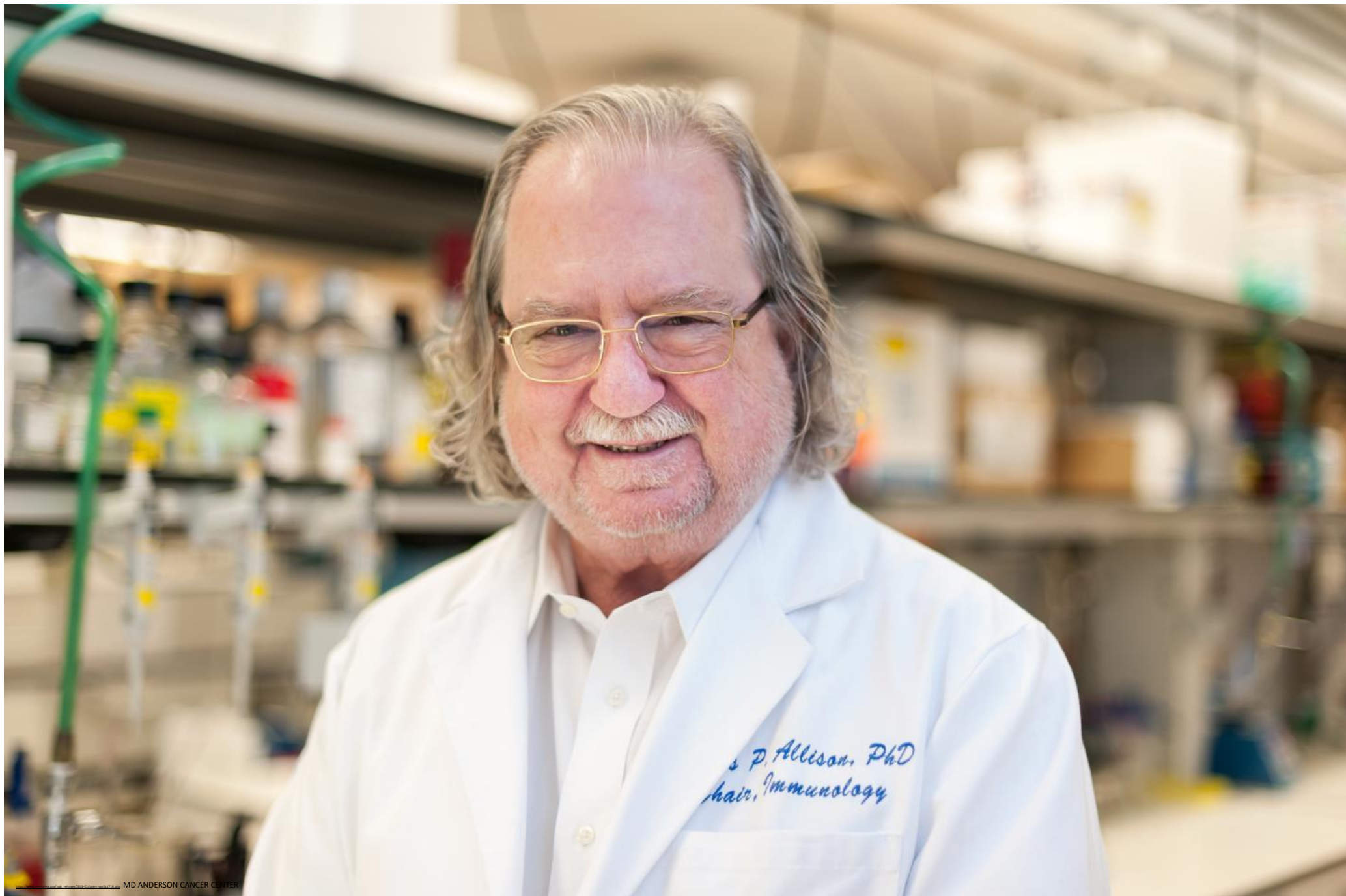


2021-2022

# Tumor Immunology

# Introduction

- The concept of immune surveillance
- Lymphocytic infiltrates around some tumors and enlargement of draining lymph nodes correlate with better prognosis
- Immunodeficient individuals have an increased incidence of some types of tumors
- Therapeutic blockade of inhibitory receptors such as PD-1 and CTLA-4 leads to tumor remission
- Evasion of host immunity is indeed a hallmark of many, if not all, human cancers



