

Effects of 5-lipoxygenase pathway inhibition on rhinovirus-associated bronchial epithelial inflammation

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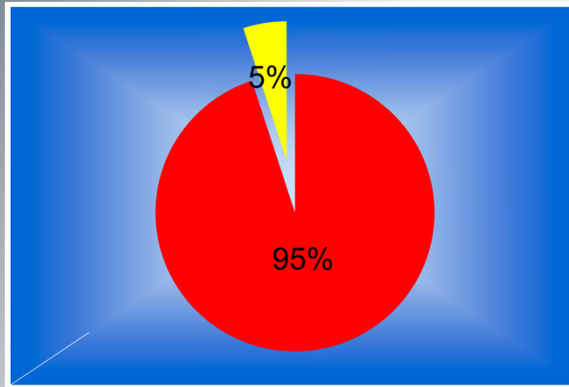
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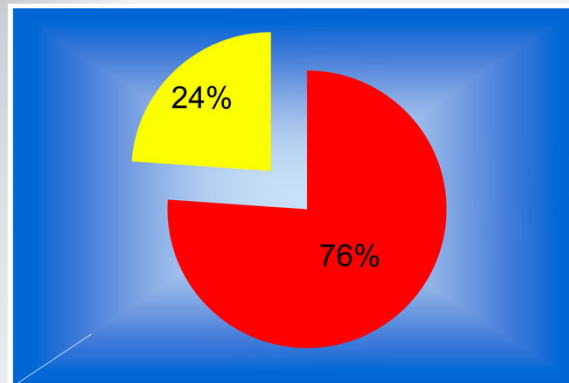
RVs and asthma exacerbations

Children

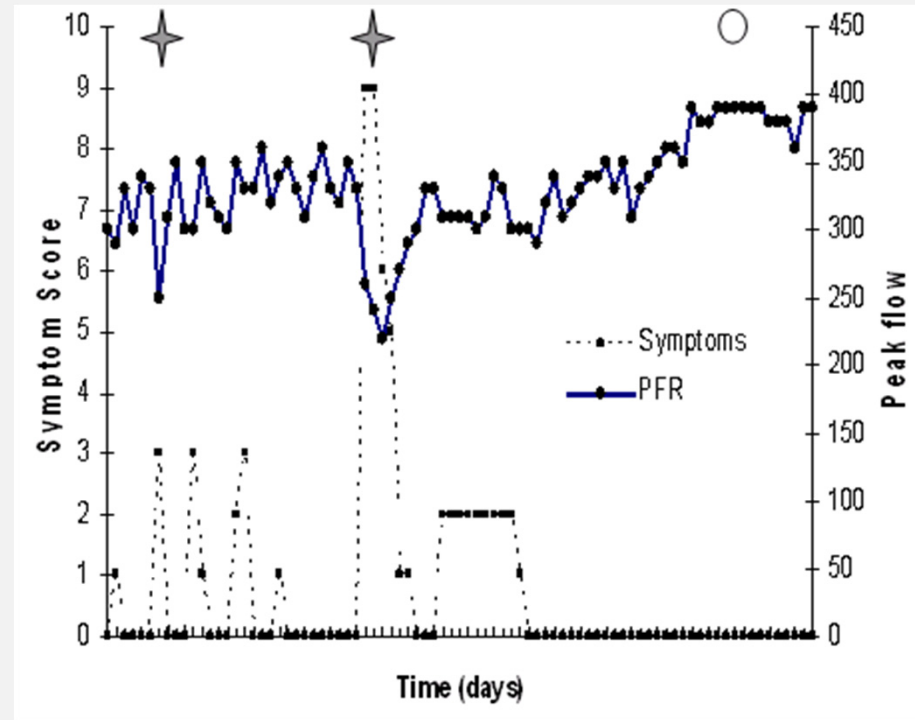


Ruuskanen et al. (2006)

