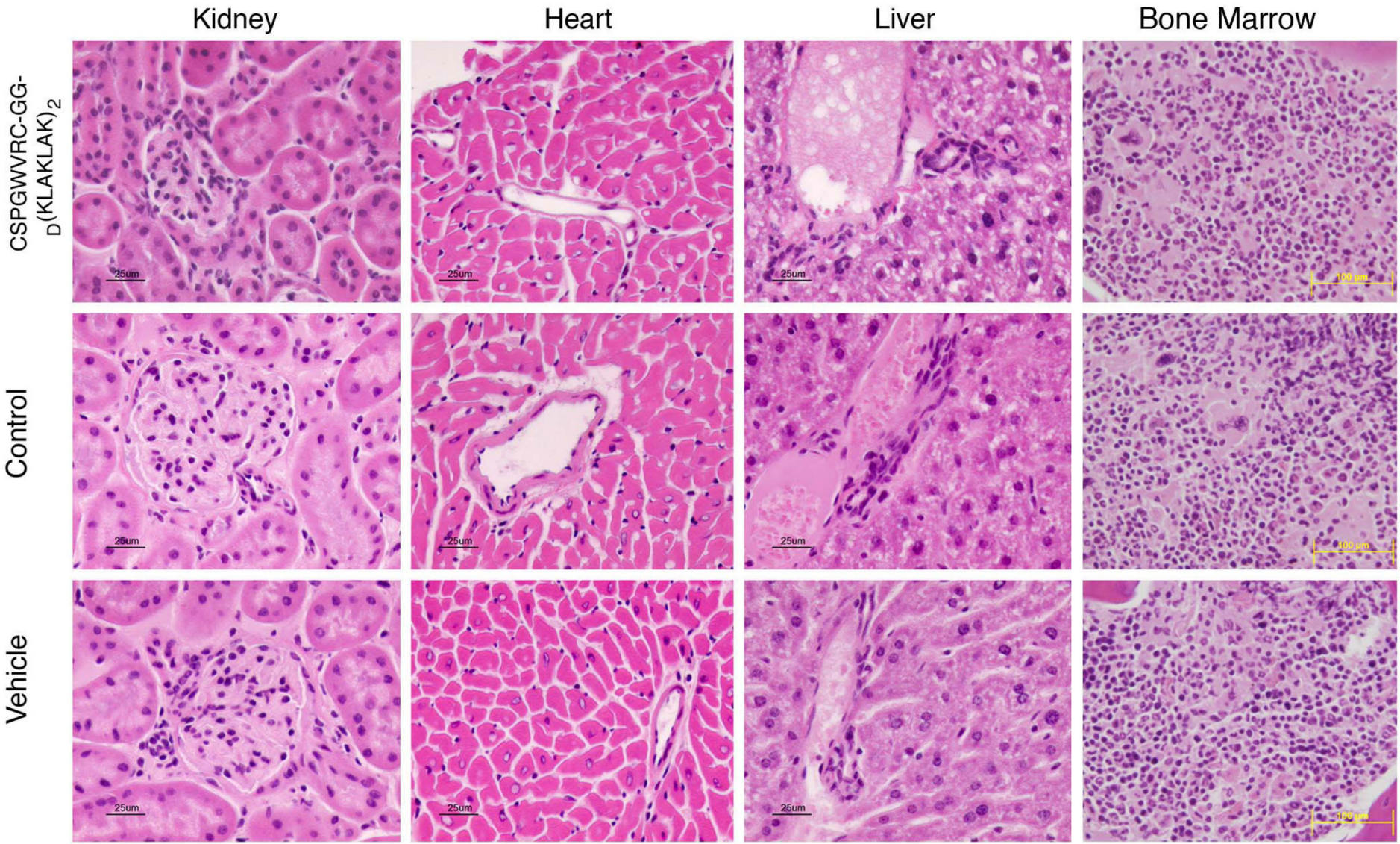
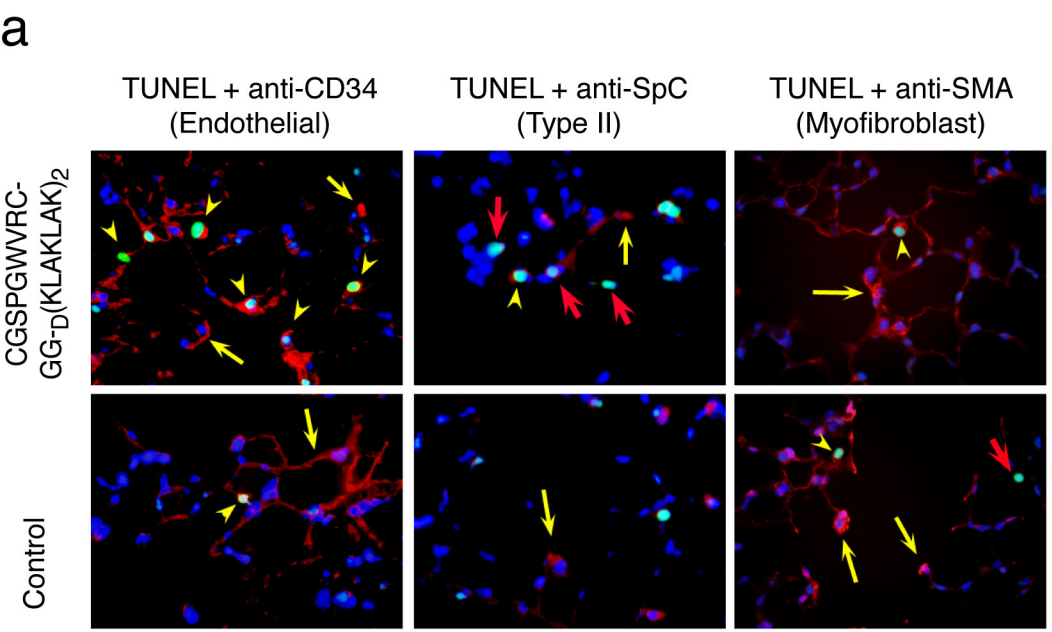
