

## Supplementary Figure Legends:

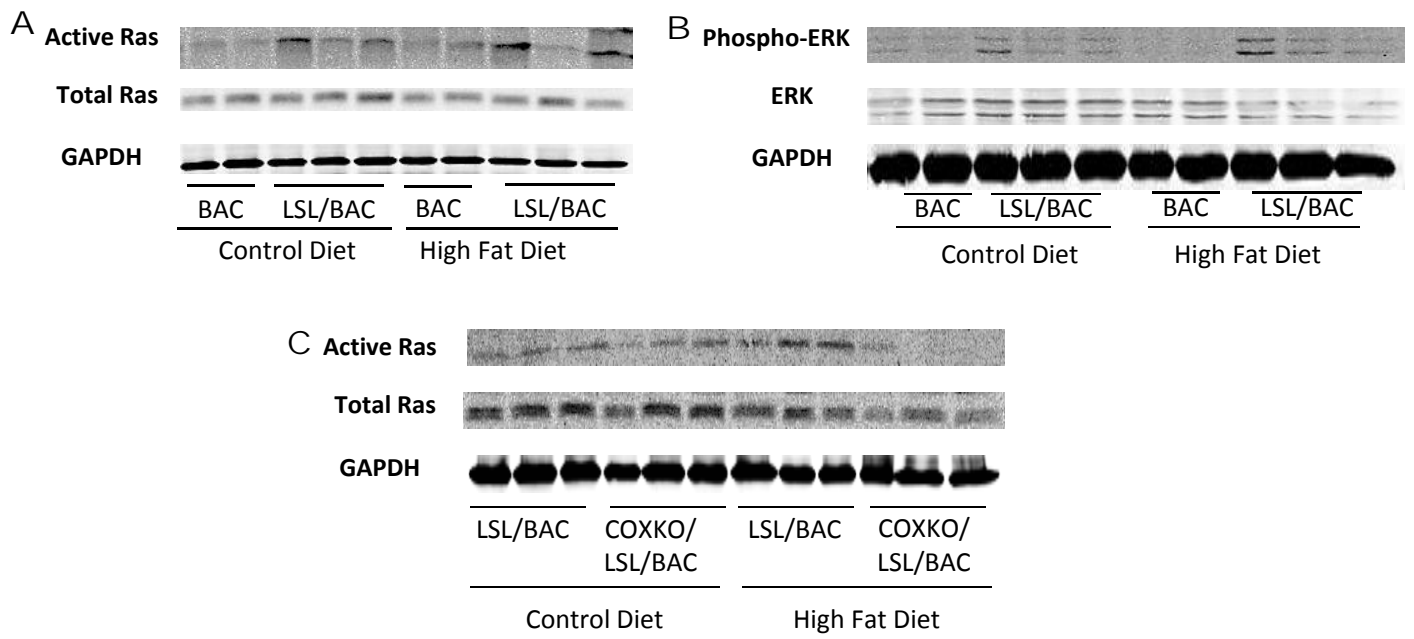
**Supplementary Figure 1: Increased Ras activity and Phospho-ERK in LSL/BAC animals blocked by Cox-2 elimination.** Representative western blot images of **(A)** GTP-bound Ras and **(B)** Phospho-ERK quantification shown in Figure 2 A and B. **(C)** Representative western blot images of GTP-bound Ras from quantification shown in Figure 3 of LSL/BAC, and COXKO/LSL/BAC animals on CD and HFD comparison.

**Supplementary Figure 2: Increased Cox-2 levels in mice expressing oncogenic K-Ras fed HFD.** **(A)** Immunofluorescence staining of Cox-2 was performed on BAC and LSL/BAC animals on CD and HFD. **(B)** Quantification of Cox-2 fluorescence intensity for groups was graphed. **(C)** Further, immunofluorescence of Cox-2 and F4/80+ macrophages co-localization is shown.

