Periostin: Update on Clinical Use

Kenji Izuhara

Saga Medical School, Japan

WISC2014 Biomarkers in Asthma: Helping Diagnosis and Treatment

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Heterogeneity of bronchial asthma

- Age of onset (Early onset vs. Late onset)
- Existence of obesity
- Inflammatory cells (Eosinophil-dominant vs. Neutrophil-dominant)
- IgE-dependency (Atopic vs. Non-atopic)
- Responsiveness to ICS (Good vs. Poor)

The status and the problems of the treatment using ICS or anti-IgE antibody (Omalizumab)

ICS

- ICS is effective and has significantly decreased deaths from asthma
- But 5-10% of the patients are resistant or hypo-responsive

Adcock, *J Endocrinol*, 2003

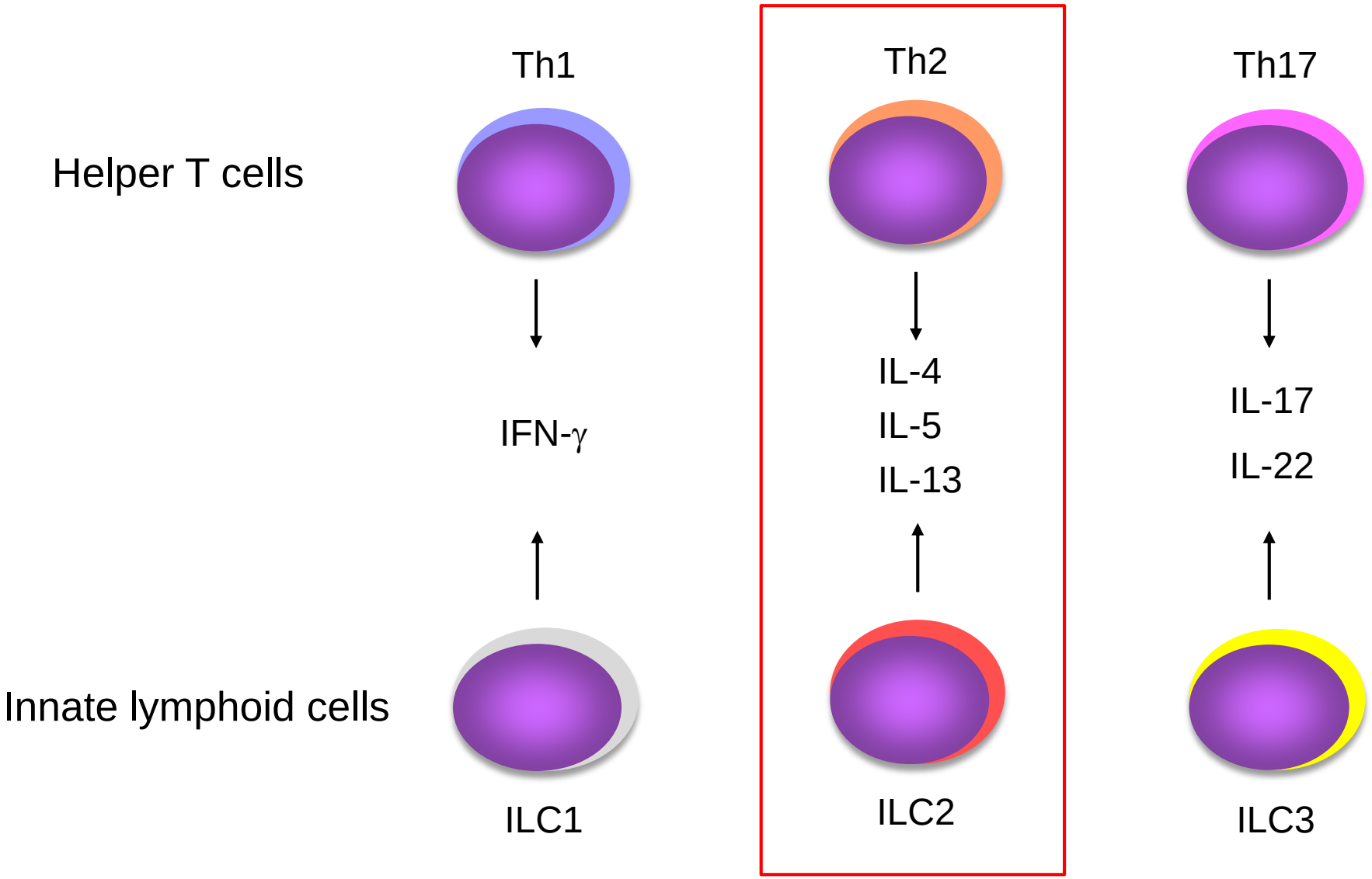
Anti-IgE antibody (Omalizumab)