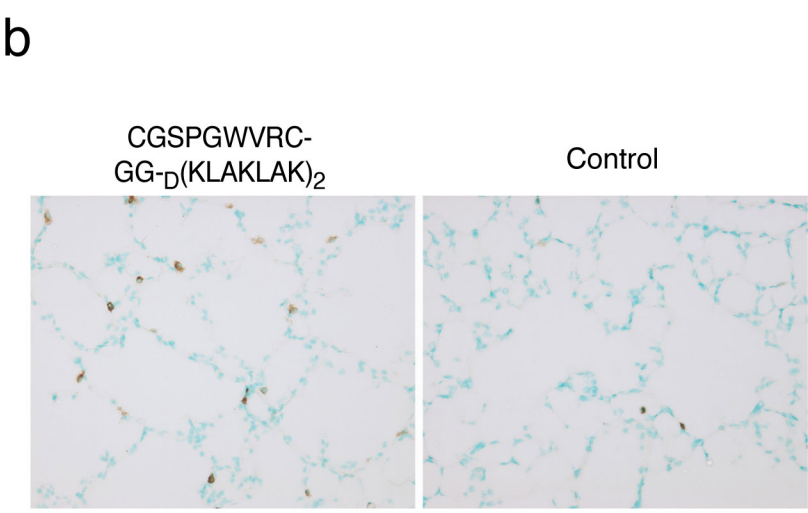
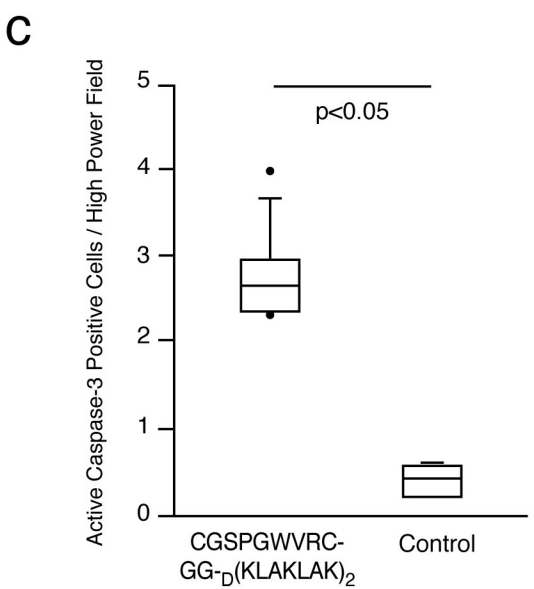


