Introduction to the immune system

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A course developed as an education program of the Federation of Clinical Immunology Societies (FOCIS)

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The development of Immunology

- The first golden age 1960-2000
  - Basic principles established
- The second golden age 1990-present
  - Development of therapeutics, especially biologicals
- The future
  - Application of new technologies: cell therapy, gene therapy, gene editing, omics – how much of the promise will be realized?

What does the immune system do?

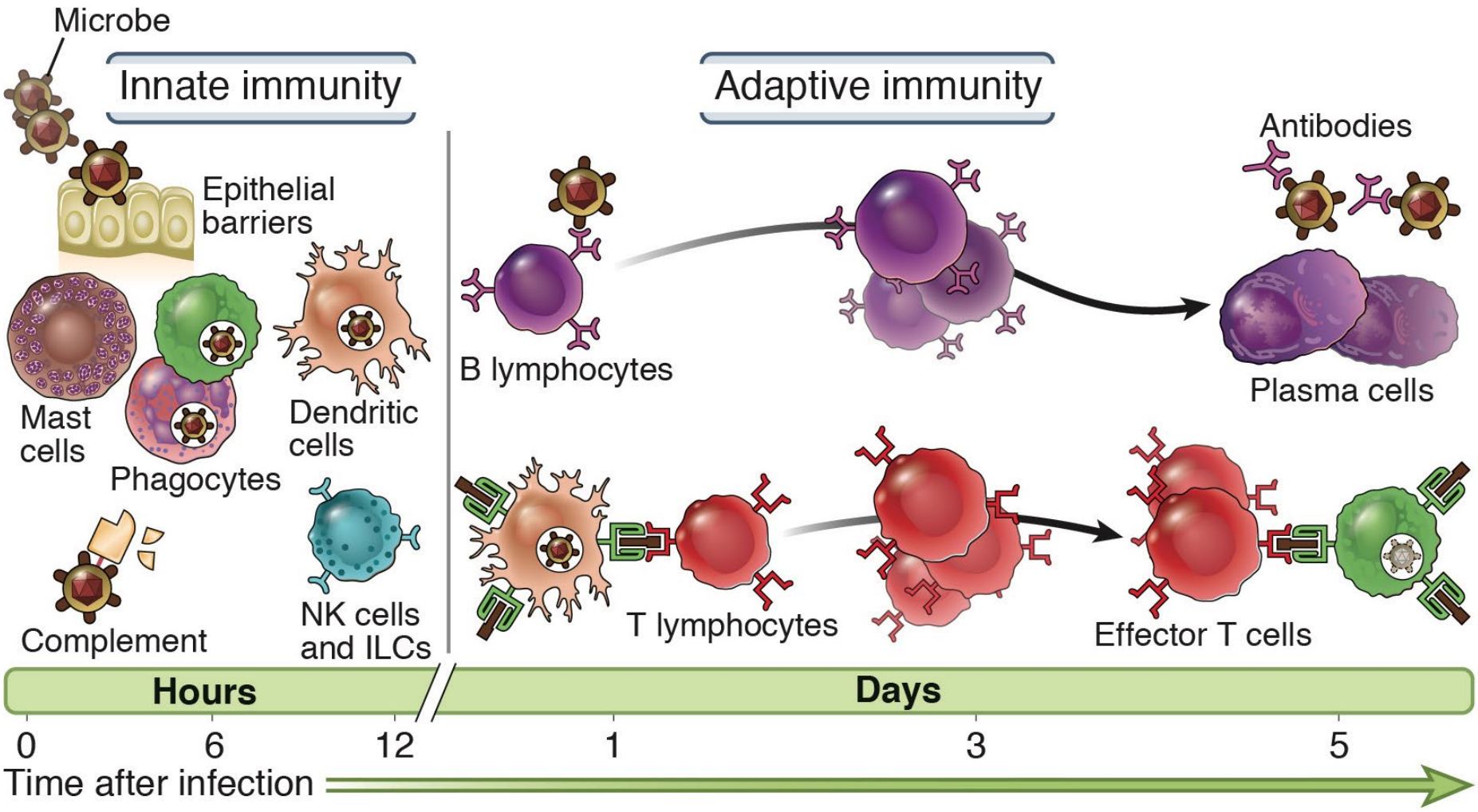
Normal functions

- Defense against infections
  - Repair of damaged tissues
- Defense against some tumors

