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Mapping of eosinophils, immune cell profiles, and microbes in COPD lung tissue

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Background: A subgroup of COPD patients (pts) displays eosinophilia, a trait targeted in several clinical drug programs. Little is known about the mechanisms underlying eosinophil (eos) infiltration into COPD lungs, or how eos infiltration relates to microbial presence and immune cell composition.

Aims: Reveal the spatial relationship between tissue eos, microbes, and immune cell patterns in lungs and lymph nodes from COPD pts.

Methods: Surgical lung tissue was collected from 35 COPD pts (GOLD I-IV) and 17 non-COPD controls. Microbes and complete immune cell profiles were identified histologically by combined in situ hybridization and multiplex immunohistochemistry, followed by computerized spatial analysis.

Results: Mean total tissue eos increased in severe COPD. The infiltration pattern was patchy with no spatial correlation to bacteria, viruses, or fungi. Multiplex imaging of major leukocyte and structural cell populations revealed spatially distinct immune cell niches in which eos-rich microenvironments occurred alongside neutrophil- and macrophage-dominated regions. Eos and type 2 foci were spatially linked to basophils, CD20+ B lymphocytes, CD20-CD19+ plasmablasts, and CD138+ plasma cells. Eos infiltration in bronchi, small airways, or alveolar regions was associated with eosinophilia in the subcapsular and medullary lymphatic sinuses in lung-draining lymph nodes.

Conclusions: Patchy eosinophilia was linked to adaptive immune niches that with spatially separated non-eos inflammation yields complex mixed inflammatory signatures that likely impact treatment response. The finding of no spatial association between microbial presence and eosinophilia suggests that other non-infectious factors are involved.