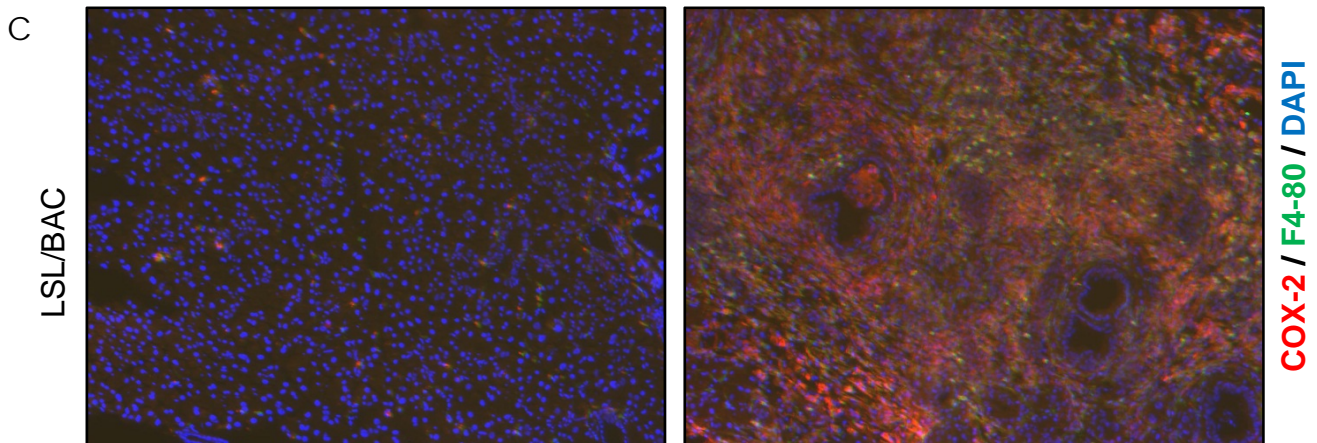
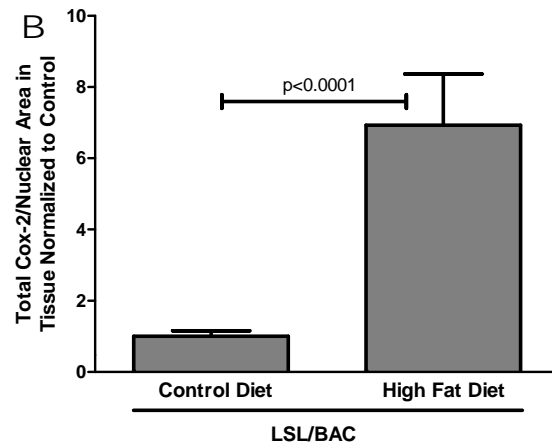
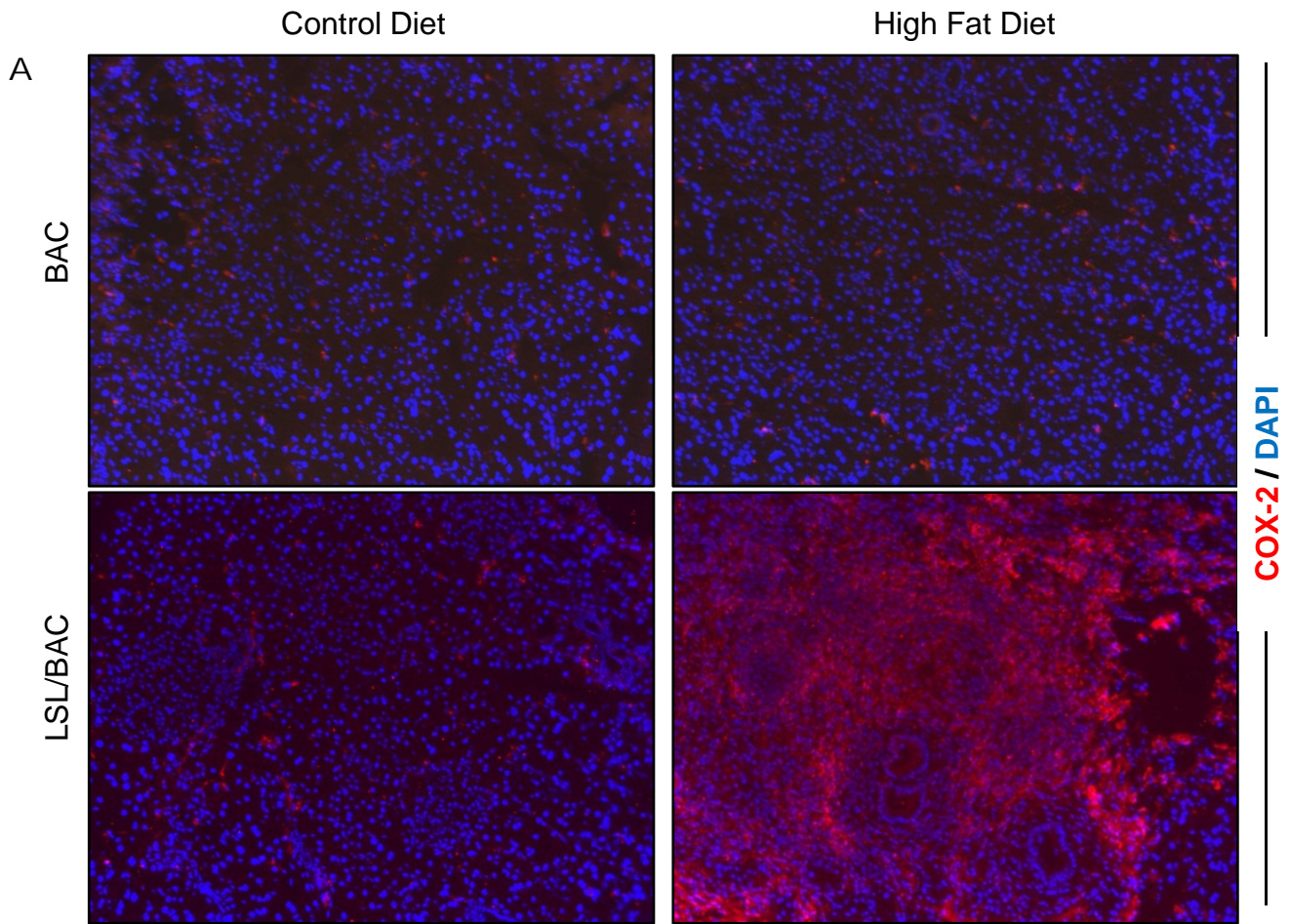
**Supplementary Figure 3: Important role of Cox-2 in Inflammation, fibrosis and PanIN development and accelerated cancer development in Pdx-Cre-K-Ras<sup>G12D</sup> fed HFD.** **(A)** Quantification data of fibrosis, inflammation and PanINs, for COXKO/BAC, and COXKO/LSL/BAC animals treated with CD and HFD compared to BAC and LSL/BAC animals data shown in Figure 1D. **(B)** Pdx-Cre-K-Ras<sup>G12D</sup> mice on CD (n=9) and HFD (n=6) were scored on the level of inflammation, fibrosis, and the number of each grade of PanINs present in the entire tissue.

**Supplementary Figure 4: Decreased level of  $\alpha$ SMA, phospho-ERK, Cox-2, and F4/80+ macrophage recruitment with Cox-2 deletion.** IHC staining of COXKO/BAC and COXKO/LSL/BAC animals fed the CD and the HFD for **(A)** alpha-SMA, **(B)** Phospho-ERK, **(C)** Cox-2, and **(D)** F4/80+ macrophages in each group.

