The role of the airway epithelium in asthma

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UNDERSTANDING THE CENTRAL ROLE OF THE EPITHELIUM IN SEVERE ASTHMA AND BEYOND

Asthma is driven by interactions between the environment, epithelium and immune system[1–6]

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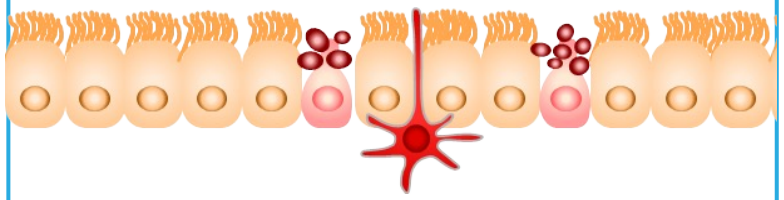
Environmental exposures[1,2]

Epithelium[2–4]

- Key role in tissue homeostasis
- Mediator between environment and immune system
- Rapid production of epithelial cytokines in response to exposures



Immune system[5,6]

- Allergic eosinophilic inflammation
- Non-allergic eosinophilic inflammation
- Non-T2 (non-eosinophilic) mechanisms
- Structural cell changes

T2, type 2

1. Pelaia G, et al. Nat Rev Drug Discov 2012;11:958–972; 2. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 3. Watson B, Gauvreau GM. Expert Opin Ther Targets 2014;18:771–785; 4. Loxham M, et al. Clin Exp Allergy 2014;44:1299–1313; 5. Brusselle G, Bracke K. Ann Am Thorac Soc 2014;11(Suppl. 5):S322–S328; 6. Gauvreau GM, et al. Expert Opin Ther Targets 2020;24:777–792

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The airway epithelium is a first point of contact for environmental exposures[1]

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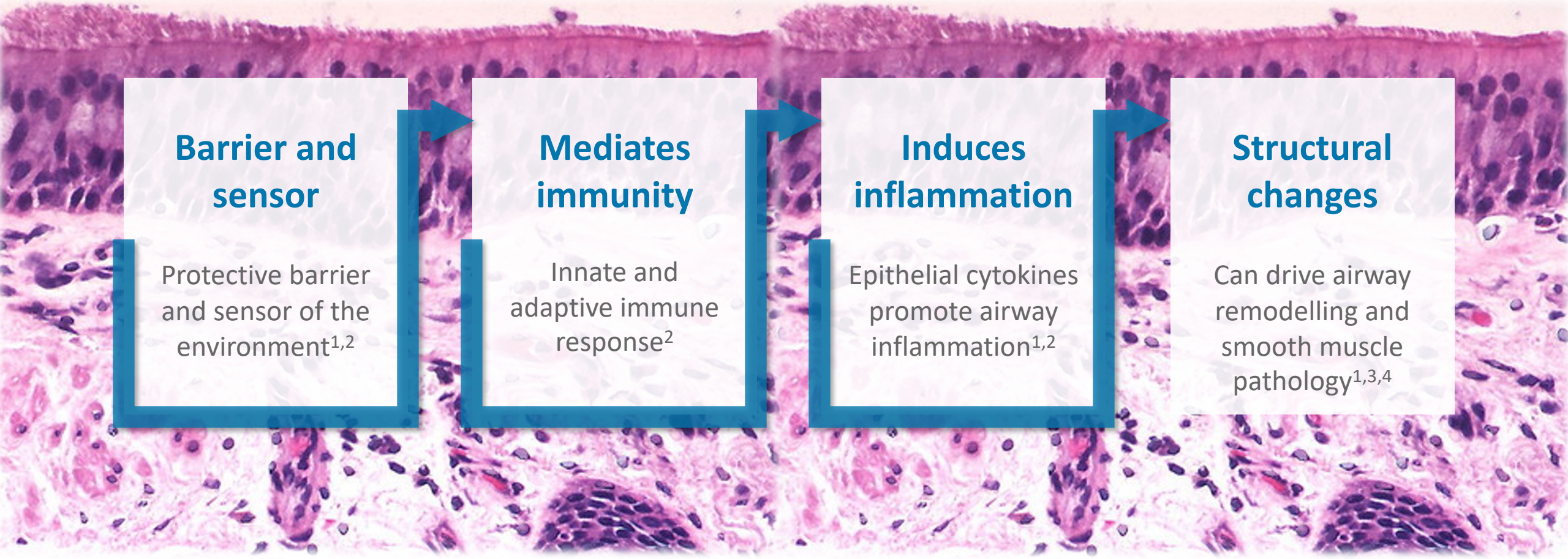

