

Ly6G protein expressed in neutrophils is a novel regulator for skin homeostasis

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The role of mast cells (MCs) in the development of allergic diseases is pivotal, with their activation triggered by allergens leading to degranulation and the release of inflammatory mediators, such as histamine. These mediators not only induce allergic diseases but also elevate vascular permeability, attracting various immune cells to the inflammatory tissues and intricately regulating allergic responses. In a previous study, utilizing a mouse model, we demonstrated that neutrophils suppress allergic reactions. Notably, we observed proximity and interaction between activated MCs and neutrophils. While neutrophils are recognized for their defense responses against foreign substances, the molecular mechanism governing MC-neutrophil interactions in allergic diseases remains elusive. In this study, our focus turned to Ly6G, a protein specific to neutrophils, to unravel the regulatory mechanism of allergic responses orchestrated by Ly6G through interactions between MCs and neutrophils. Ly6G was found to migrate to MCs through neutrophil-MC interactions, with its migration significantly heightened upon allergen stimulation. To probe the function of Ly6G, we produced recombinant Ly6G (rLy6G) and confirmed its binding to MCs using flow cytometry. Further analysis revealed that rLy6G mitigated allergen stimulation-dependent enhancement of MC degranulation. Intriguingly, rLy6G tended to increase mRNA expression and protein secretion of TNF α and CCL2 in MCs. To identify functional sequences, we synthesized nine peptides, derived from Ly6G sequence. Several peptides were identified to suppress MC degranulation, but TNF α and CCL2 secretion were upregulated. To assess the impact of rLy6G on allergic responses in a disease model, we employed a Passive Cutaneous Anaphylaxis (PCA) model. Administration of rLy6G demonstrated a reduction in the increase in vascular permeability, a marker of anaphylactic symptoms, compared to control mice. These results collectively indicate that Ly6G plays a pivotal role in regulating allergic responses through MC-neutrophil interactions.