10 ANNI DI TERAPIA ANTI-IGE: ANCORA INNOVAZIONI IN ASMA GRAVE E CSU

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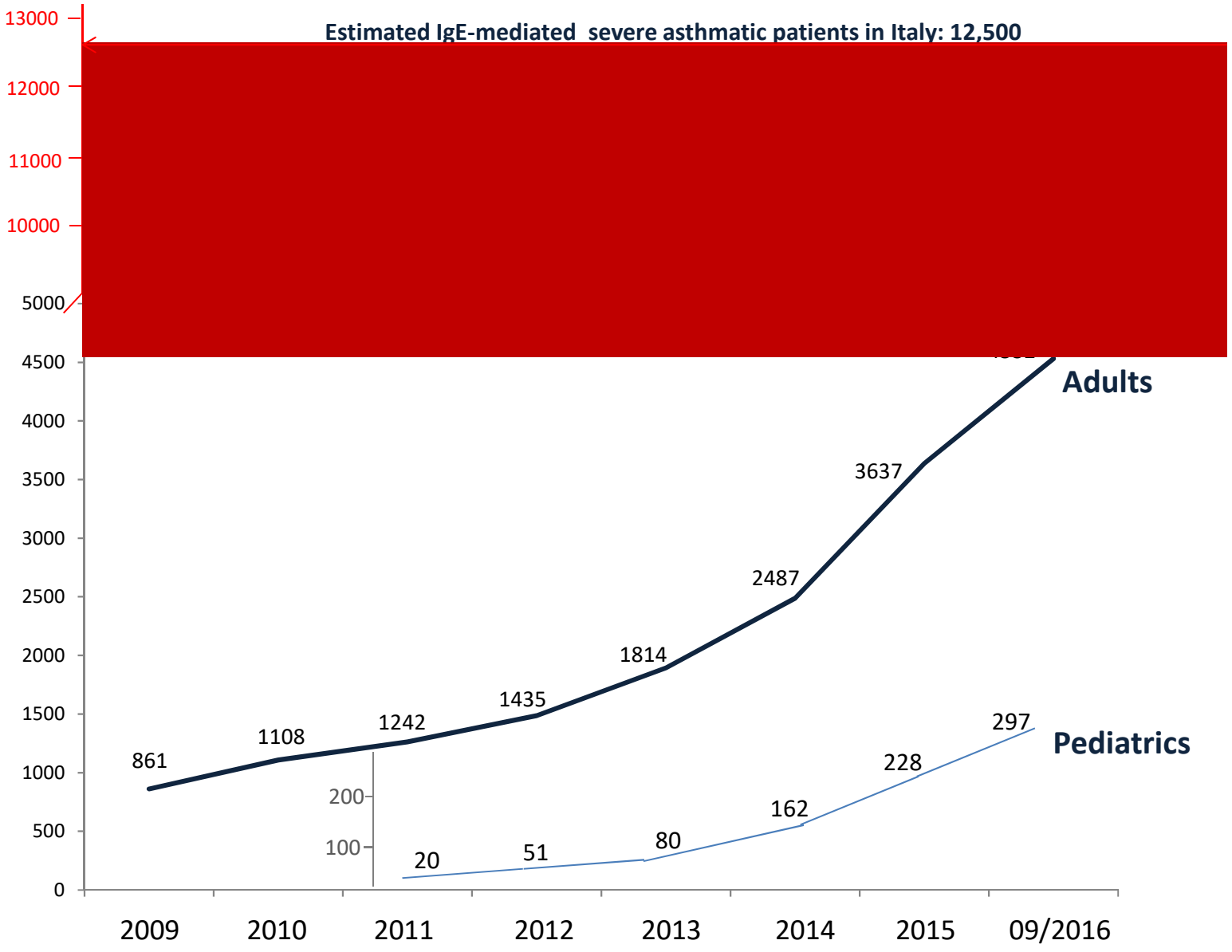
Italian SAA patients treated with Omalizumab



