Basic Immunology

17th lecture:

Suppression of the immune response

Main steps of the immune response

Recognition

Activation

Differentiation

Effector function

Memory

Suppression

1. Antigen as the main regulator

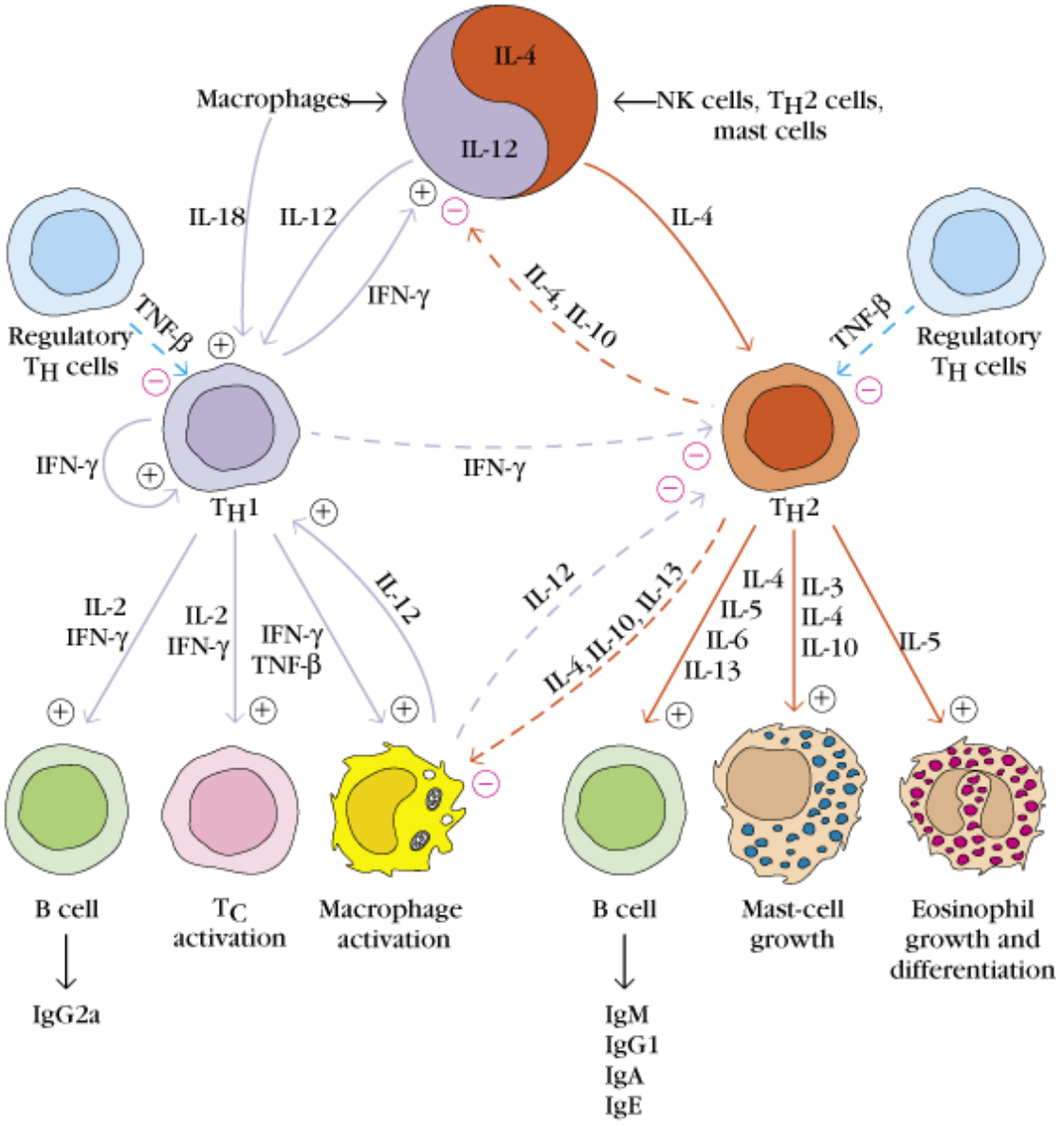
Activates T and B cells

Antigen nature, dose, location influence the immune response