Disease and therapeutic implications

- Cause of disease (autoimmunity, allergy)
- Barrier to transplantation, gene therapy

Innate and adaptive immunity



Innate immunity: always present (ready to attack); many pathogenic microbes have evolved to resist innate immunity

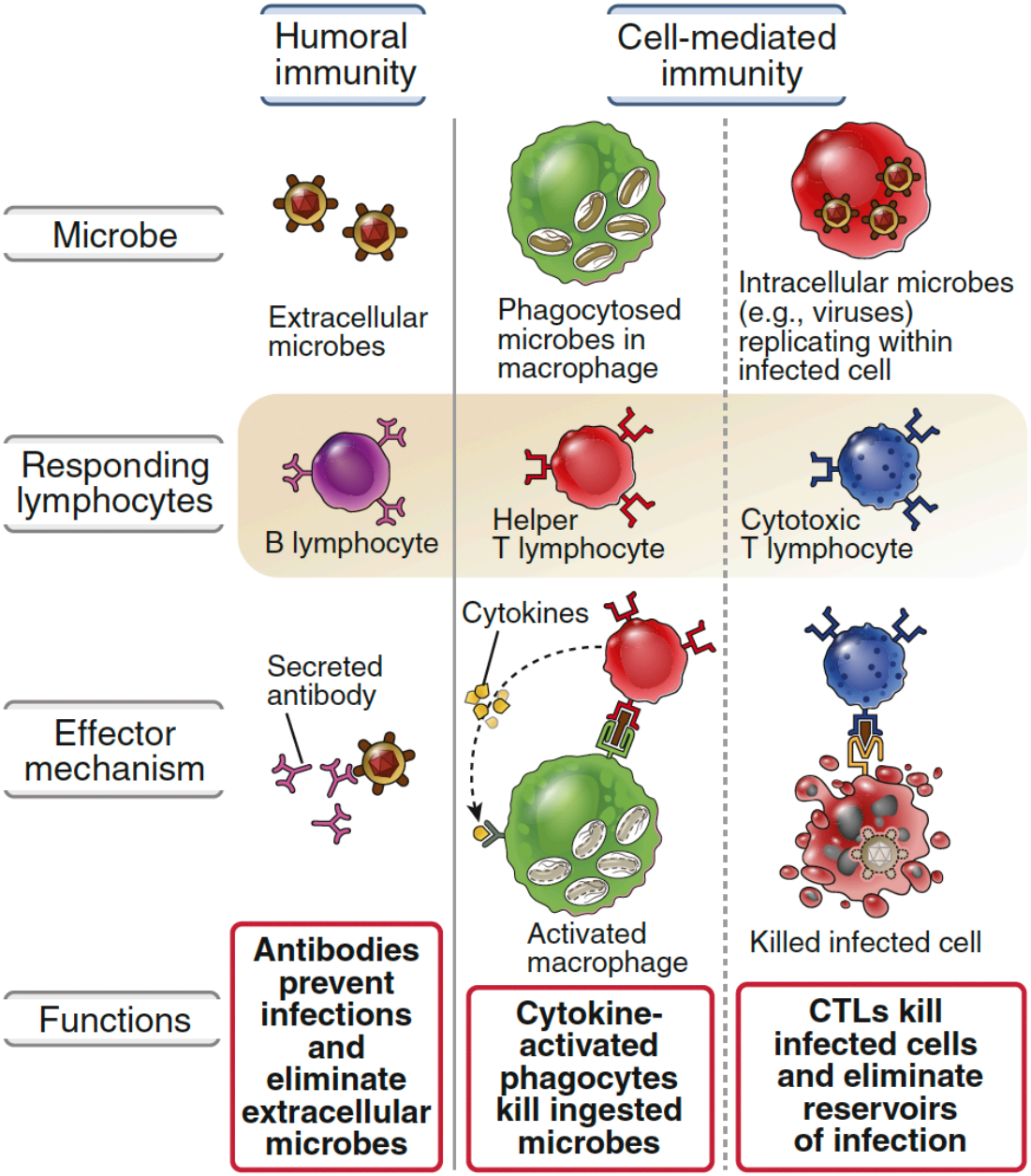
Adaptive immunity: stimulated by exposure to microbe; more potent