Adults

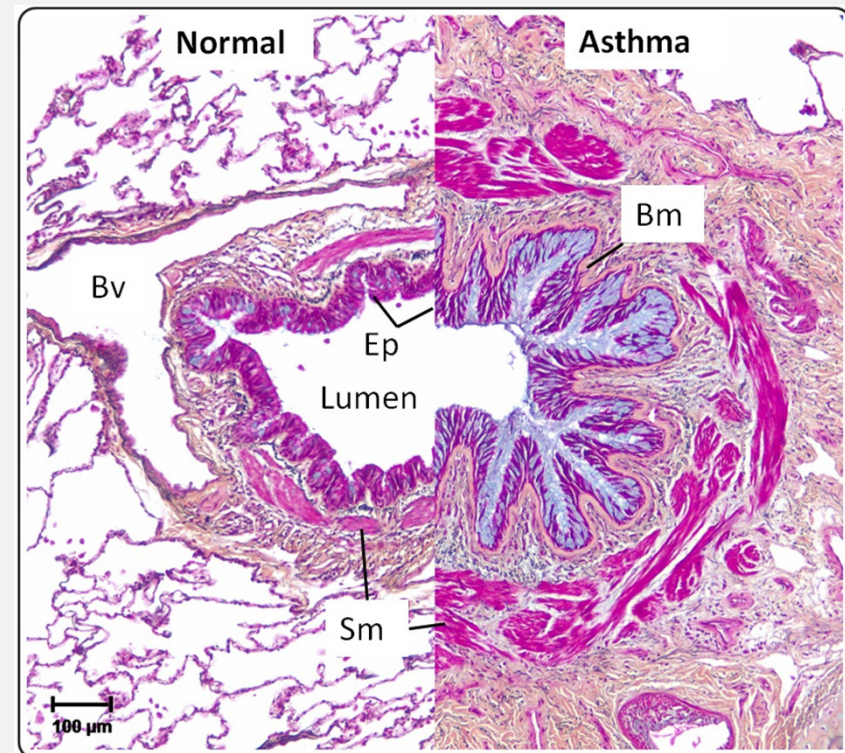
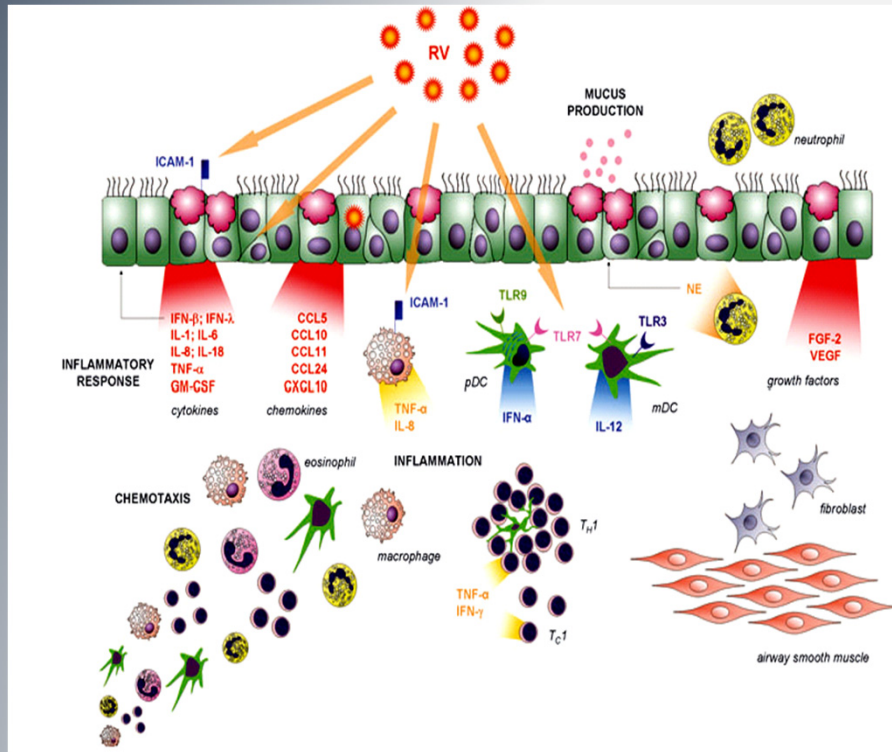


Wark et al. ERJ (2002)