- 61% of severe asthma patients show improvement of QOL
- Serum IgE cannot predict the responsiveness

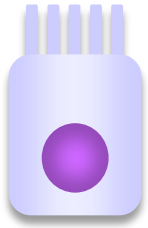
Bousquet, *Respr Med*, 2007

- Expensive cost

T cell subsets and innate lymphoid cells important for immune responses



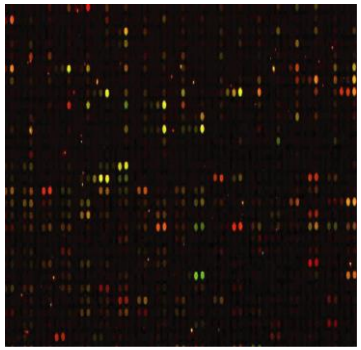
Identification of periostin as a novel mediator in bronchial asthma

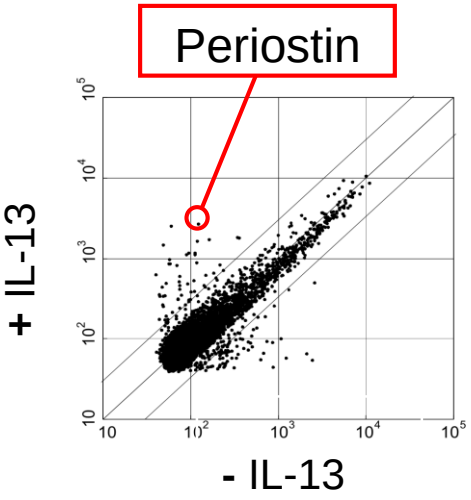


Airway epithelial cell

± IL-13

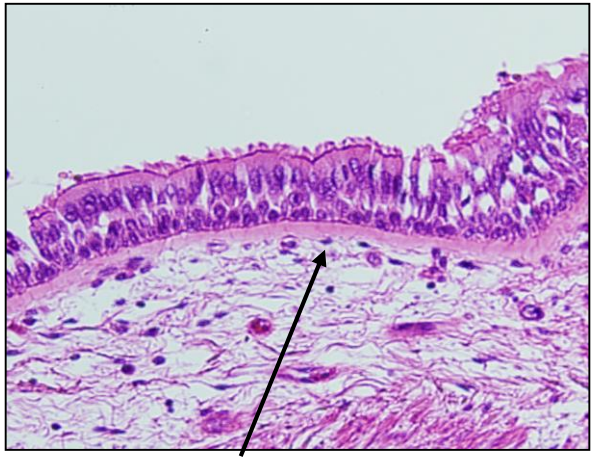
DNA microarray





Yuyama, *Cytokine*, 2002

H&E staining



Thickened Basement Membrane

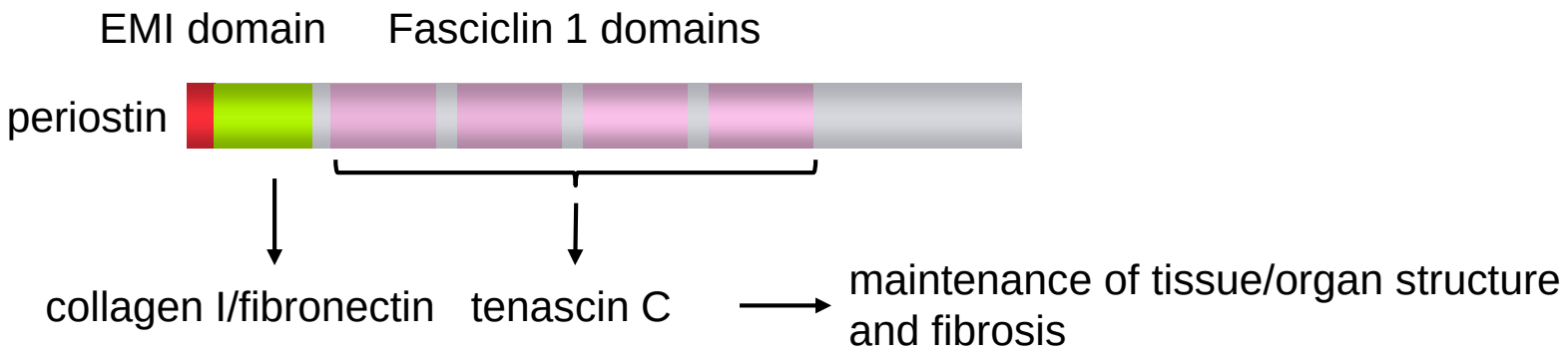
Periostin staining

Periostin

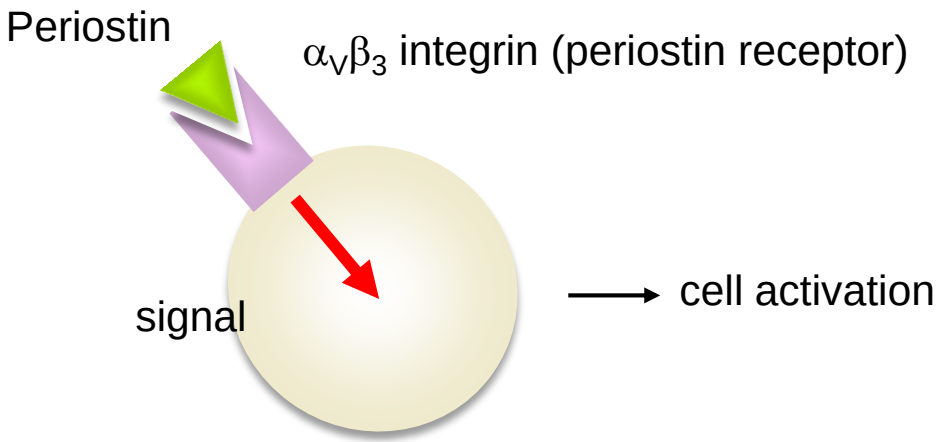