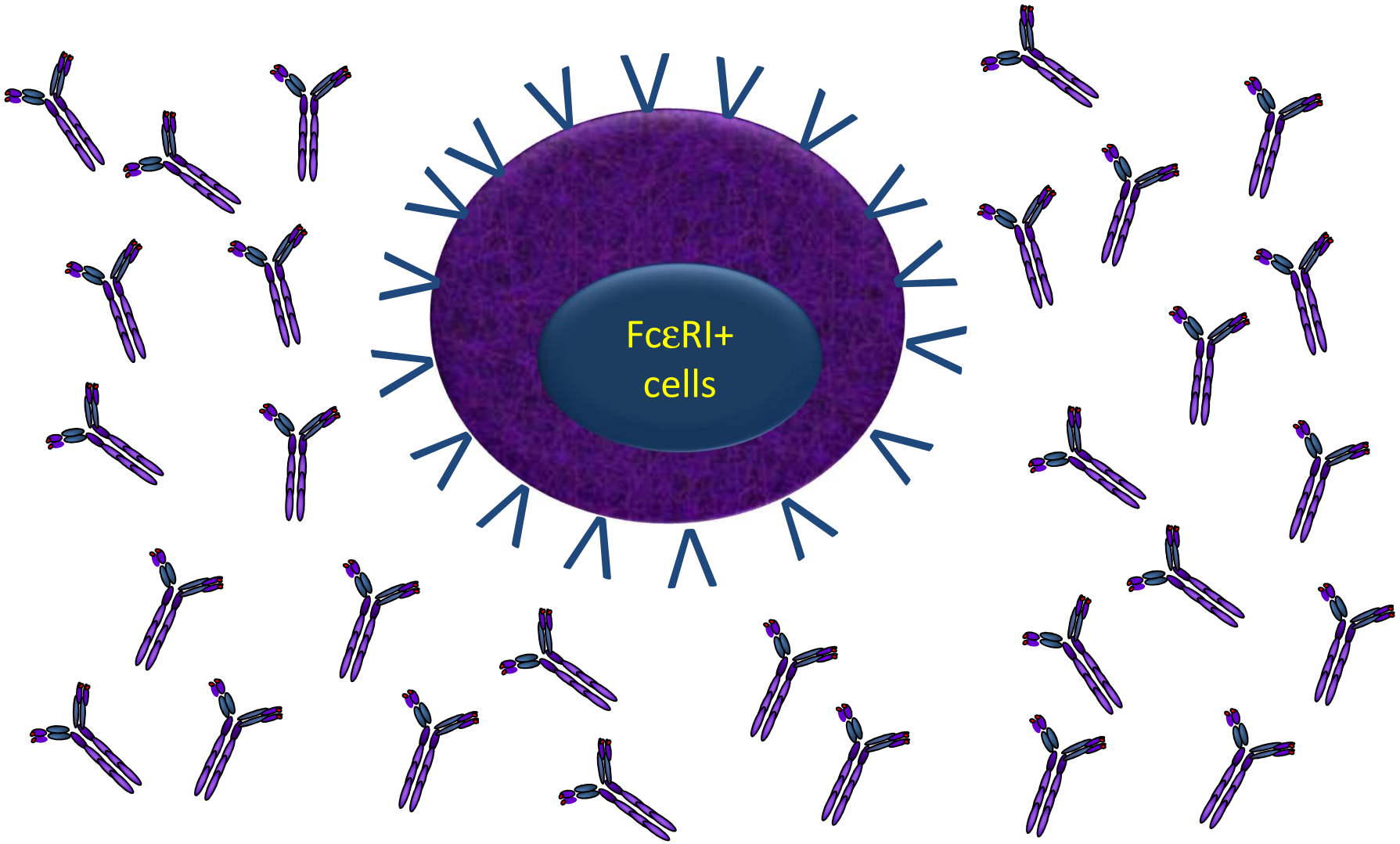
Matucci A; Vultaggio A. Highlights 2016 (Data from Novartis, October 2016)

Why should we use an anti-IgE strategy in severe asthma ?

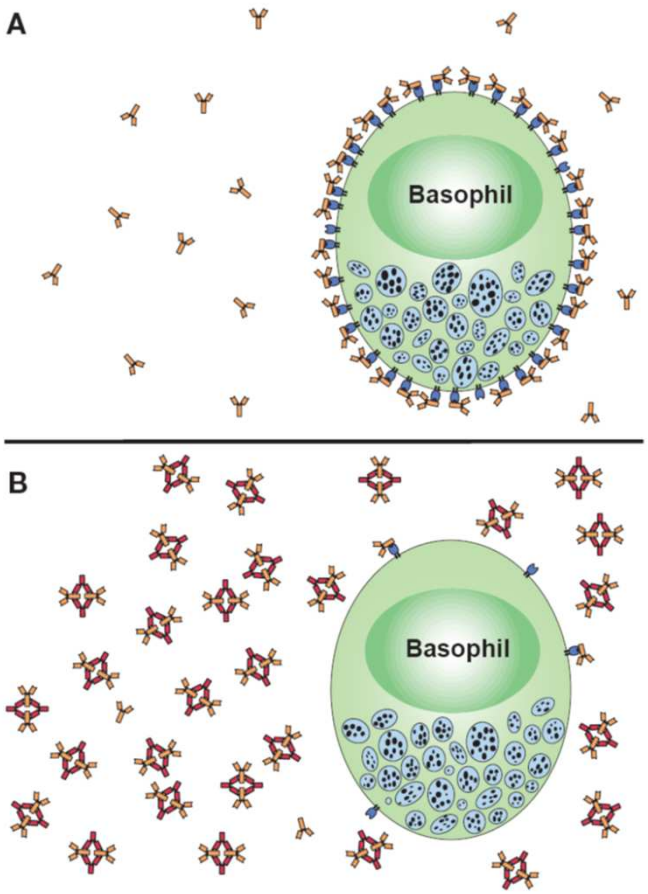
RATIONALE OF OMALIZUMAB USE IN ASTHMATIC PATIENTS

