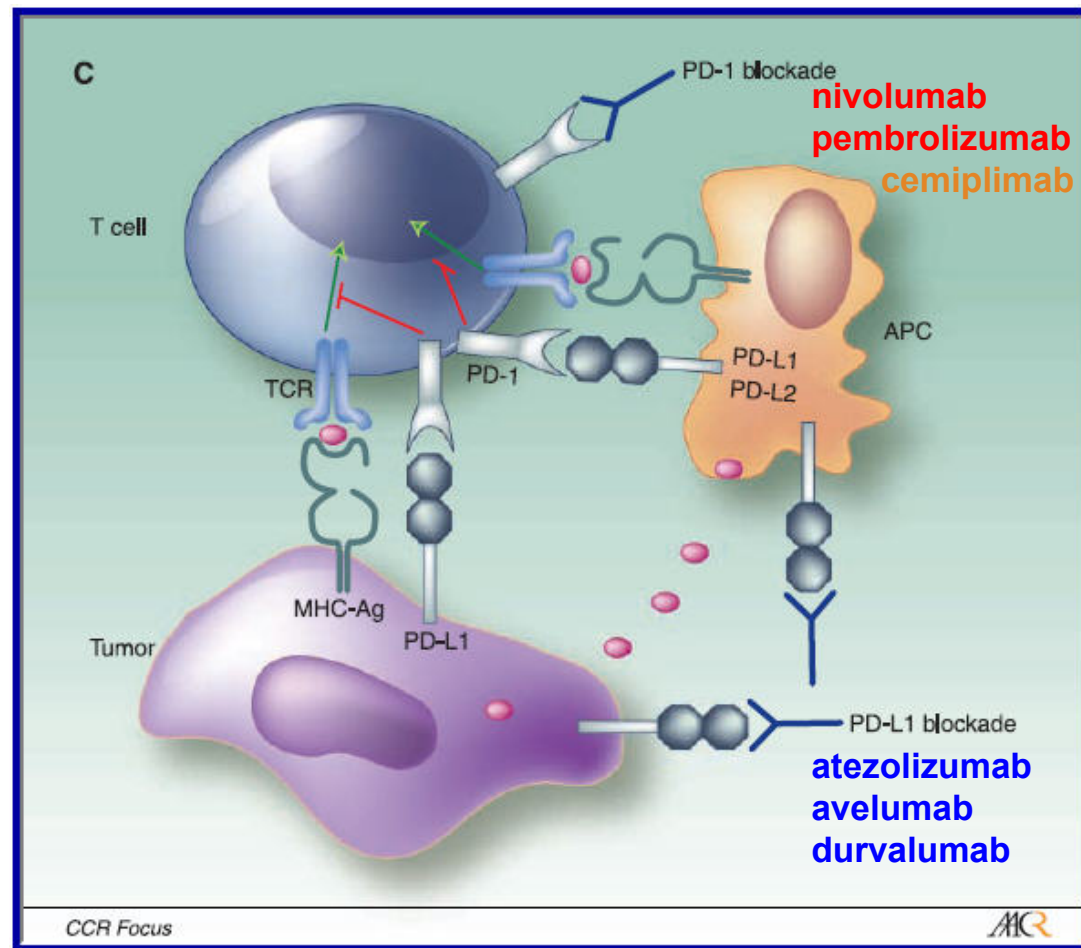


2018
 Nobel Prize



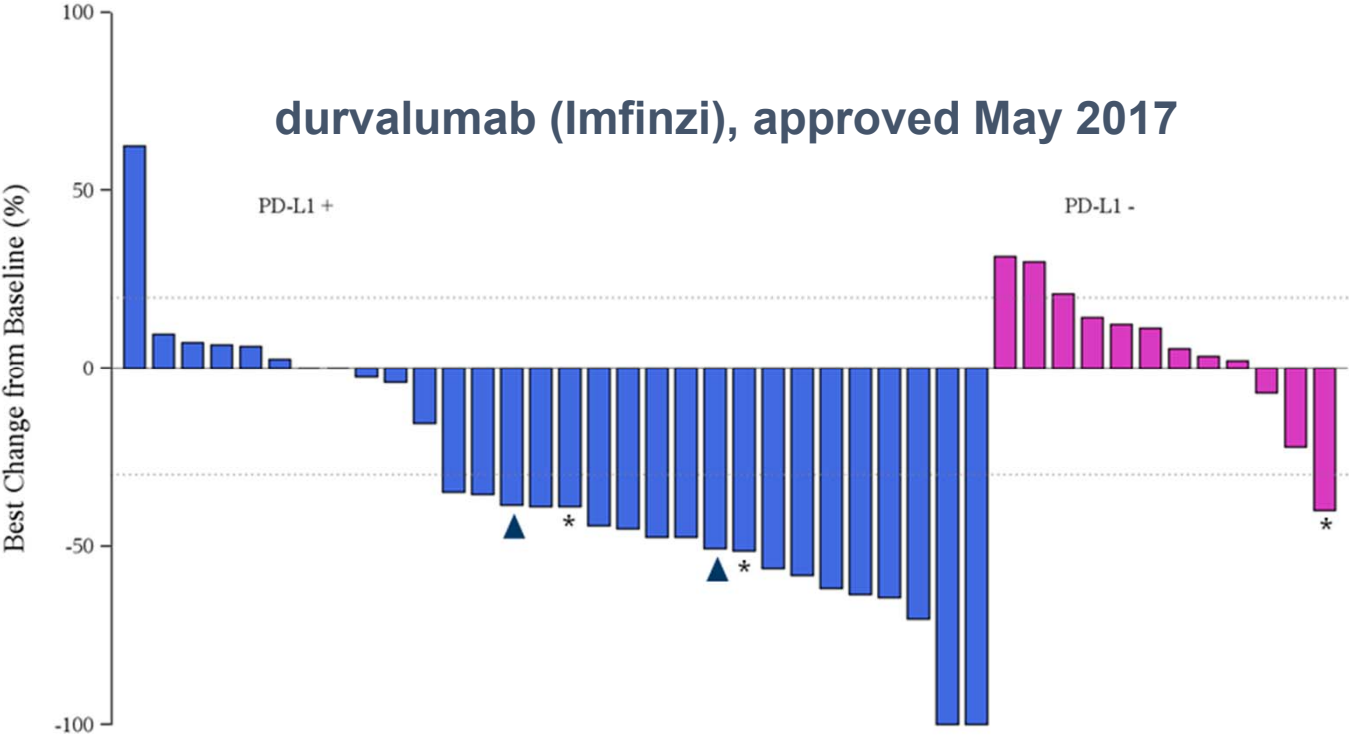
Jim Allison, PhD
 MD Anderson

Signals on tumors turn cancer immunity off

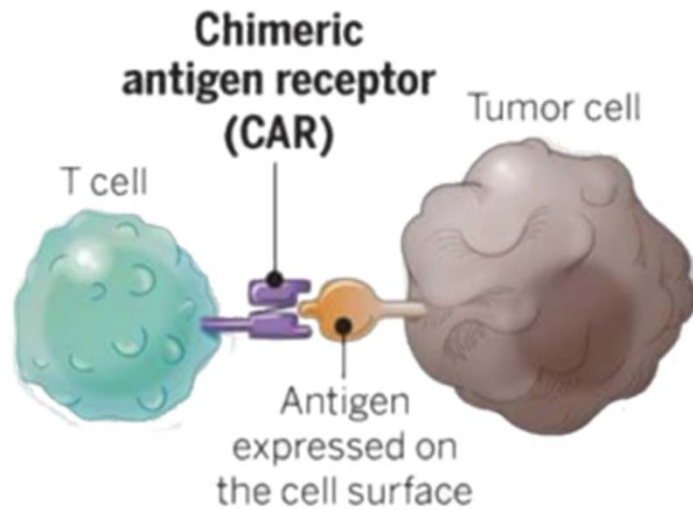


Anti-PD-L1 antibody treats advanced stage bladder cancer

J Clin Onc, 2016 35(26):3119



CAR T cells are FDA-approved for some lymphomas and leukemias



T cells are withdrawn from the body, engineered to express a tumor recognition receptor and infused back into patient