Takayama, *J Allergy Clin Immunol*, 2006

Two faces of periostin

- A conventional extracellular matrix (ECM) protein



- A matricellular protein



Izuhara, *Allergol Int*, 2014

Characteristics pf periostin in bronchial asthma

1. A novel component of thickened basement membrane downstream of IL-13 signals

   Takayama, *J Allergy Clin Immunol*, 2006, Hayashi, *Proc Natl Acad Sci USA,* 2007

2. A surrogate biomarker of type 2 immune responses

   Woodruff, *Am J Respir Crit Care Med*, 2009

3. A companion diagnostic for antagonists against type 2 immune responses

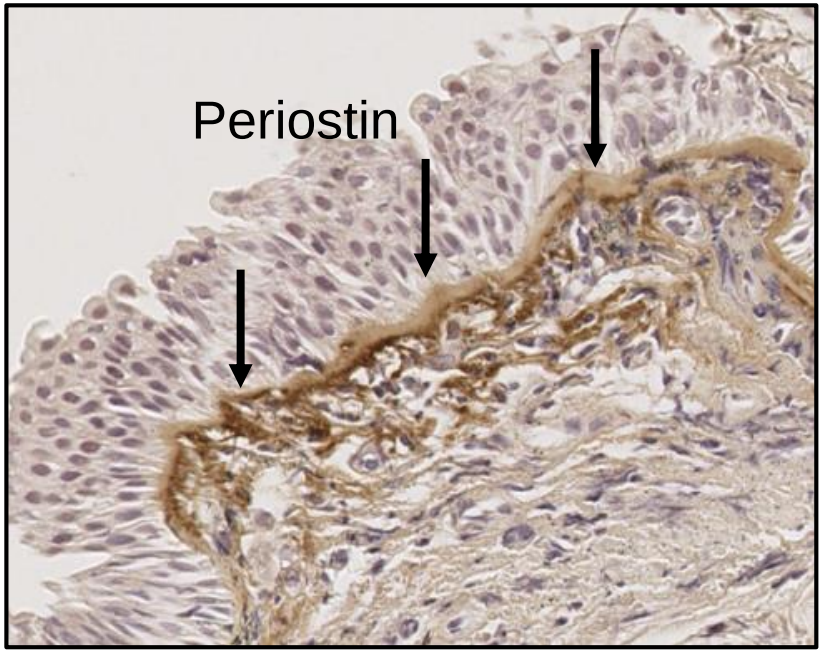
   Corren, *N Engl J Med*, 2011, Hanania, *Am J Respir Crit Care Med*, 2013