*P. Allison, PhD  
Chair, Immunology*

# Tumor antigens

= passenger mutations

= driver mutations

## Tumor cells expressing different types of tumor antigens

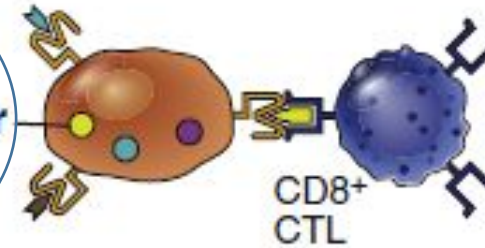
## Examples

Mutated self protein that does not contribute to tumorigenesis



Various mutant proteins in carcinogen or radiation-induced animal tumors and in human tumors

Product of oncogene or mutated tumor suppressor gene



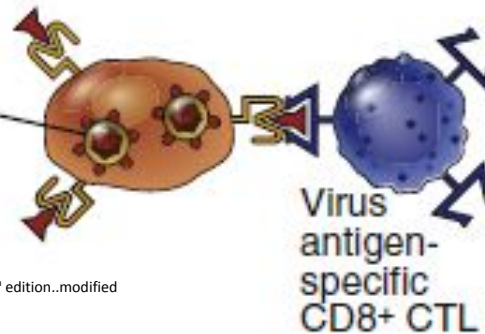
Oncogene products: mutated Ras, Bcr/Abl fusion proteins  
Tumor suppressor gene products: mutated p53 protein

Overexpressed or aberrantly expressed self protein



Tyrosinase, gp100, cancer/testis antigens in various tumors

Oncogenic virus



Human papilloma virus E6, E7 proteins in cervical carcinoma; EBNA proteins in EBV-induced lymphomas

# Tumor antigens, cont'd

...also: oncofetal antigens...

- carcinoembryonic antigen (CEA)

- $\alpha$ -fetoprotein (AFP)

...also: altered cell surface glycolipids and glycoproteins

...also: cell type-specific differentiation antigens

# HPV

- Cervix, anogenital & oropharyngeal (esp., tonsils)

- E6 & E7 gene products

degrades p53 (p53 is a tumor suppressor gene)

-binds *RB* and release E2F from it  
-also inactivates p21 & p27 (CDKIs)

= cyclin-dependent kinase inhibitors  
...when inactivated: cyclin-dependent  
kinases will induce cell proliferation

So it will become free and induce cell proliferation

**TSTA &**

**TATA**

**???**

# Mechanisms

- ...like any cytoplasmic protein, tumor antigens may enter the class I MHC antigen-processing pathway and be recognized by CD8+ T cells
- ...these antigens may enter the class II antigen-processing pathway in antigen presenting cells that have phagocytosed dead tumor cells, and thus be recognized by CD4+ T cells also



# Mechanisms, cont'd

- Natural killer cells:
  - ...induced by IL-2 and IL-15
  - ...these cytokines may be used for treatment
- Role of macrophages

# Escape from immune system

- **Selective outgrowth of antigen-negative variants**
- **Loss or reduced expression of MHC molecules.**  
...but may trigger NK cells
- **Activation of immunoregulatory pathways**  
...downregulation of costimulators on APCs  
...as a result: CTLA-4 is engaged more than CD28  
...PD-L1 and PD-L2 surface proteins → These are expressed more on tumor cells  
...will activate PD-1 receptor on T cell

# Escape from immune system, cont'd

- **Secretion of immunosuppressive factors by cancer cells**
  - TGF-beta
  - Galectins
  - IL-10
  - ...etc.
- **Induction of regulatory T cells (Tregs)**

# Therapies

- Cytokines
- Monoclonal antibodies
- Vaccines

**Thank  
You**