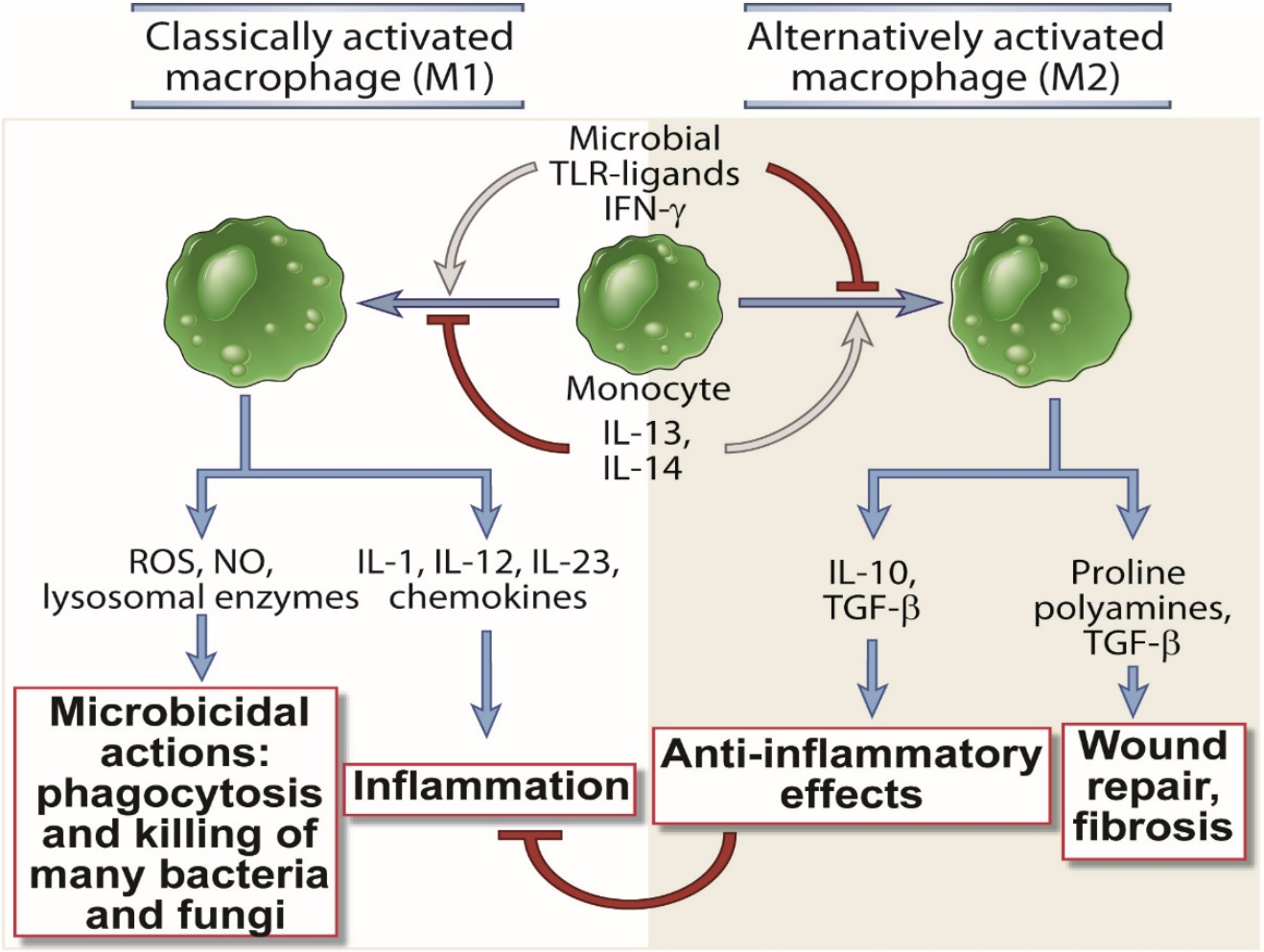
T_H1 vs T_H2

Withdrawal/elimination of the antigen stops further activation

1. Antigen as the main regulator



