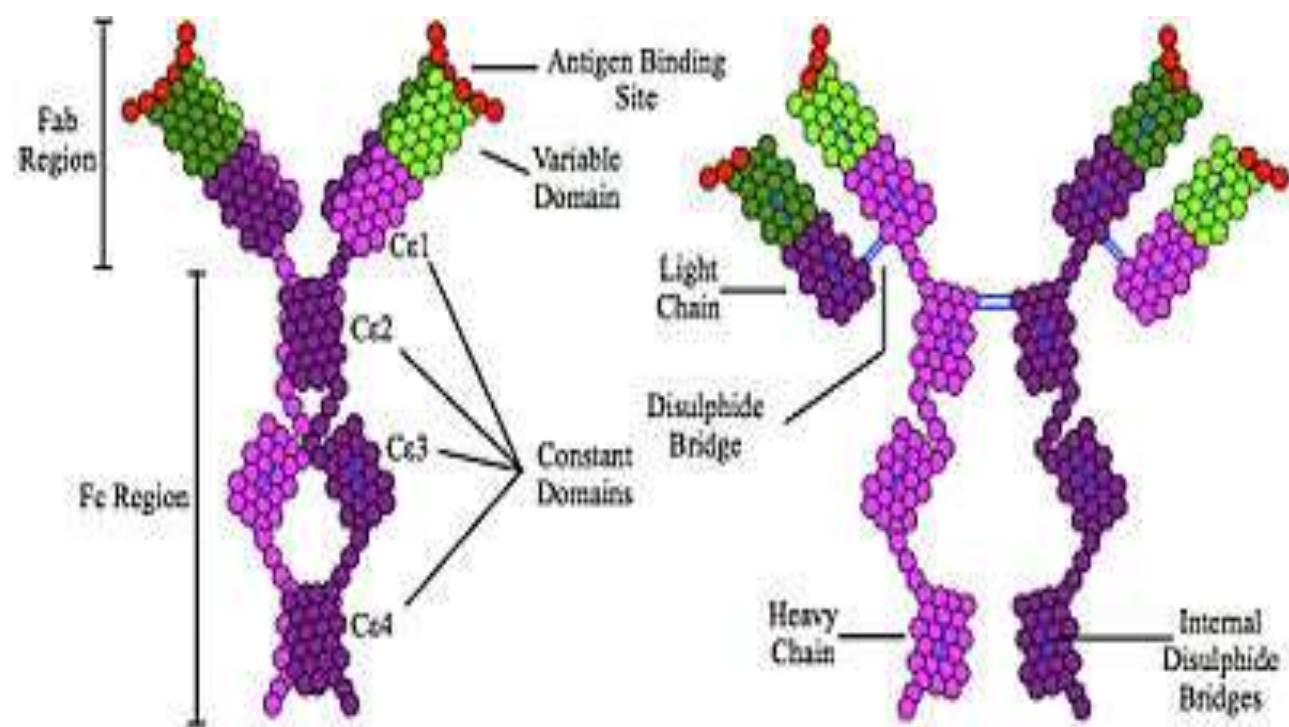


IgE İlişkili Hastalıklar

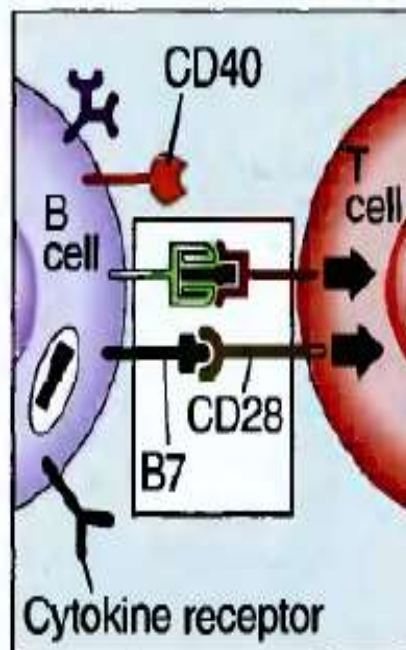
Prof. Dr. İnsu Yılmaz

Erciyes Üniversitesi Tıp Fakültesi Göğüs Hastalıkları AD

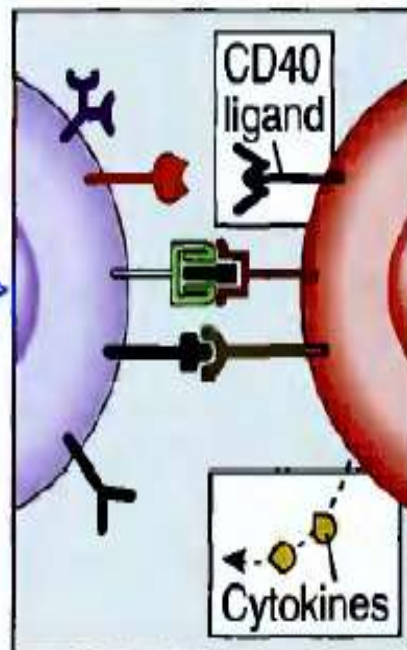
İmmünoloji ve Allerji Hastalıkları BD



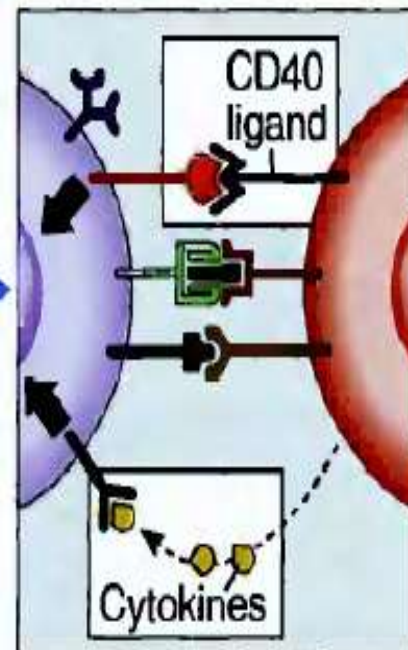
B cell presents antigen to helper T cell