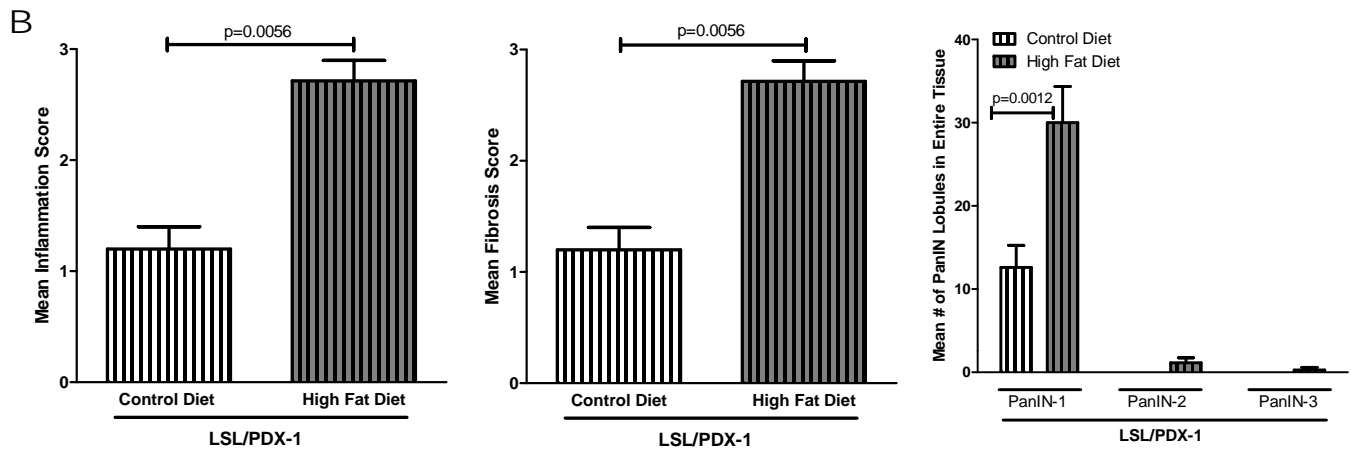
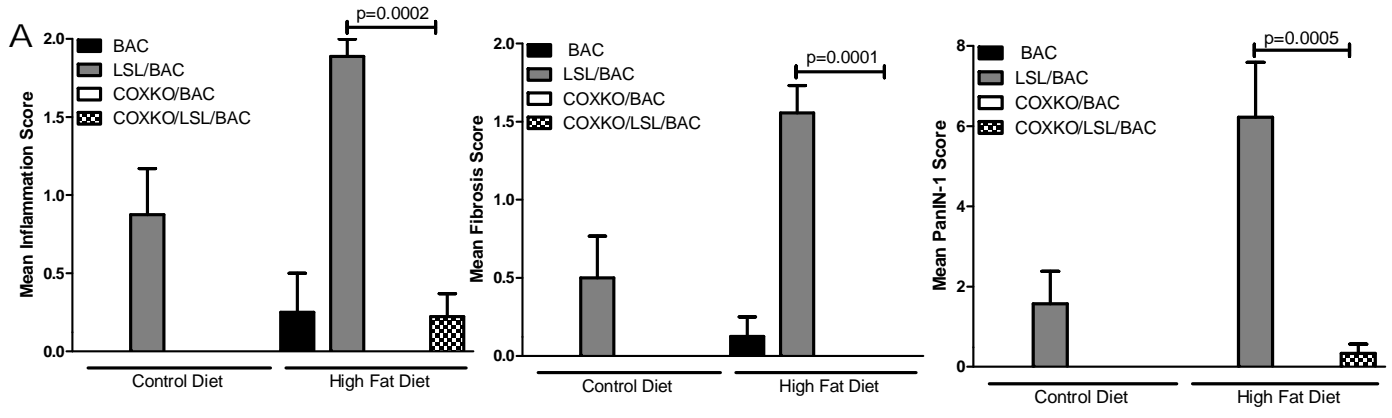
**Supplementary Figure 5: Histological scoring for inflammation, fibrosis, and area of PanIN lobules.** Representative images of **(A)** level 1 for inflammation and fibrosis, **(B)** intermediate level 2 for inflammation and fibrosis, and **(C)** level 3 for inflammation and fibrosis scoring described in methods is shown. **(D)** Representative PanIN lesions lobules scoring described in methods and collagen staining at lower magnification of LSL/BAC tissues in HDF analyzed is also presented.