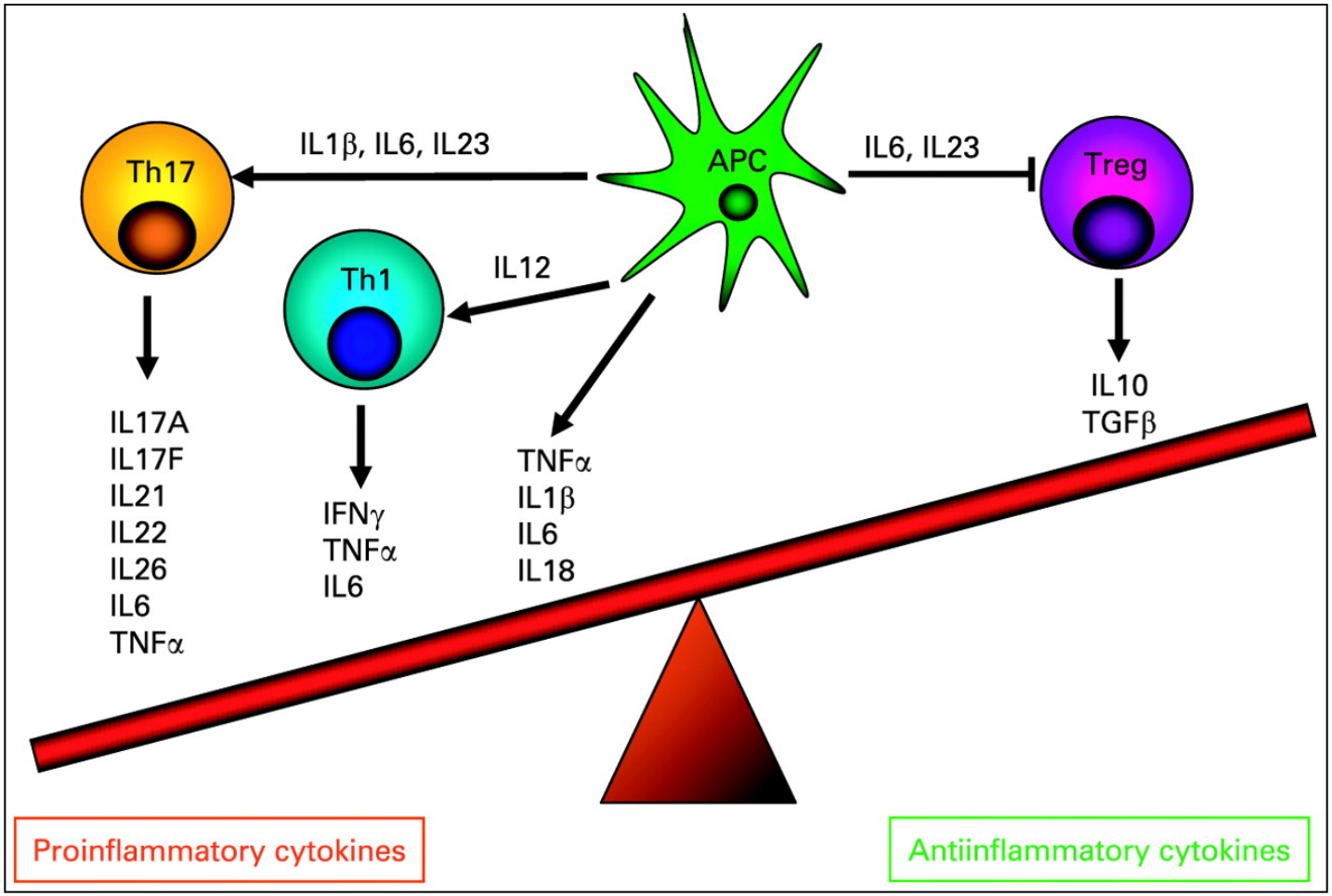
Polarization of macrophages



Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

Cytokine balance of inflammation



2. Need for costimulation