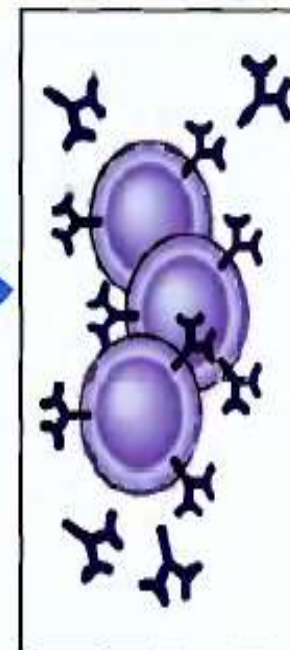
Helper T cell is activated; expresses CD40L, secretes cytokines

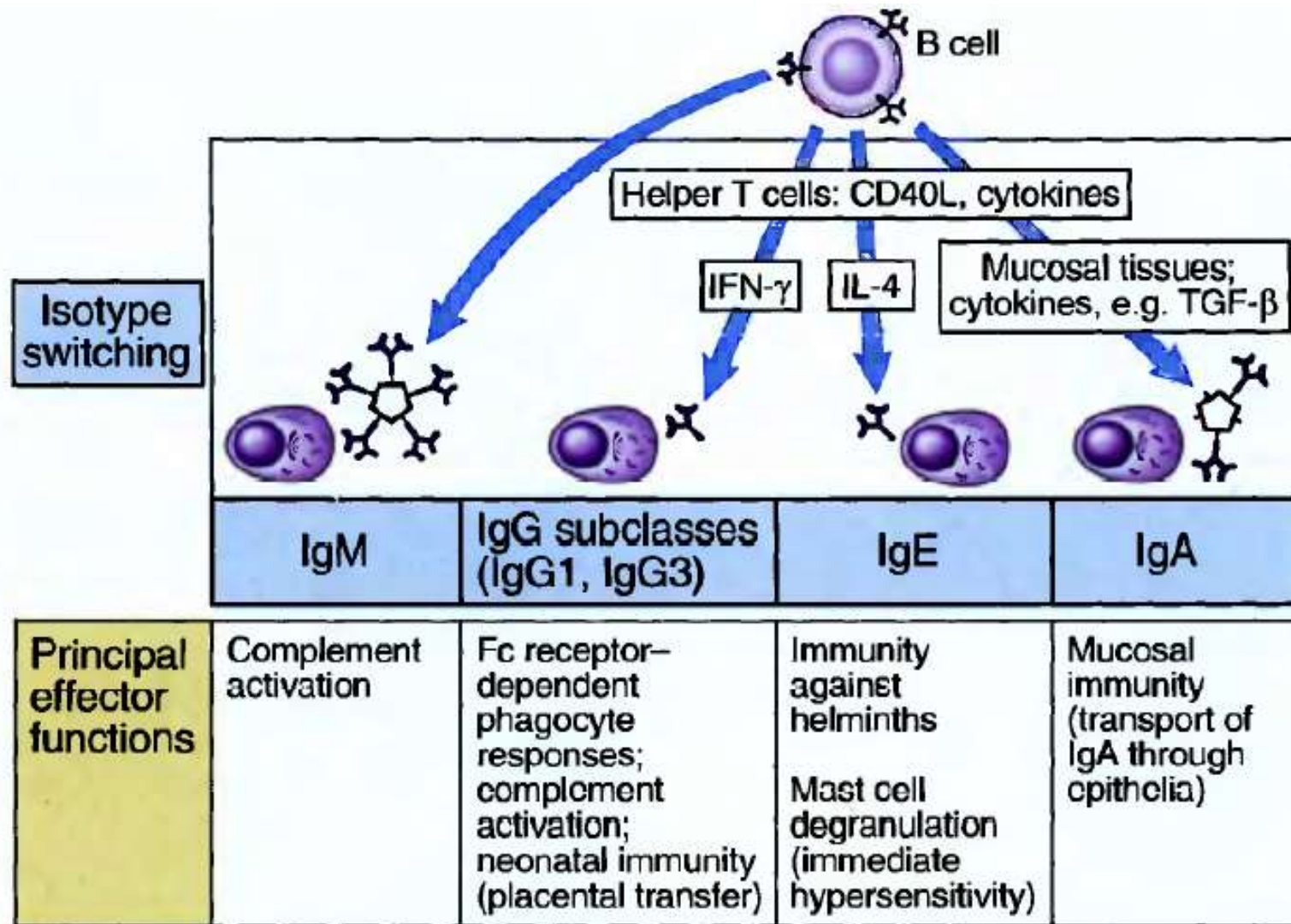


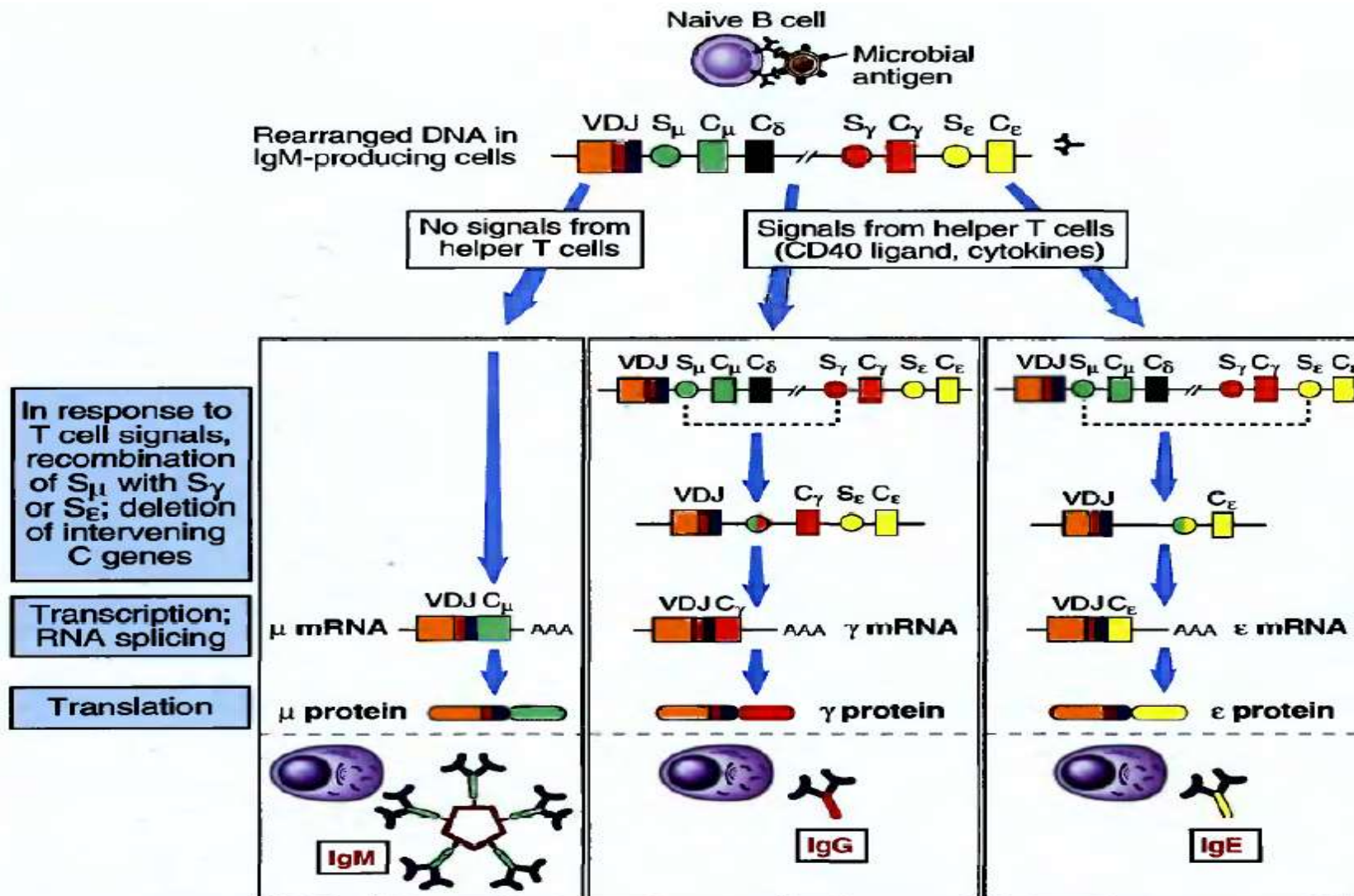
B cells are activated by CD40 engagement, cytokines