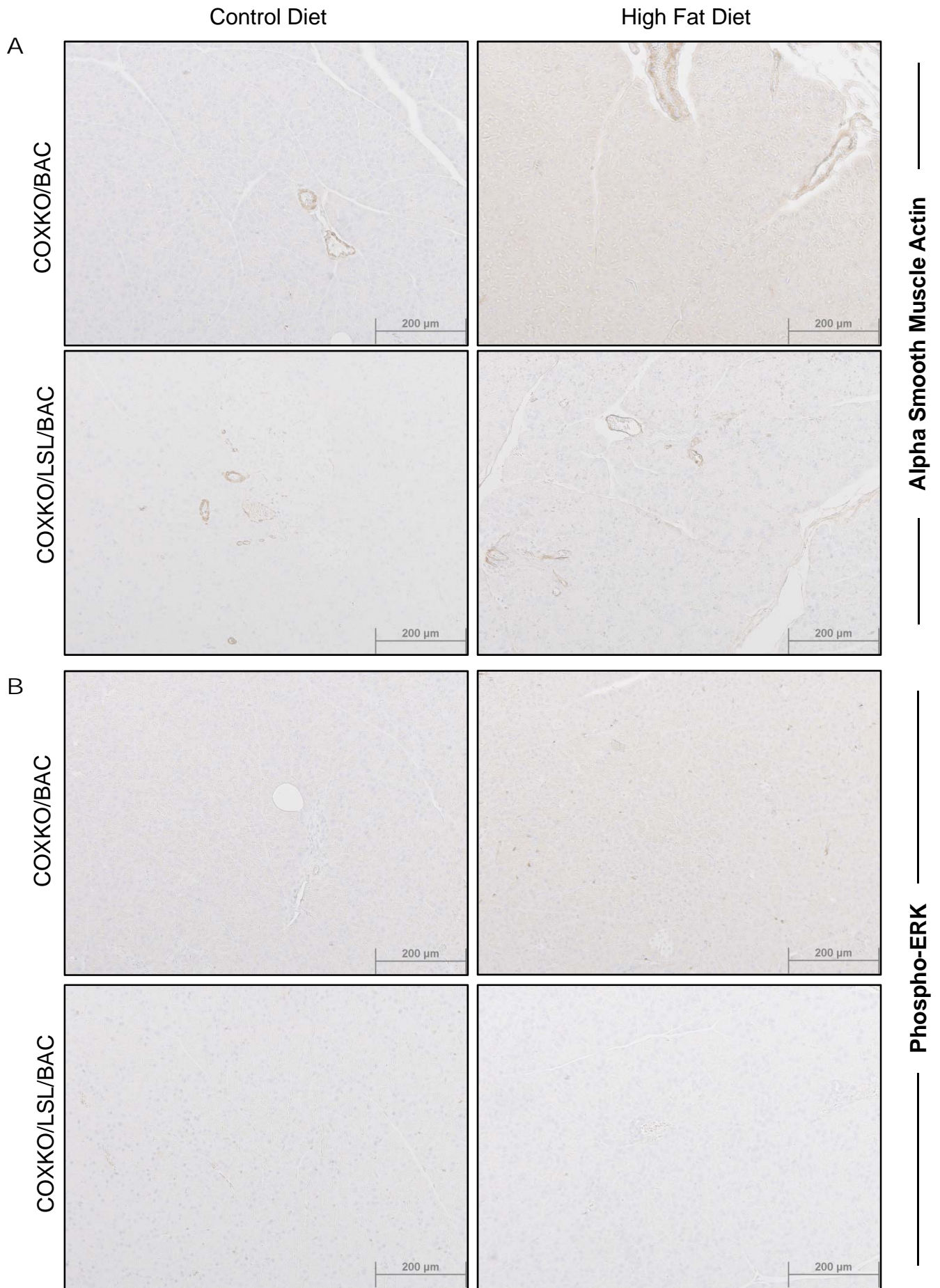
**Supplementary Figure 1**



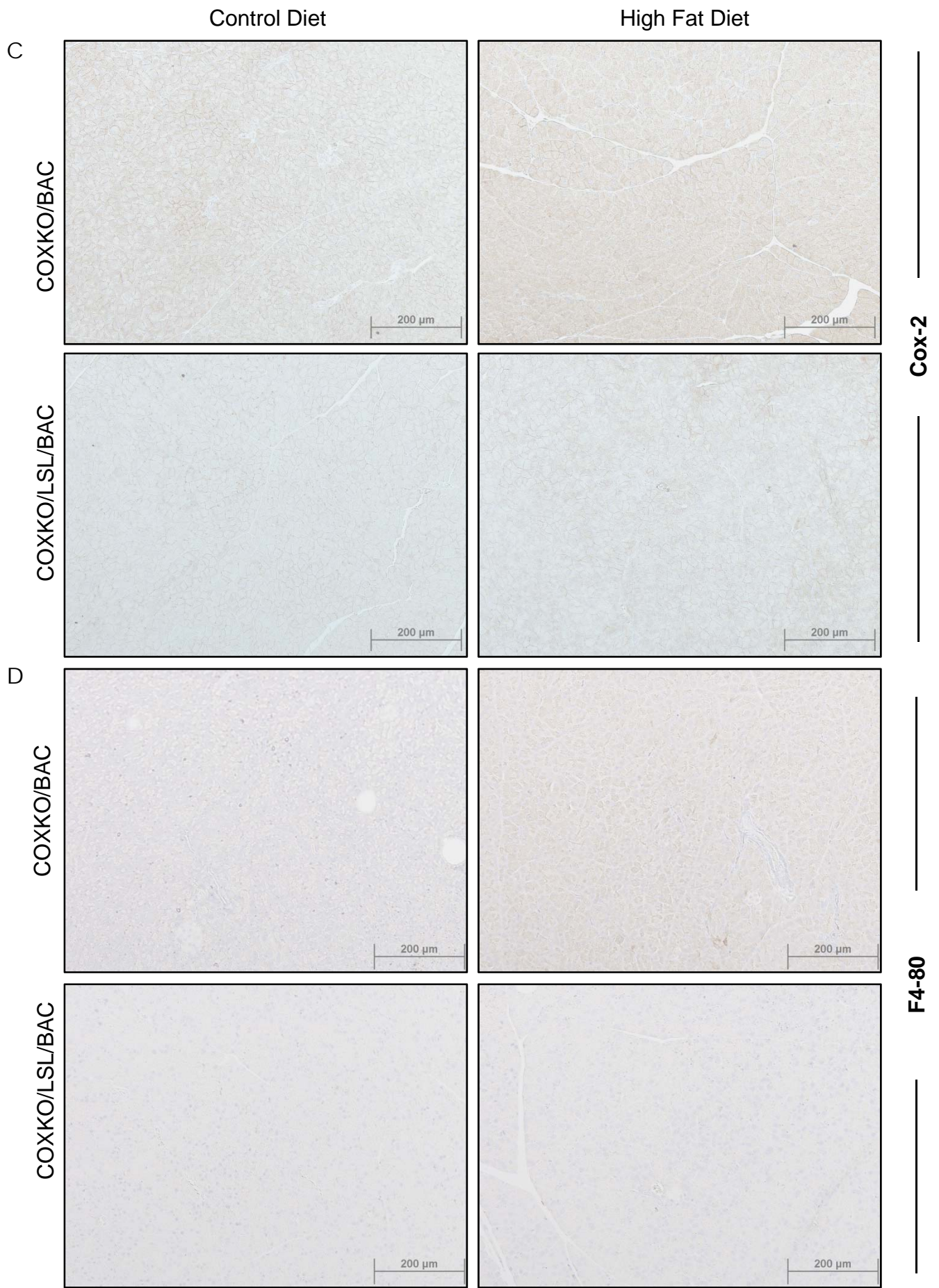