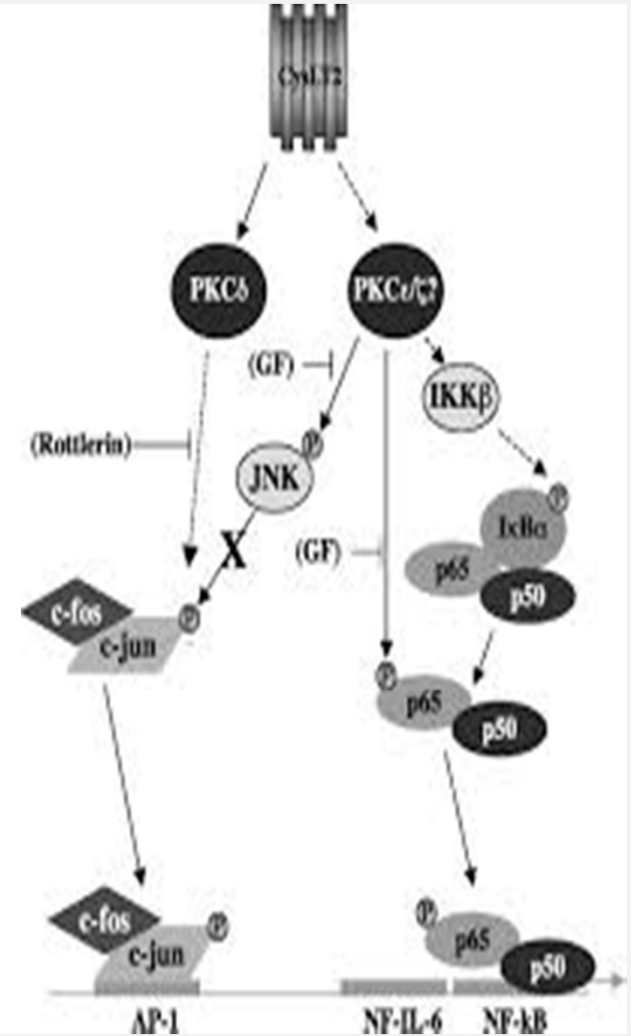
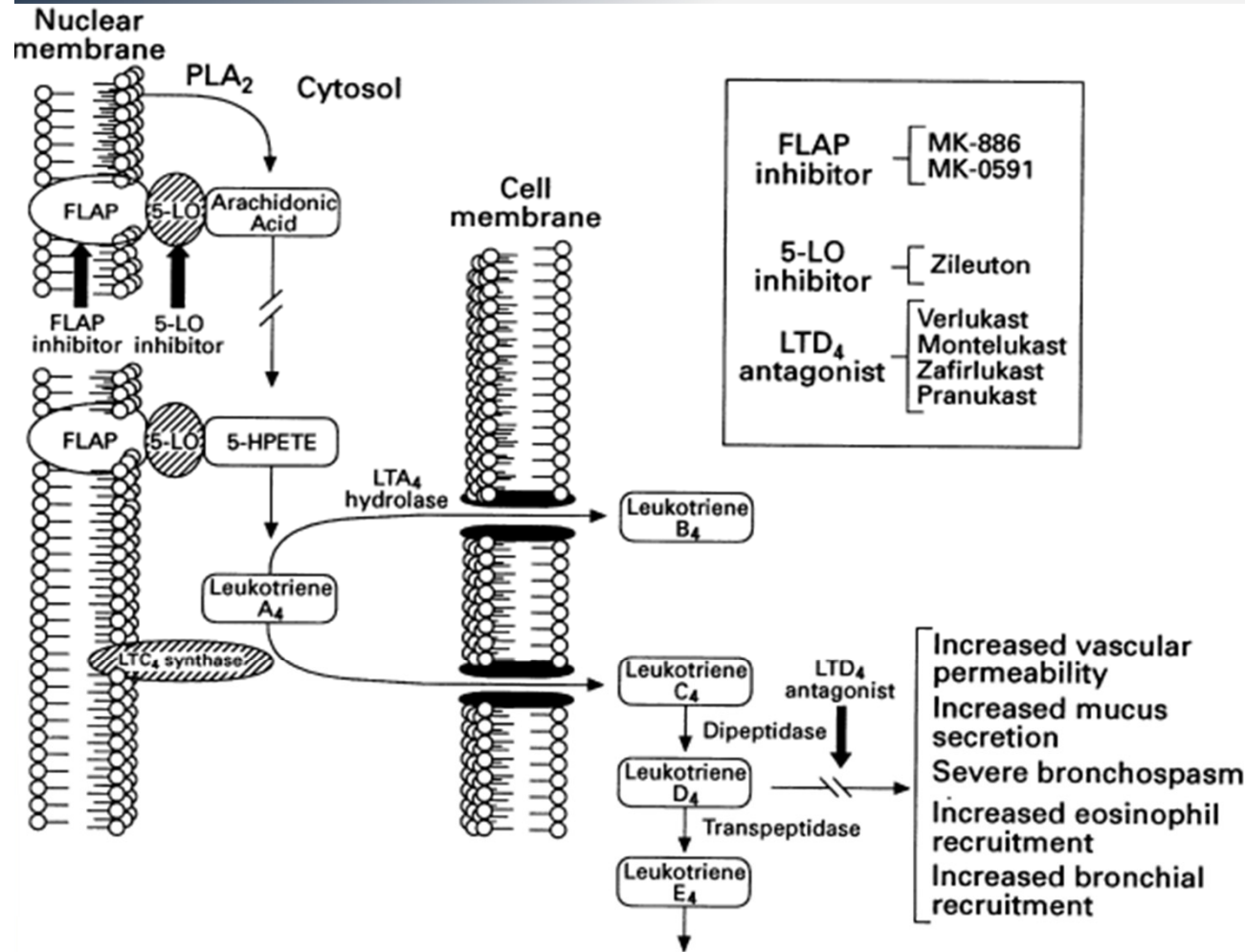


NG Papadopoulos and CL Skevaki. Asthma: An atlas of investigation and management, 1st ed, 2006

