Figure S1. Full-length images of the immunoblots in Figure 1. Black dot line boxes indicate the cropped images used in Fig. 1. (A) Western blot analysis of p53 in HCT116$^{sh\ control}$ or HCT116$^{sh\ p53}$ cells. (B) Western blot analysis of APJ and α-SMA in CCD-18Co cells co-cultured with HCT116$^{sh\ control}$ or HCT116$^{sh\ p53}$ cells. (C) Western blot analysis of APJ and α-SMA in CCD-18Co cells co-cultured with HCT116 or Caco-2 cells. (D) Western blot analysis of APJ and α-SMA in CCD-18Co cells co-cultured with SW480 or DLD-1 cells. shRNA, short hairpin RNA; α-SMA, alpha-smooth muscle actin; APJ, apelin receptor.

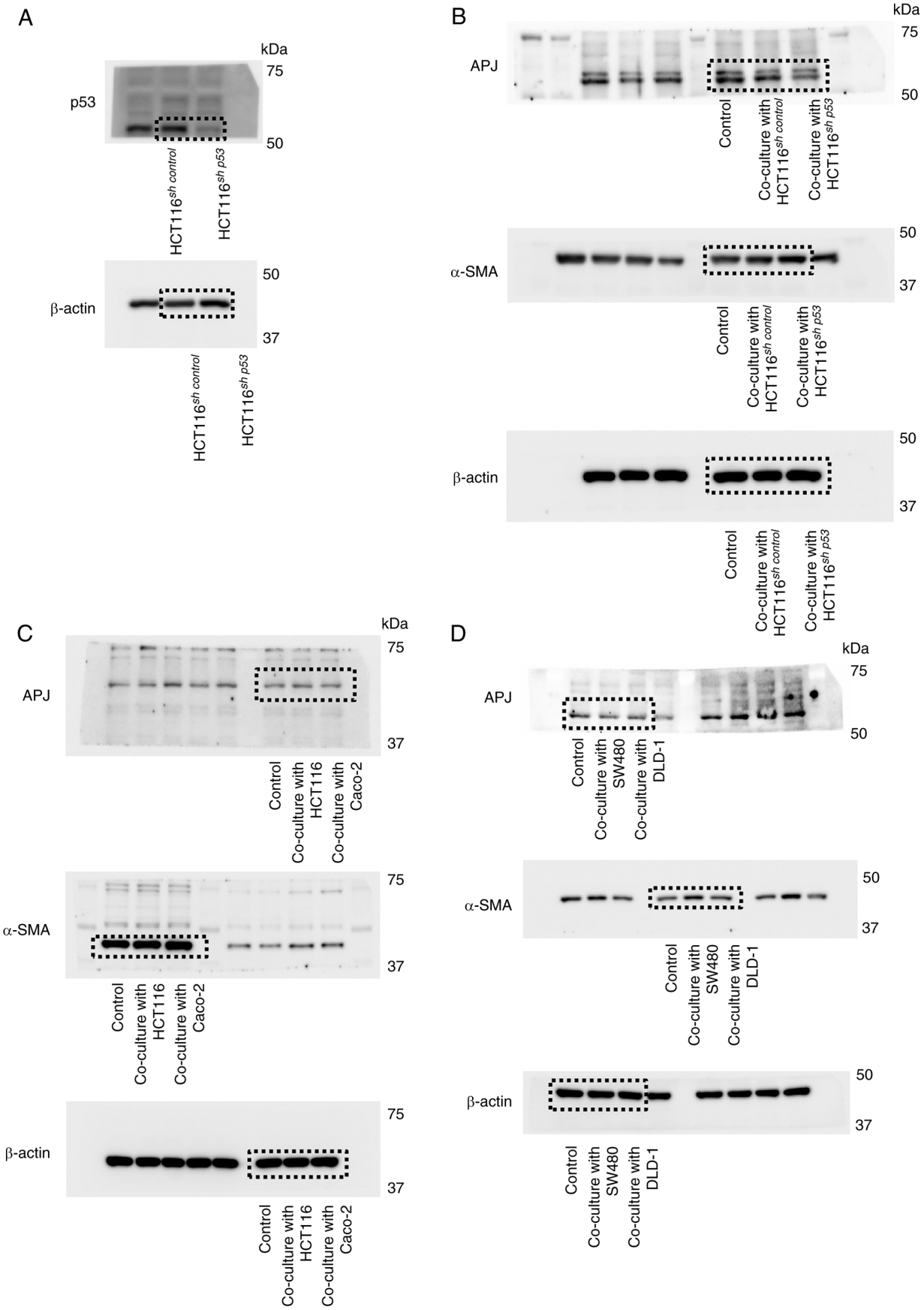

Figure S2. Full-length images of the immunoblots in Fig. 2. Black dot line boxes indicate the cropped images used in Fig. 2. Western blot analysis of α-SMA in CCD-18Co cells with ML221 (10 μM). α-SMA, alpha-smooth muscle actin.