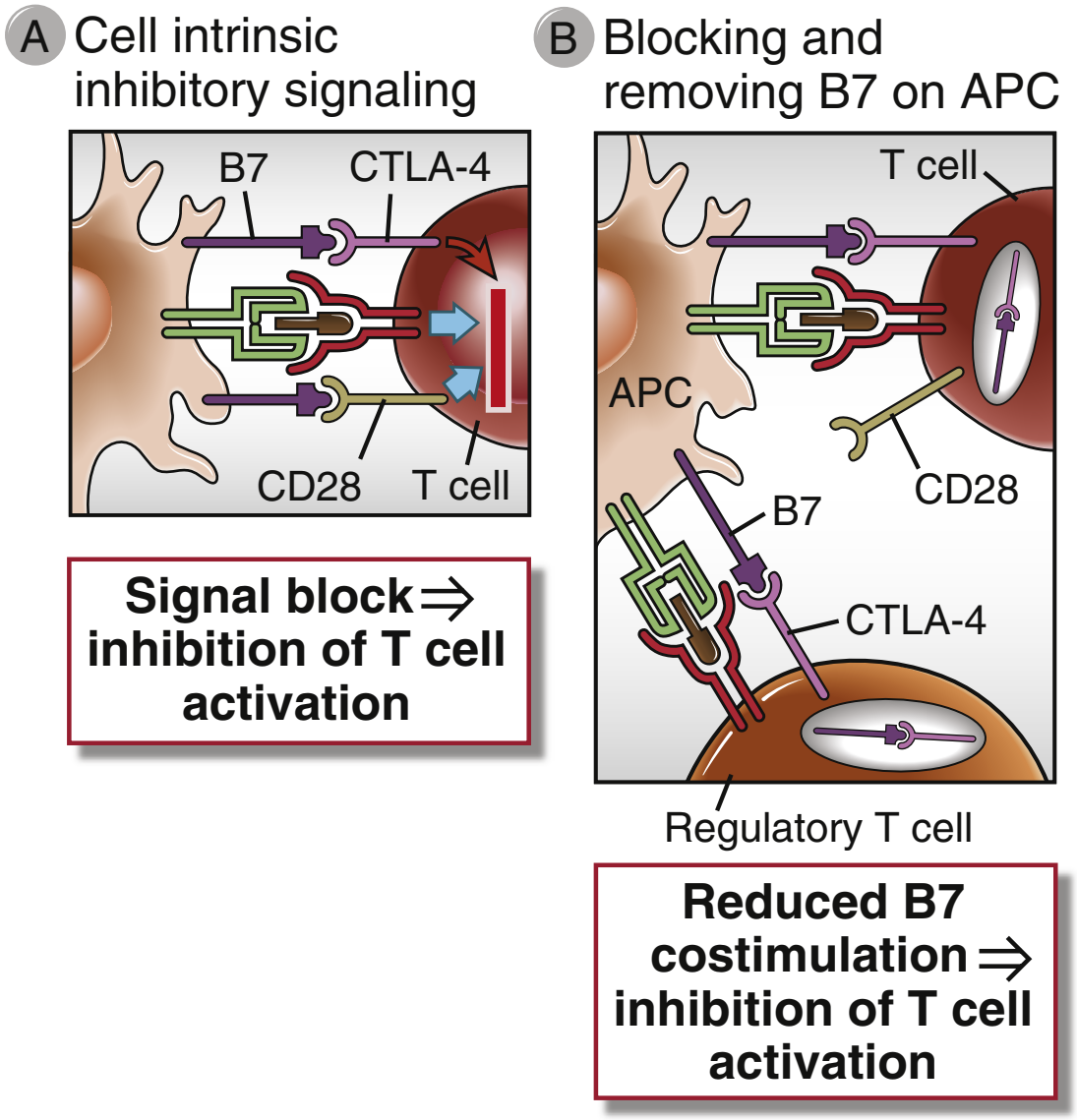


Fig 15-6

3. Regulatory T cells

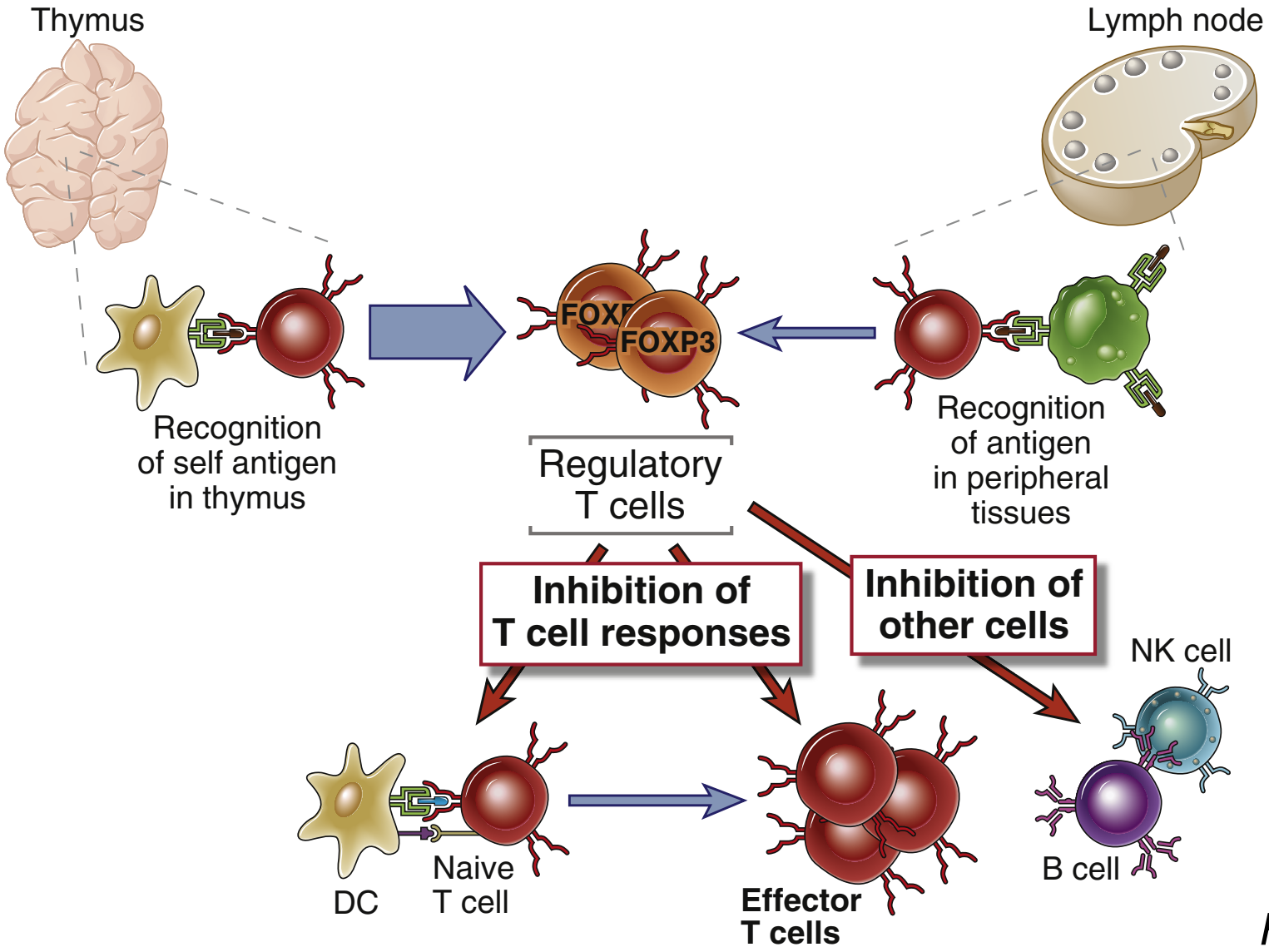
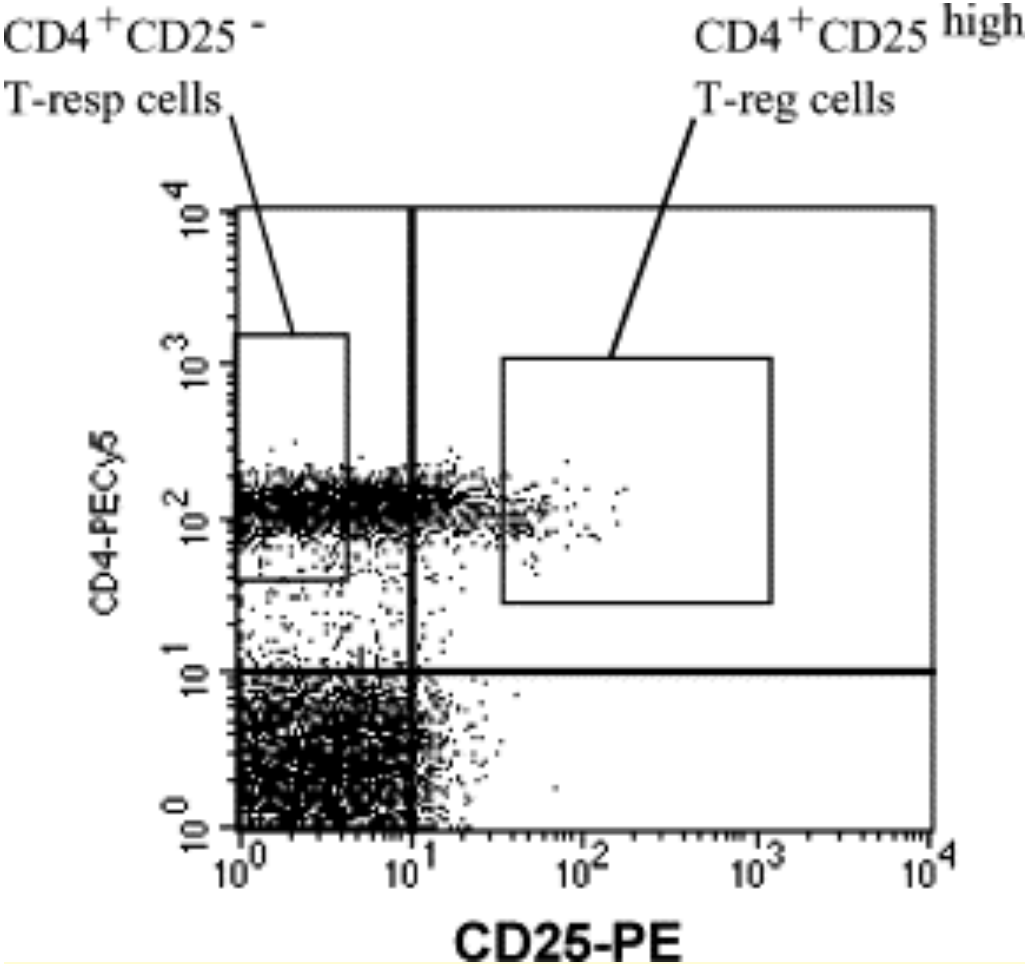