Cells of the immune system

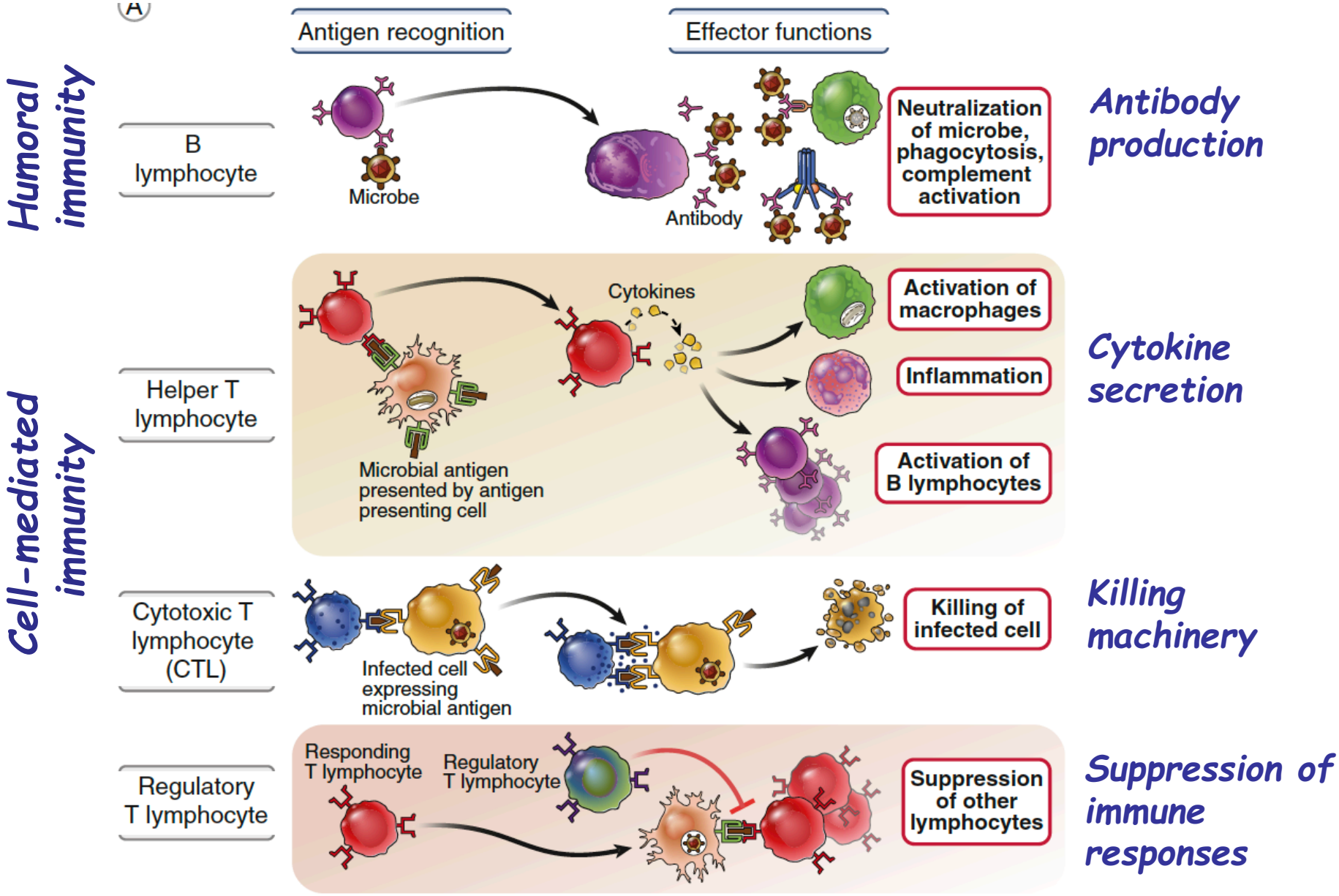
- **Lymphocytes:** the cells of adaptive immunity; recognize antigens and develop (differentiate) into cells that perform the defense functions
  - Following activation, some lymphocytes differentiate into **effector cells** that perform different functions in immunity (the effects of the immune response)

