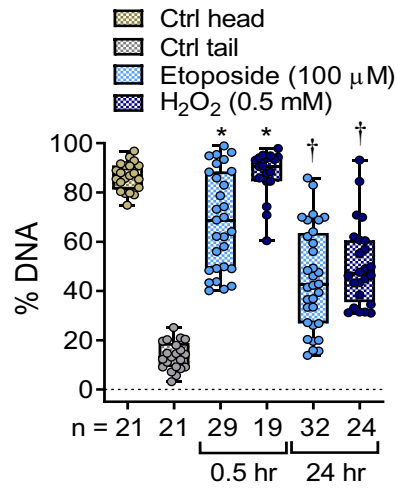
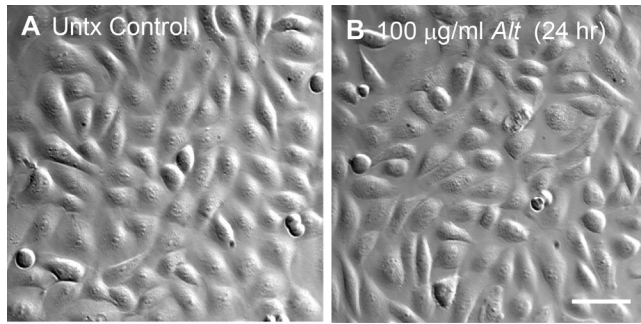


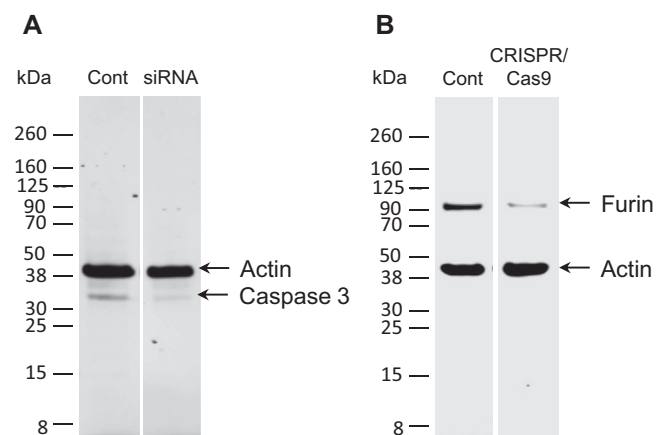
**FIG E1.** Heat treatment of *Alternaria* extract inhibits DNA release. **(A)** eDNA (*white arrows*) detected by DAPI staining of hBE cell monolayers exposed to *Alternaria* (100  $\mu\text{g}/\text{mL}$ ) for 30 minutes (400 $\times$ ; scale bar 10  $\mu\text{m}$ ). **(B and C)** DNA release indicated by YoYo-1 fluorescence does not occur when hBE cells are stimulated with heat-treated (100°C for 10 minutes) *Alternaria* extract (200 $\times$ ; scale bar 10  $\mu\text{m}$ ).



**FIG E2.** Apoptosis induction and H<sub>2</sub>O<sub>2</sub> exposure elicits sustained DNA fragmentation. The apoptosis inducer etoposide (100 μmol) and H<sub>2</sub>O<sub>2</sub> (0.5 mmol) produced DNA fragmentation after 0.5 hours, and partial repair was observed after 24 hours (\**P* < .0001 compared to control [tail]; †*P* < .0004 compared to etoposide or H<sub>2</sub>O<sub>2</sub> at 0.5 hours, respectively; Brown-Forsythe and Welch ANOVA followed by Dunnett T3 posttest).



**FIG E3.** hBE cells remain viable after 24 hours of exposure to *Alternaria*. **(A)** Phase contrast image (original magnification 200 $\times$ ) of untreated control hBE cells before *Alternaria* (100  $\mu$ g/mL) exposure. **(B)** Appearance of cells after continuous *Alternaria* treatment for 24 hours (scale bar = 10  $\mu$ m).



**FIG E4.** RNA interference and CRISPR/Cas9 knockdown of caspase-3 and furin. **(A)** Representative Western blot showing ~85% knockdown of caspase-3 protein expression in cells treated with siRNAs targeting caspase-3 (n = 3). **(B)** Representative Western blot showing that CRISPR/Cas9 gene editing of furin in hBE cells produced 93% knockdown of furin protein expression (n = 3).

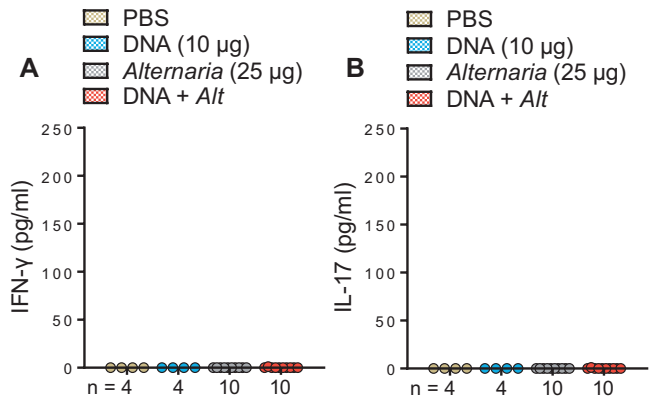
## Human Pro-Caspase 3 (P42574-1)

MENTENSVDS KSIKNLEPKI IHGSESMSG ISLDNSYKMD YPEMGLCIII  
NNKNFHKSTG MTSRSGTDVD AANLRETFRN LKYEVRNKND LTREEIVELM  
RDVSKEDHSK RSSFVCVLLS HGEEGIIFGT NGPVDLKKIT NFFRGDRCS  
LTGKPKLFII QACRGTELDG GIETDSGVDD DMACHKIPVE ADFLYAYSTA  
PGYYSWRNSK DGSWFIQSLC AMLKQYADKL EFMHILT RVNRK VATEFESF  
SFDATFHAKK QIPCIVSMLT KELYFYH



Furin  
cleavage site

**FIG E5.** Sequence of human pro-caspase-3. Amino acid sequence of human pro-caspase-3 showing the location of a furin cleavage site (*red*) in the C-terminal region of the enzyme.



**FIG E6.** *Alternaria* does not induce IFN- $\gamma$  or IL-17 secretion. (**A** and **B**) Sub-maximal, intranasal (i.n.) *Alternaria* (25  $\mu$ g) exposure does not stimulate IFN- $\gamma$  or IL-17 release into BAL fluid, and coadministration of mouse genomic DNA (10  $\mu$ g) does not alter or amplify the response.