RVs induce inflammation and remodeling



Leukotriene pathway and inflammation



Hypothesis

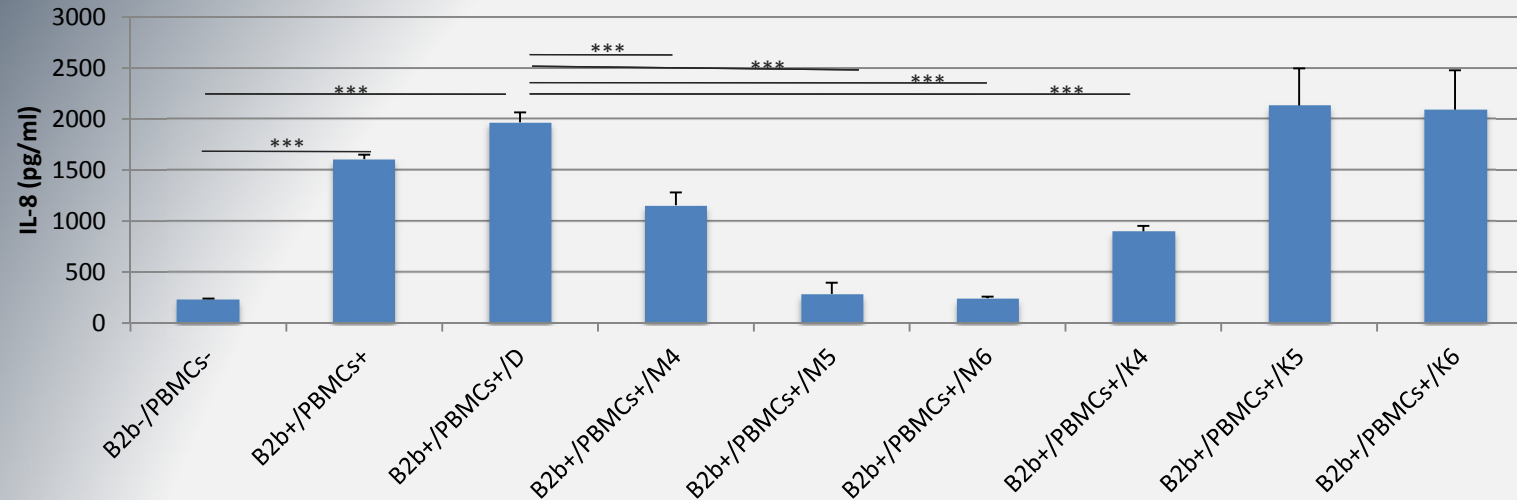
Anti-leukotriene treatment of epithelial cells with or without exposure to supernatants of RV-infected PBMCs may inhibit RV-induced up-regulation of inflammatory cytokines.

Methods

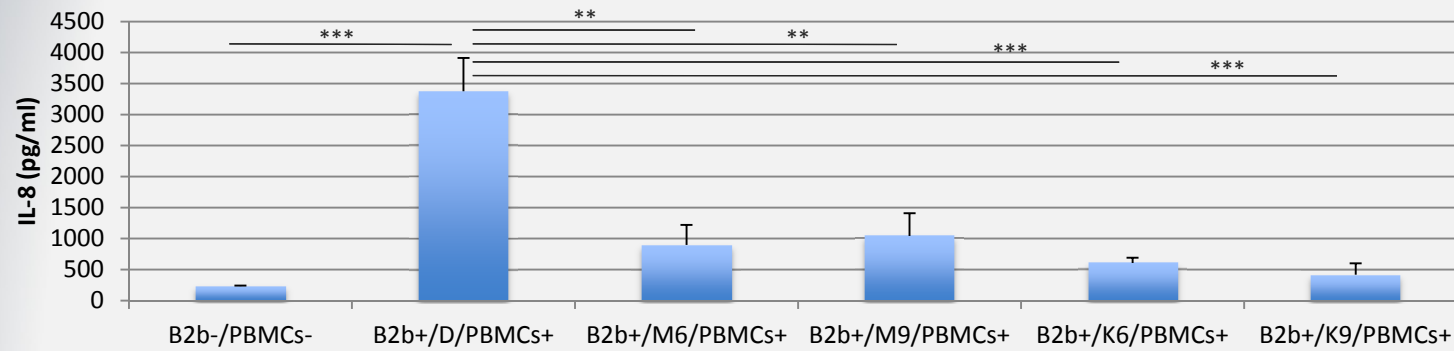
- PBMCs isolation: healthy donor – non atopic-non astmatic
- BEAS-2B cell culture
- *In-vitro* infection of BEAS-2B cells and/or PBMCs with A1B
- *In-vitro* treatment of BEAS-2B cells and/or PBMCs with Montelukast (cysLT receptor antagonist) or MK-886 (FLAP inhibitor)
- Incubation at 33° C, 5% CO₂ for 48 hours
- Evaluation of the concentration of inflammatory cytokines: IL-8, RANTES, IL-11, IL-6, IP-10

Results(I) IL-8

BEAS-2b, IL-8 release (drug treated PBMCs)