- **Myeloid cells:**
  - Include macrophages and neutrophils (phagocytes), antigen-presenting cells (mostly dendritic cells), other leukocytes (eosinophils), mast cells

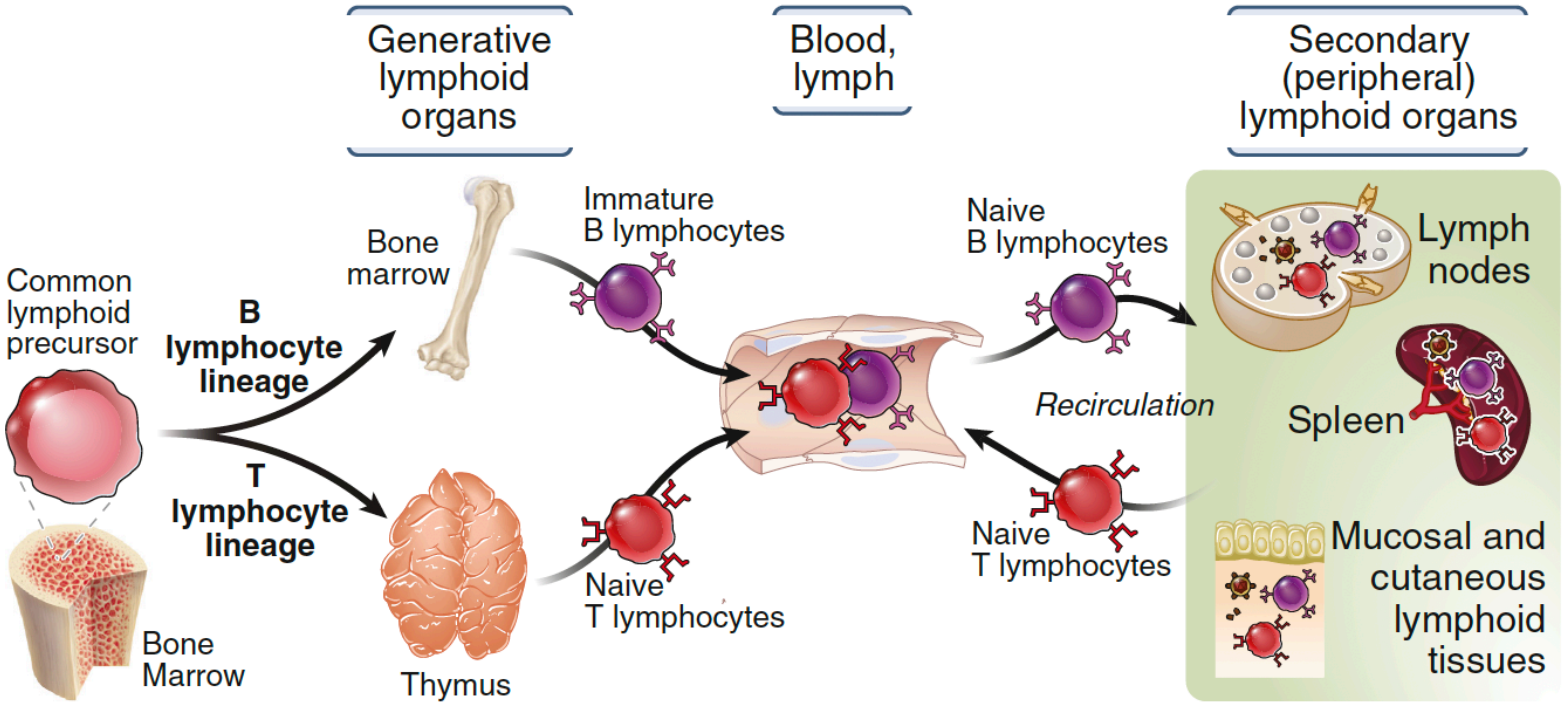