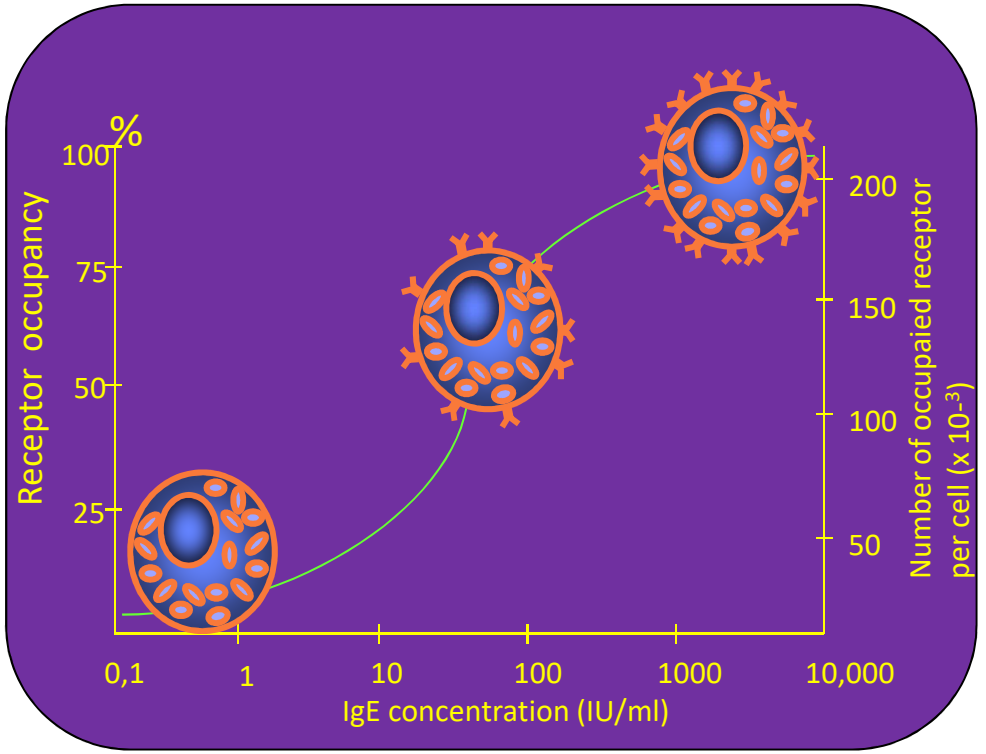
Are IgE involved in the pathogenesis of bronchial asthma (Chronic phase) ?	Have clinical trials and real-life studies displayed positive results?	OMALIZUMAB TREATMENT

THE EXPRESSION OF IGE RECEPTORS IS DIRECTLY RELATED TO IGE SERUM LEVELS



THE EXPRESSION OF HIGH AFFINITY FCE RECEPTORS IS DIRECTLY RELATED TO TOTAL IGE SERUM LEVELS





Owen CE. Pharmacol Therap 2007, 113, 121-133

Chanez P, et al. Respir Med. 2010;104:1608-17

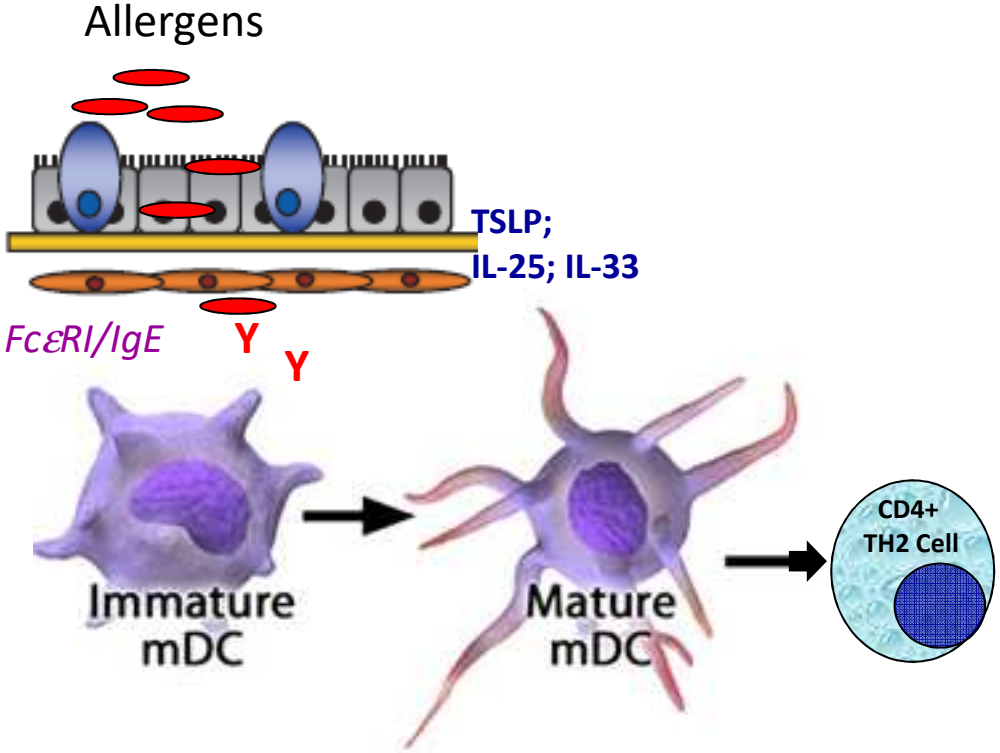
Time of decrease of FcεRI:

- Basophils 7 days 88%
- Mast cells 70 days 90%

IgE Indirectly Affect Eosinophils

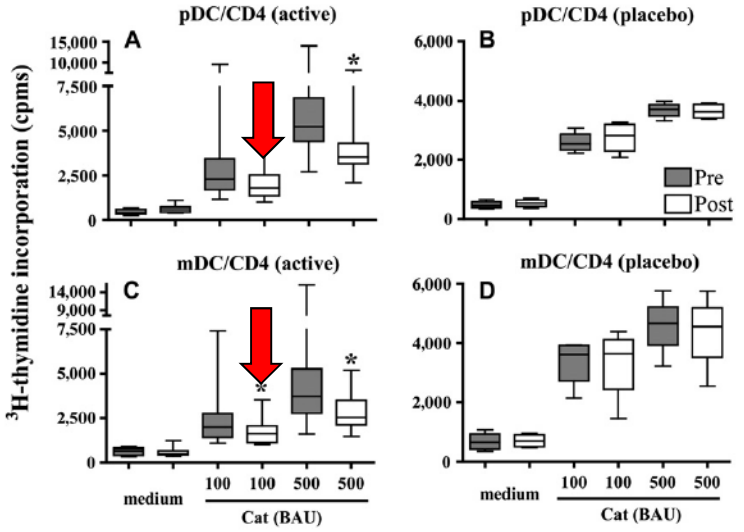
Decreases in human dendritic cell–dependent T_H2-like responses after acute *in vivo* IgE neutralization

John T. Schroeder, et al. J Allergy Clin Immunol 2010;125:896-901.