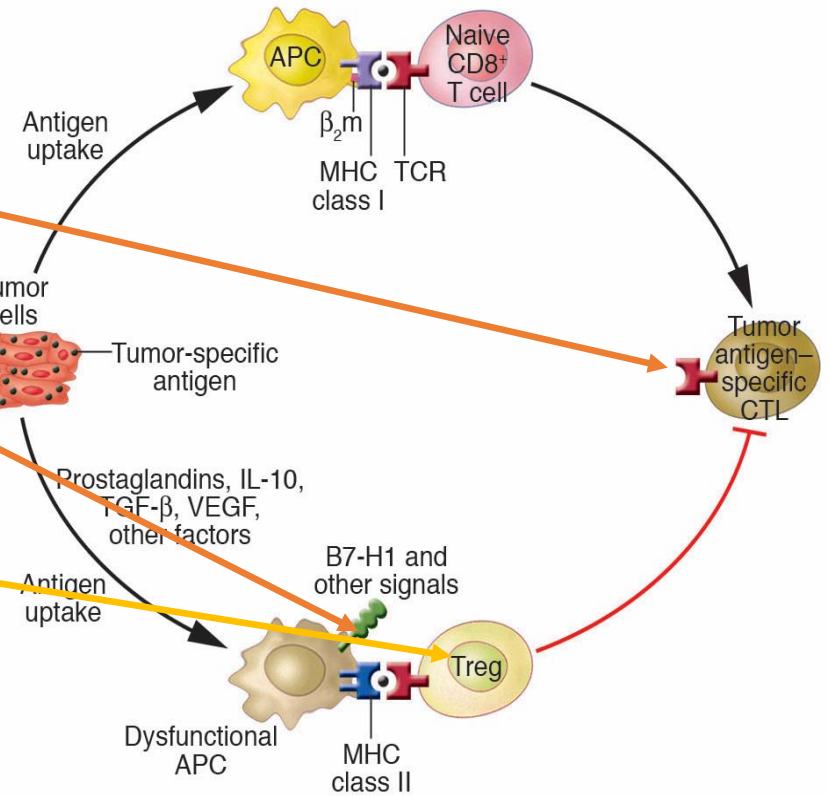
Carl June, MD
University of Pennsylvania

SO FAR

- Giving CAR T cells (good cells)
- Checkpoint antibodies

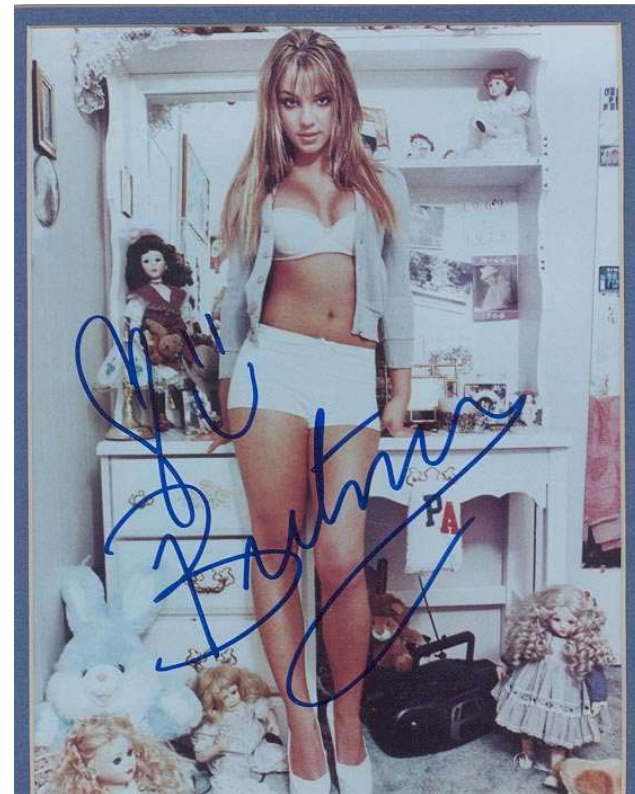
NOW

Regulatory T cells (bad cells)