Types of adaptive immunity



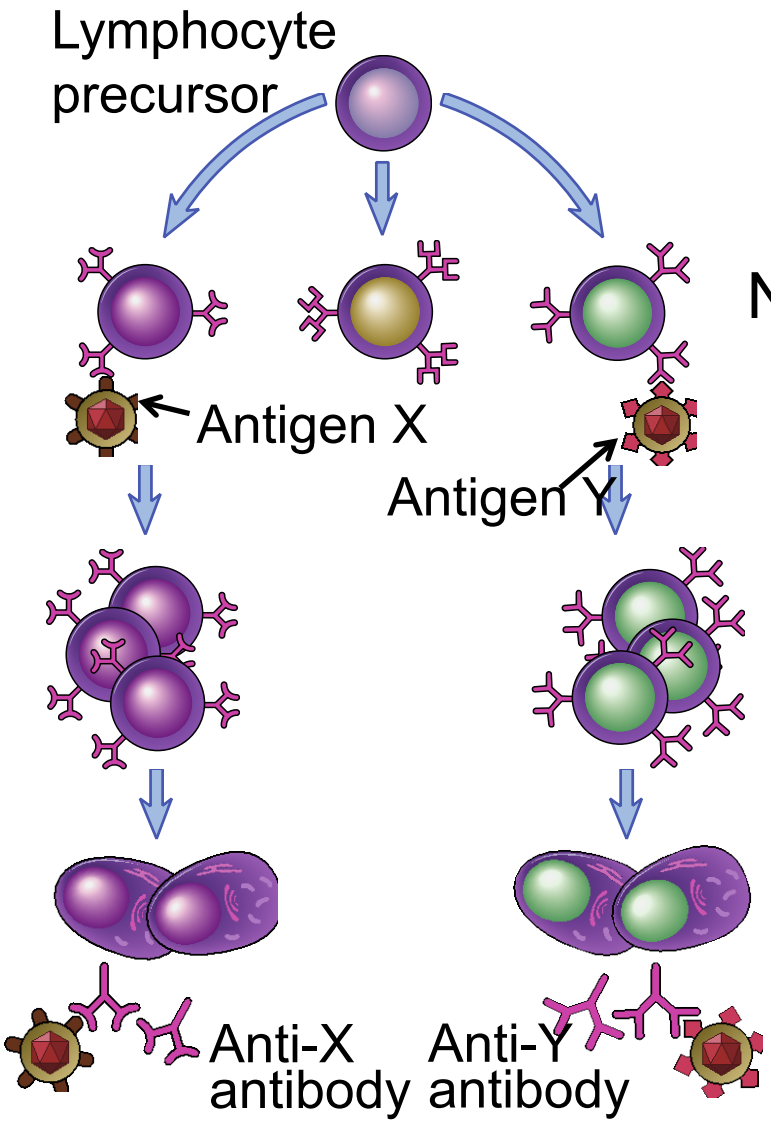
Classes of lymphocytes



Maturation of lymphocytes



Lymphocyte diversity and clonal selection