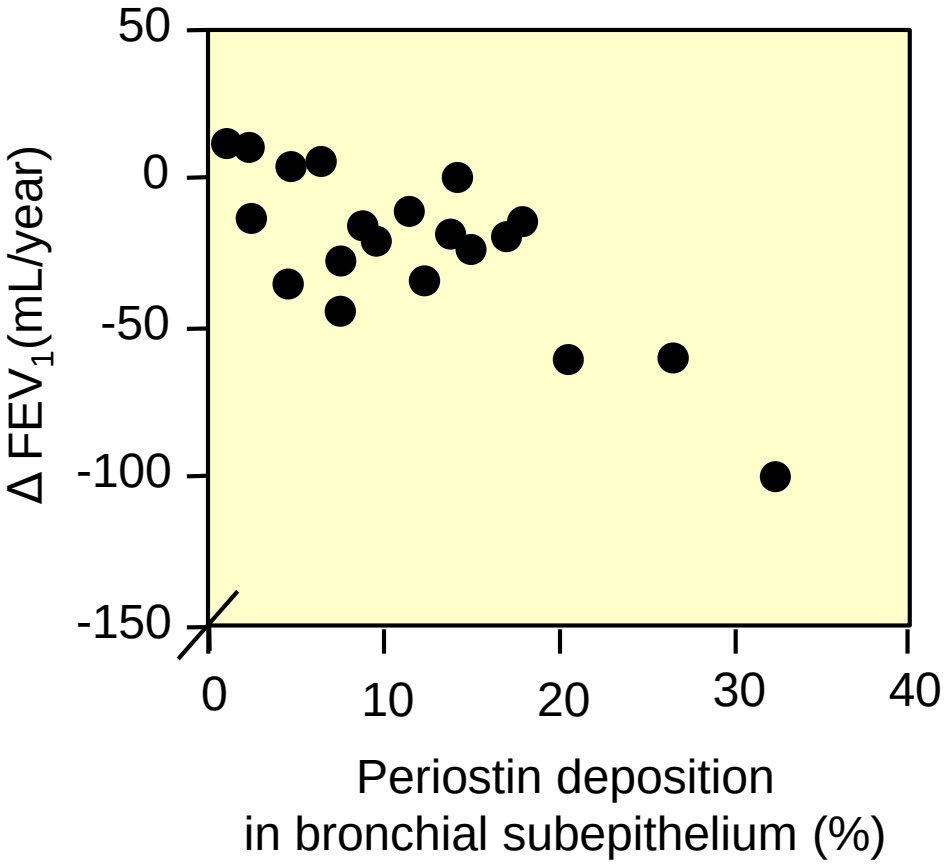
4. Still controversial whether it is a good guy or a bad guy

   Sehra, *J Immunol*, 2011, Gordon, *Clin Exp Allergy*, 2011

   Blanchard, *Mucosal Immunol*, 2008, Bentley, *J Allergy Clin Immunol,* in press

Periostin deposition is associated with 20-year decline of pulmonary function in asthma patients