QUIZ #2

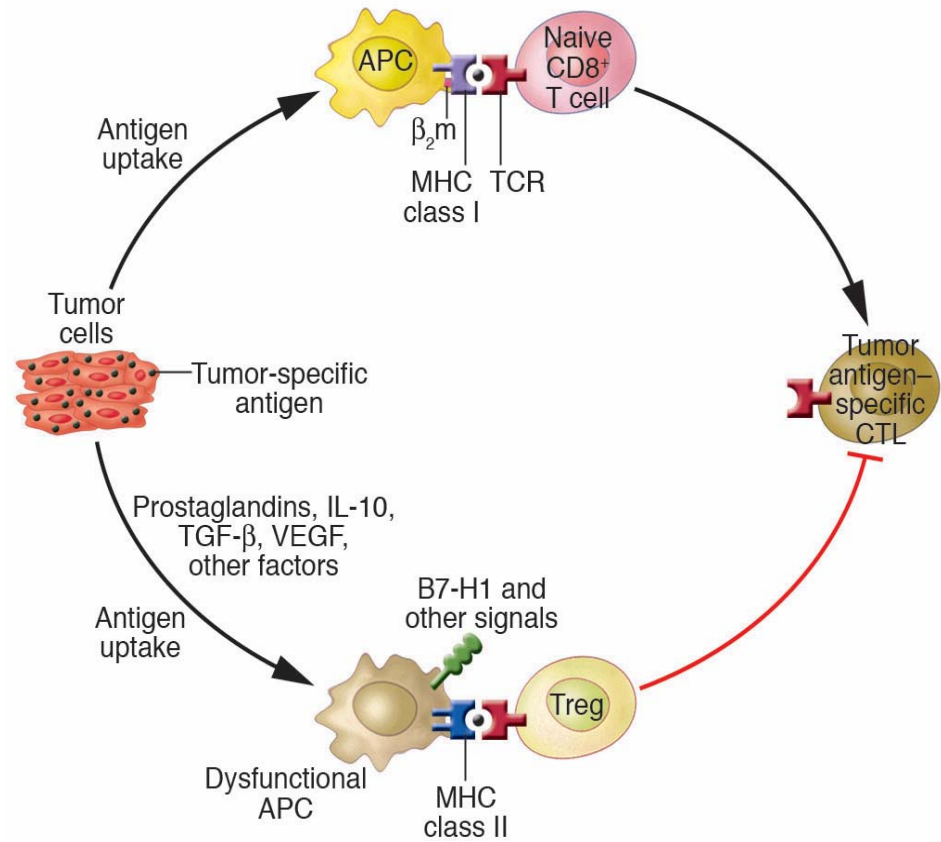
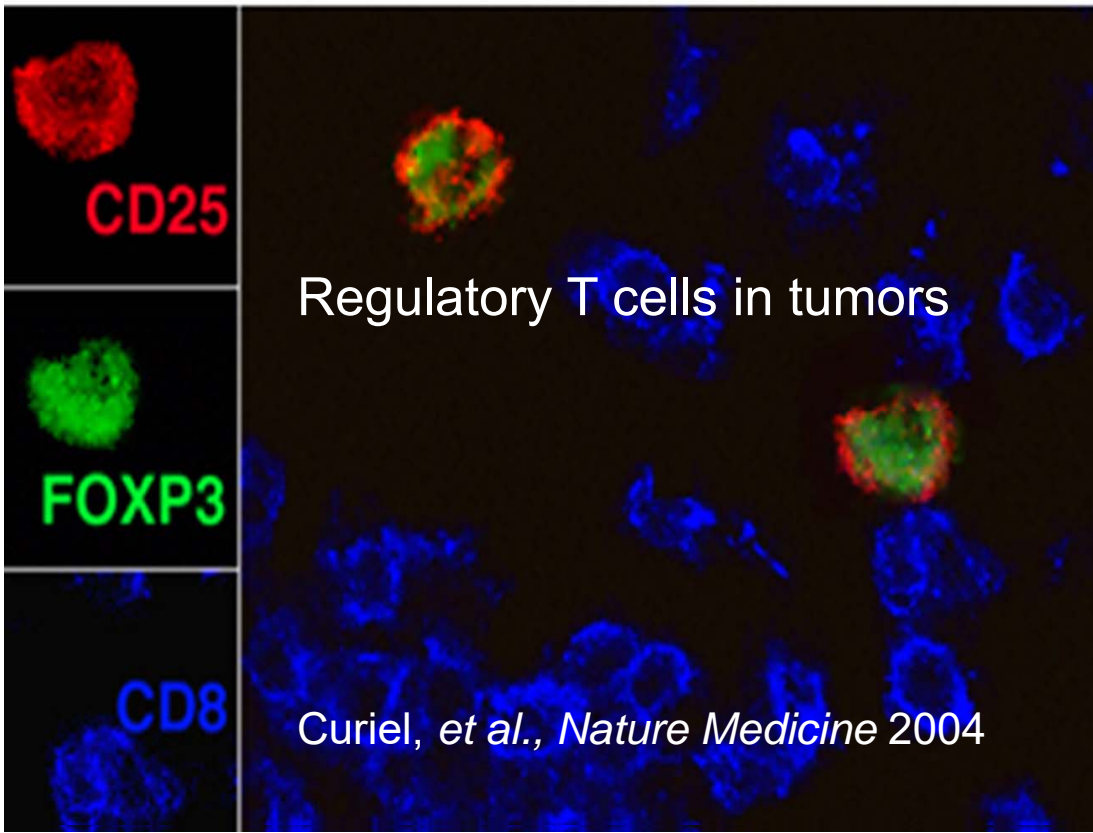
The new immunologic you



