Supplemental Figure 1. CS induces cell injury in an in vitro model of COPD. (A) HK-2 cell viability upon exposure for 24h to increasing concentrations of cigarette smoke extract (CSE), measured by alamar Blue assay. Data are mean ± SEM. ***P<0.001 by one-way ANOVA with Bonferroni post-hoc test, dot plots represent quantitation of 3 independent experiments.
Supplemental Figure 2. Cigarette smoke induces oxidative stress and mitochondrial injury in a murine model of COPD. (A) Electron transport chain (ETC) complexes expression in kidney tissue of mice exposed to 6 months of cigarette smoke (CS) vs. room air (RA) control (n = 5 in each group). (B) Expression of proteins that regulate mitochondrial dynamics in the kidney tissue from mice exposed to 6 months CS or RA, Mitofusin1 (MFN1), Mitofusin2 (MFN2) and Dynamin-like 120-kDa protein (OPA1) (n = 6 in each group). All data are mean ±SEM.*P<0.05, ***P<0.001, NS (non-significant) by Student’s t test.
Supplemental Figure 3: Autophagy is selectively induced in mouse kidneys after cigarette smoke exposure. (A) Representative blots from additional autophagy cascade proteins such as autophagy-related protein 7 (ATG7) and 5 (ATG5) and p62/SQSTM1 expression in kidney tissue from mice exposed to CS or RA for 6 months (n = 3 in each group). (B) Anti- and pro-apoptotic proteins Bcl-2 and Bax expression in CS-exposed vs. control RA-exposed mice (n = 3 in each group). (C) Cleaved caspase-3 levels measured by ELISA in whole kidney tissue homogenates (n = 8 in each group). Data are mean ±SEM, analyzed by 2-tailed Student’s t-test. (D) Representative western blot of necroptosis proteins: receptor-interacting serine/threonine-protein kinase-1 (RIPK1), receptor-interacting serine/threonine-protein kinase-3 (RIPK3) and mixed lineage kinase domain-like (MLKL) expression in kidney tissue after 6 months of CS or RA exposure (n = 4 in each group).
Supplemental Figure 4. The Beclin-1 response in kidney is specific for CS-mediated renal damage. (A) Beclin-1 expression upon blockage of autophagic flux in vitro with chloroquine. (B) Quantification of Beclin-1 expression in the liver (n = 8 in each group) and heart tissues (n = 8 for RA, n = 7 for CS) of mice exposed to CS for 6 months, data are mean ± SEM. NS (non-significant) by 2-tailed Student’s t test. (C) Beclin-1 expression in kidney tissue after in vivo elastase exposure (n = 2 for control, n = 3 for elastase).
Supplemental Figure 5: *Becn1*−/− mice have decreased mitophagy at baseline which does not increase after CS exposure. (A) Diagram representing calcium-binding and coiled-coil domain-containing protein2 (NDP52) mediated mitophagy. Injured mitochondria are ubiquitinated and recognized by autophagosomes via LC3B binding units present in mitophagy receptors such as NDP52. (B) Quantification of Western blots from Parkin and Optineurin (OPTN), proteins involved in the mitophagy cascade (n = 6 in each group). All data are mean ± SEM, NS (non-significant) analyzed by Student’s t test.
Full unedited gel for Figure 1

Fibronectin

Actin
Full unedited gels for Figure 2
Full unedited gels for Figure 4

fig 4b (left)

LC3B

fig 4b (right)

59kDa

Beclin-1

14kDa

LC3b

42kDa

β-Actin

figure 4C

59kDa

Beclin-1

14kDa

LC3b

42kDa

β-Actin
Full unedited gel for Figure 5
Full unedited gel for Figure 7
Western blots for supplemental Figure 3

**PANEL S3A**

- 80kDa
- 50kDa
- 42kDa

ATG7

ATG5

Actin

**PANEL S3B**

- 50kDa
- 42kDa
- 25kDa
- 42kDa

Bcl2

Actin

Bax

Actin

**PANEL S3D**

- 50kDa
- 42kDa

RIP3

RIP1

Actin

MLKL

Actin
Western blots for Supplement Figure 4.

Panel S4A

Panel S4C