

**Loss of IL-4R $\alpha$ -mediated PI3K signaling accelerates the onset and progression of  
IgE/mast cell-mediated reactions**

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**Supplementary Figure S1. No impact of loss of IL-4R $\alpha$ -PI3K signaling on total IgE.**

Total IgE levels in the serum of OVA-sensitized, intragastric (i.g.) OVA-challenged WT and IL-4R $\alpha$ <sup>Y500F</sup> mice following the seventh challenge. Each filled circle represents an individual mouse. Data represents mean  $\pm$  SD.

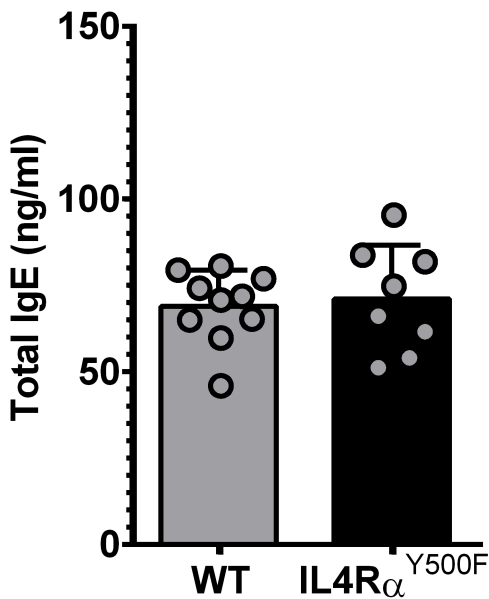
**Supplementary Figure S2. A Positive relationship between vascular leak and shock response in murine oral antigen-induced anaphylaxis.**

Correlation between hematocrit and systemic symptoms of oral antigen-induced anaphylaxis. Spearman's rank correlation coefficient between hematocrit and temperature change from 0 to 60 minutes after the seventh i.g. OVA challenge in OVA-sensitized WT mice. Individual symbols represent 1 mouse.

**Supplementary Figure S3. Systemic anaphylaxis in WT and IL-4R $\alpha$ <sup>Y500F</sup> mice is dependent on Histamine.**

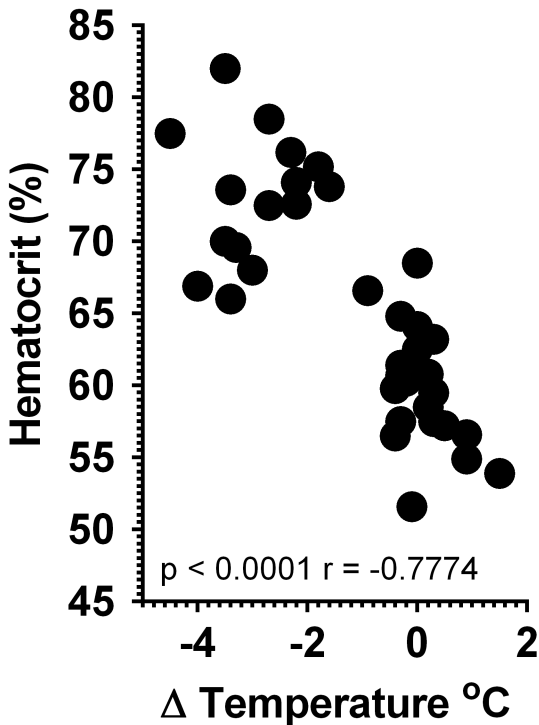
Temperature change from 0 to 30 minutes in OVA-sensitized, intragastric (i.g.) OVA-challenged (A). WT and (B). IL-4R $\alpha$ <sup>Y500F</sup> mice following the sixth and seventh intragastric (i.g.) OVA challenge. OVA-sensitized WT and IL-4R $\alpha$ <sup>Y500F</sup> mice receive repeated i.g. OVA challenges and Temperature change from 0 to 30 minutes was determined following the sixth challenge. Prior to the seventh challenge mice were administered histamine Type 1 and Type 2 receptor antagonists Triprolidine (200 $\mu$ g) and Cimetidine (200 $\mu$ g) i.v. (200 $\mu$ l final volume) 30 minutes prior to OVA challenge. Each filled circle represents an individual mouse. Data represents the temperature change from 0 to 30 minutes following the sixth and seventh challenge; p values as indicated.

**Supplementary Figure S4. Histamine and DHEA-induced PI3K activation in human vascular endothelial cell line EA.hy926.** Representative Western blot analyses probing for PI3K p85-full-length-protein and actin in protein lysates from human vascular endothelial cell line EA.hy926 following 0, 1, 5, 15, 30 and 60 minutes stimulation with Histamine (20nM) or DHEA (100nM).

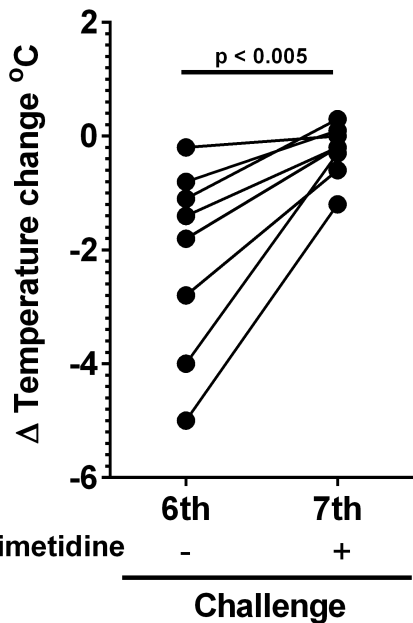


**Supplemental Figure S1.**

# Supplemental Figure S2



**(A). WT**

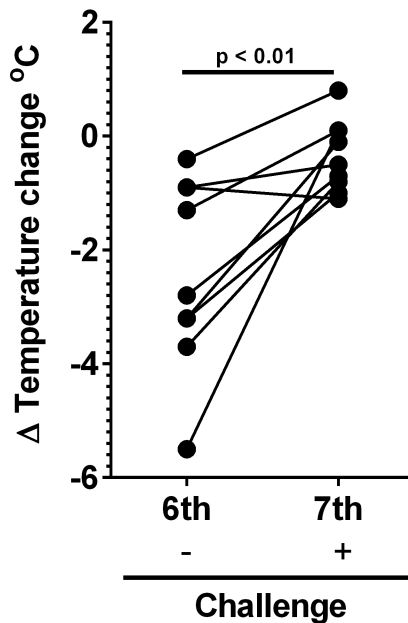


Tripolridine / Cimetidine

- +

Challenge

**(B). II4R $\alpha$ <sup>Y500F</sup>**



- +

Challenge

**Supplemental Figure S3.**

**Supplemental Figure S4**

