Alveolar macrophage P2Y6 receptors counterbalance leukotriene-dependent type 2 lung immunopathology priming function

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Introduction
Type 6 purinergic (P2Ys) receptors are high affinity G protein-coupled receptors (GPCRs) on alveolar macrophages (UDP). Previously, we found that P2Y6 receptors inhibit type 2 immunity in lung allergic inflammation by incompletely understood mechanisms. In this study, we sought to identify key steps and cell types responsive for the protective effect of P2Y6 receptors. We also determined the potential consequence of P2Y6 receptor blockade by CysLT1-R antagonist ifexin existence vivo and in vivo.

Methods
P2y6flox/flox;Nos2aCreERT2(TTA) (Cre+/-) and P2y6flox/flox;Nos2aCreERT2(TTA) HET controls were treated with tamoxifen before or after the initial sensitization. The mice were sensitized with an extract from Dermatophagoides farinae (DF) intranasally (i.n.) on days 0, 1, 14, and 15. We examined the physiologic functions of alveolar macrophage at sensitization using cell depletions, adoptive transfers, CysLT1-R antagonist (Zafirlukast, MK571), and relevant controls and comparisons.

Figure #1

A Tamoxifen
B Eosinophils

Figure #2

Figure #3

A BAL (2 d) B BAL UDP level (2 d) C NAC / Cre/+ Eosinophils

Figure #4

A BAL cells (Wtg 2 d) B BAL (2 d)

Figure #5

A AHR /Gapdh x Cells B BAL cells (Wtg 2 d)

Figure #6

A IL-12p40 B IL-12p40 (Wtg mice, 16 d)

Acknowledgments
The authors thank Erica Fabi and Andrew Zech for intellectual and strategic input,Huber Ito and John to help with statistical analyses. This work was supported by generous contributions from the Vinik Family, the Kaya Family, by National Institute of Health Grants AI078065, HL111113, HL117945, AI000001, AI000001, R01HL118293, R01AI131517, and U01AI095210, and by an American Heart Association Grant (19SDG34610001) awarded to J. Nagai and an Overseas Research Fellowship Award (28-348) awarded to J. Nagai. The authors declare no competing financial interests.

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