Generation of mature lymphocytes with many different antigen receptors

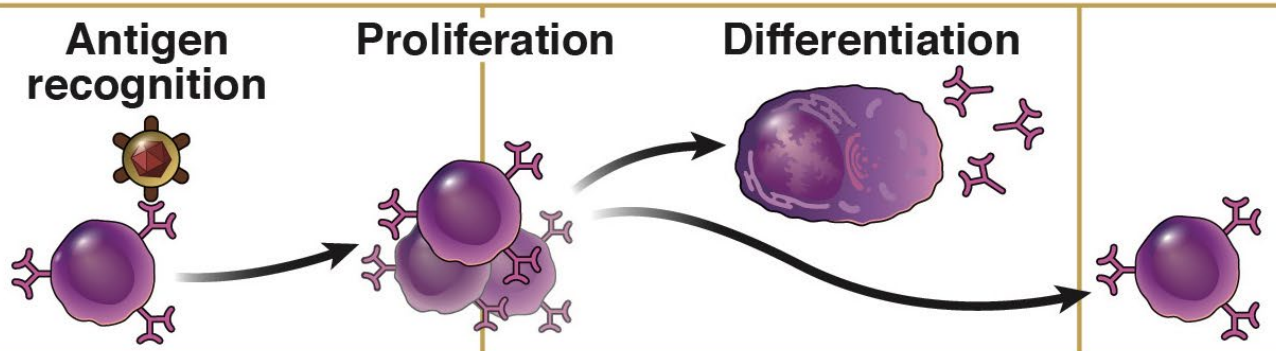
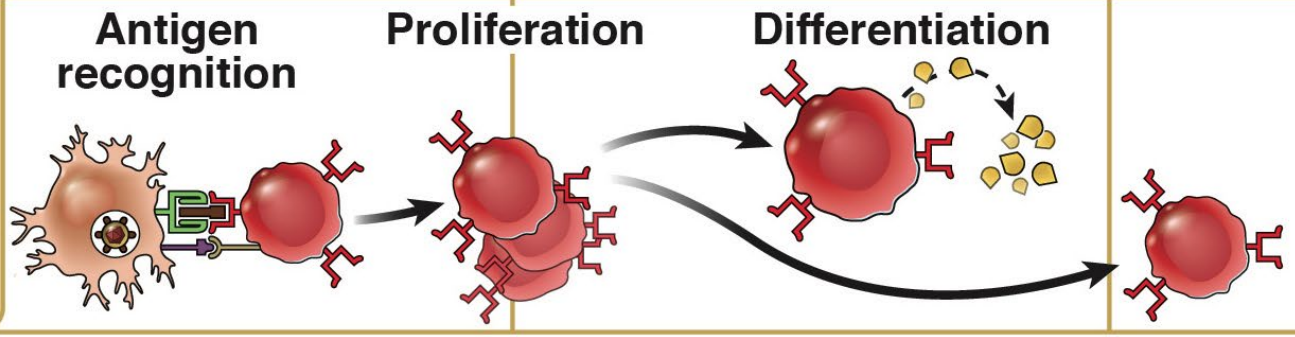
Naïve lymphocytes circulate through lymphoid organs