B cell proliferation and differentiation

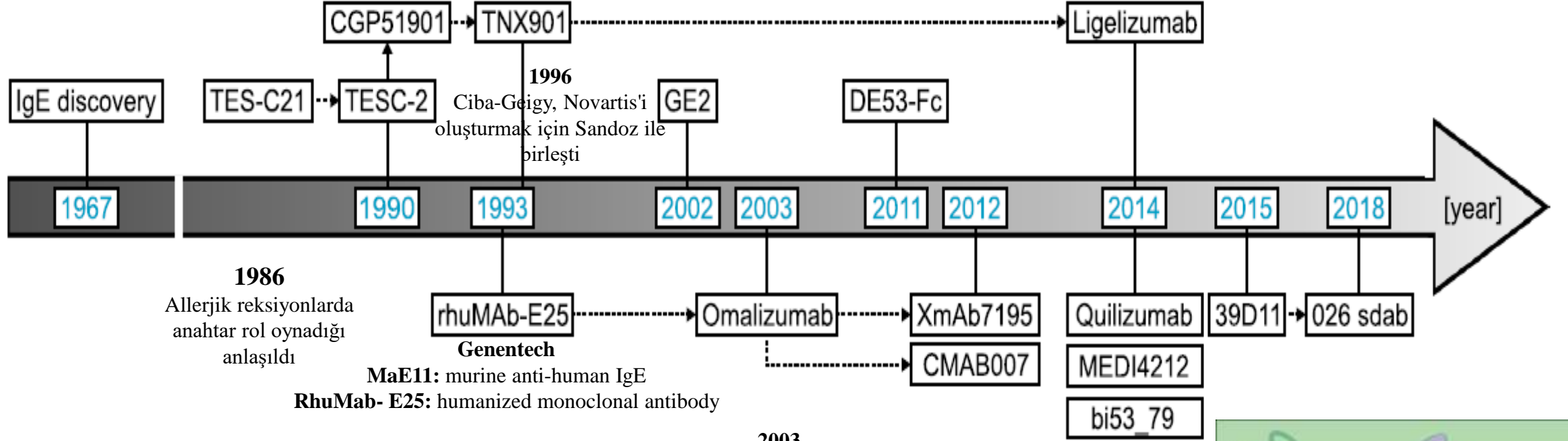






Allerjik rinit Faz 1 ve 2
Doz bağımlı serbest IgE azalma
Rinit semptomlarında azalma
Yüksek tolerabilite

