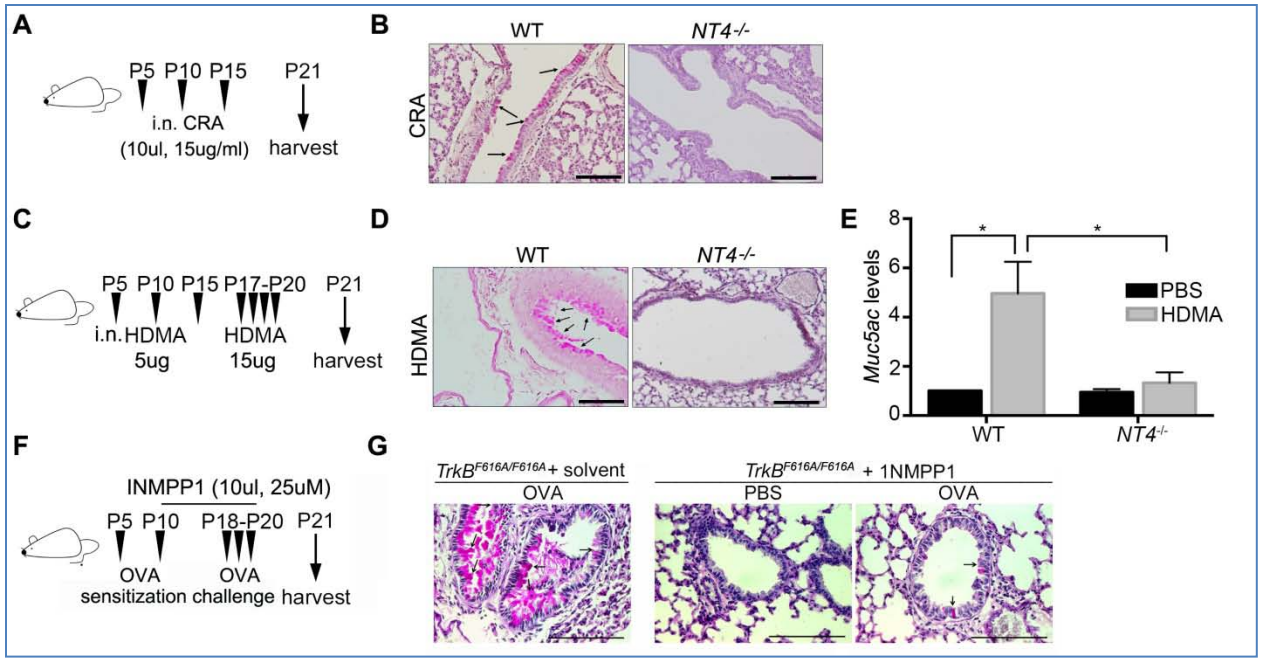
Supplementary Materials and Methods

Mice: *Gad1*$^{f/f}$ mice were kindly provided by Dr. Jun Ding (Stanford University, Stanford, CA, USA). *TrkB*$^{F616A/F616A}$ mice were kindly provided by Dr. David Ginty (Harvard Medical School, MA, USA). *Gad2*$^{CreERT2/+}$ (stock number: 010702), and *Rosa(lacZ)* (stock number: 003309) were purchased from The Jackson Laboratories (Bar Harbor, ME, USA).

Allergen exposure. For cockroach allergen exposure, mice were given intra-nasally cockroach antigen (CRA) (10µl, 15µg/ml; Cat. #B26, Greer Labs) at P5, P10, and P15. For house dust mite allergen (HDMA) exposure, mice were given intra-nasally HDMA (5µg; Cat. # XPB70D3A2.5, Greer Labs) at P5, P10, and P15 followed by daily intranasal instillations (15µg) between P17-P20. Control pups received PBS intra-nasally. At day 21, mice were sacrificed for blood and lung harvest.

Airway contraction assay using lung slices. Individual lung slices were placed in each well of 24-well plates, secured with a ring of nylon mesh together with a metal washer. The plate was imaged with an inverted microscope (DMI6000B; Leica Microsystems, Buffalo Grove, IL, USA). Mid-sized airways with a baseline luminal area between 14,000µm^2 and 20,000µm^2 were selected for imaging. Lung slices were stimulated with increasing concentrations of Mch to induce contraction. Each airway was imaged every minute for a total duration of 35 min. The airway luminal area was measured using NIH Image J and normalized to the baseline value.

Supplementary Figures



Supplementary Figure 1. NT4 and TrkB signaling were required for early life allergen-induced mucus overproduction in mice. (*A*) Scheme of cockroach allergen (CRA) exposure in early life. Controls received saline. (*B*) Representative images of PAS staining of lung sections of wild type (WT) and *NT4*$^{-/-}$ mice at P21 following CRA exposure. (*C*) Scheme of house dust mite allergen (HDMA) exposure in early life. Controls received saline. (*D*) Representative images of PAS staining of lung sections of WT and *NT4*$^{-/-}$ mice following HDMA exposure. (*E*) *Muc5ac* gene expression in WT and *NT4*$^{-/-}$ mice following exposure to saline or HDMA were analyzed by qPCR. Data were normalized to *18S* rRNA. *P<0.05. (*F*) Scheme of 1NMPP1 treatment of *TrkB*$^{F616A/F616A}$ mice between P10-P20 during OVA exposure. Controls were injected with the solvent for 1NMPP1. (G) Representative images of PAS staining of lung sections of *TrkB*$^{F616A/F616A}$ mice with and without 1NMPP1 treatment. Arrows point to mucus^{+} cells in airways. Scale bars, 100µm. N=5 for each group.