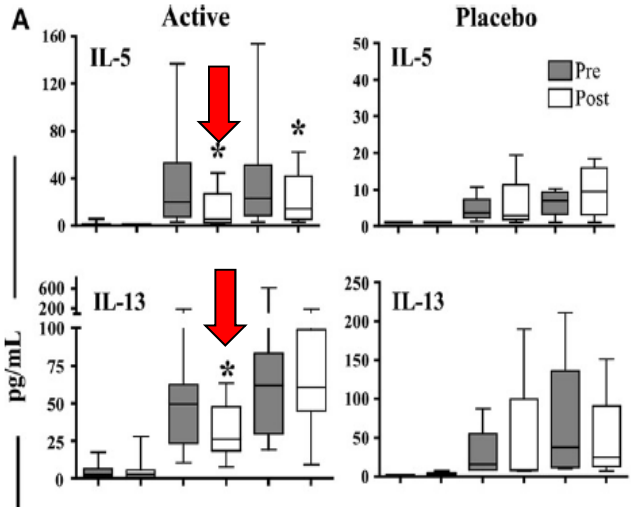


Omalizumab induces a decrease in expression of FcεRI on pDC

Inhibition of T cell proliferation

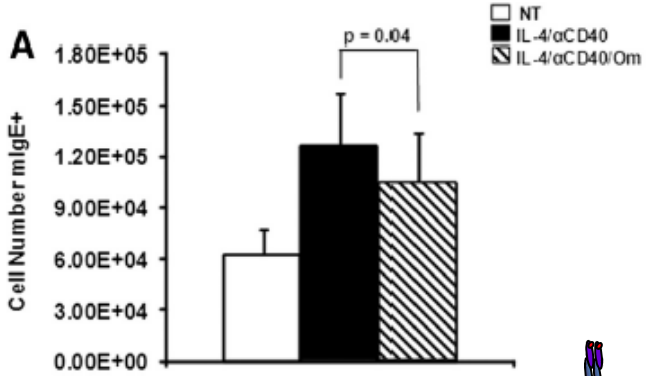


Decreased production of IL-5 and IL-13

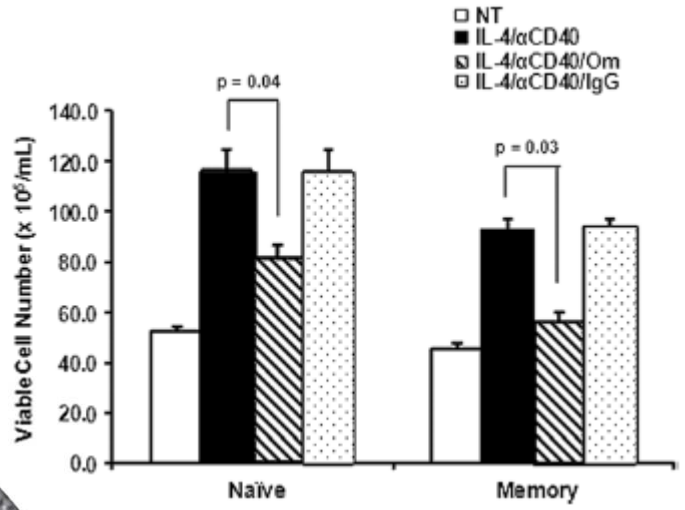


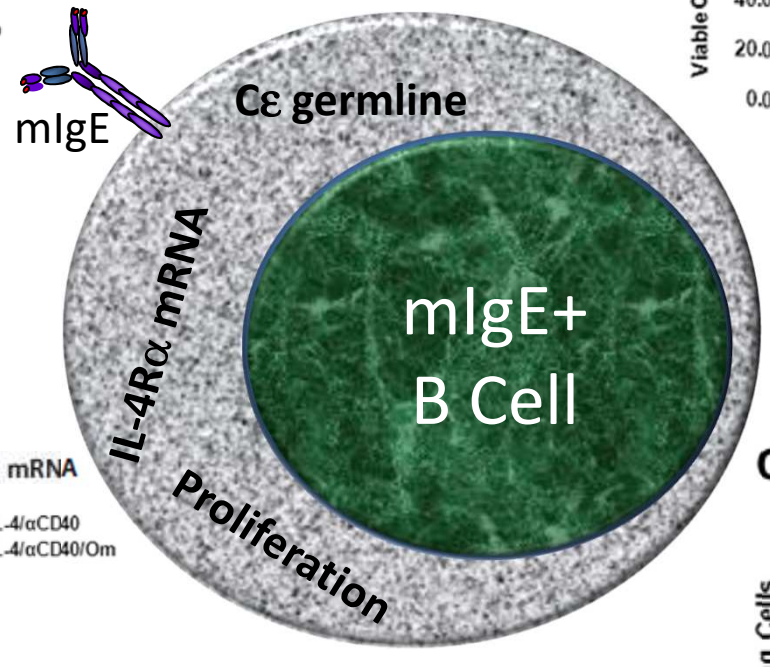
Omalizumab's effects on IgE-bearing B lymphocytes

