

Barrier Dysfunction, Type 2 Inflammation, and Neuroimmune Dysregulation Interact to Drive the Pathophysiology of AD, Asthma, CRSwNP, and EoE¹⁻¹⁷

A triad of interacting mechanisms

- Type 2 inflammation
- Barrier dysfunction
- Neuroimmune dysregulation

Underlie multiple pathophysiological processes across multiple diseases¹⁻¹⁷

Are associated with recurring and debilitating symptoms, and progressive tissue damage in a range of diseases with type 2 inflammation component¹⁻¹⁷

Type 2 inflammatory cytokines have key roles in pathogenic processes in diseases with type 2 inflammation component⁵⁻¹²

Predominant driver of systemic effects, including activation of Th2 cells and other immune cells^{2,5,10,11}

Drivers of local tissue responses, inflammation and various disease symptoms^{2,5,7,10}

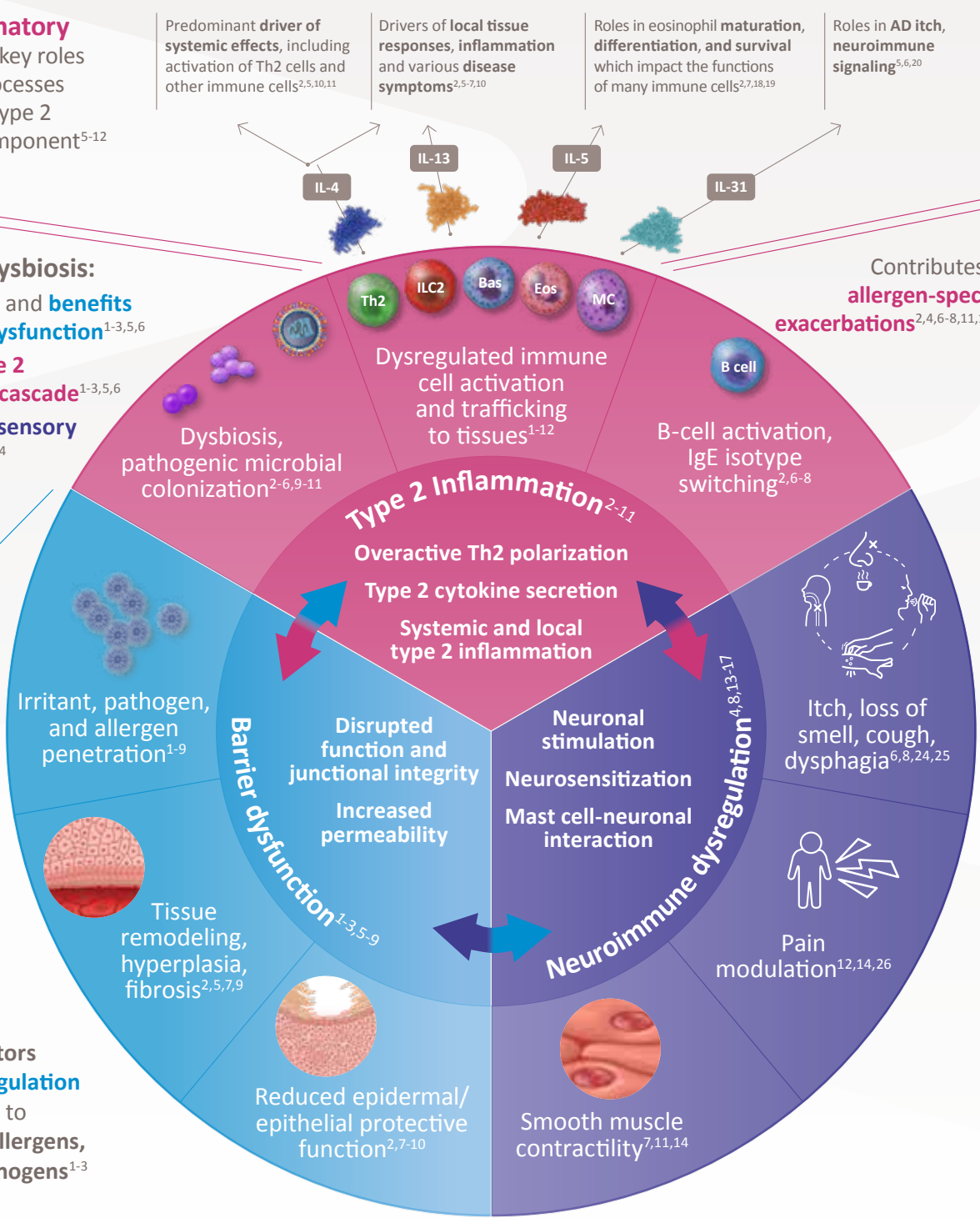
Roles in eosinophil maturation, differentiation, and survival which impact the functions of many immune cells^{2,7,18,19}

