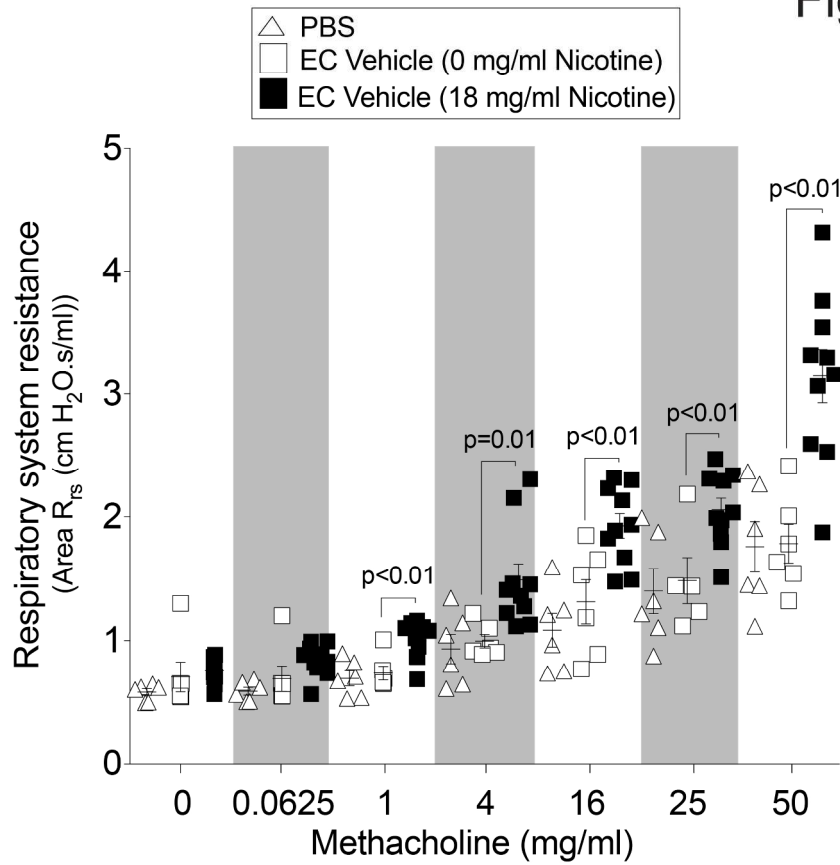
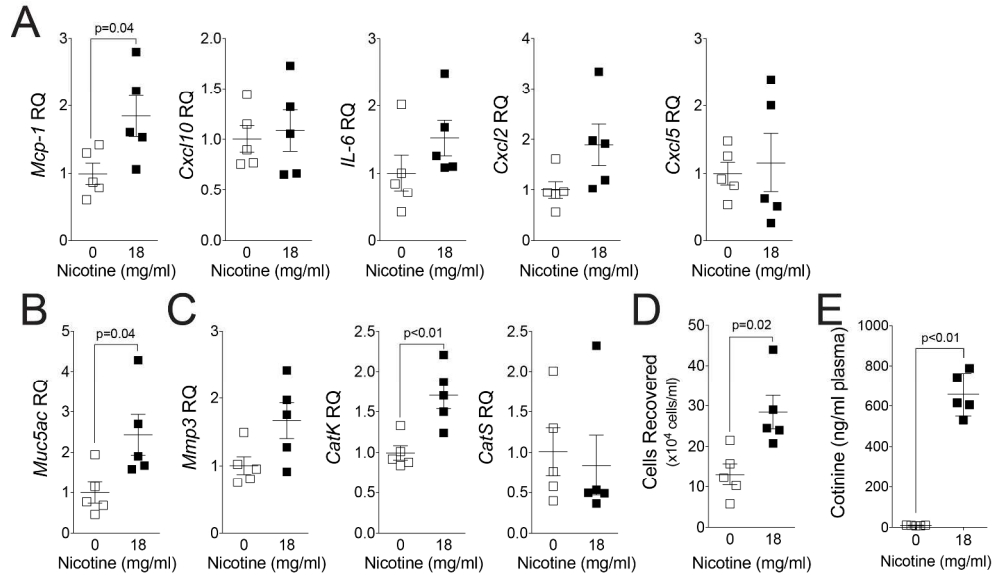


Figure S1



Supplemental Figure S1. Airway hyperresponsiveness to increasing doses of methacholine in mice exposed to inhaled PBS, nicotine-free and nicotine-containing e-cigarette fluids. Mice were exposed daily to inhaled PBS, nicotine-free (EC vehicle, 0 mg/ml) or nicotine-containing (EC vehicle, 18 mg/ml) e-cigarette liquids for 4 months. Airway hyperresponsiveness to increasing doses of methacholine was assessed in each animal group. Graph is represented as mean \pm s.e.m. p values shown, comparing both treatments connected by a line. All $n \geq 6$ /group. The comparisons between two individual groups were determined by student t-tests. ANOVA analyses were used for comparisons between three or more groups.

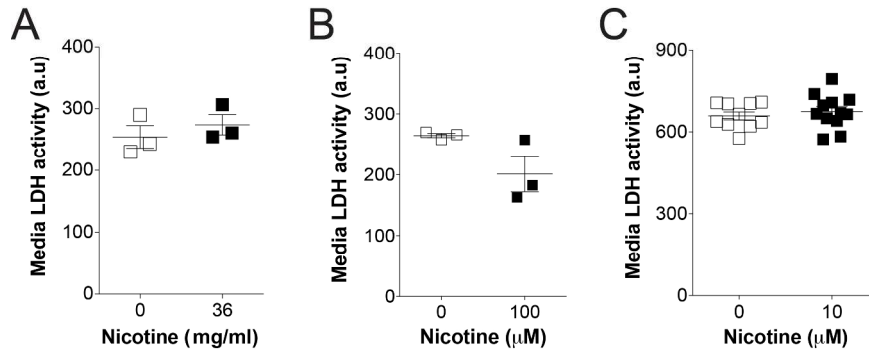
Figure S2



Supplemental Figure S2. Cytokine, protease and mucin responses in lungs from mice exposed to inhaled nicotine-free or nicotine-containing e-cigarette fluids for 2 weeks. Mice were exposed to inhaled nicotine-free (0 mg/ml) or to nicotine-containing (18 mg/ml) e-cigarette for 2 weeks. (A) Gene expression analysis by qPCR for the cytokines MCP-1, CXCL10, IL-6, CXCL2 and CXCL5, (B) Muc5ac and (C) proteases MMP-3, Cathepsin K and Cathepsin S. (D) Total BALF cells were quantified in mice exposed daily for 2 weeks. (E)

Mice were exposed daily to inhaled PBS, nicotine-free (EC vehicle, 0 mg/ml) or nicotine-containing (EC vehicle, 18 mg/ml) e-cigarette liquid for 2 weeks and nicotine absorption was confirmed by plasma cotinine levels. Graphs are represented as mean \pm s.e.m. p values shown, comparing both treatments connected by a line. All n=5/group. The comparisons between two individual groups were determined by student t-tests.

Figure S3



Supplemental Figure S3. Cell viability following E-cigarette vapor and nicotine exposures. Fully differentiated NHBE cells, grown at an ALI, were exposed to (A) vapor from nicotine-free (0 mg/ml) or from nicotine-containing (36 mg/ml) e-cigarettes, (B) nebulized nicotine (final apical concentration estimated at 100 nM) or (C) media supplemented with nicotine. LDH release was recorded. Graphs are represented as mean \pm s.e.m. p values shown, comparing both treatments connected by a line. All $n \geq 3$ donors/group. The comparisons between two individual groups were determined by student t-tests.