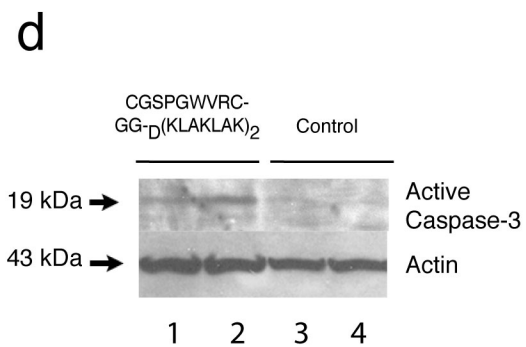
Giordano *et al.* - Fig.1S (Supplemental Data)

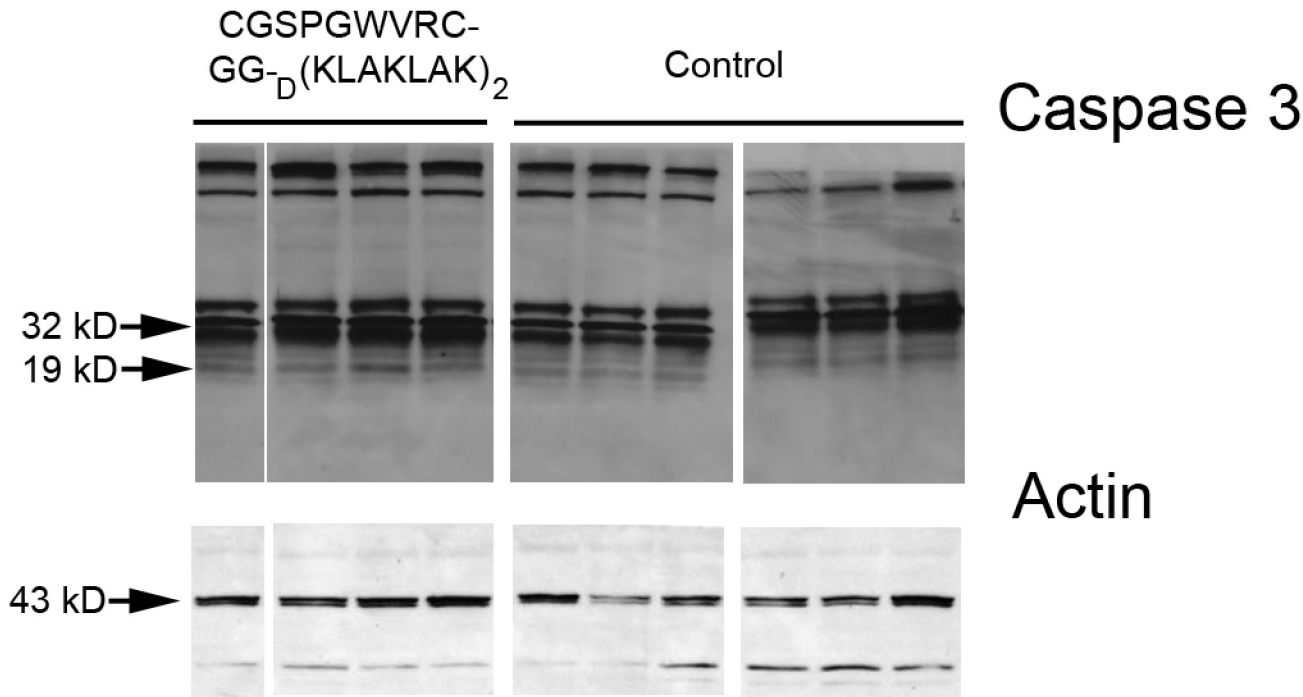




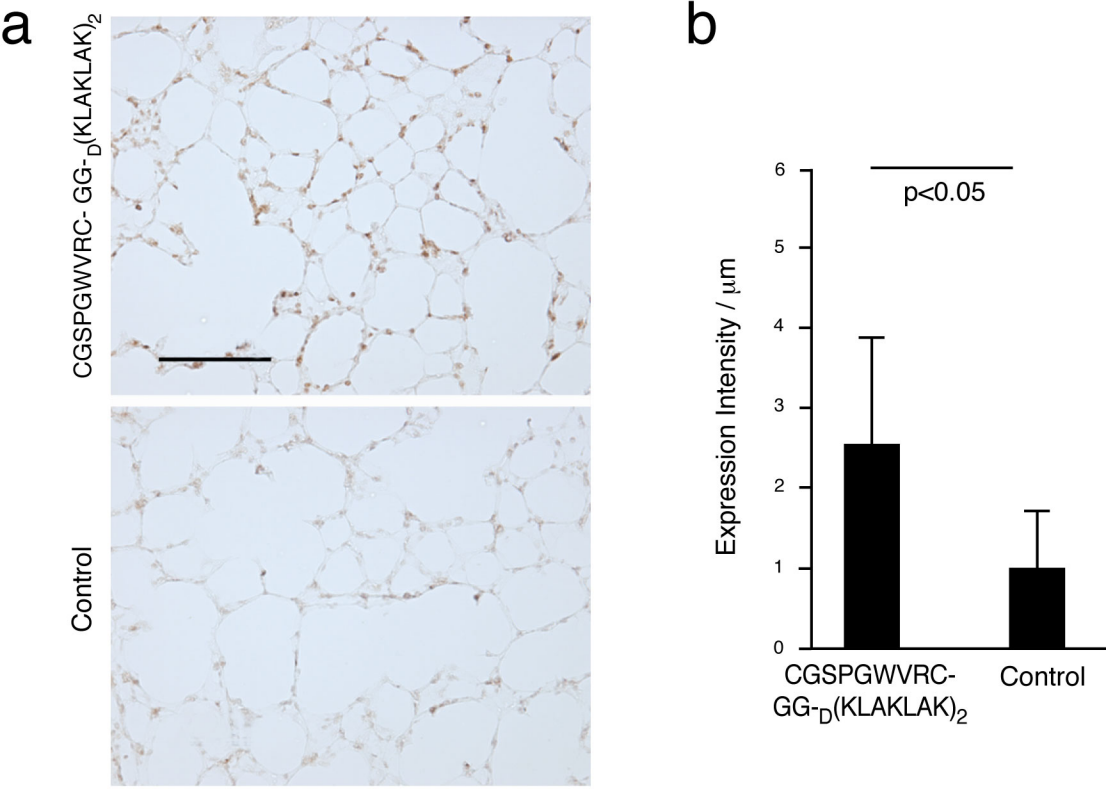


Giordano *et al.* - Fig.2S
