Biologics for type 2 severe asthma: Understanding the mechanism of action

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The key molecules targeted by biologic therapies in severe type 2 asthma

Key therapeutic targets

Type 2 cytokines (IL-4, IL-5 and IL-13) and IgE have a pivotal role in asthma pathophysiology

- **IgE** plays a significant role in allergic asthma
- **IL-4, IL-5 and IL-13** drive eosinophilic inflammation
- **IL-4 and IL-13** drive IgE synthesis in type 2 asthma

Targeted biologic therapies

Five mABs have been developed targeting these pathways:

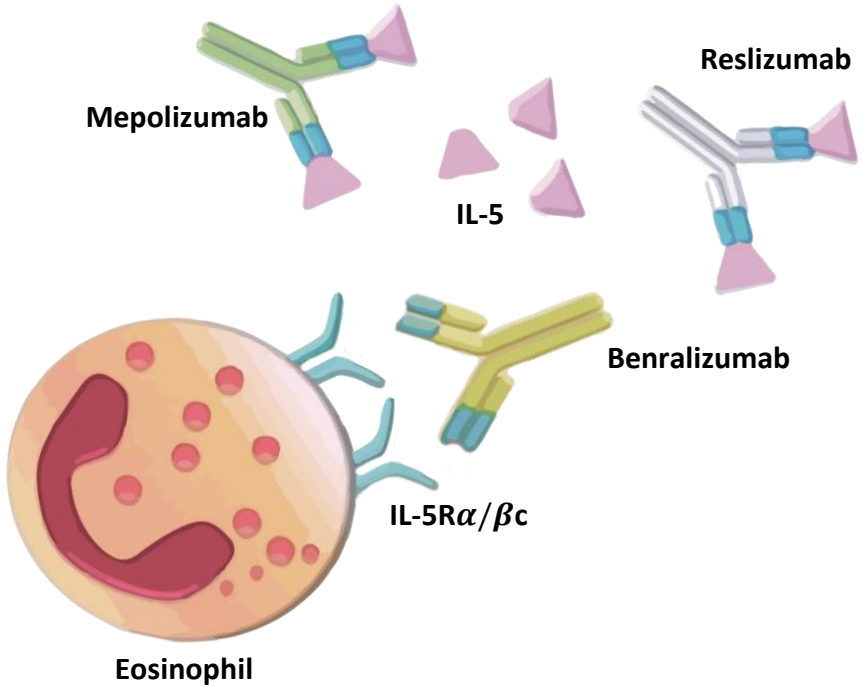
- Omalizumab (IgE)
- Mepolizumab (IL-5)
- Reslizumab (IL-5)
- Benralizumab (IL-5 receptor)
- Dupilumab (IL4R binding IL-4/IL-13)

Ig, immunoglobulin; IL, interleukin; mAB, monoclonal antibody

1. Robinson D et al. *Clin Exp Allergy*. 2017;47:161–75.

Mechanism of action of mepolizumab, reslizumab and benralizumab

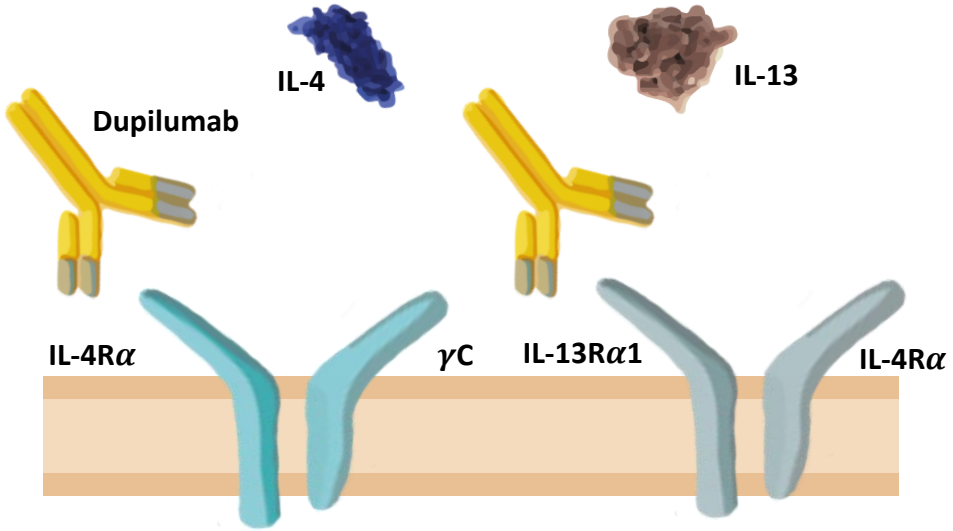
- Mepolizumab and reslizumab bind to and neutralise IL-5
- Benralizumab targets and blocks the IL-5 receptor