Specific lymphocytes recognize antigens

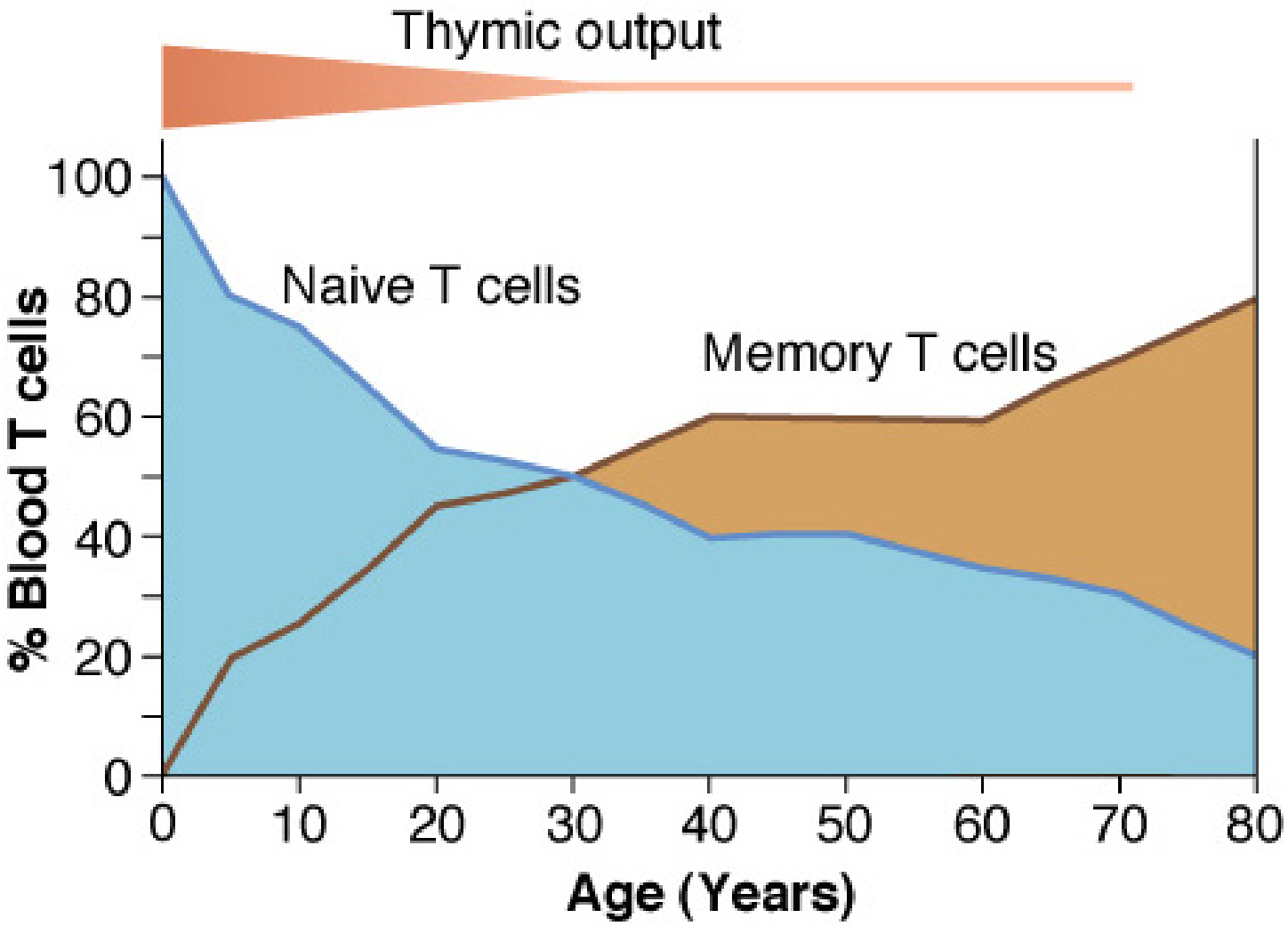
Lymphocytes are activated to proliferate and to differentiate into effector cells

Lymphocytes with highly specific and diverse antigen receptors develop prior to exposure to antigens

Stages in the life history of lymphocytes

Cell type	Stage		
	Naive cell	Activated or effector lymphocyte	Memory lymphocyte
B lymphocytes			
T lymphocytes			