(Supplemental Data)





Giordano *et al.* - Fig.3S
(Supplemental Data)



Giordano *et al.* - Fig.4S
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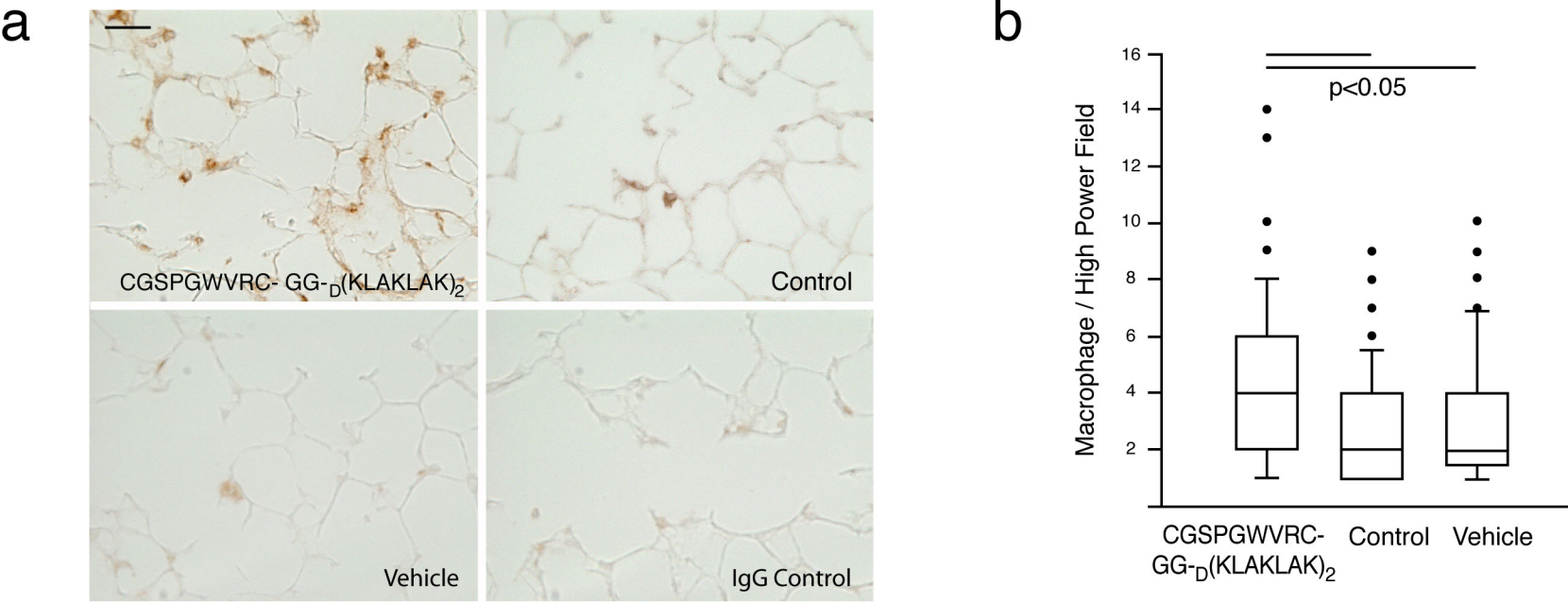