Kanemitsu, *Am J Respir Crit Care Med,* 2014

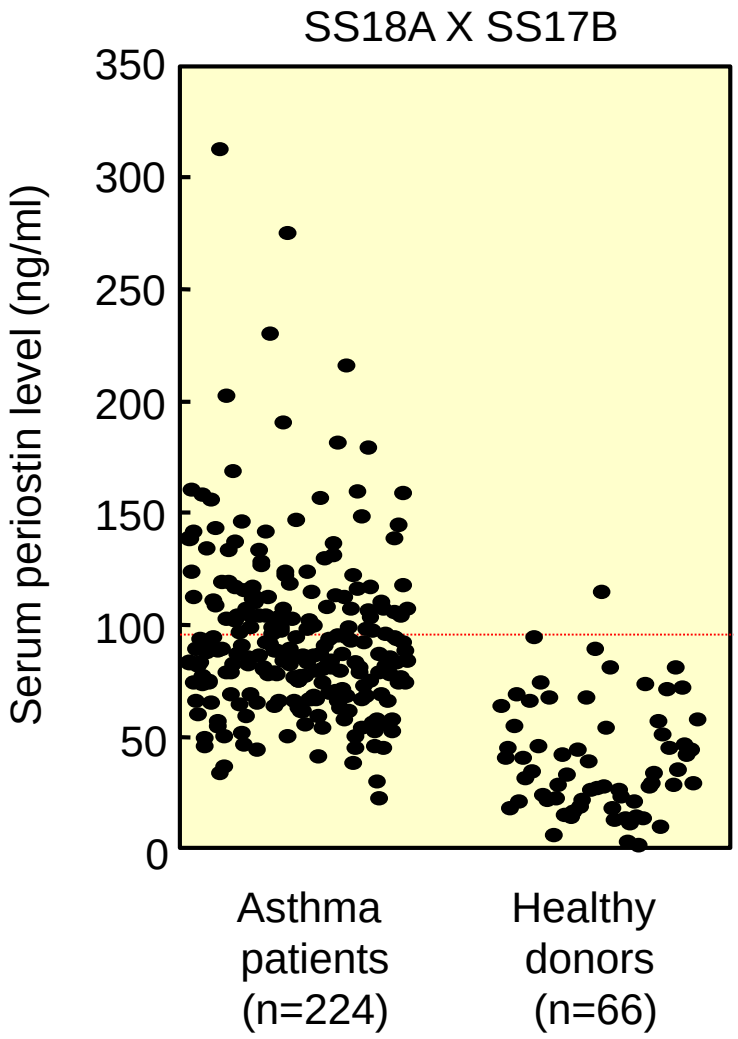
Why is periostin useful as a biomarker?

- Easily moves from the lesions to blood
- Basal concentration in blood is appropriate (periostin: 10-90 ng/ml)

  not too high (fibronectin/vitronectin: ~100 μg/ml)

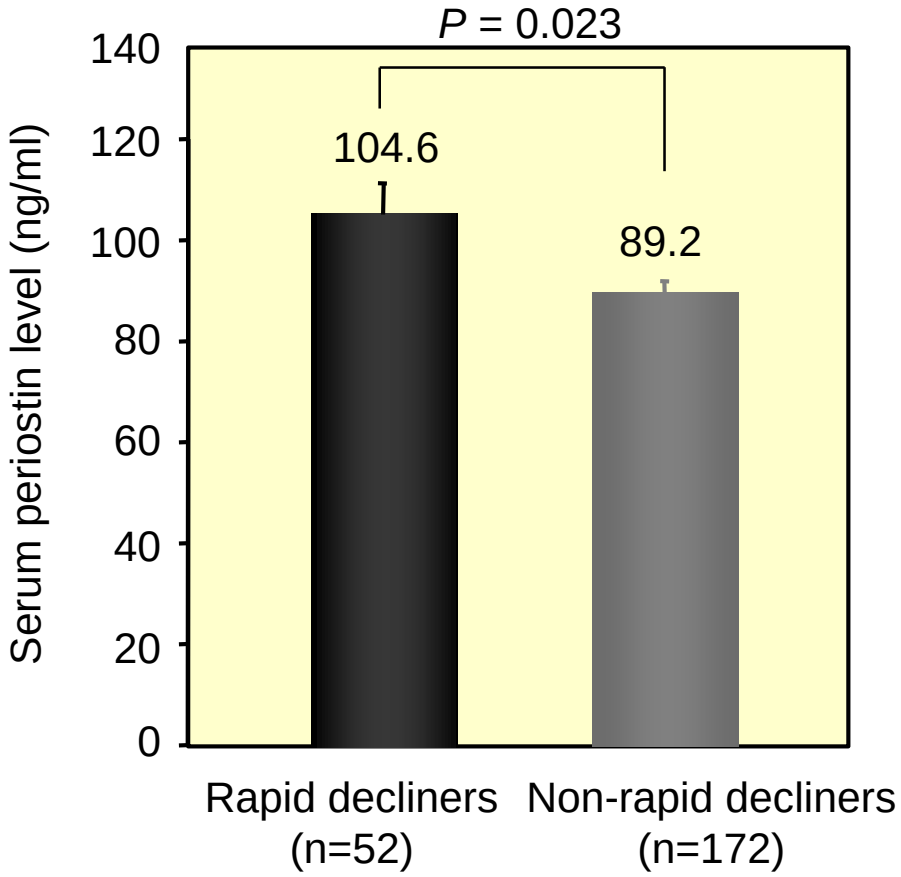
  not too low (cytokines: ~10 pg/ml)
- A kit with low detection limit (20 pg/ml) is available

