Periostin: Update on Clinical Use

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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


Anti-IgE antibody (Omalizumab)

• 61% of severe asthma patients show improvement of QOL

• Serum IgE cannot predict the responsiveness


• Expensive cost
T cell subsets and innate lymphoid cells important for immune responses

Helper T cells

- Th1
  - IFN-γ

Innate lymphoid cells

- ILC1
- ILC2
- ILC3

Th17
- IL-17
- IL-22

Th2
- IL-4
- IL-5
- IL-13

Th1

Identification of periostin as a novel mediator in bronchial asthma

Airway epithelial cell

DNA microarray

Periostin staining

H&E staining

Thickened Basement Membrane

Periostin

Two faces of periostin

- A conventional extracellular matrix (ECM) protein

  EMI domain  Fasciclin 1 domains
  
  periostin
  
  collagen I/fibronectin  tenascin C  → maintenance of tissue/organ structure and fibrosis

- A matricellular protein

  Periostin  \( \alpha \nu \beta_3 \) integrin (periostin receptor)

  signal  → cell activation

Izuhara, *Allergol Int*, 2014
Characteristics of periostin in bronchial asthma

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

2. A surrogate biomarker of type 2 immune responses
   

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

4. Still controversial whether it is a good guy or a bad guy
   
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 $\Delta$FEV$_1$ decline in asthma patients.

Rapid decliners (n=52)
Non-rapid decliners (n=172)

Serum periostin level (ng/ml)

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**
- Early onset
- Non-atopic

**Cluster 2**
- Late onset
- Atopic

**Cluster 3**
- Late onset
- Eosinophil-dominant

**Cluster 4**
- Poor control
- Low FEV$_1$
- High IL-6

Serum periostin levels are well correlated with decline of FEV$_1$ in cluster 3

Algorithm for treatment of asthma

Asthma patients → Clusterization

- Neutrophils
- Eosinophils

Cluster 1 → Good response to ICS
Cluster 2
Cluster 3
Cluster 4 → Poor response to ICS

Measurement of serum periostin levels

Good response to ICS ← Low
Poor response to ICS ← High

Addition of type2 antagonists
Characteristics of periostin as a biomarker

- A type 2 biomarker
  \[\rightarrow\text{ Useful to predict efficacy of type 2 antagonists}\]

- A remodeling biomarker
  \[\rightarrow\text{ Useful to predict hypo-responsiveness to ICS}\]
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