Giordano *et al.* - Fig.5S
(Supplemental Data)

Supplementary Fig. S1. Control tissue sections from mice treated for 21 days with CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide, control peptides [CGSPGWVRC and $_D$(KLAKLAK)$_2$] and vehicle were stained with H&E. No apparent changes in the lung histology were detected in CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$-treated animals. Scale bar, 25 μm (except in the rightmost column, 100 μm).

Supplementary Fig. S2. CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ causes lung cell apoptosis after 4 days of treatment. **a**, Identification of apoptotic (TUNEL; green) endothelial cells (CD34-specific antibody; red), type II epithelial cells (SpC-specific antibody; red) and myofibroblast cells (SMA-specific antibody) in the lungs of CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$, or control peptide [CGSPGWVRC or (KLAKLAK)$_2$]-treated mice after 4 days of treatment. Cell nuclei were stained with DAPI (blue). Shown are merged images, with co-localization of cell-specific markers and apoptosis (yellow arrowheads); examples of non-apoptotic cells with positive cell specific marker are indicated by yellow arrows while red arrows point to apoptotic cells lacking staining for a cell-specific marker. **b**, Active caspase-3 expression in lung sections of mice 4 days after treatment with CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ or control peptides [CGSPGWVRC or $_D$(KLAKLAK)$_2$]. CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide-treated lungs show abundant active caspase-3-positive cells in the alveolar septa in contrast to control-treated lungs. **c**, Quantification of number of alveolar septal cells positive for active caspase-3. **d**, Increased expression of active caspase-3 was detected in CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$-treated mice lungs in comparison with the control treated mice lungs as detected by Western blot analysis of lung tissue lysates with anti-active caspase-3 antibody. Densitometric quantification of active caspase-3 expression levels obtained in Western blot analysis normalized to actin were: lane-1, 0.58; lane-2, 0.42; lane-3, 0.18; lane-4, 0.15 densitometric units.

Supplementary Fig. S3. Western blot analysis of lung tissue lysates with anti-active caspase-3 and anti-actin antibodies after 21 days of treatment (image shows the whole gel scan of region highlighted in Fig. 5c). Arrows indicate actin (43 kDa), full length procaspase-3 (32 kDa) and active caspase-3 (19 kDa) bands.

Supplementary Fig. S4. CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide induces oxidative damage to mouse lungs as indicated by increasing 8-oxo-HG-dG levels. **a**, Immunohistochemical staining of 8-oxo-dG in lung sections from mice treated for 4 days with CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide or control peptides [CGSPGWVRC or $_D$(KLAKLAK)$_2$]. Lung sections from the CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide-treated mice show increased 8-oxo-HG-dG expression when compared to the lung sections from the control treated mice. Scale bar, 100 μm. **b**, Quantification of the 8-oxo-dG intensity in the lung tissues from CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide-treated mice show increased 8-oxo-dG expression when compared to the lung tissues of the control peptide-treated mice.

Supplementary Fig. S5. CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide treatment induces an influx of macrophages into mouse lungs **a**, Lung sections from mice treated for 21 days with vehicle, CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$ peptide or with control peptides [CGSPGWVRC and $_D$(KLAKLAK)$_2$ peptides] were stained with the Mac-3 antibody to identify macrophages. Scale bar, 50 μm. **b**, An increased number of macrophages is seen in CGSPGWVRC-GG-$_D$(KLAKLAK)$_2$-treated animals in comparison to control animals.