Serum periostin levels are associated with ΔFEV_1 decline in asthma patients



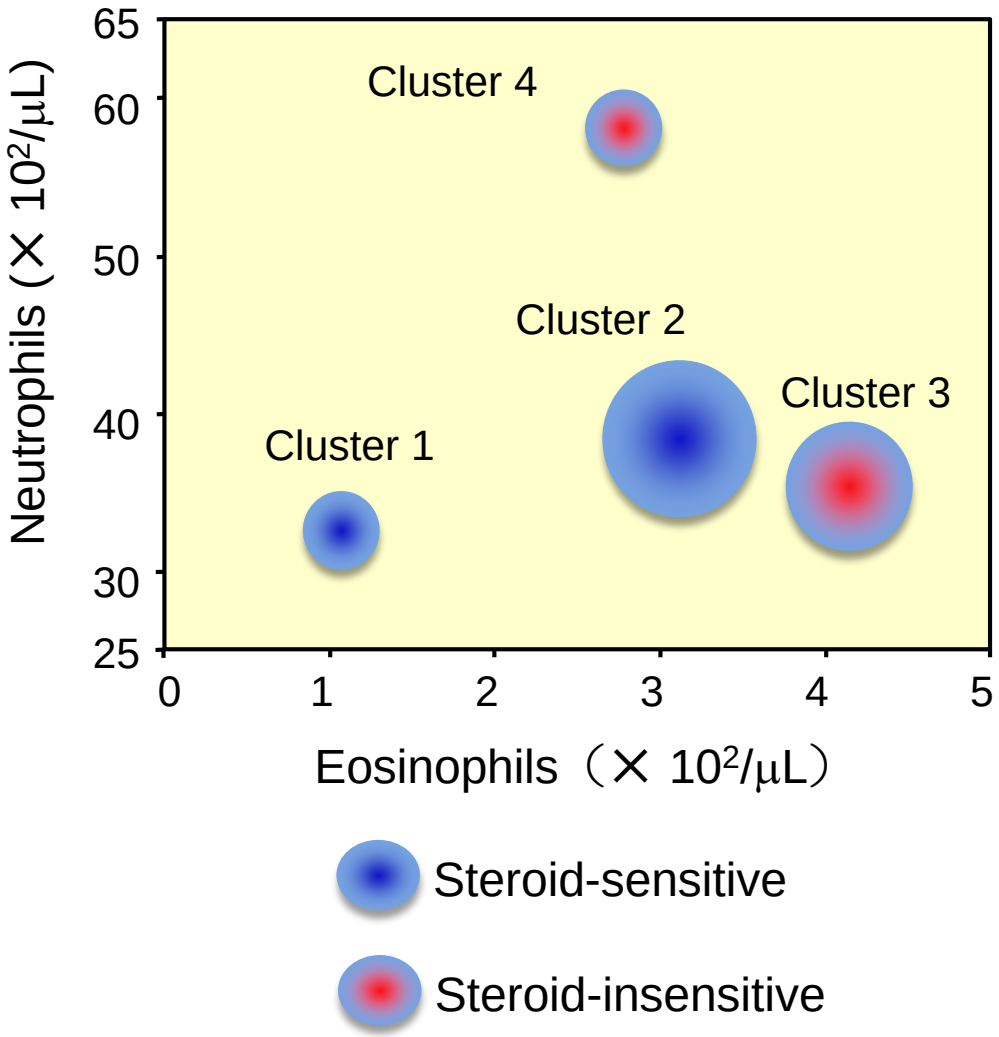
Rapid decliners : $\Delta FEV_1 < -30$ ml/yr