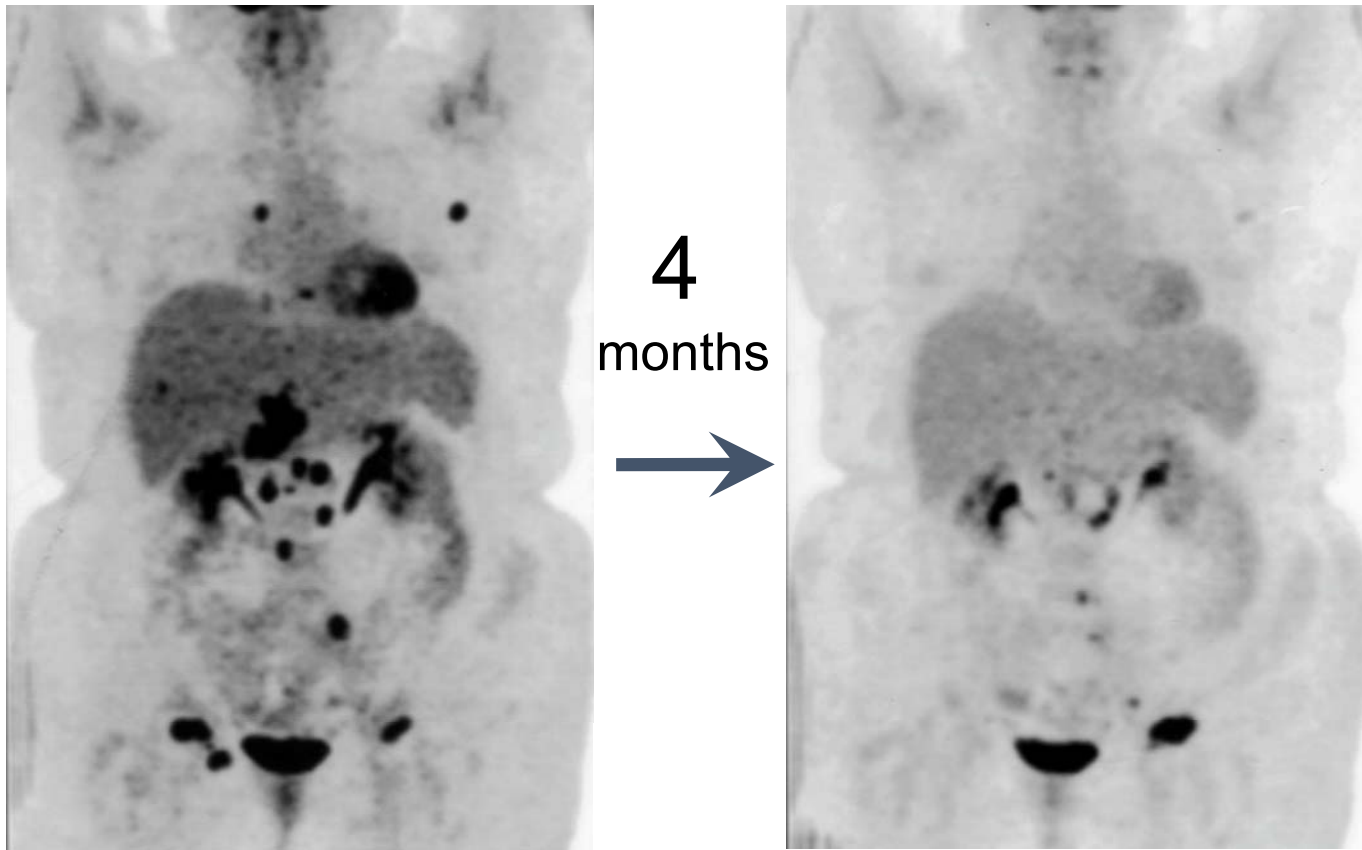
At puberty, the body makes a whole host of new proteins: breasts, breast milk, gonads, etc.