Barrier and sensor

Protective barrier and sensor of the environment[1,2]

Mediates immunity

Innate and adaptive immune response[2]

Induces inflammation

Epithelial cytokines promote airway inflammation[1,2]

Structural changes

Can drive airway remodelling and smooth muscle pathology[1,3,4]

Image of normal lung; bronchus by Yale Rosen, available at https://www.flickr.com/photos/pulmonary_pathology/3661529896 (Accessed 6 January 2022)
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1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Roan F, et al. J Clin Invest 2019;129:1441–1451; 3. Wang Y, et al. Respir Med 2008;102:949–955; 4. Corren J. J Allergy Clin Immunol Pract 2019;7:1394–1403

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The airway epithelium plays a fundamental role in asthma[1–4]

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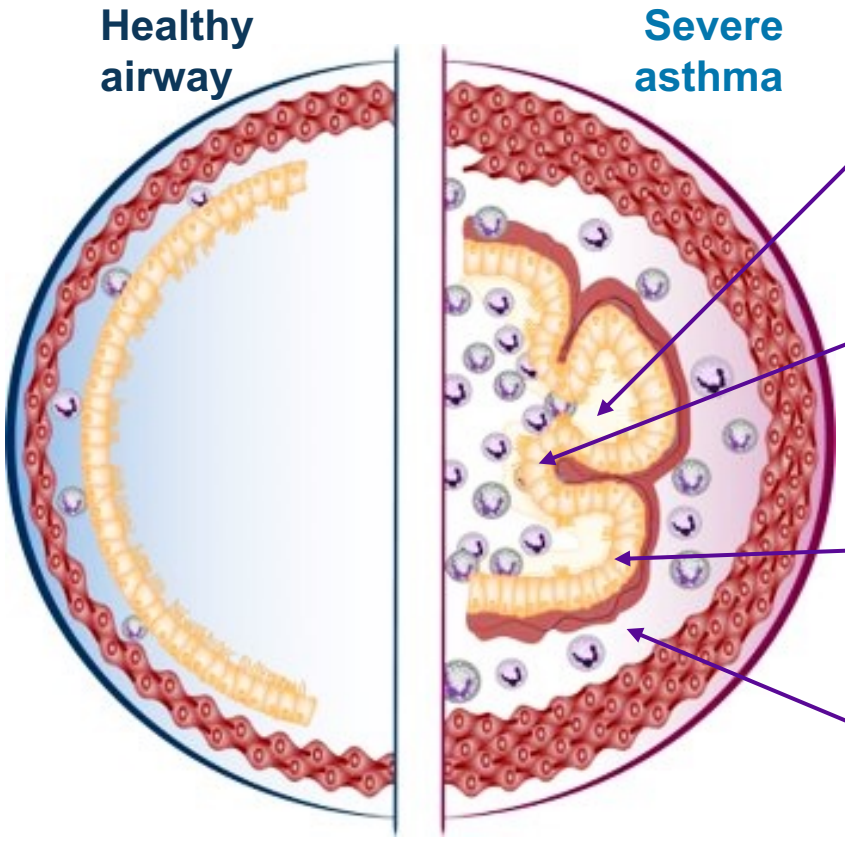
The airway epithelium serves as a barrier/sensor and mediates airway immunity[1,2]

In severe asthma, the epithelium is significantly altered[1–4]



↑ Goblet cell hyperplasia and ↑ mucus production[1,3]
Leads to airway blockage

↓ Epithelial tight-junction number and integrity[3,4]
Tissue damage as external insults penetrate the airway wall

↑ Basal membrane thickness[1,3,5]
Increased matrix deposition → airway narrowing

Sub-epithelial inflammation and fibrosis[5]
Can lead to fixed airway obstruction

Figure adapted from the Centre of Excellence in Severe Asthma as part of the Centre of Research Excellence in Severe Asthma (https://toolkit.severeasthma.org.au) (Accessed 6 January 2022) .

