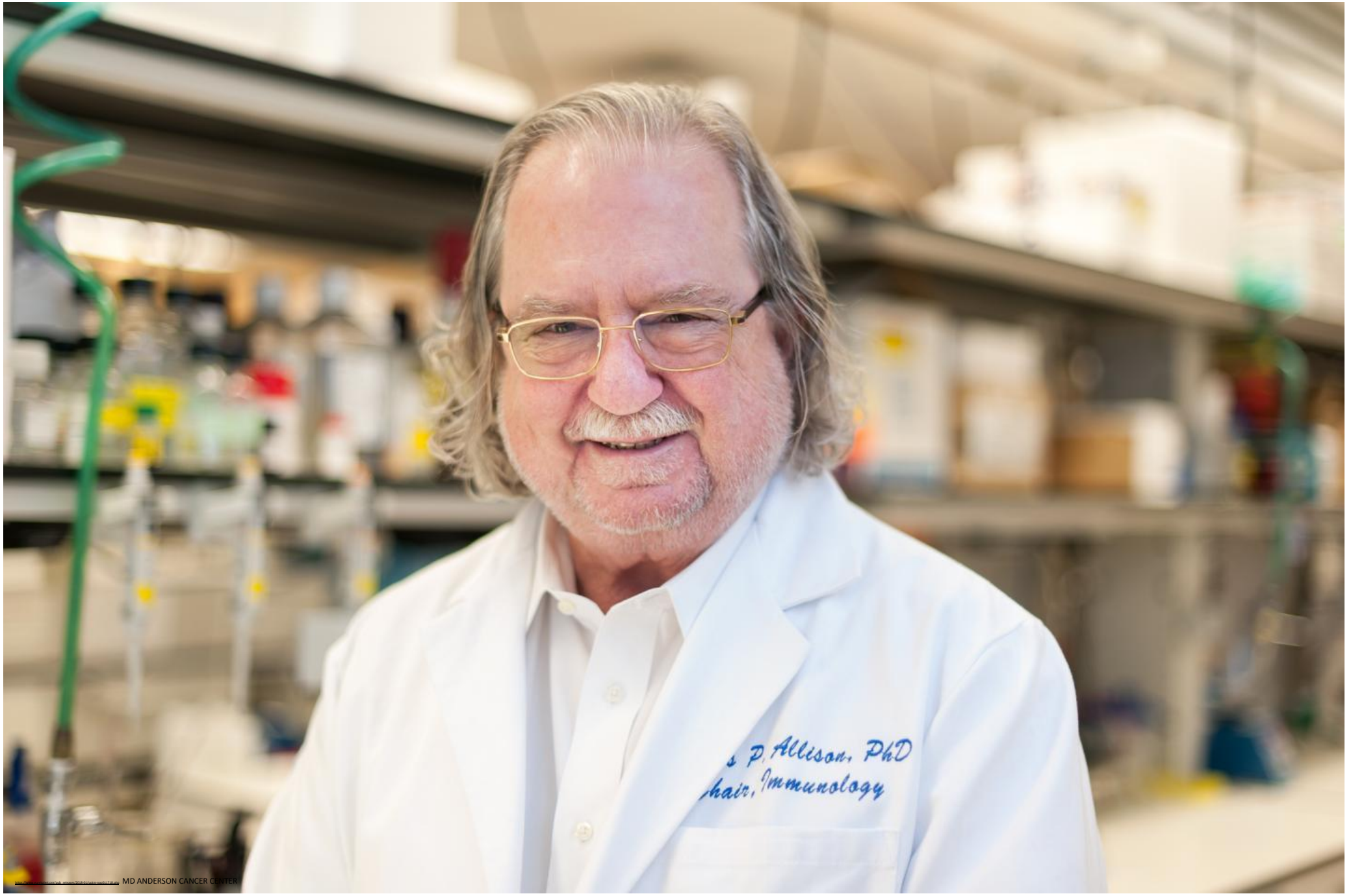
2021-2022

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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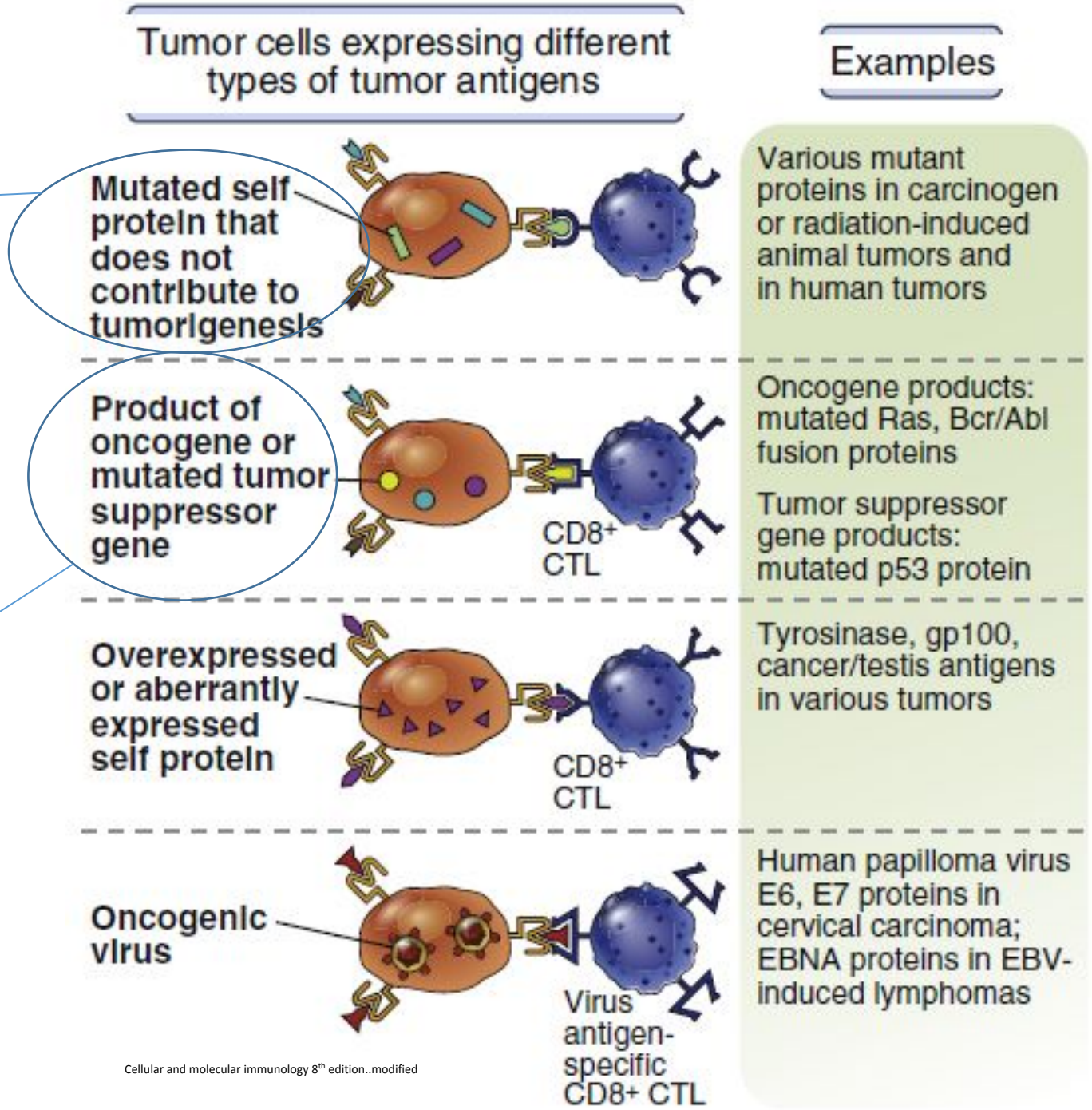
Tumor antigens

= passenger mutations

= driver mutations



Cellular and molecular immunology 8th edition..modified

Tumor antigens, cont'd

…also: oncofetal antigens…