TNX56901=TNX901=Talizumab:
humanized monoclonal anti-IgE antibody

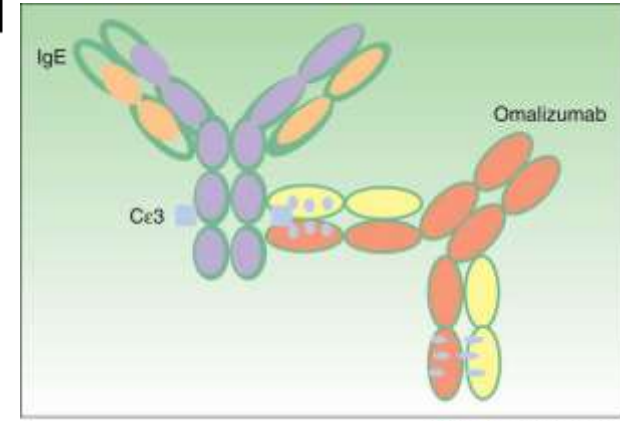


Giba-Geigy, farklı fare modellerinde kavram ispatı
Tanox, ilk monoklonal mürin anti-human IgE antikor **TES-C21**

Giba Giagy+Tanox
Chimeric mouse/human monoclonal antibody
TESC-2 = CGP51901

2003
Genentech+TANOX+ Novartis
rhuMAb=Omalizumab (Xolair)
İlk terapötik anti-IgE antikor

IgE antikorunu nötralize eden
IgG1 alt sınıfında antikor



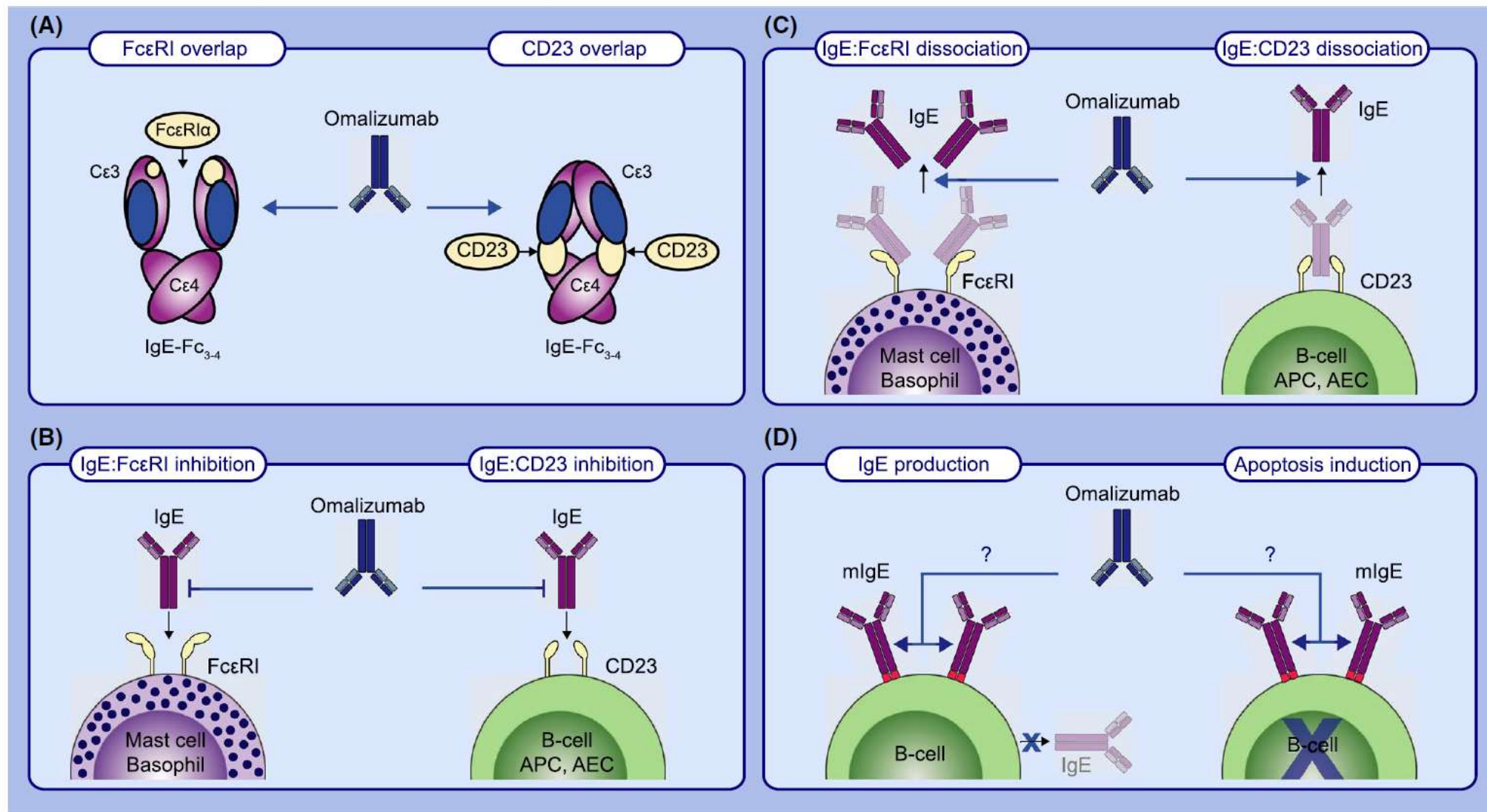


FIGURE 2 Binding characteristics and modes-of-action of omalizumab. A, Schematic overview of omalizumab (blue)-, FcεRIα (left panel)- and FcεRII/CD23 (right panel)-binding sites as well as their relative overlap on IgE-Fc₃₋₄ (purple). B, Omalizumab-mediated inhibition of free IgE binding to FcεRI or CD23. C, Omalizumab-mediated accelerated dissociation of pre-formed IgE:FcεRI and IgE:CD23 complexes. D, Potential mechanisms leading to suppression of IgE production by omalizumab

