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Spotlight on Leading Edge Research

Frontline Science: Eosinophil - deficient MBP - 1 and EPX double - knockout mice link pulmonary remodeling and airway dysfunction with type 2 inflammation

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Abstract

Eosinophils and the release of cationic granule proteins have long been implicated in the development of the type 2–induced pathologies linked with respiratory inflammation. Paradoxically, the ablation of the two genes encoding the most abundant of these granule proteins, major basic protein - 1 (*MBP - 1*) and eosinophil peroxidase (*EPX*), results in a near collapse of eosinophilopoiesis. The specificity of this lineage ablation and the magnitude of the induced eosinopenia provide a unique opportunity to clarify the importance of eosinophils in acute and chronic inflammatory settings, as well as to identify potential mechanism(s) of action linked with pulmonary eosinophils in those settings. Specifically, we examined these issues by assessing the induced immune responses and pathologies occurring in MBP - $1^{-/-}$/$EPX^{-/-}$ mice after 1) ovalbumin sensitization/provocation in an acute allergen - challenge protocol, and 2) crossing MBP - $1^{-/-}$/$EPX^{-/-}$ mice with a double - transgenic model of chronic type 2 inflammation (i.e., I5/hE2). Acute allergen challenge and constitutive cytokine/chemokine expression each induced the accumulation of pulmonary eosinophils in wild - type controls that was abolished in the absence of MBP - 1 and EPX (i.e., MBP - $1^{-/-}$/$EPX^{-/-}$ mice). The expression of MBP - 1 and EPX was also required for induced lung expression of IL - 4/IL - 13 in each setting and, in turn, the induced pulmonary remodeling events and lung dysfunction. In summary, MBP - $1^{-/-}$/$EPX^{-/-}$ mice provide yet another definitive example of the immunoregulatory role of pulmonary eosinophils. These results highlight the utility of this unique strain of eosinophil - deficient mice as part of in vivo model studies investigating the roles of eosinophils in health and disease settings.

Citing Literature