1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Roan F, et al. J Clin Invest 2019;129:1441–1451; 3. Holgate ST. Immunol Rev 2011;242:205–219; 4. Heijink IH, et al. Clin Exp Allergy 2014;44:620–630; 5. Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145

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The airway epithelium structure is significantly altered in severe asthma[1–5]

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In bronchial biopsies of patients with severe asthma versus healthy controls:[5]

↑ Epithelial thickness
versus normal airway (**A**)

↑ Epithelial cell proliferation
versus normal airway (**B**)

↑ Apoptosis
versus normal airway

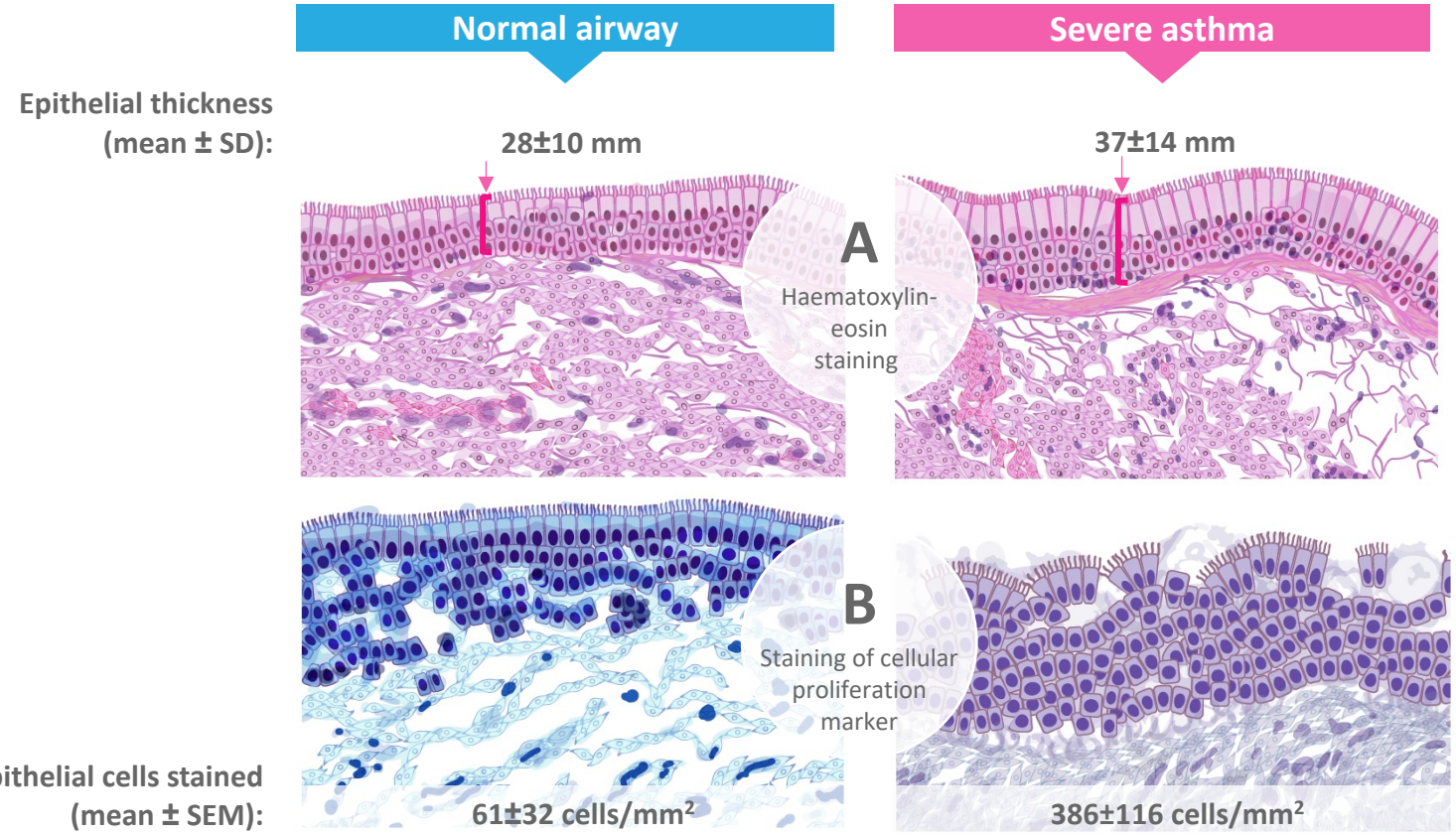

Figure adapted from Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145
SD, standard deviation; SEM, standard error of the mean

1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Holgate ST. Immunol Rev 2011;242:205–219; 3. Heijink IH, et al. Clin Exp Allergy 2014;44:620–630; 4. Caminati M, et al. World Allergy Organ J 2018;11:13; 5. Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145

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Environmental exposures trigger airway inflammation at the epithelium[1–4]

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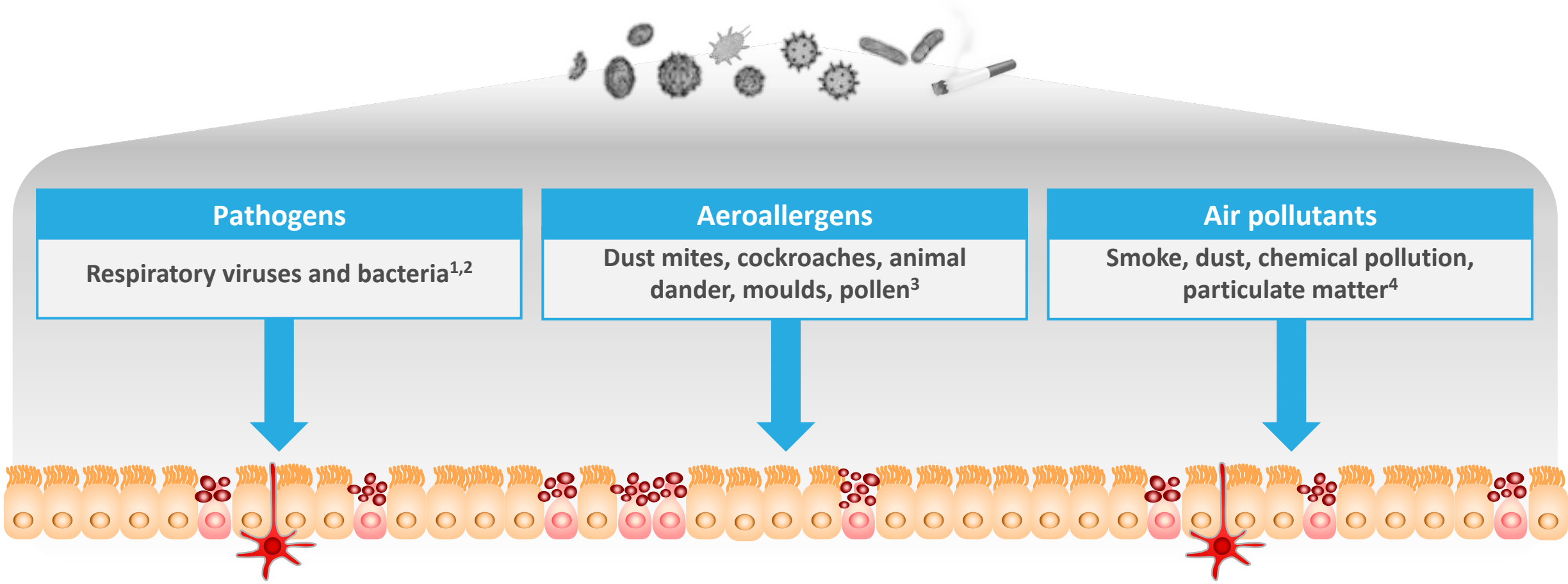