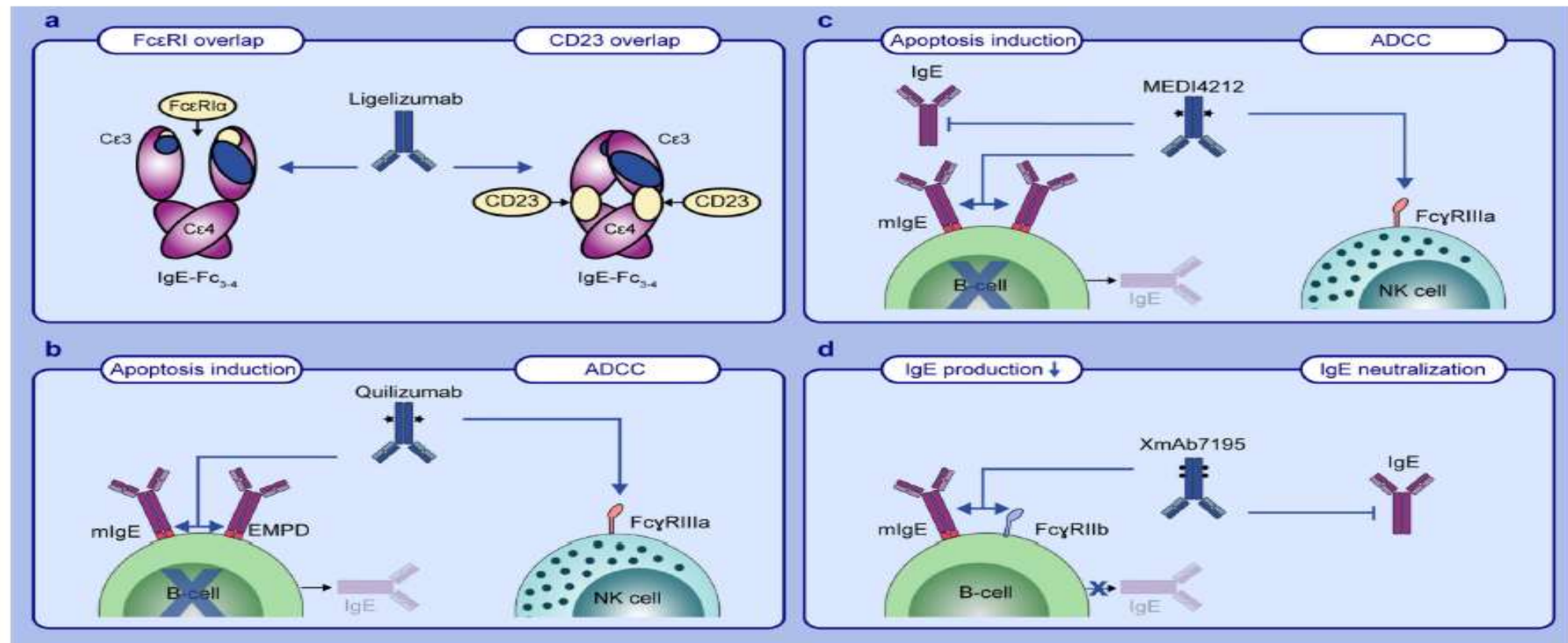


Fig. 3. Binding characteristics and modes-of-action of different anti-IgE antibodies.

a) Schematic overview of ligelizumab (blue), FcεRIα (left panel) and FcεRII/CD23 (right panel) binding sites as well as their relative overlap on IgE-Fc₃₋₄ (purple). **b)** Two mechanisms of quilizumab mediated suppression of IgE production through induction of B-cell apoptosis or antibody dependent cellular cytotoxicity (ADCC). Afucosylation of quilizumab is indicated with stars. **c)** Mechanisms of MEDI4212 mediated neutralization of free IgE and suppression of IgE production through induction of B-cell apoptosis or antibody dependent cellular cytotoxicity (ADCC). Afucosylation of MEDI4212 is indicated with stars. **d)** XmAb7195 mediated neutralization of free IgE and suppression of IgE production through co-aggregation of mIgE and FcγRIIb on B-cells. Mutations in the antibody Fc-part are indicated with dots.