Non-rapid decliners : $\Delta FEV_1 \geq -30$ ml/yr



Kanemitsu, *J Allergy Clin Immunol,* 2013

Asthma can be categorized into four clusters by eosinophils and neutrophils



Cluster 1

- Late onset
- Non-atopic

Cluster 2

- Early onset
- Atopic

Cluster 3

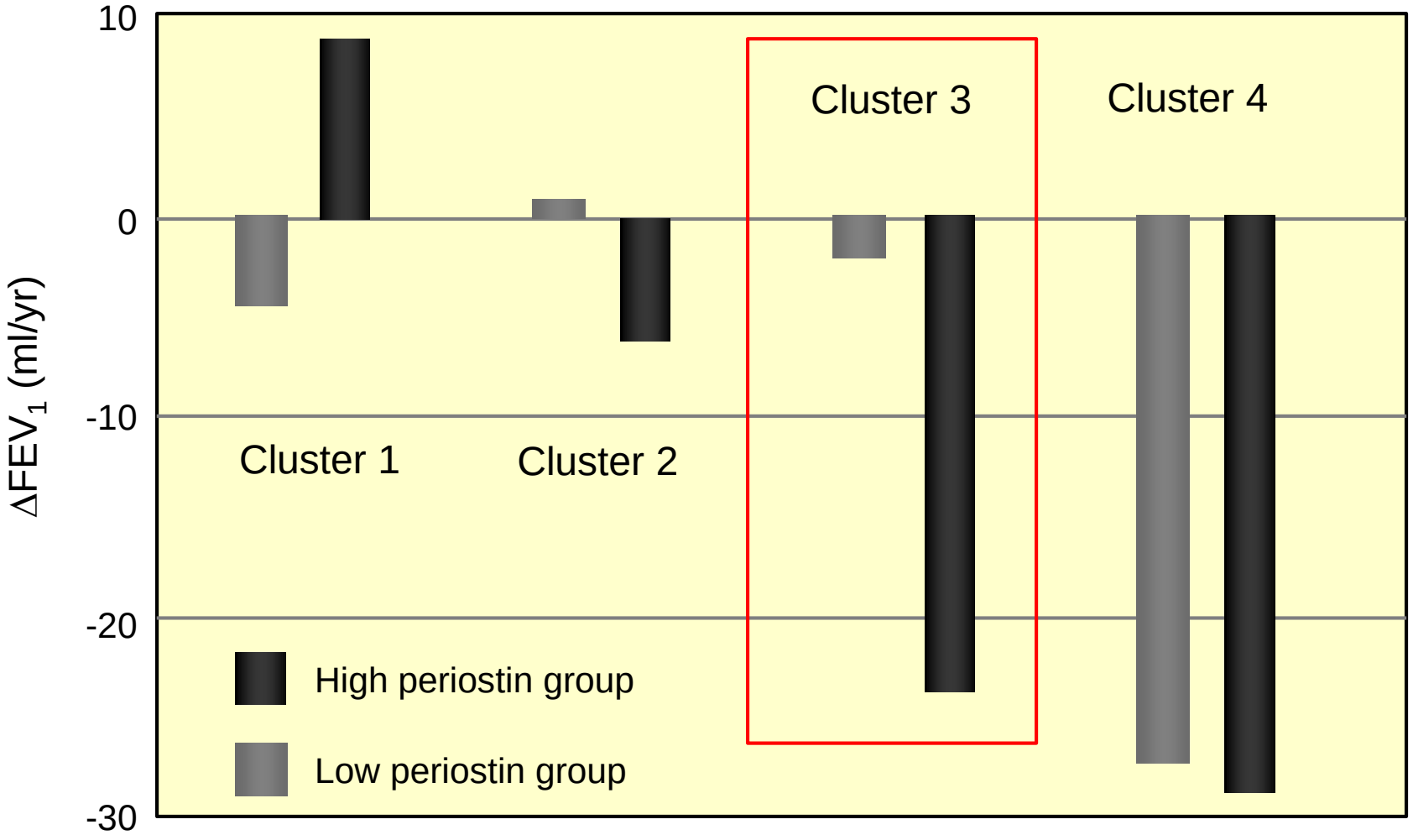
- Late onset
- Eosinophil-dominant

Cluster 4

- Poor control
- Low FEV_1
- High IL-6

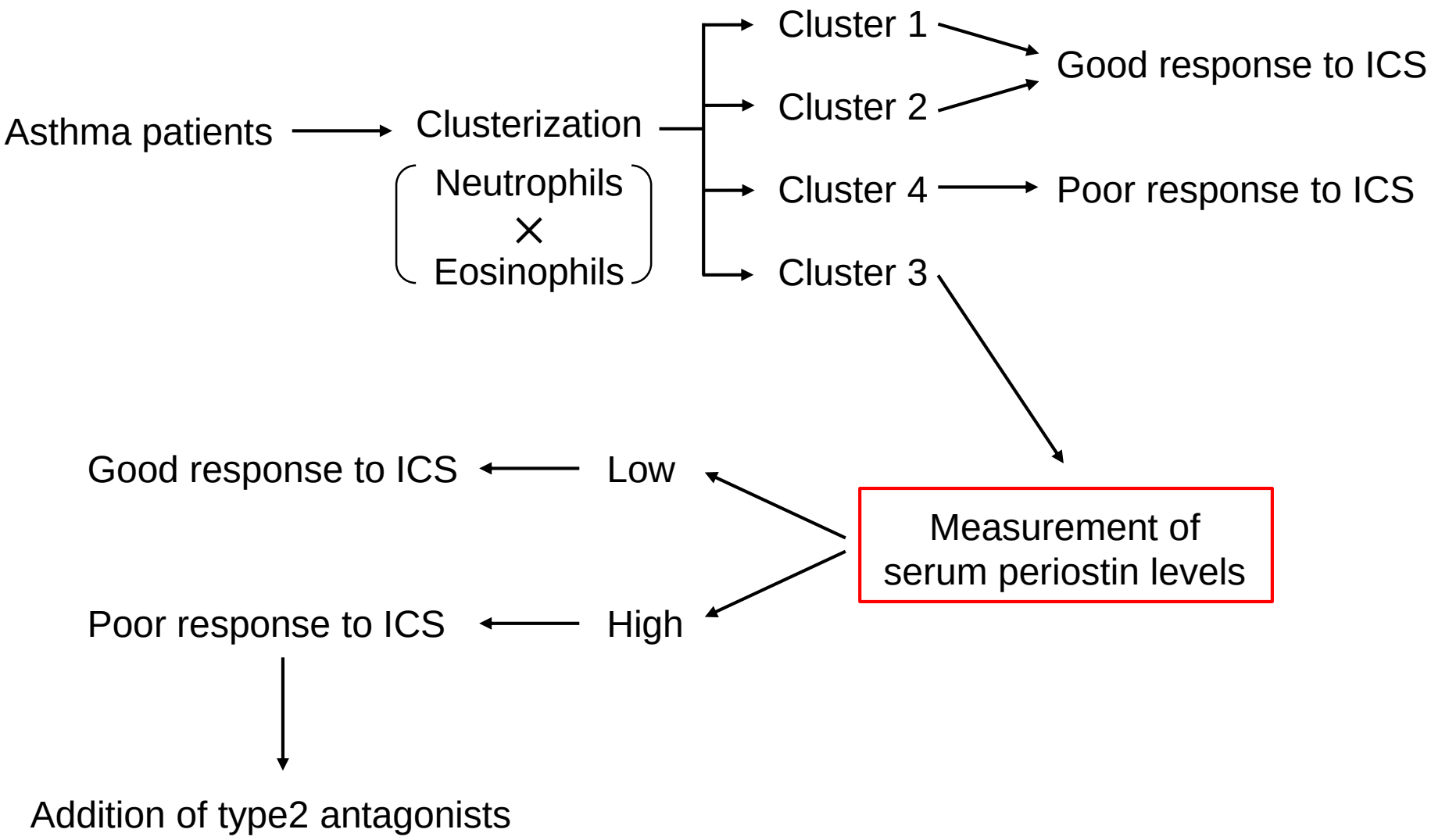
Nagasaki, *J Allergy Clin Immunol,* 2014

Serum periostin levels are well correlated with decline of FEV_1 in cluster 3



Nagasaki, *J Allergy Clin Immunol,* 2014

Algorithm for treatment of asthma



Characteristics of periostin as a biomarker

- A type 2 biomarker

→ Useful to predict efficacy of type 2 antagonists

- A remodeling biomarker

→ Useful to predict hypo-responsiveness to ICS

Acknowledgment

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