**Supplementary Results**

**Anti-inflammatory potential of Ze339 is not restricted to cells derived from atopic donors**

Since IL-8 production and neutrophil chemotaxis are hallmarks of allergic as well as non-allergic inflammation, we assessed whether Ze339 might act on the proinflammatory response of HNEC from both, atopic and non-atopic donors. Therefore, the atopy status of the HNEC donors was determined by Immuno-CAP assay, and results were calculated separately according to the atopy status. As shown in **Supp. fig. 1**, PolyIC stimulation of HNEC induced the secretion of IL-8 and other pro-inflammatory mediators (G-CSF, CCL-5, IL-6, IL-1α), an effect that was most pronounced in cells derived from non-atopic donors. Ze339 significantly reduced the PolyIC-induced cytokine and chemokine response in cells derived from both, non-atopic and atopic donors.

**Ze339 and Petasins do not induce enhanced cytotoxicity in nasal epithelial cells**

To evaluate the viability of stimulated HNECs, the lactate dehydrogenase (LDH) activity in supernatants of stimulated HNECs was quantified. Stimulation with Ze339 or the petasin isofroms did not lead to a significant increased LDH production (**Supp. fig. 2**), even when cells were treated in combination with PolyIC compared to medium control (**Supp. fig. 3**).

**Supplementary figure legends**

**FIGURE S1**

**Ze229 decreases the cytokine- and chemokine response in primary nasal epithelial cells derived from non-atopic and atopic donors.**

HNEC of non-atopic (n=4) and atopic donors (n=5) were incubated for 24h medium, PolyIC (10µM) or PolyIC plus Ze339 (3µM), and cell-culture supernatants were analysed for the pro-inflammatory mediators using Bioplex assay: IL-8 (a), G-CSF (b), CCL-5 (c), IL-6 (d), and IL-1α (e). \*: p<0.05; \*\*: p<0.01, Wilcoxon test.

**FIGURE S2**

**Ze339 and petasin isoforms are not cytotoxic on primary nasal epithelial cells.**

HNEC were stimulated for 24h with medium or indicated concentrations of Ze339 (a), isopetasin (b), petasin (c) or neopetasin (d). Lactate dehydrogenase (LDH) levels were determined in supernatants of HNEC. Shown are results of n=3 experiments, normalized to cells lysed with Triton X-100.

**FIGURE S3**

**Ze339 and petasin isoforms do not induce cytotoxicity in PolyIC-stimulated HNEC.**

HNECs were stimulated for 24h with medium, PolyIC (10µg/ml) or PolyIC plus indicated concentrations of the stimulants Ze339 (a), isopetasin (b), petasin (c) or neopetasin (d), petasin isoform mixture (e). After 24h, lactate dehydrogenase (LDH) levels were determined in lysates and normalized to cells lysed with Triton x-100. Shown are results of n=5 experiments.