IgE ilişkili hastalıklar

- Allerjik rinit
- Allerjik konjonktivit
- Arı allerjileri
- Anafilaksi
- Allerjik astım
- Eozinofilik astım
- Gıda allerjileri
- Tip 2 KRS/NP
- KSÜ
- Atopik dermatit
- HES
- KEP
- EGPA
- ABPA
- Eozinofilik özefajit
- Enfestasyonlar (Paraziter hastalıklar)
- Enfeksiyonlar
- Otoimmün hastalıklar
- Lenforetiküler maligniteler
- Solid organ maligniteleri
- Primer immün yetmezlikler
- Pemfigus vulgaris
- İnflamatuar bağırsak hastalıkları
- Allograft rejeksiyon
- Ateroskleroz
- Yanık, travma

IgE ilişkili hastalıklar

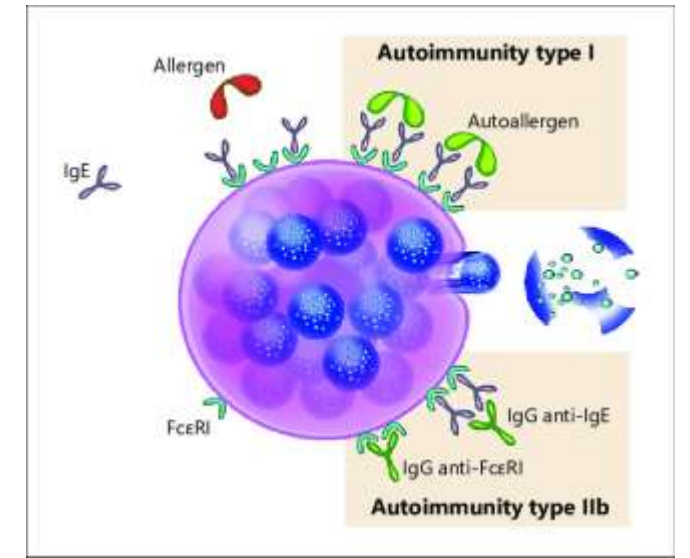
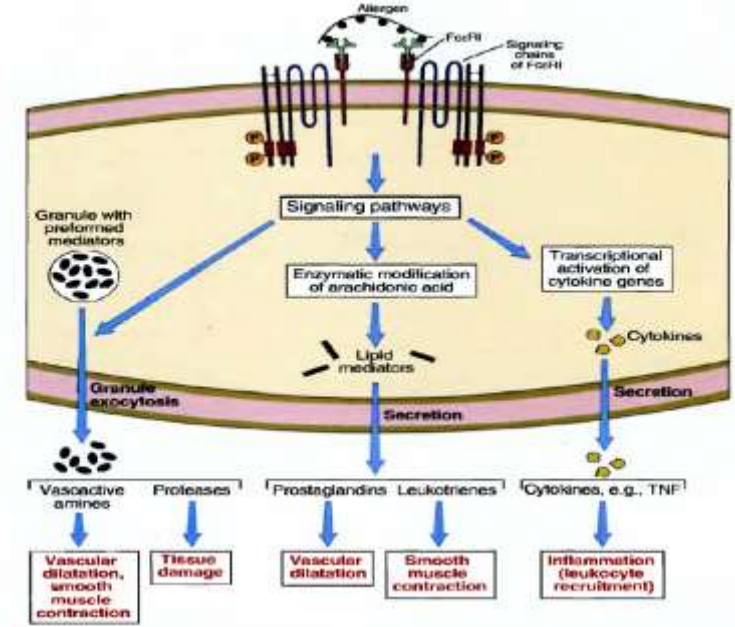
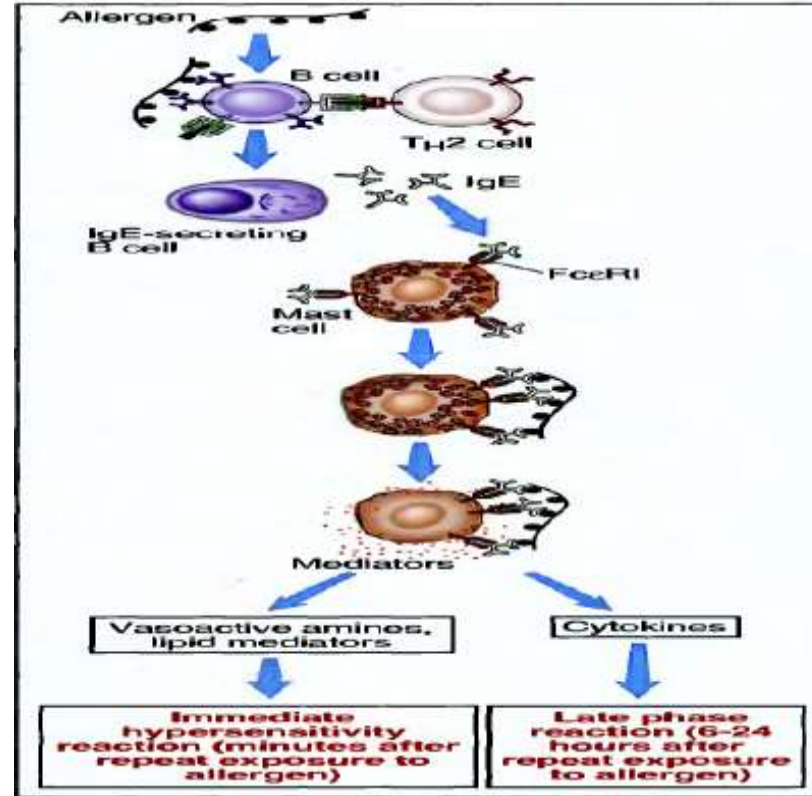
- **Allerjik rinit**
- Allerjik konjonktivit
- Arı allerjileri
- Anafilaksi
- Allerjik astım
- Eozinofilik astım
- Gıda allerjileri
- Tip 2 KRS/NP
- KSÜ
- Atopik dermatit
- HES
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- ABPA
- Eozinofilik özefajit
- Enfestasyonlar (Paraziter hastalıklar)
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- Pemfigus vulgaris
- İnflamatuar bağırsak hastalıkları
- Allograft rejeksiyon
- Ateroskleroz
- Yanık, travma