**Supplementary Figure 2**



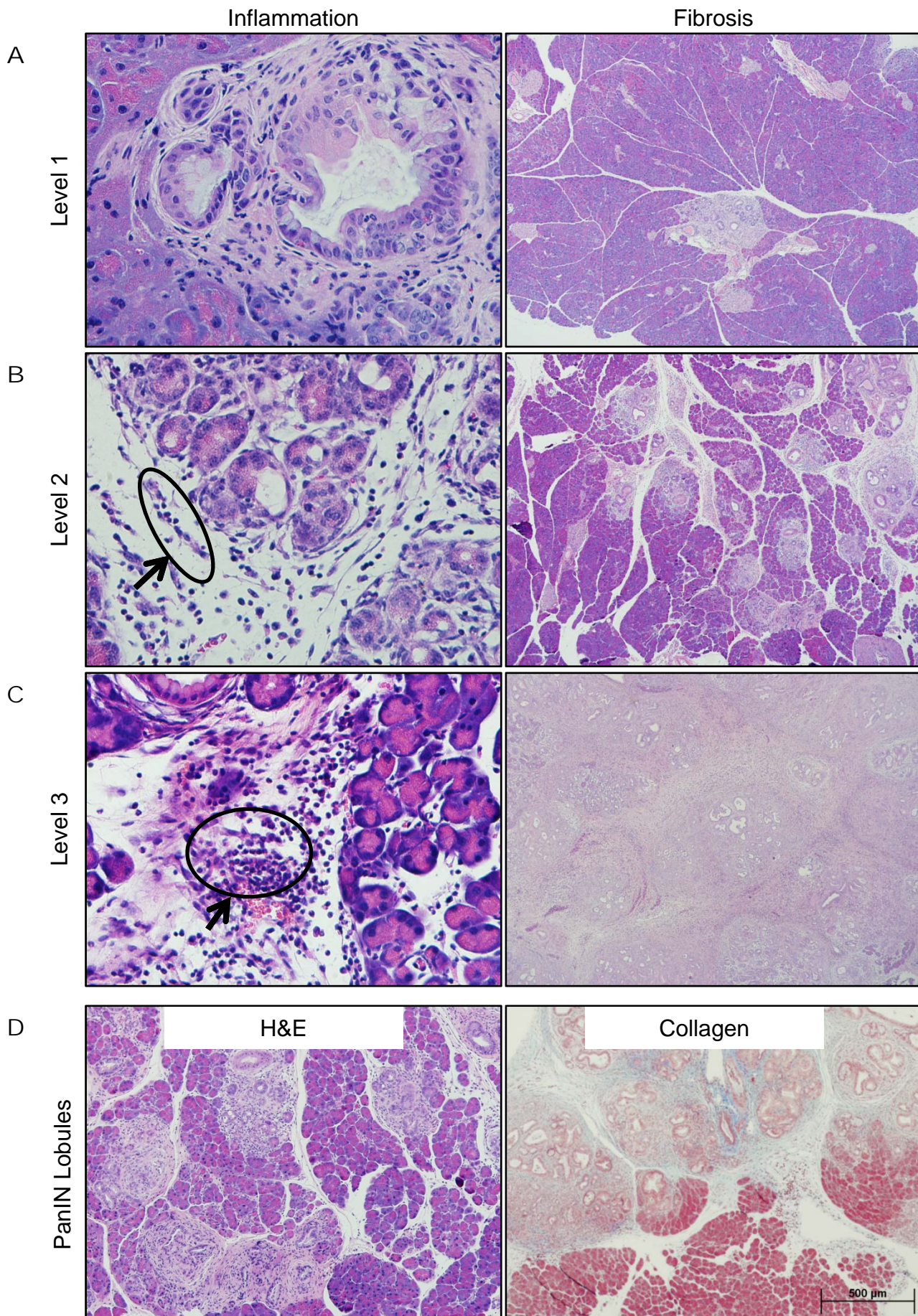
Supplementary Figure 3



**Supplementary Figure 4**



**Supplementary Figure 4**



**Supplementary Figure 5**