Omalizumab reduced the number of membrane IgE+

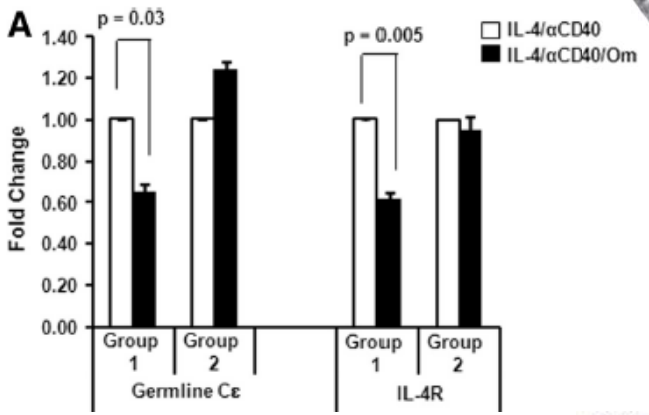


Omalizumab reduced viable human B cell numbers.

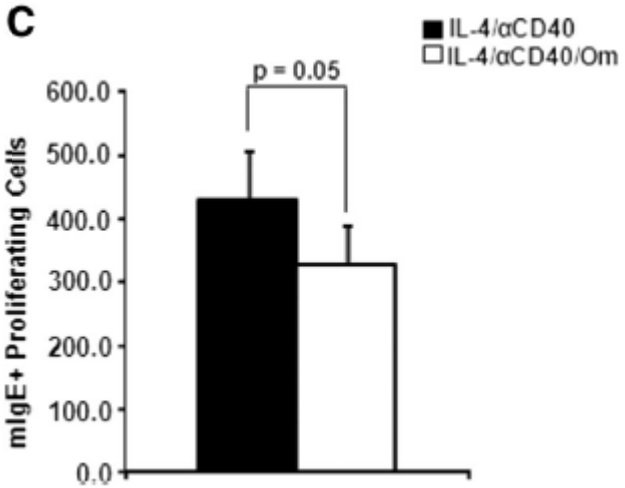




Omalizumab reduced germline Cε and IL-4Rα mRNA

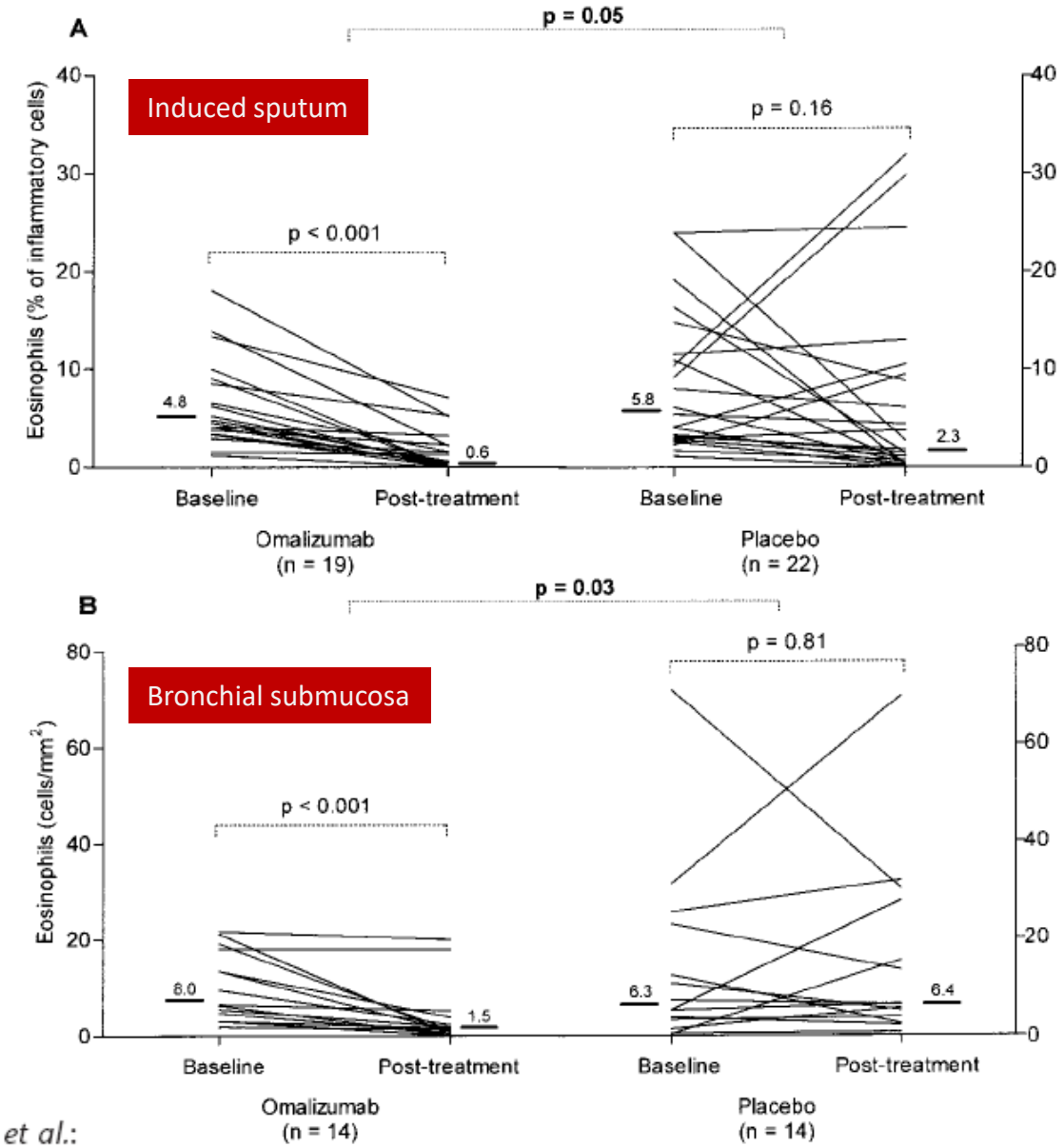


Omalizumab reduced proliferating mIgE+ B cells.