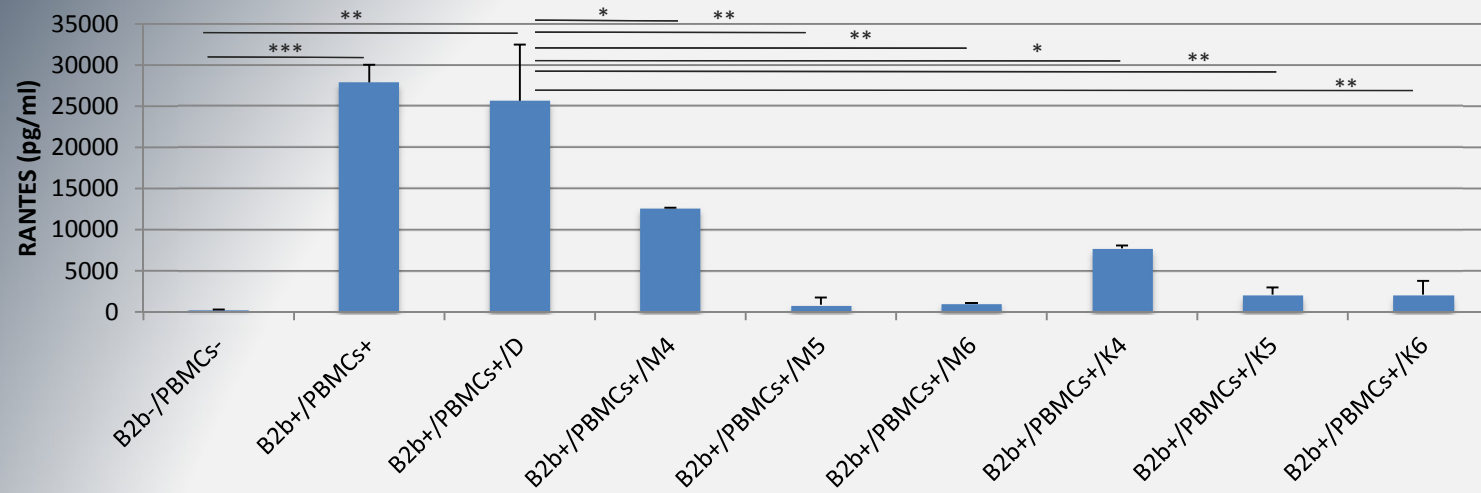


BEAS-2b, IL-8 release (PBMCs, drug treated)