Your immune system accepts these.

Regulatory T cells stop autoimmunity, which includes cancer immunity



Denileukin diftitox reduces metastatic tumor in treatment-refractory ovarian cancer



2013, 2013, IX, 483 p. 19 illus., 16 in color.

Printed book

Hardcover

▶ 139,95 € | £126.00 | \$189.00

▶ *149,75 € (D) | 153,94 € (A) | CHF 186.50

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T.J. Curiel, University of Texas Health Science Center, San Antonio, TX, USA (Ed.)

Cancer Immunotherapy

Paradigms, Practice and Promise

▶ In-depth discussion over the entire field of tumor immunotherapy, past, present, and future

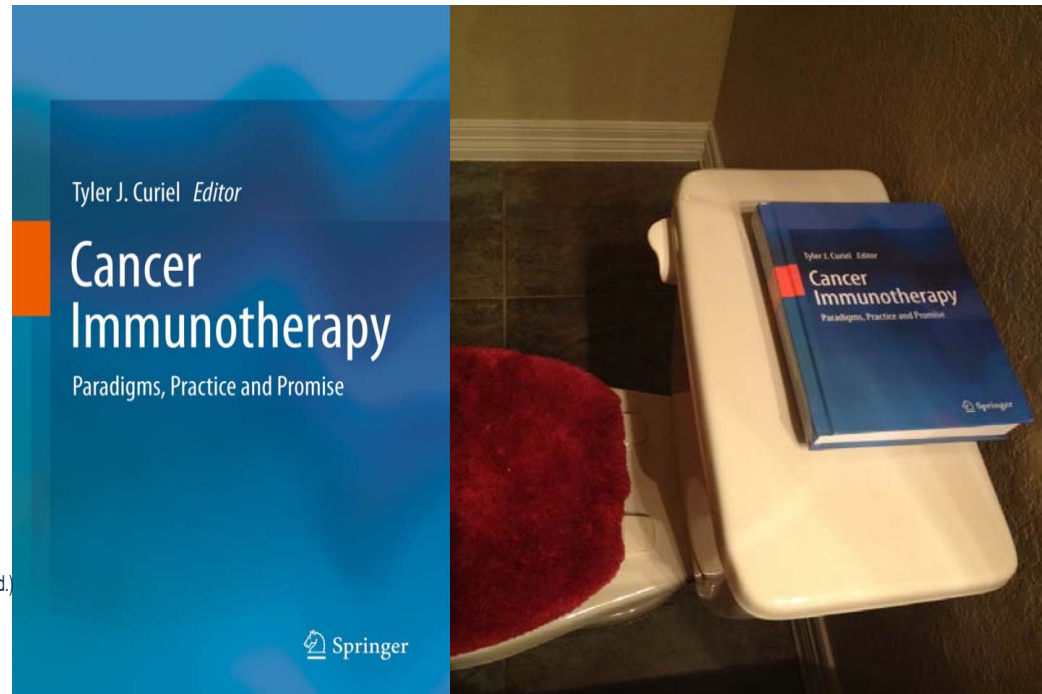
▶ Comprehensive list of contributors discussing a broad range of topics

