Defective epithelial barrier in allergy

Cezmi A. Akdis
Swiss Institute of Allergy and Asthma Research (SIAF)
Role of Tissues in Immune Tolerance

J Immunol 1997
J Immunol 1999
EJI 2000
J Clin Invest 2000
J Allergy Clin Imm 2001
J Invest Derm 2001
J Allergy Clin Imm 2002
J Allergy Clin Imm 2003
J Immunol 2003
Faseb J 2003
Curr Opin Imm 2004
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JACI 2007-2008
Basinski et al. JACI 2009
Meyer et al. JACI 2010, 2012
Zimmermann JACI 2011
Soyka JACI 2012
Rebane JACI 2012
Chalubinsky, Wanke 2013
Wawrzyniak 2014
Wanke 2014
EPITHELIAL BARRIER VERSUS PERMISSIVENESS
Tight Junctions – Seal of the Epithelium

E-cadherin

desmosomes

gap junctions

www.invitrogen.com

Niessen, 2007
Functions

• Closed tight junctions: preventive and protective

• Open tight junctions: to drain inflammation, but allow allergen, toxin accessibility

TJs PROTEINS:

3-membrane domains
• occludin
• claudins (24 proteins)
• tricellulin (novel - between 3 neighbouring cells)

1-membrane domain
• JAMs – junction adherent proteins
Epithelial Barrier is Defective in Asthma, CRS, AD, ...

a. an inherited defect
b. epigenetically modified
Defective epithelial barrier function in asthma

Chang Xiao, et al.
The Journal of Allergy and Clinical Immunology
Volume 128, September 2011, Pages 549–556.e12

• The bronchial epithelial barrier in asthma is compromised. This defect may facilitate the passage of allergens and other agents into the airway tissue, leading to immune activation and may thus contribute to the end organ expression of asthma.

Tight junction defects in patients with atopic dermatitis

Anna De Benedetto, et al.
The Journal of Allergy and Clinical Immunology
Volume 127, March 2011, Pages 773-786.e7,

• An impairment in tight junctions contributes to the barrier dysfunction and immune dysregulation observed in AD subjects and that this may be mediated in part by reductions in claudin-1.
Defective epithelial barrier in chronic rhinosinusitis: The regulation of tight junctions by IFN-γ and IL-4

Michael B. Soyka et al.
The Journal of Allergy and Clinical Immunology

A defective epithelial barrier was found in patients with CRS with nasal polyps along with a decreased expression of TJ proteins.

The broad spectrum of interepithelial junctions in skin and lung

Jeannette I. Kast et al.
The Journal of Allergy and Clinical Immunology

TJ network is complex and involves many proteins
Disrupted TJs in CRS

**Figure 1**
Soyka et al.
A

IL-4 and IFN-γ open TJs

Soyka et al. 2012
The effects of allergen derived proteases on airway epithelial cells obtained from asthmatic and healthy individuals and associated mechanisms

- **Cells:** Asthmatic and healthy primary BEC

- **Allergenes:**
  - Der p1 (cysteine protease)
  - Dermatophagoides serine protease extract
  - Bla g 2 (aspartic protease)
  - Lolium perenne (serine protease)

- **Experiments:** Effects of allergenic protease on BEC will be determine as follows:
  - Confocal staining for Tight Junctions (TJ)
  - TEER measurements for epithelial integrity
  - RT with Taq Man microfluidic cards (22 genes for TJ and 14 genes for epithel derived proteins)
  - ELISA for cytokine/chemokine production
Tissue factors that contribute to immune tolerance

Quae medicamenta non sanant, ferrum sanat, quae ferrum non sanat, ignis sanat

Hippocrates

keep away, wash away, suppress
Acknowledgements

Kerstin Wanke
Paulina Wawrzyniak
Marcin Wawrzyniak
Jeannette Kast
Michael Soyka
Beate Rückert

Marek Sanak
Bogdan Jakieła
Christian J. Virchow
Marco Idzco

Project supported by a grant from Switzerland through the Swiss Contribution to the enlarged European Union