Fig 15-7

3. Regulatory T cells



3. Regulatory T cells

Phenotype: $CD3^+$ $CD4^+$ $CD25^+$ $FoxP3^+$

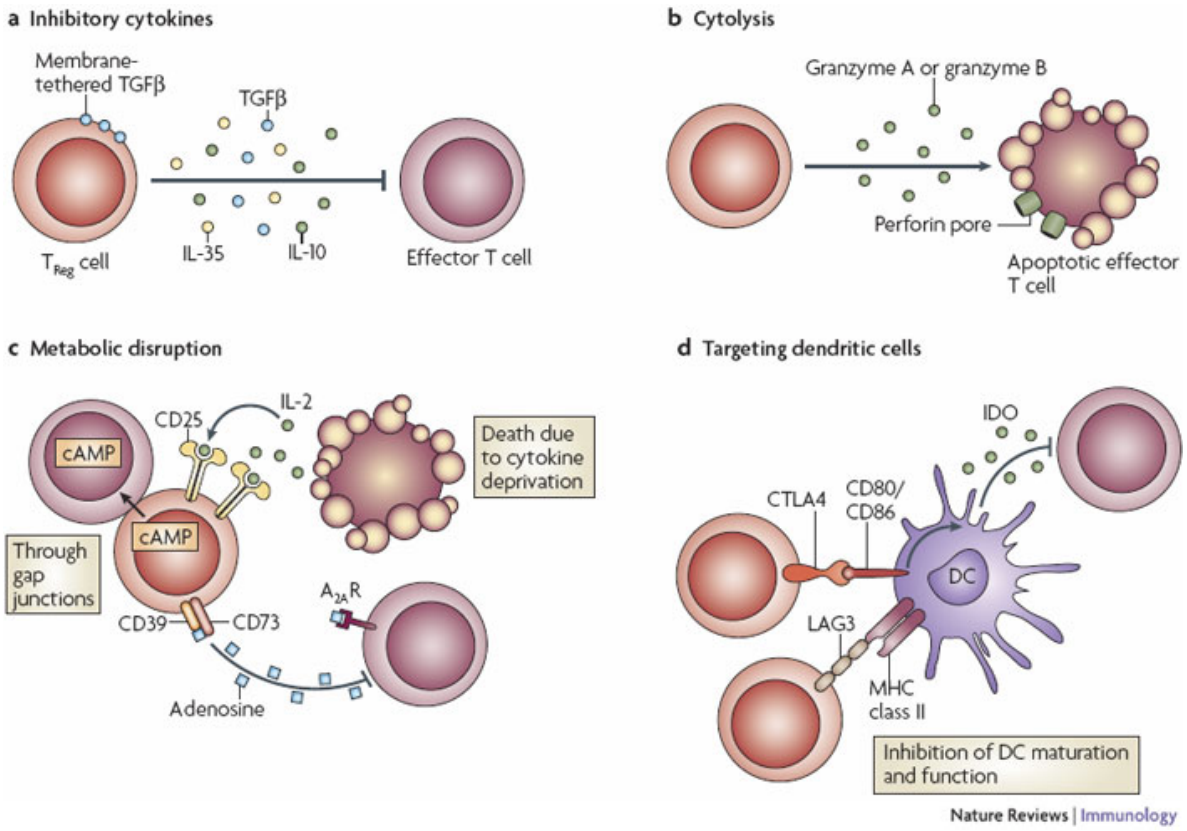
FoxP3 Mutation: IPEX Syndrom (immune dysregulation, polyendocrinopathy, enteropathy, X-linked)

Origin: Thymus (natural) or periphery (induced)

Suppression mechanism:

- Cytokine secretion: IL-10, TGFβ
  - *IL-10$^{-/-}$ mice: colitis*
- Blocking costimulation via CTLA-4
- IL-2 “consumption” via IL-2Rα (CD25, high-affinity IL-2R)