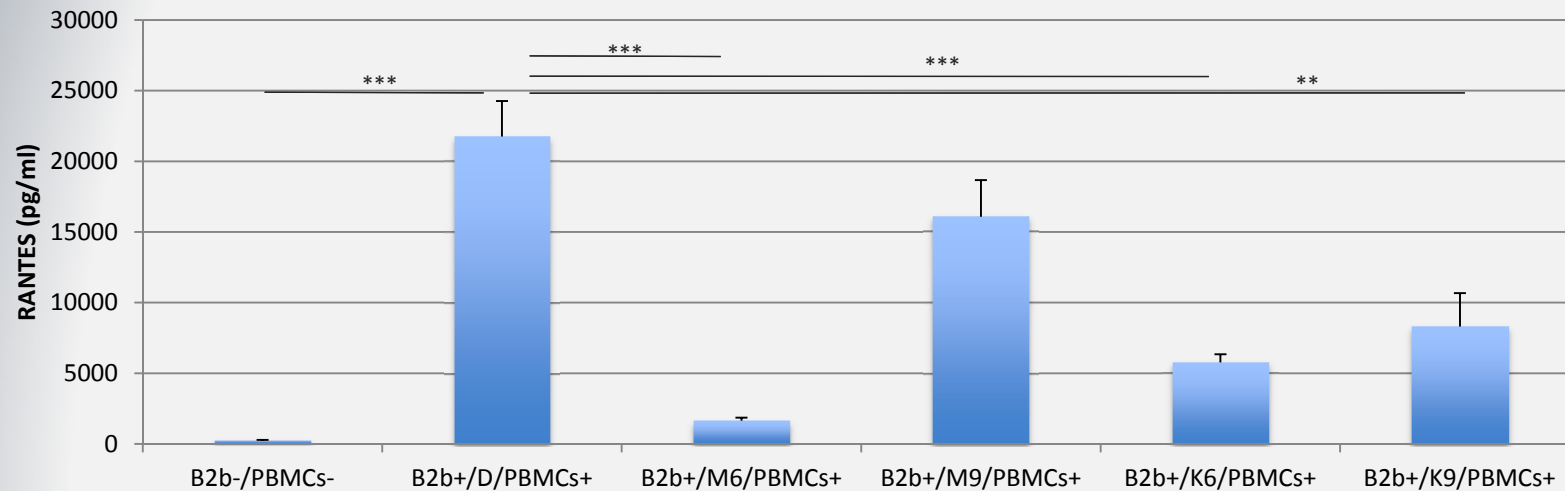


Results(II) RANTES

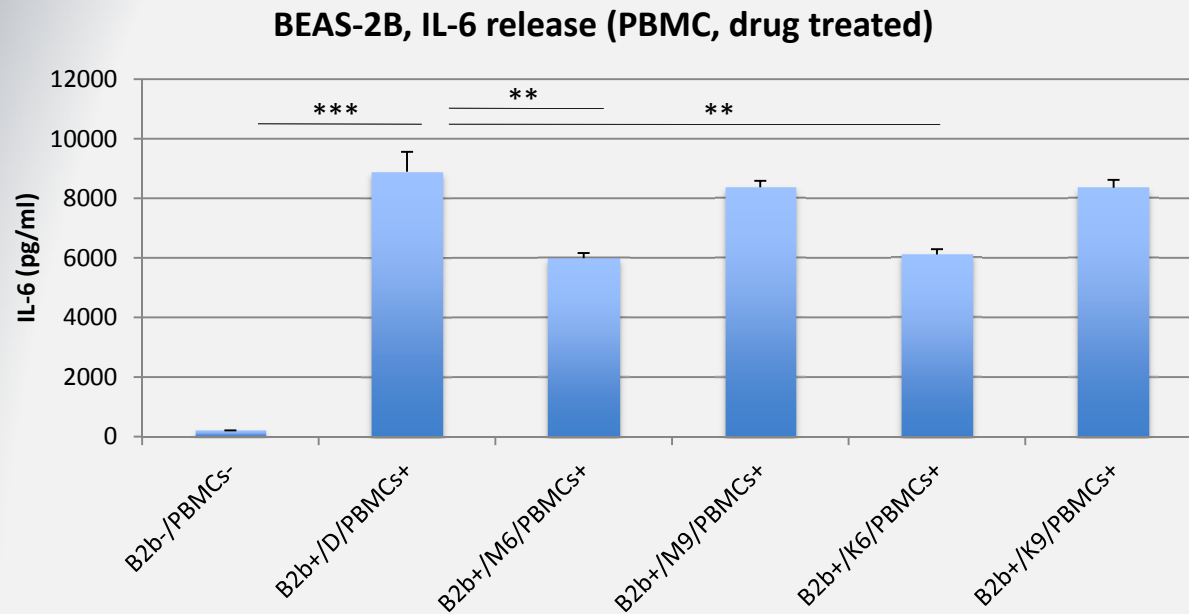
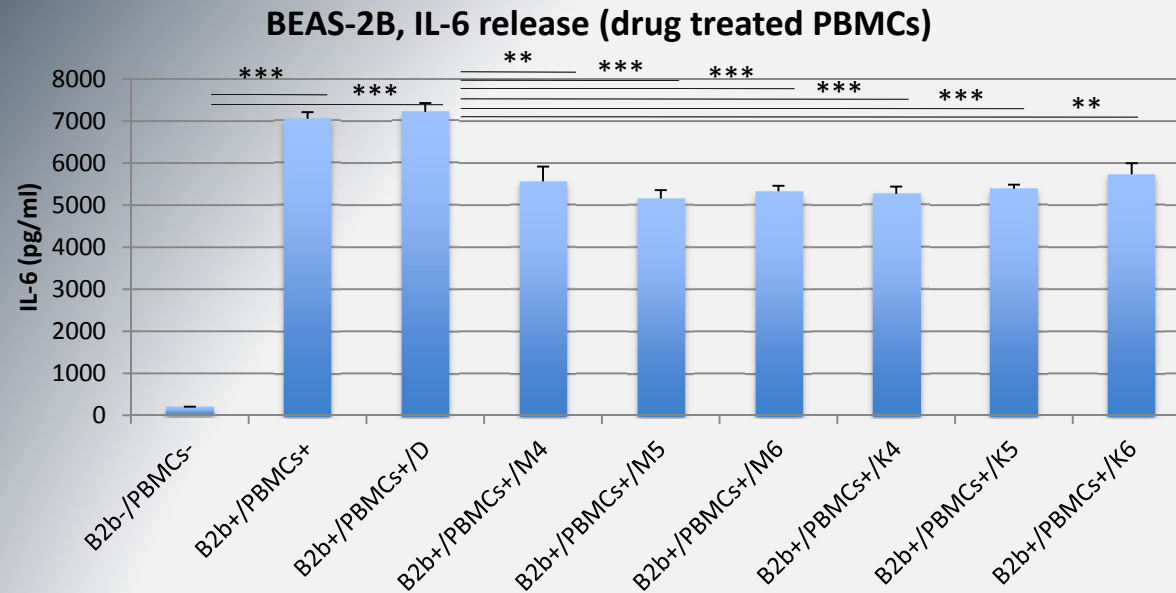
BEAS-2b, RANTES release (drug treated PBMCs)



BEAS-2b, RANTES release (PBMCs, drug treated)