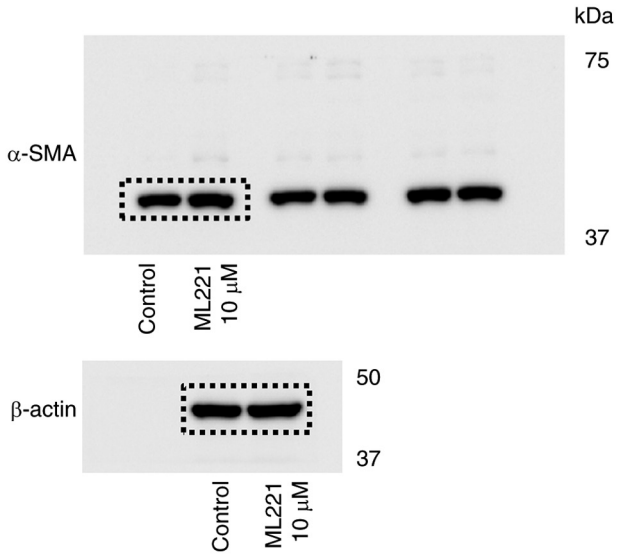

Figure S3. Full-length images of the immunoblots in Fig. 3. Black dot line boxes indicate the cropped images used in Fig. 3. Western blot analysis of APJ and α-SMA in CCD-18Co cells with APJ siRNA compared to si control. siRNA, short interfering RNA; α-SMA, alpha-smooth muscle actin; APJ, apelin receptor.

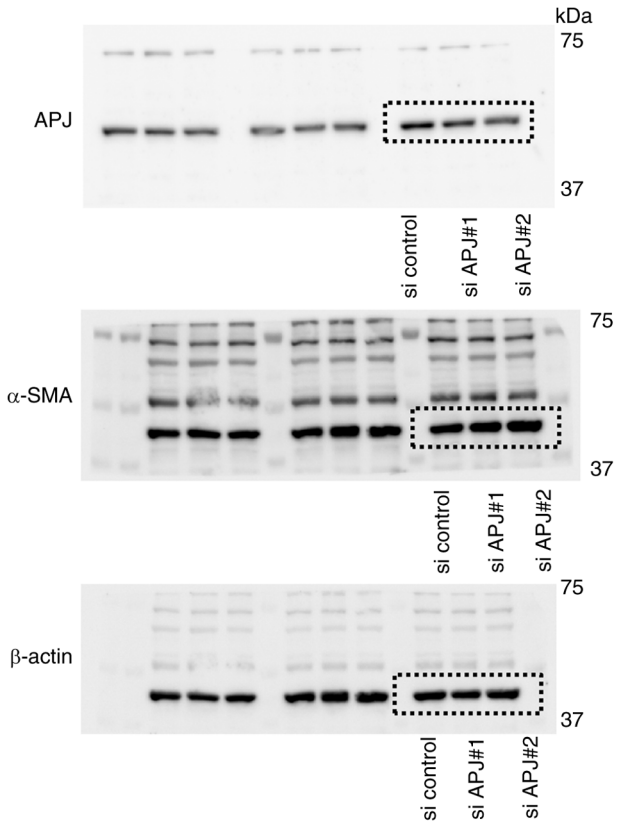

Figure S4. Full-length images of the immunoblots in Figure 4. Black dot line boxes indicate the cropped images used in Fig. 4. Western blot analysis of phosphorylated Smad2/3, Smad2/3 and α-SMA in CCD-18Co cells with or without apelin-13 in the 10-1,000 nM range and/or rhTGF-β1 (10 ng/ml). rhTGF-β1, recombinant human transforming growth factor beta 1; APLN, apelin-13; P-Smad2/3, phosphorylated Smad2/3; α-SMA, alpha-smooth muscle actin.