1. Wark PA, Gibson PG. Thorax 2006;61:909–915; 2. Iikura M, et al. PLoS One 2015;10:e0123584; 3. Baxi SN, Phipatanakul W. Adolesc Med State Art Rev 2010;21:57–71; 4. Lambrecht BN, et al. Immunity 2019;50:975–991

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The triggers of asthma are diverse[1]

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Self-reported asthma triggers (N=1202)

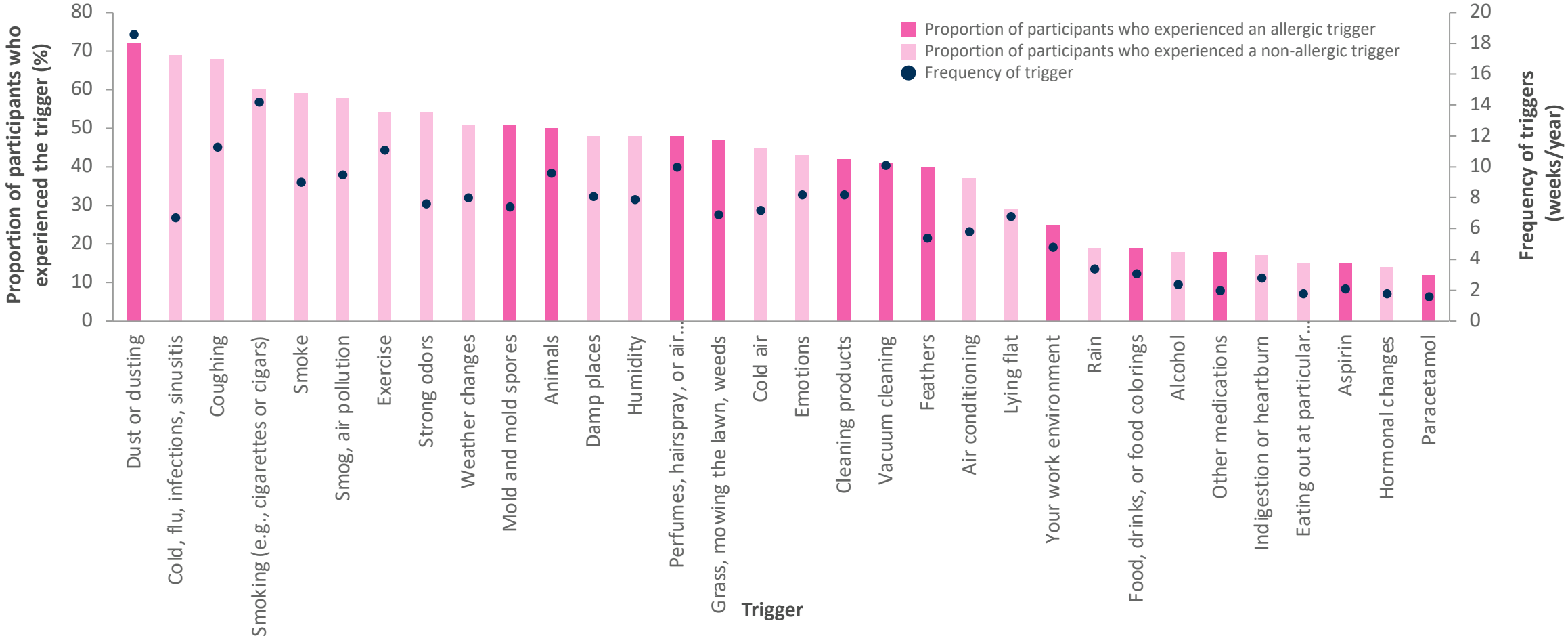

Figure adapted from Price D, et al. J Asthma. 2014;51:127–135 (http://creativecommons.org/licenses/by/3.0) (Accessed 6 January 2022).

1. Price D, et al. J Asthma 2014;51:127–135

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