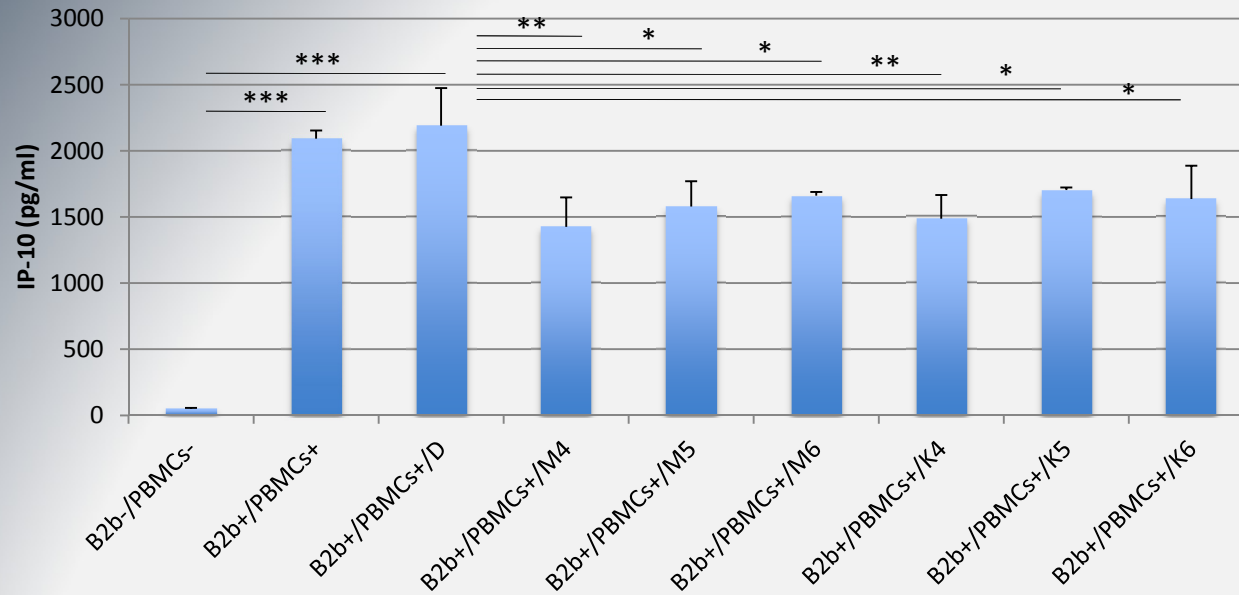


Results(III) IL-6

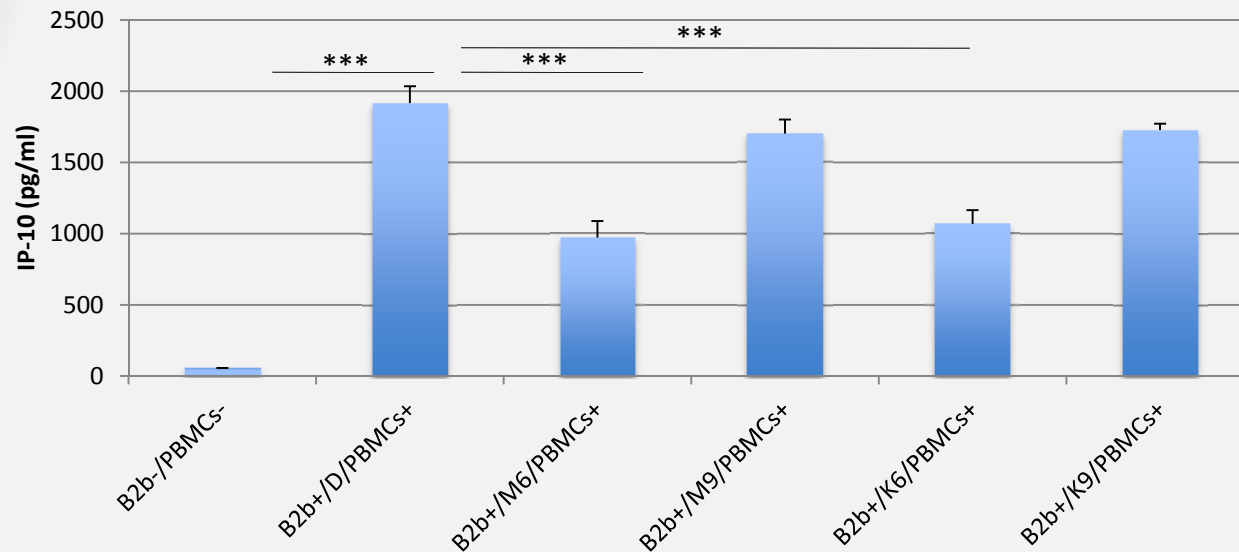


Results(V) IP-10

BEAS-2B, IP-10 release (drug treated PBMCs)