-carcinoembryonic antigen (CEA)

-α-fetoprotein (AFP)

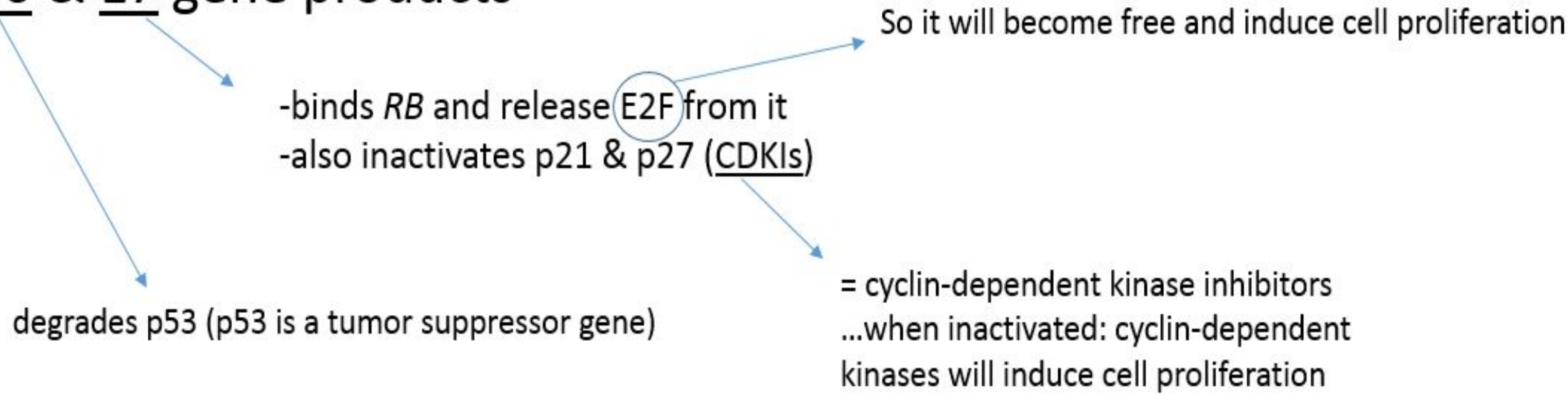
…also: altered cell surface glycolipids and glycoproteins

…also: cell type-specific differentiation antigens

HPV

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

- E6 & E7 gene products



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