▶ The field is very active with many researchers working with immunotherapy and cell biology

This volume is a comprehensive discussion of the major factors affecting tumor immunology and a discussion of all major anti-cancer immunotherapeutic agents approved by the Food and Drug Administration of the United States and by European agencies. Many promising but unapproved agents in clinical trials are also discussed, as are key pre-clinical developments. The major challenges and intellectual issues facing investigators developing novel immunotherapeutics are discussed in detail as are conceptual developments influencing current and future treatment strategies.

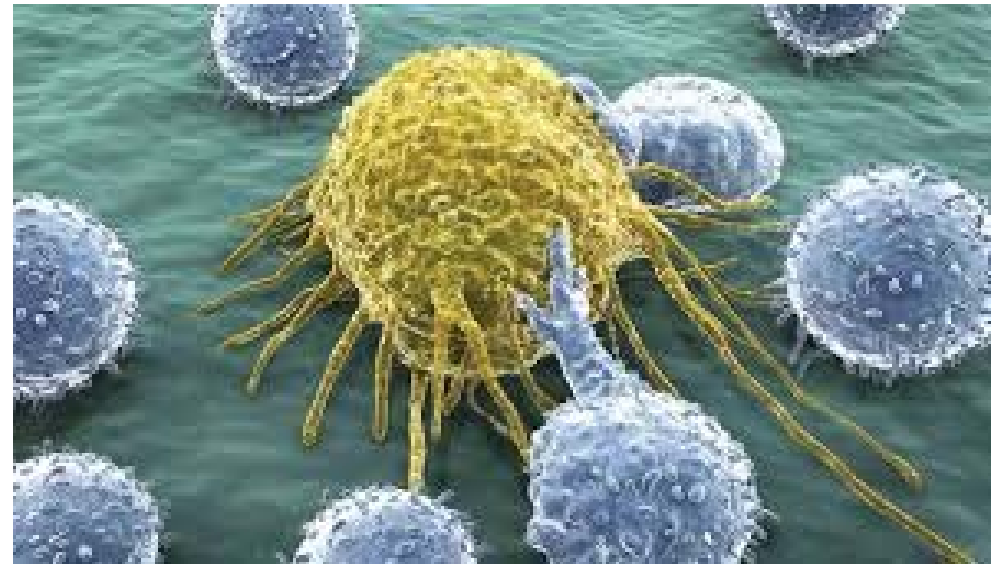
Each chapter begins by defining all relevant key terms and concepts and provides pertinent background information so that the text will be accessible to newcomers to the field as well as to the expert. This text book should provide an excellent reference resource for investigators in tumor immunology, life sciences students, drug developers designing novel anti-cancer immunotherapeutics, and to other individuals with some scientific training wishing to gain a better understanding of the field of tumor immunotherapy.

Although the field is evolving rapidly, we have taken pains to ensure that information was as up to date as possible as the text went to press



Summary of Cancer Immunotherapy in 2019

- Immune checkpoint antibodies are the most successful class of cancer drugs ever developed
- However, most patients still do not respond well enough
- Immunotherapy could work theoretically for any cancer
- Many new agents are coming very soon
- Consider clinical trials



Immunotherapy trials coming to Mays CC in 2019

- **Bladder cancer**
 - Immune checkpoint antibodies plus standard chemotherapy
- **Breast cancer**
 - Immune checkpoint antibodies plus a personalized vaccine plus standard chemo
- **All carcinomas**
 - Treg depletion agent alone or plus other agents
 - Novel immune checkpoint blockers

<https://imgur.com/gallery/R5K7Zx4>

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