Roles in AD itch, neuroimmune signaling^{5,6,20}

Microbiome dysbiosis:

- Contributes to and benefits from barrier dysfunction^{1-3,5,6}
- Intensifies type 2 inflammatory cascade^{1-3,5,6}
- Interacts with sensory mechanisms^{4,14}

Contributes to allergen-specific exacerbations^{2,4,6-8,11,13,16}



Contributing factors for barrier dysregulation include exposure to environmental allergens, irritants and pathogens¹⁻³

AD, atopic dermatitis; Bas, basophil; CRSwNP, chronic rhinosinusitis with nasal polyps; EoE, eosinophilic esophagitis; Eos, eosinophil; ILC2, innate lymphoid type-2 cell; MC, mast cell; Th2, T helper 2 cell.

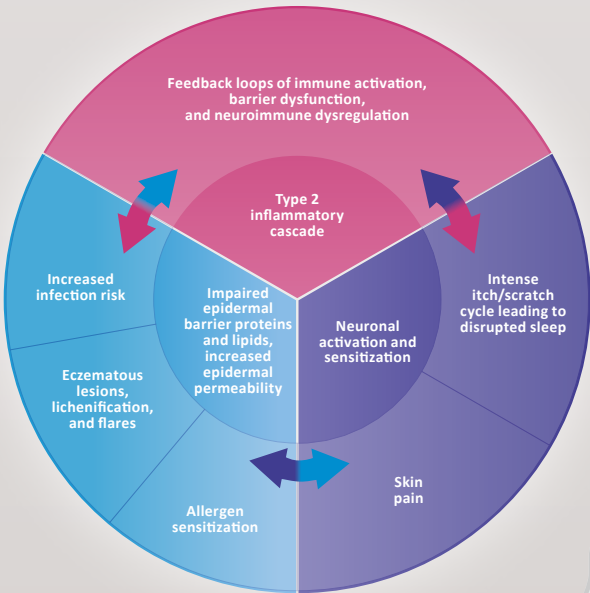


Triad of Dysregulated Mechanisms Driven by Type 2 Inflammation Impacts Patients' Quality of Life²⁻¹⁰

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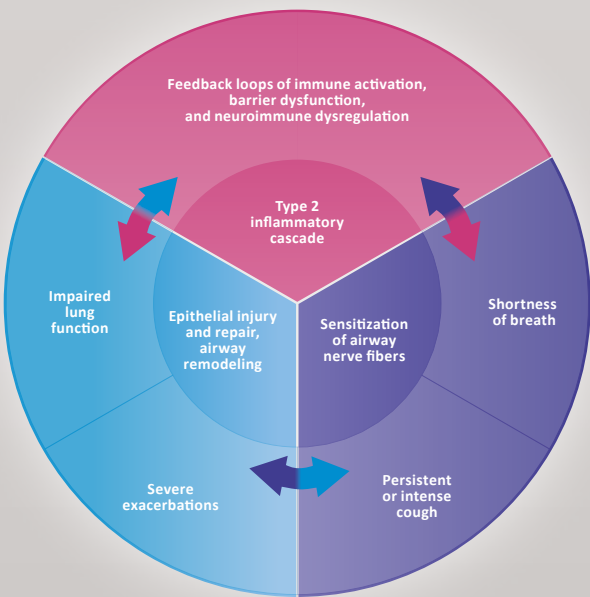
ATOPIC DERMATITIS^{1-3,5,6,22,23}



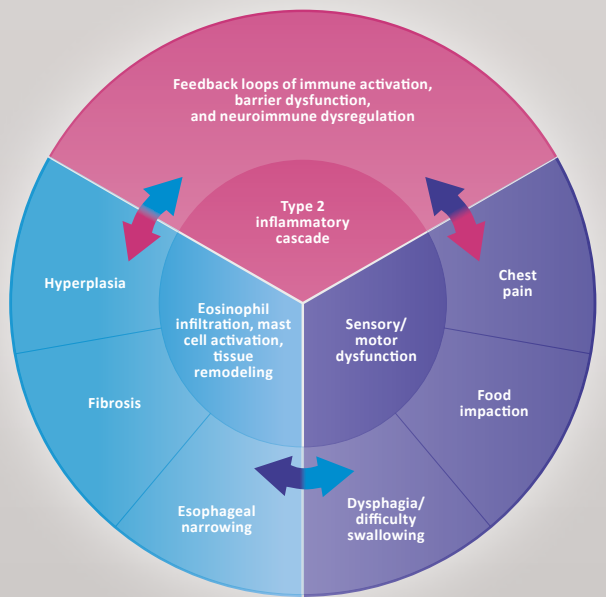
CHRONIC RHINOSINUSITIS WITH NASAL POLYPS^{1-3,9-12,15,17}



ASTHMA^{1-4,7,8}



EOSINOPHILIC ESOPHAGITIS^{1-3,11-13}



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