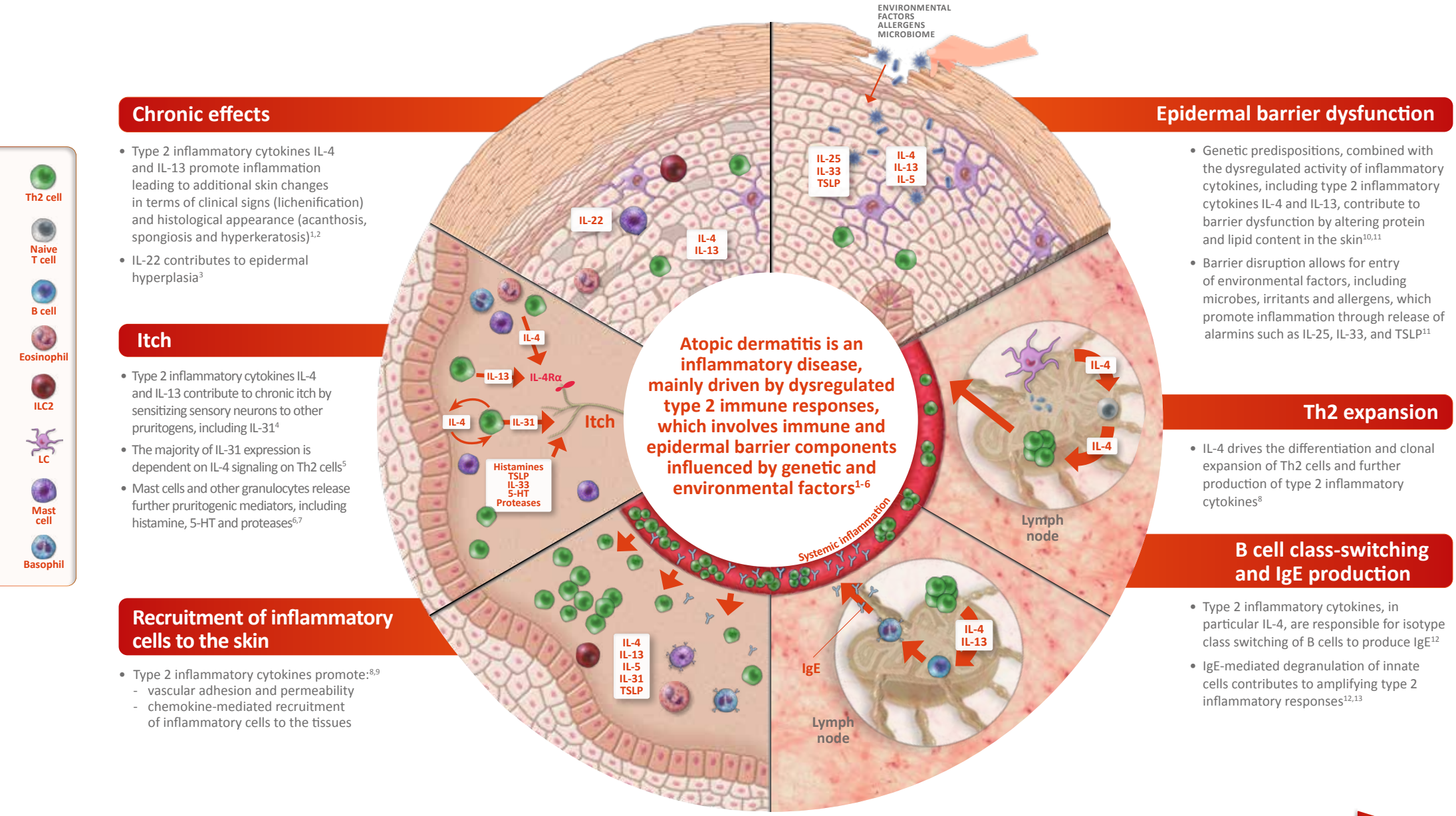
ATOPIC DERMATITIS, A CHRONIC, PROGRESSIVE TYPE 2 INFLAMMATORY DISEASE



Chronic effects

- Type 2 inflammatory cytokines IL-4 and IL-13 promote inflammation leading to additional skin changes in terms of clinical signs (lichenification) and histological appearance (acanthosis, spongiosis and hyperkeratosis)[1,2]
- IL-22 contributes to epidermal hyperplasia[3]

Itch

- Type 2 inflammatory cytokines IL-4 and IL-13 contribute to chronic itch by sensitizing sensory neurons to other pruritogens, including IL-31[4]
- The majority of IL-31 expression is dependent on IL-4 signaling on Th2 cells[5]
- Mast cells and other granulocytes release further pruritogenic mediators, including histamine, 5-HT and proteases[6,7]

Recruitment of inflammatory cells to the skin

- Type 2 inflammatory cytokines promote:[8,9]
  - vascular adhesion and permeability
  - chemokine-mediated recruitment of inflammatory cells to the tissues

Epidermal barrier dysfunction

- Genetic predispositions, combined with the dysregulated activity of inflammatory cytokines, including type 2 inflammatory cytokines IL-4 and IL-13, contribute to barrier dysfunction by altering protein and lipid content in the skin[10,11]
- Barrier disruption allows for entry of environmental factors, including microbes, irritants and allergens, which promote inflammation through release of alarmins such as IL-25, IL-33, and TSLP[11]

Th2 expansion

- IL-4 drives the differentiation and clonal expansion of Th2 cells and further production of type 2 inflammatory cytokines[8]

B cell class-switching and IgE production

- Type 2 inflammatory cytokines, in particular IL-4, are responsible for isotype class switching of B cells to produce IgE[12]
- IgE-mediated degranulation of innate cells contributes to amplifying type 2 inflammatory responses[12,13]

5-HT, 5-hydroxytryptamine

The figure above is a simplified representation of cells, cytokines and alarmins involved in type 2 inflammation, not meant to be exhaustive in nature.

1. Kim K, et al. *Int J Mol Sci.* 2022;23(4):2116. **2.** Pappa G, et al. *J Clin Med.* 2022;11:5633. **3.** Padhi A, et al. *J Invest Dermatol.* 2022; 142(2):333-342.e6. **4.** Moniaga CS, et al. *Diagnostics* (Basel). 2021;11(11):2090. **5.** Furue M, Furue M. *J Clin Med.* 2021;10(9):1906. **6.** Kwiatkowska D, Reich A. *Acta Derm Venereol.* 2021;101(10):350. **7.** Koumaki D, et al. *J Clin Med.* 2023;12:2091. **8.** Haddad EB, et al. *Dermatol Ther* (Heidelb). 2022;12:1501-1533. **9.** Fania L, et al. *Int. J Mol Sci.* 2022;23:2684. **10.** Chong AC, et al. *J Asthma Allergy.* 2022;15:1681-1700. **11.** Beck L, et al. *JID Innovations.* 2022;2:100131. **12.** Sweeney A, et al. A*llergy Asthma Clin Immunol.* 2021;17:30. **13.** Wang F, et al. *Cell.* 2021;184(2):422-440.e17.

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