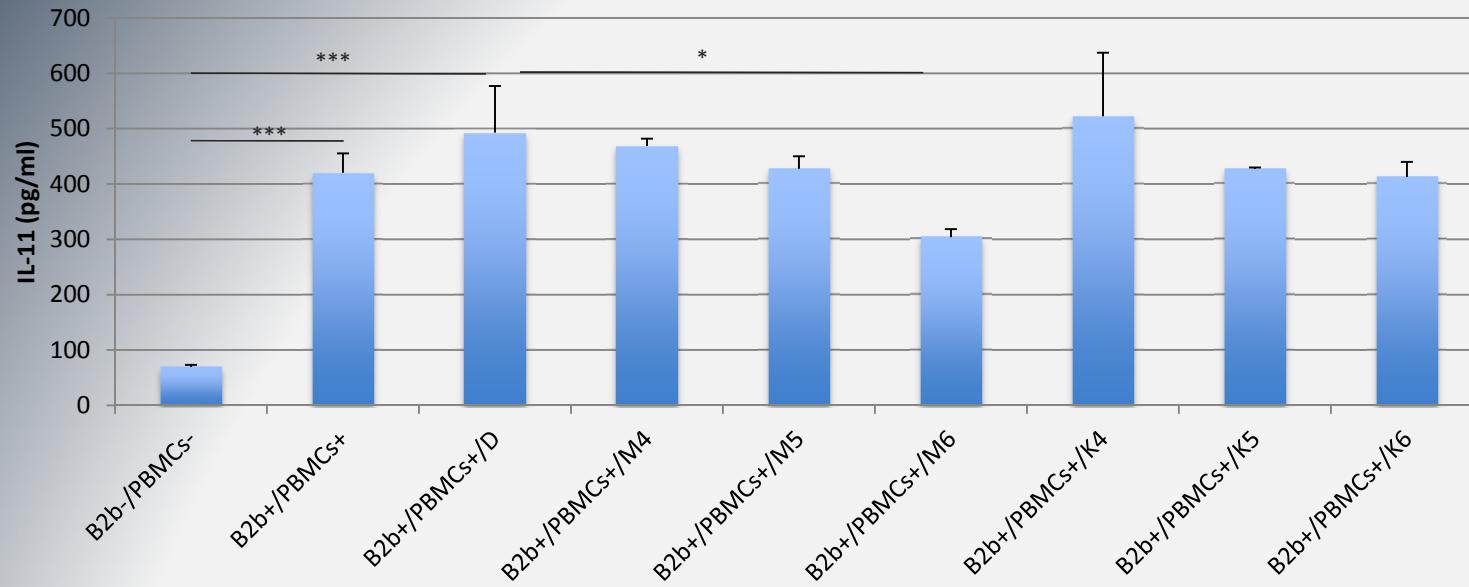


BEAS-2B, IP-10 release (PBMCs, drug treated)

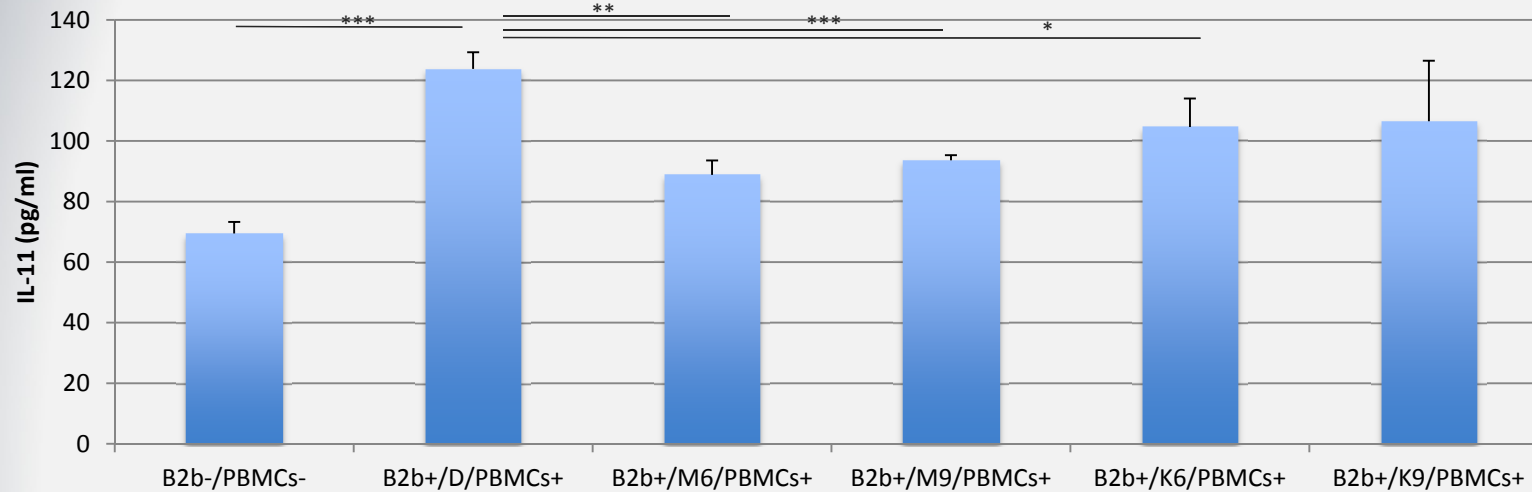


Results(IV) IL-11

BEAS-2b, IL-11 release (drug treated PBMCs)



BEAS-2b, IL-11 release (PBMCs, drug treated)



Conclusion

Anti-leukotriene treatment of RV-infected bronchial epithelial cells suppresses epithelial RV-mediated pro-inflammatory (IL-6, IL-8, RANTES, IP-10) and anti-inflammatory (IL-11) cytokine response.

These observations may represent an indirect mode of action of anti-leukotriene medication in virus-induced asthma.