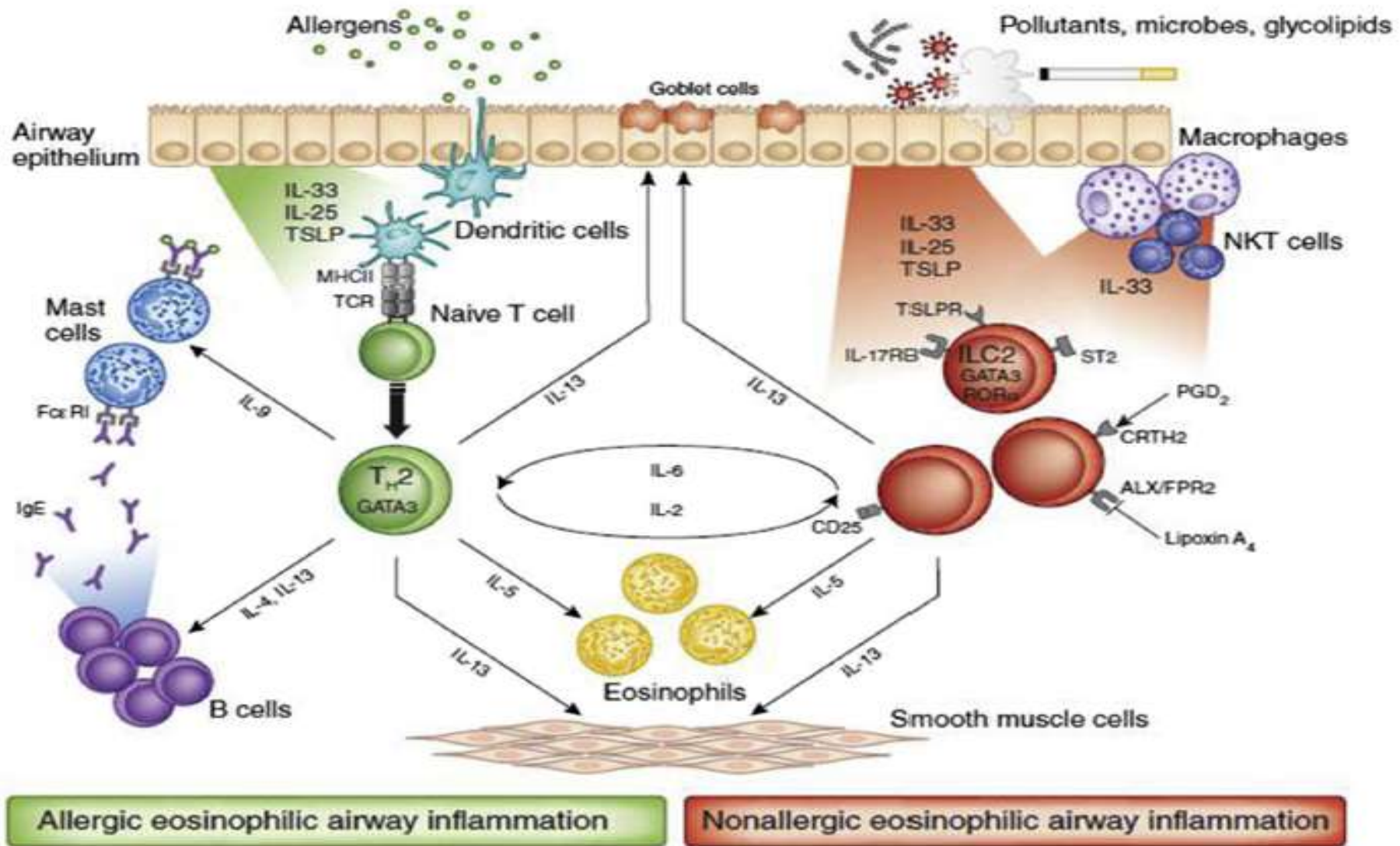
Hastalık patofizyolojisinde IgE'nin yer aldığı hastalıklar

- Allerjik rinit
- Allerjik konjonktivit
- Arı allerjileri
- Anafilaksi (IgE aracılı)
- Allerjik astım
- Eozinofilik astım
- Gıda allerjileri (IgE aracılı)
- Tip 2 KRS/NP
- KSÜ
- EGPA
- ABPA
- Paraziter hastalıklar

IgE'nin hastalık patofizyolojisinde majör rol aldığı hastalıklar

- Allerjik rinit
- Allerjik konjonktivit
- Arı allerjileri
- Anafilaksi (IgE aracılı)
- Gıda allerjileri (IgE aracılı)
- KSÜ (otoimmün)
- **Allerjik/eozinofilik astım**
- **Tip 2 KRS/NP**