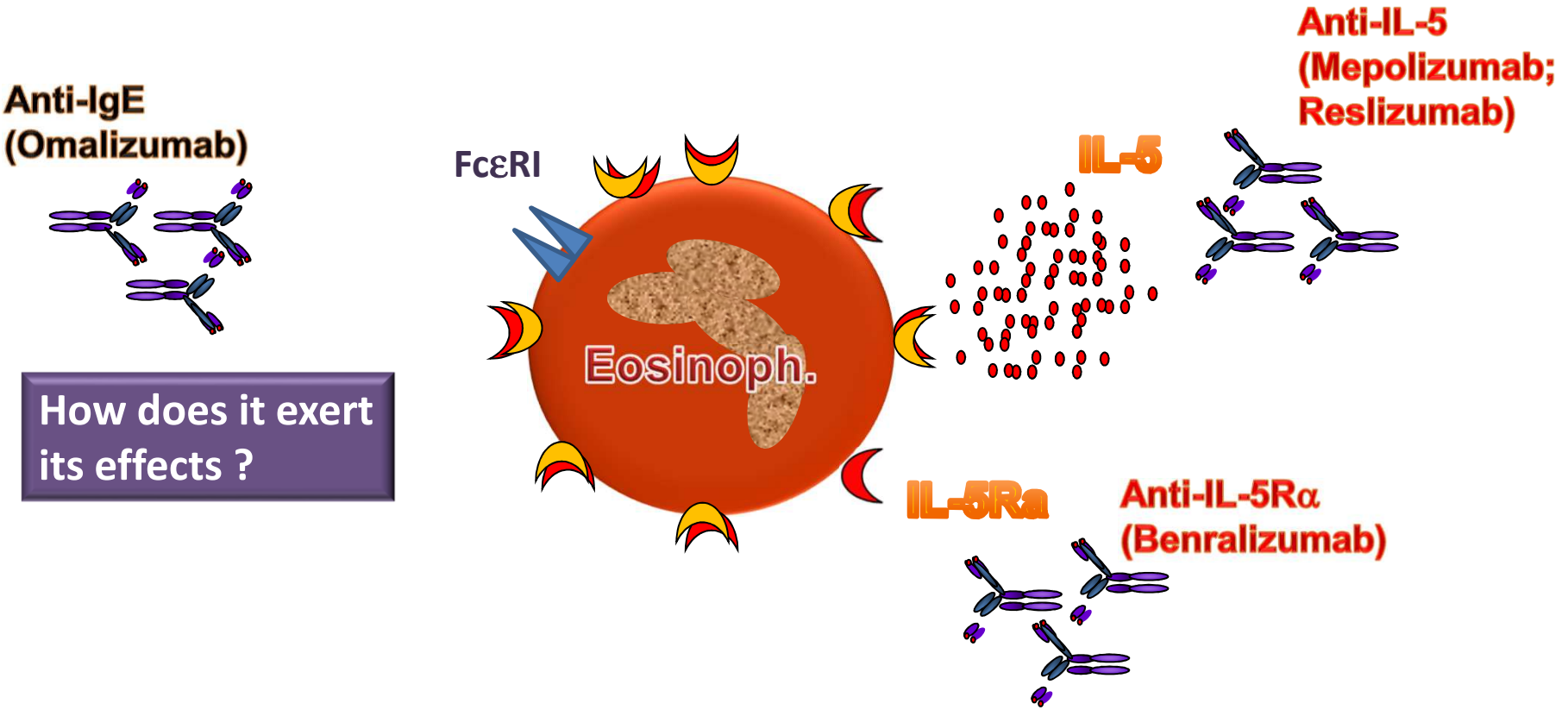
Chan *et al. Clinical and Translational Allergy* 2013, **3**:29

Effect of 16 weeks of treatment with either Omalizumab or placebo on Eosinophil counts.



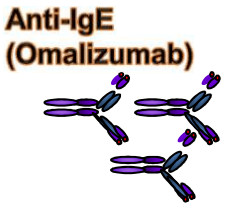
Djukanović, Wilson, Kraft, *et al.*:
Am J Respir Crit Care Med Vol 170. pp 583–593, 2004