1. Pelaia G et al. *Ther Clin Risk Manag.* 2016;12:1075–82.
Image adapted from Pelaia G et al. *Ther Clin Risk Manag.* 2016.

Dupilumab mechanism of action

- Dupilumab binds to the IL-4α subunit of IL-4 and IL-13 receptors[1]
- Dupilumab blocks signalling of IL-4 and IL-13, key cytokines that promote production of IgE, recruitment of inflammatory cells and can trigger airway remodelling[2]



1. Vatrella A et al. *J Asthma Allergy* 2014;7:123–30; 2. Robinson D et al. *Clin Exp Allergy*. 2017;47:161–75.
Image adapted from Vatrella A et al. *J Asthma Allergy* 2014.

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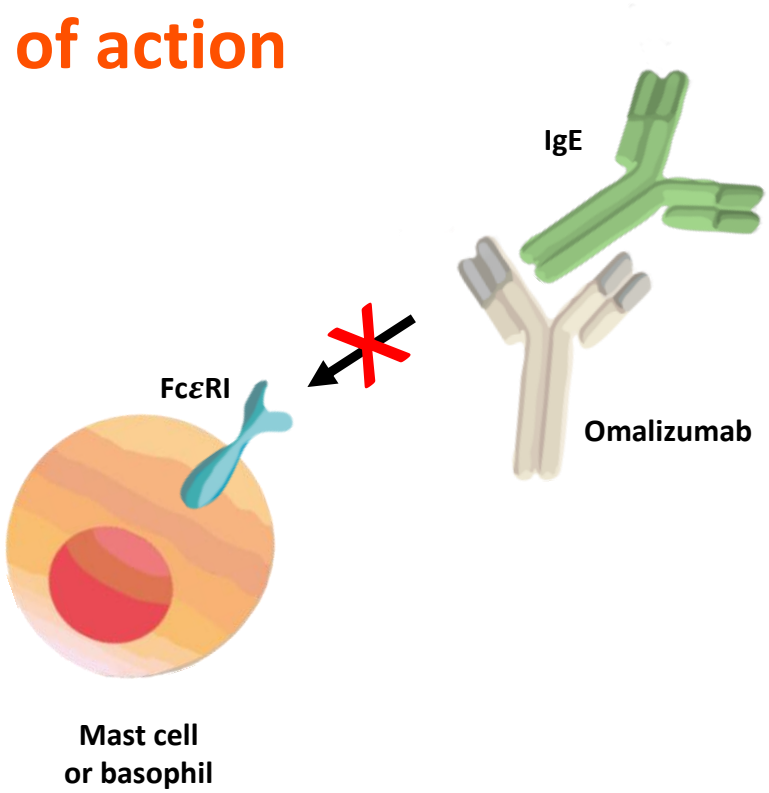
Omalizumab mechanism of action

- Omalizumab is an anti-IgE antibody that prevents IgE from binding to its high-affinity receptor on mast cells and basophils[1]
- Dampens release of proinflammatory mediators and reduces inflammatory response[1]



1. Busse WW. *Allergol Int*. 2019;68(2):158–66.
Image adapted from: https://www.creativebiolabs.net/omalizumab-overview.htm

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