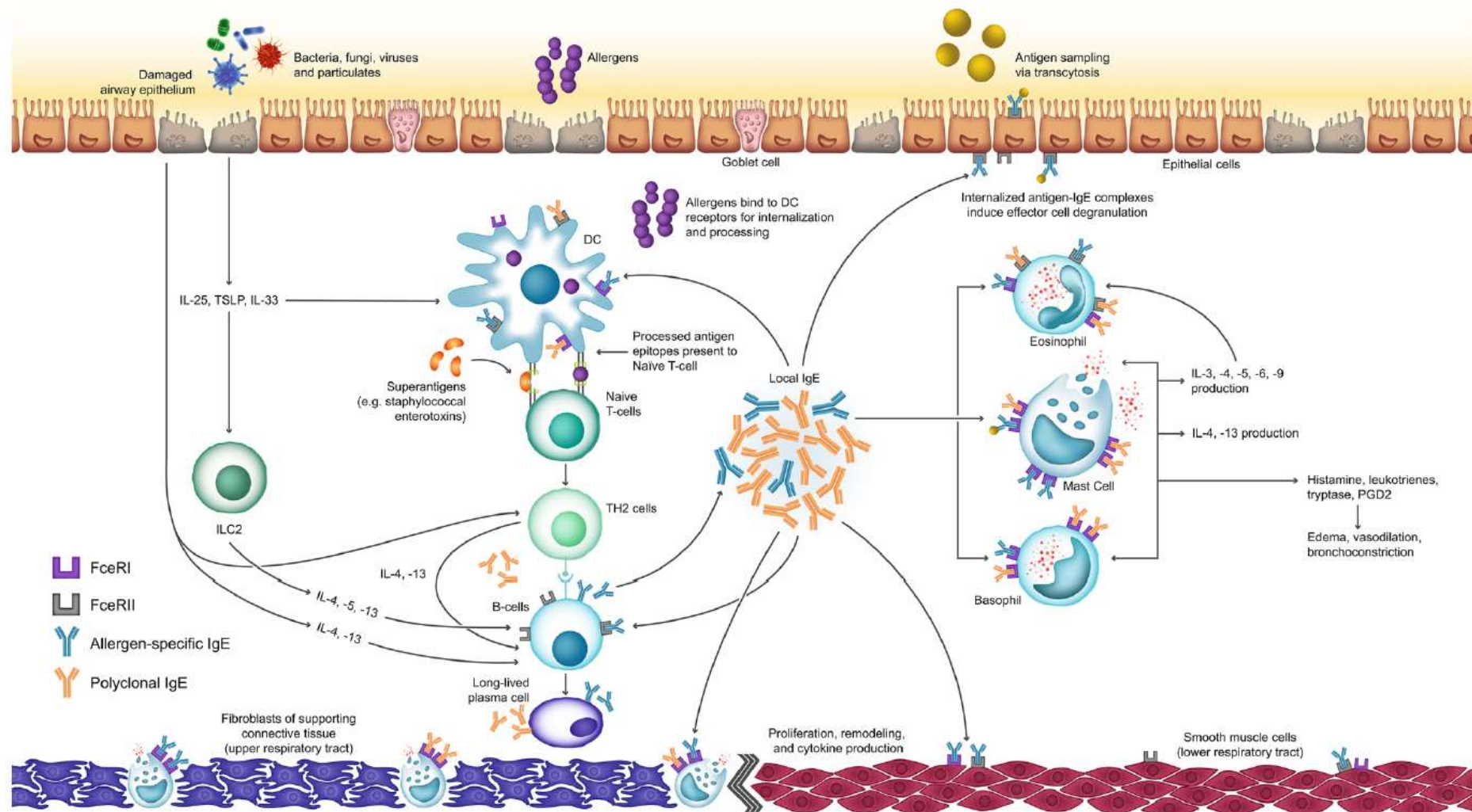


Fig. 1 Mechanism of IgE-mediated upper and lower airway disease. In response to allergen exposure, dendritic cells present allergen-specific antigens to naïve T cells, which are activated and differentiate into Th2 cells. These Th2 cells produce key cytokines (IL-4, IL-13), prompting B cells to produce allergen-specific IgE. Alternatively, exposure to external stimuli such as bacteria, fungi, viruses, and particulates promotes epithelial release of IL-25, TSLP, and IL-33. These factors stimulate ILC2 cells to produce IL-5, IL-13, and to a lesser extent, IL-4, which in turn promote B cell production of IgE. Finally, superantigens, including *Staphylococcal* enterotoxins, can directly cross-link antigen-presenting cells with naïve T cells, bypassing the antigen presentation step, yielding polyclonal IgE. Once produced, local IgE acts on the FcεRI receptors of tissue-resident mast cells and basophils, prompting the release of histamine, leukotrienes, tryptase, and prostaglandin, which manifest as edema, vasodilation, and

bronchoconstriction as part of the early response. IgE also binds to FcεRII receptors on B cells for enhanced antigen presentation. Later release of key cytokines recruits proinflammatory cells, including eosinophils and basophils, to the site of inflammation, and additionally promotes the overexpression of mucus-producing goblet cells and contributes to airway hyperresponsiveness. Crosstalk within the inflammatory pathway promotes a self-propagating cycle of chronic inflammation. The lower left side of the figure depicts the fibroblasts and mast cells within the supporting connective tissue of the nasal cavity, while the lower right side depicts the smooth muscle cell layer surrounding the lower respiratory airway. DC, dendritic cell; FcεRI, high-affinity immunoglobulin E receptor; FcεRII, low-affinity immunoglobulin E receptor; IgE, immunoglobulin E; IL, interleukin; ILC, innate lymphoid cell; PGD2, prostaglandin D2; Th2, T helper 2; TSLP, thymic stromal lymphopoietin



TEŞEKKÜRLER