Eosinophils as a Target for Biological Agents



Matucci A.; Vultaggio A. Master in Allergologia; Napoli 2015

Omalizumab Targets Eosinophils Through Direct and Indirect Effects



Decreased FCεR expression

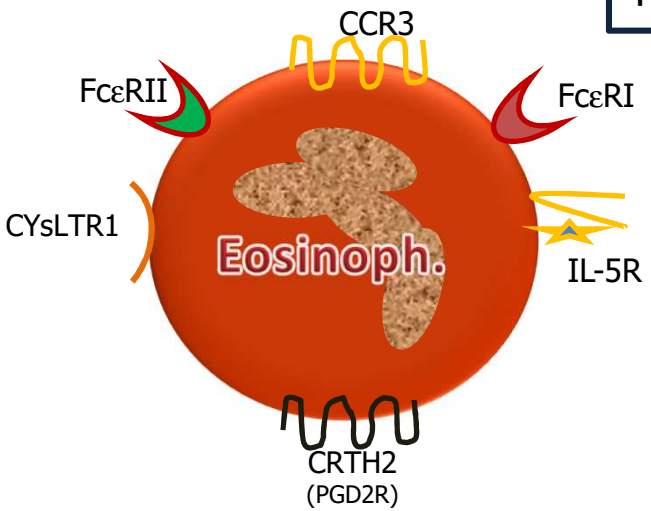
Direct

Indirect

Decreased activation and mediator release; induces apoptosis

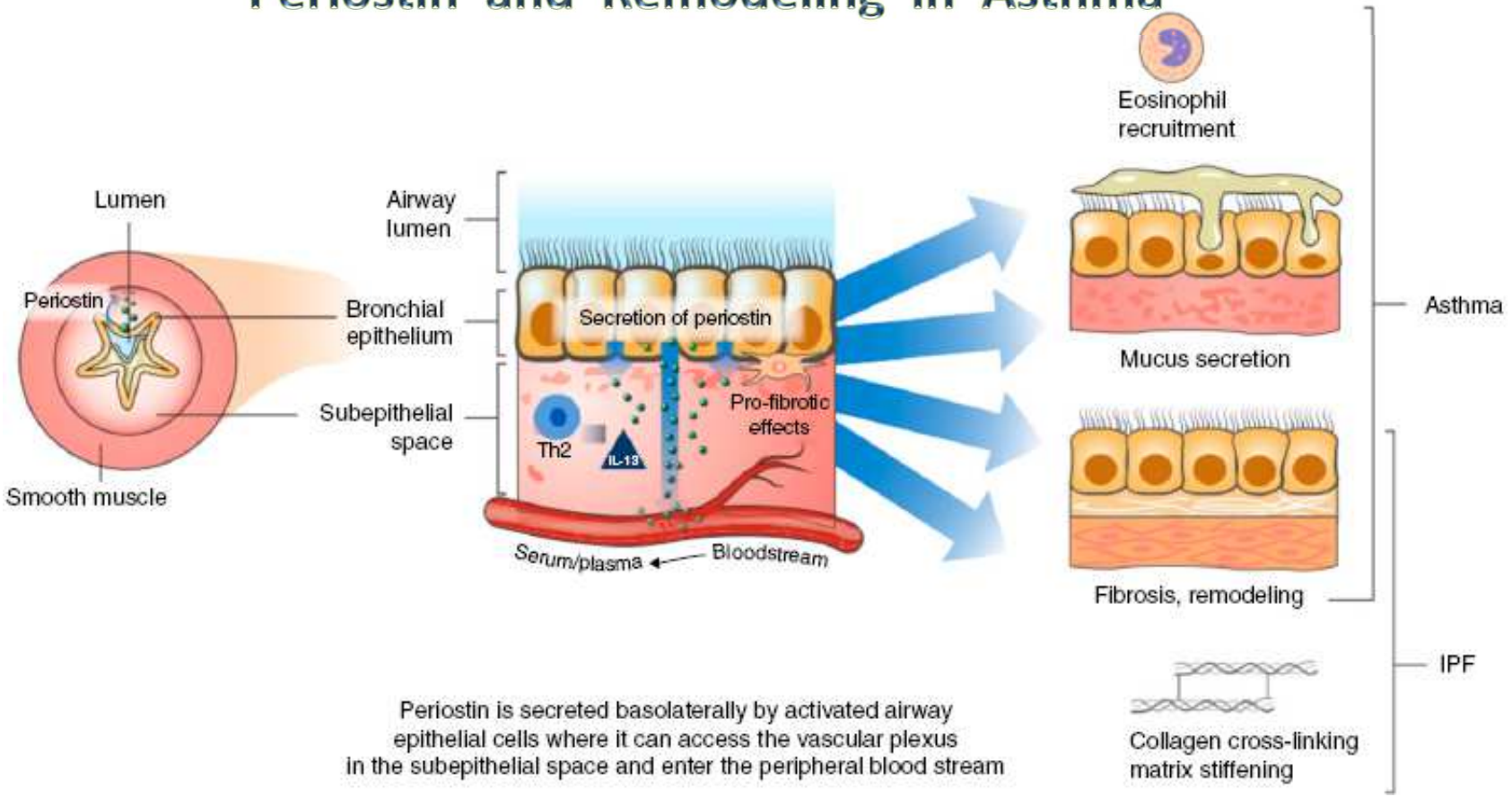
Decreased release of IL-5, IL-3; GM-CSF by Mast cells/basophils

Decreased Ag uptake and presentation by DC: decreased release of IL-5, IL-3, IL-13, GM-CSF, Eotaxin, RANTES by Th2 cells



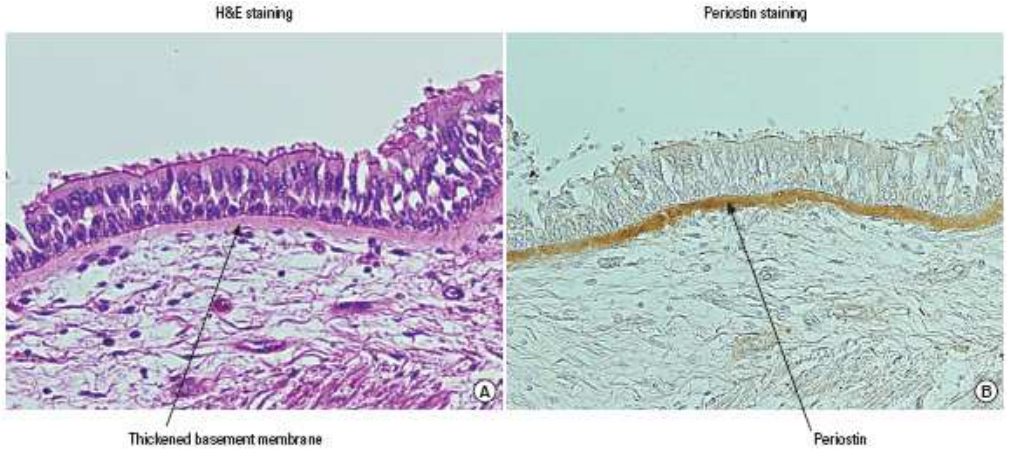
- ↓ Differentiation
- ↓ Activation
- ↓ Migration
- ↑ Apoptosis

