

# PATHWAYS TO DISEASE: INFLAMMATION IN COPD

COPD is a chronic, heterogeneous, and often progressive inflammatory airway disease associated with persistent airflow limitation, respiratory symptoms, and exacerbations<sup>1</sup>



#### SYMPTOMS<sup>1</sup>

Dyspnea, cough, sputum production

#### **Common Phenotypes**

## BRONCHITIS, SMALL AIRWAYS DISEASE<sup>2,3</sup>

Chronic inflammatory damage to airways, mucus overproduction, and hypersecretion

#### EMPHYSEMA<sup>2</sup>

Loss of elasticity, hyperinflation, and alveolar destruction

# COPD PATHOPHYSIOLOGY





**GASES** 





which cause pathophysiological processes:



MUCUS HYPERSECRETION<sup>2</sup>

AIRWAY REMODELING AND FIBROSIS<sup>5-7</sup>

EMPHYSEMA<sup>2</sup>

## with clinical impacts:



PERSISTENT SYMPTOMS<sup>1</sup>



PROGRESSIVE LUNG FUNCTION DECLINE<sup>2</sup>





SYSTEMIC EFFECTS<sup>1</sup>

COPD, chronic obstructive pulmonary disease.

#### REFERENCES

- I. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2024. Accessed April 26, 2024. https://goldcopd. org/2024-gold-report/
- 2. Rodrigues S, da Cunha C, Soares G, Silva PL, Silva AR, Gonçalves-de-Albuquerque CF. Mechanisms, pathophysiology and currently proposed treatments of chronic obstructive pulmonary disease. *Pharmaceuticals (Basel)*. 2021;14(10):979.
- 3. David B, Bafadhel M, Koenderman L, De Soyza A. Eosinophilic inflammation in COPD: from an inflammatory marker to a treatable trait. *Thorax.* 2021;76(2):188-195.
- 4. Barnes PJ. Oxidative stress in chronic obstructive pulmonary disease. *Antioxidants (Basel)*. 2022;11(5):965.
- 5. Aghapour M, Raee P, Moghaddam SJ, Hiemstra PS, Heijink IH. Airway epithelial barrier dysfunction in chronic obstructive pulmonary disease: role of cigarette smoke exposure. *Am J Respir Cell Mol Biol.* 2018;58(2):157-169.
- 6. Caramori G, Casolari P, Barczyk A, Durham AL, Di Stefano A, Adcock I. COPD immunopathology. Semin Immunopathol. 2016;38(4):497-515.
- 7. Araya J, Cambier S, Markovics JA, et al. Squamous metaplasia amplifies pathologic epithelial-mesenchymal interactions in COPD patients. *J Clin Invest.* 2007;117(11):3551-3562.
- 8. Hikichi M, Mizumura K, Maruouka S, Gon Y. Pathogenesis of chronic obstructive pulmonary disease (COPD) induced by cigarette smoke. *J Thorac Dis.* 2019;11(suppl 17):S2129-S2140.
- 9. Guo-Parke H, Linden D, Weldon S, Kidney JC, Taggart CC. Mechanisms of virus-induced airway immunity dysfunction in the pathogenesis of COPD disease, progression, and exacerbation. *Front Immunol.* 2020;11:1205.
- 10. Calderon AA, Dimond C, Choy D, et al. Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD. *Eur Respir Rev.* 2023;32(167):220144.
- 11. Gandhi NA, Bennett BL, Graham NMH, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov.* 2016;15(1):35-50.
- 12. Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease.

  J Allergy Clin Immunol. 2016;138(1):16-27.

- 13. Maspero J, Adir Y, Al-Ahmad M, et al. Type 2 inflammation in asthma and other airway diseases. *ERJ Open Res.* 2022;8(3):00576-2021.
- 14. Alevy YG, Patel AC, Romero AG, et al. IL-13-induced airway mucus production is attenuated by MAPK13 inhibition. *J Clin Invest.* 2012;122(12):4555-4568.
- 15. Fritzsching B, Zhou-Suckow Z, Trojanek JB, et al. Hypoxic epithelial necrosis triggers neutrophilic inflammation via IL-1 receptor signaling in cystic fibrosis lung disease. *Am J Respir Crit Care Med.* 2015;191(8):902-913.
- 16. Hogg JC, Chu F, Utokaparch S, et al. The nature of small-airway obstruction in chronic obstructive pulmonary disease. *N Engl J Med.* 2004;350(26):2645-2653.
- 17. Mall MA. Unplugging mucus in cystic fibrosis and chronic obstructive pulmonary disease. *Ann Am Thorac Soc.* 2016;13 suppl 2:S177-S185.
- 18. Smithgall MD, Comeau MR, Yoon BRP, Kaufmann D, Armitage R, Smith DE. IL-33 amplified both Thland Th2-type responses through its activity on human basophils, allergen-reactive Th2 cells, iNKT and NK cells. *Int Immunol.* 2008;20(8):1019-1030.
- 19. Ruysseveldt E, Martens K, Steelant B. Airway basal cells, protectors of epithelial walls in health and respiratory disease. Front Allergy. 2021;2:787128.
- 20. Lee CG, Homer RJ, Zhu Z, et al. Interleukin-13 induces tissue fibrosis by selectively stimulating and activating transforming growth factor β1.

  J Exp Med. 2001;194(6):809-821.
- 21. Eapen MS, Lu W, Hackett TL, et al. Increased myofibroblasts in the small airways, and relationship to remodelling and functional changes in smokers and COPD patients: potential role of epithelial-mesenchymal transition. *ERJ Open Res.* 2021;7(2):00876-2020.
- 22. Doyle AD, Mukherjee M, LeSuer WE, et al. Eosinophil-derived IL-13 promotes emphysema. *Eur Respir J.* 2019;53(5):1801291.
- 23. Skjøt-Arkil H, Clausen E, Nguyen QH, et al. Measurement of MMP-9 and -12 degraded elastin (ELM) provides unique information on lung tissue degradation. *BMC Pulm Med*. 2012;12:34.
- **24.** Annunziato F, et al. *J Allergy Clin Immunol.* 2015;135(3):626-635.
- **25.** Bai S, Zhao L. Imbalance between injury and defense in the COPD emphysematous phenotype. *Front Med (Lausanne)*. 2021;8:653332.