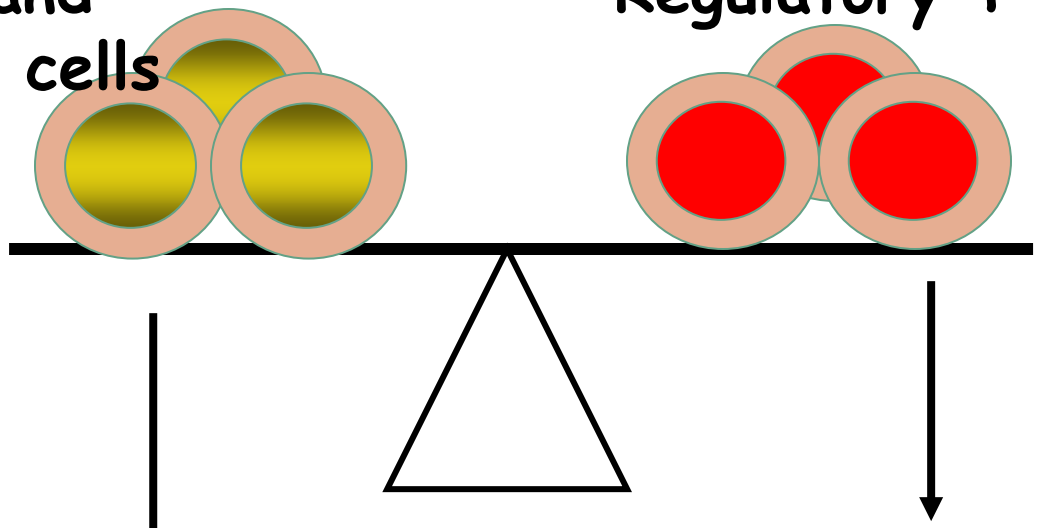
Accumulation of memory T cells with age



The immunological equilibrium: balancing lymphocyte activation and control

Activation → Effector and memory T cells

Tolerance Regulatory T cells



Normal: reactions against pathogens

Pathologic: inflammatory disease, e.g. caused by reactions against self

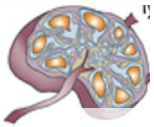
No response to self

Controlled response to pathogens

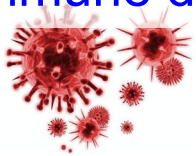
Checks and balances

- The immune system has inbuilt controls that limit responses
  - Physiologic function: to prevent damaging immune responses against self, commensals, and other harmless antigens
  - To limit excessive reactions to microbes (prevent collateral damage)
  - Examples:
    - Regulatory T cells
    - "Coinhibitors"

Immunological basis of human disease




Immune deficiency



Cancer

Allergy

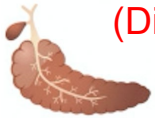
COPD

Activation Regulation

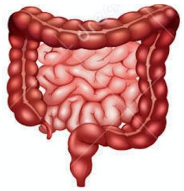
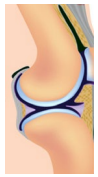
Psychological Disorders
(Alzheimer's, PTSD, depression, bipolar)

Cardiovascular Disease
(Atherosclerosis, hypertension, stroke)

Metabolic Disorders
(Diabetes, Fatty liver dis.)



Autoimmunity
(T1D, MS, RA, IBD)

Muscular Dystrophy


Transplantation
Fetal tolerance

Osteoporosis

Aging

The significance of recent advances

- Provides a solid foundation of basic principles
- Better understanding of disease mechanisms
- Development of novel therapies

Challenges in Immunology

- **Explosion of information creates complexity**
  - "Big data" (CyTOF, single-cell RNAseq) reveals many complex cell populations and pathways, and possible connections between them ("hypothesis generating")
  - Defining biological significance requires functional analyses that are difficult and not always feasible ("hypothesis proving" remains a challenge)

- **Translating results from mouse to human**
  - Mouse models are critical for understanding fundamental mechanisms but are poor at mimicking human diseases or predicting therapeutic responses