Periostin and Remodeling in Asthma



Periostin is secreted basolaterally by activated airway epithelial cells where it can access the vascular plexus in the subepithelial space and enter the peripheral blood stream

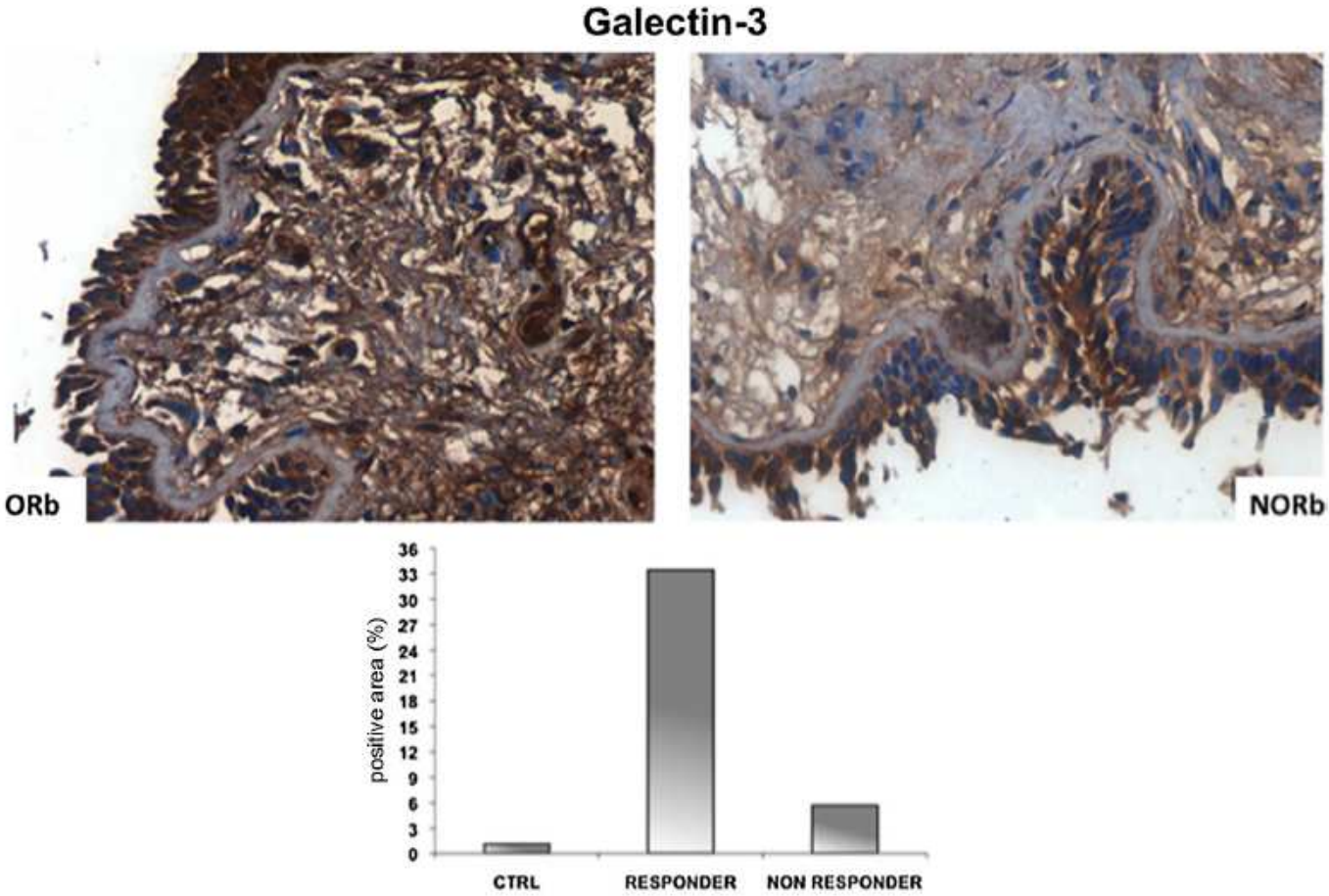
Am J Respir Crit Care Med Vol 193, Iss 9, pp 949–956, May 1, 2016



Allergy Asthma Immunol Res. 2016 November;8(6):491-498.

Proteomics of bronchial biopsies: Galectin-3 as a predictive biomarker of airway remodelling modulation in omalizumab-treated severe asthma patients

Pierluigi Mauri[a,1], Anna Maria Riccio[b,1], Rossana Rossi[a], Dario Di Silvestre[a], Louise Benazzi[a], Laura De Ferrari[b], Roberto Walter Dal Negro[c], Stephen T. Holgate[d], Giorgio Walter Canonica[b,*]



Immunology Letters 162 (2014) 2–10