Treg suppression mechanisms



a.) Inhibitory cytokines include IL-10, IL-35 and TGFβ.
b.) Cytolysis includes granzyme-A- and granzyme-B-dependent and perforin-dependent killing
c.) Metabolic disruption includes high-affinity CD25 (IL-2 receptor)-dependent cytokine-deprivation-mediated apoptosis, cAMP-mediated inhibition, and CD39- and/or CD73-generated adenosine receptor 2A-mediated immunosuppression.
d.) Targeting dendritic cells (DCs) includes mechanisms that modulate DC maturation and/or function such as lymphocyte-activation gene 3 (LAG3; also known as CD223)–MHC-class-II-mediated suppression of DC maturation, and cytotoxic T-lymphocyte antigen-4 (CTLA4)–CD80/CD86-mediated induction of indoleamine 2,3-dioxygenase (IDO), which is an immunosuppressive molecule made by DCs.

4. Suppression via antibody feedback

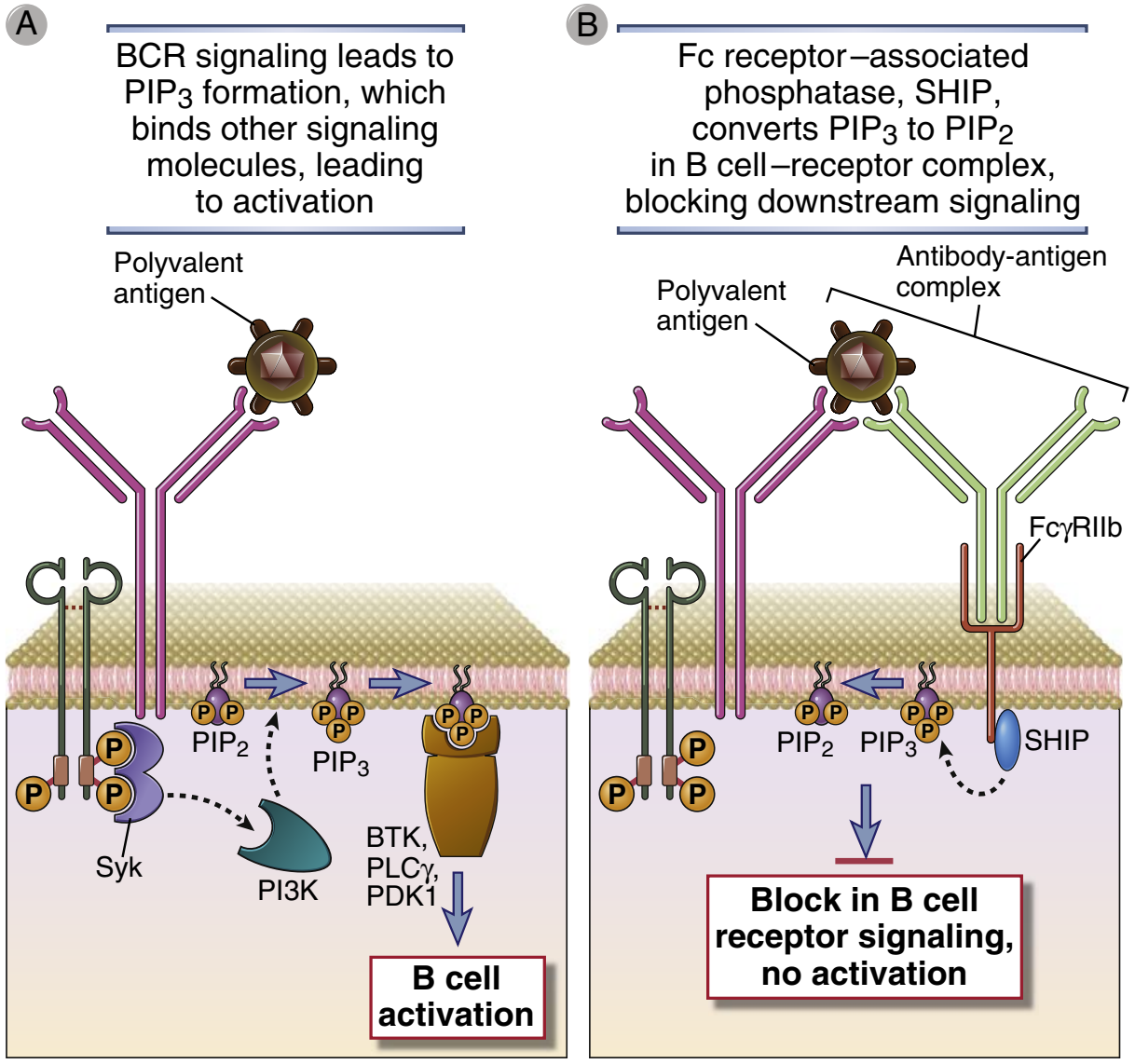


Fig 12-21

4. Suppression via antibody feedback

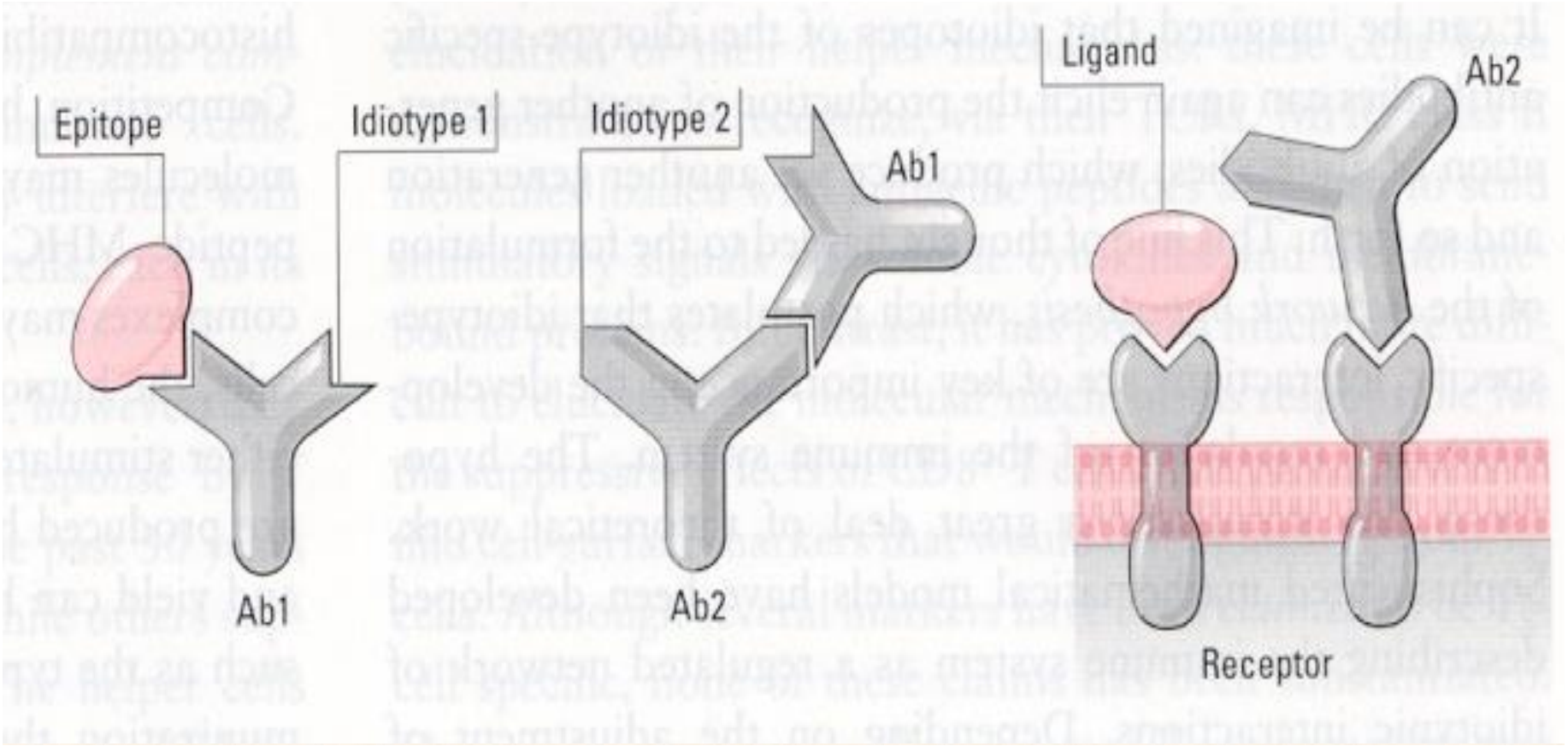
High levels of antibodies block further B cell activation

IgG + antigen immunocomplex inhibits B cell function by binding to FcγRIIb

(IgM + antigen immunocomplex promotes further B cell activation!)

5. Anti-idiotype antibodies

Network hypothesis (Niels Jerne): suppression via antibodies



5. Anti-idiotype antibodies

Function:

Suppression of B and T cells

Functional memory formation

Biological mimicry (insulin – anti-insulin – anti-anti-insulin)