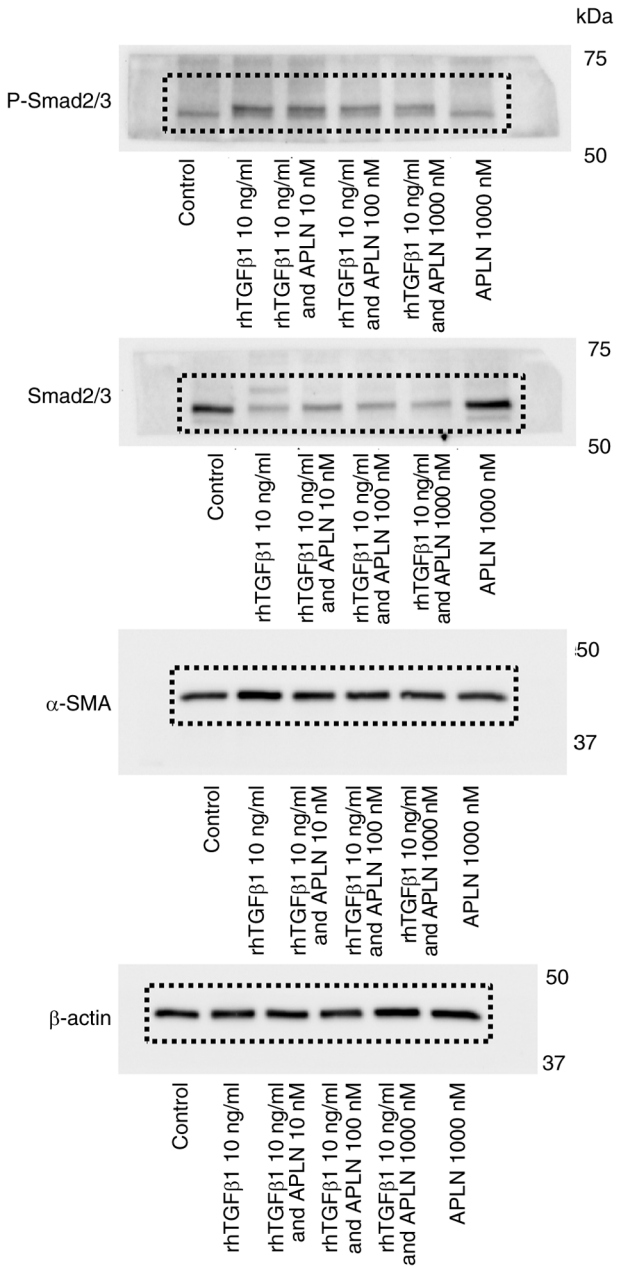

Figure S5. Full-length images of the immunoblots in Figure 4. Black dot line boxes indicate the cropped images used in Fig. 4. (A) Western blotting was performed for phosphorylated Smad2/3 and Smad2/3 in CCD-18Co cells with ML221 (10 μM). (B) Western blotting was performed for phosphorylated Smad2/3 and Smad2/3 in CCD-18Co cells with APJ siRNA. (C) Western blotting was performed for phosphorylated Smad2/3 and Smad2/3 in CCD-18Co cells co-cultured with HCT116$^{sh\ control}$ or HCT116$^{sh\ p53}$ cells. (D) Western blotting was performed for phosphorylated Smad2/3 and Smad2/3 in CCD-18Co cells co-cultured with SW480 cells. P-Smad2/3, phosphorylated Smad2/3; siRNA, short interfering RNA; shRNA, short hairpin RNA.

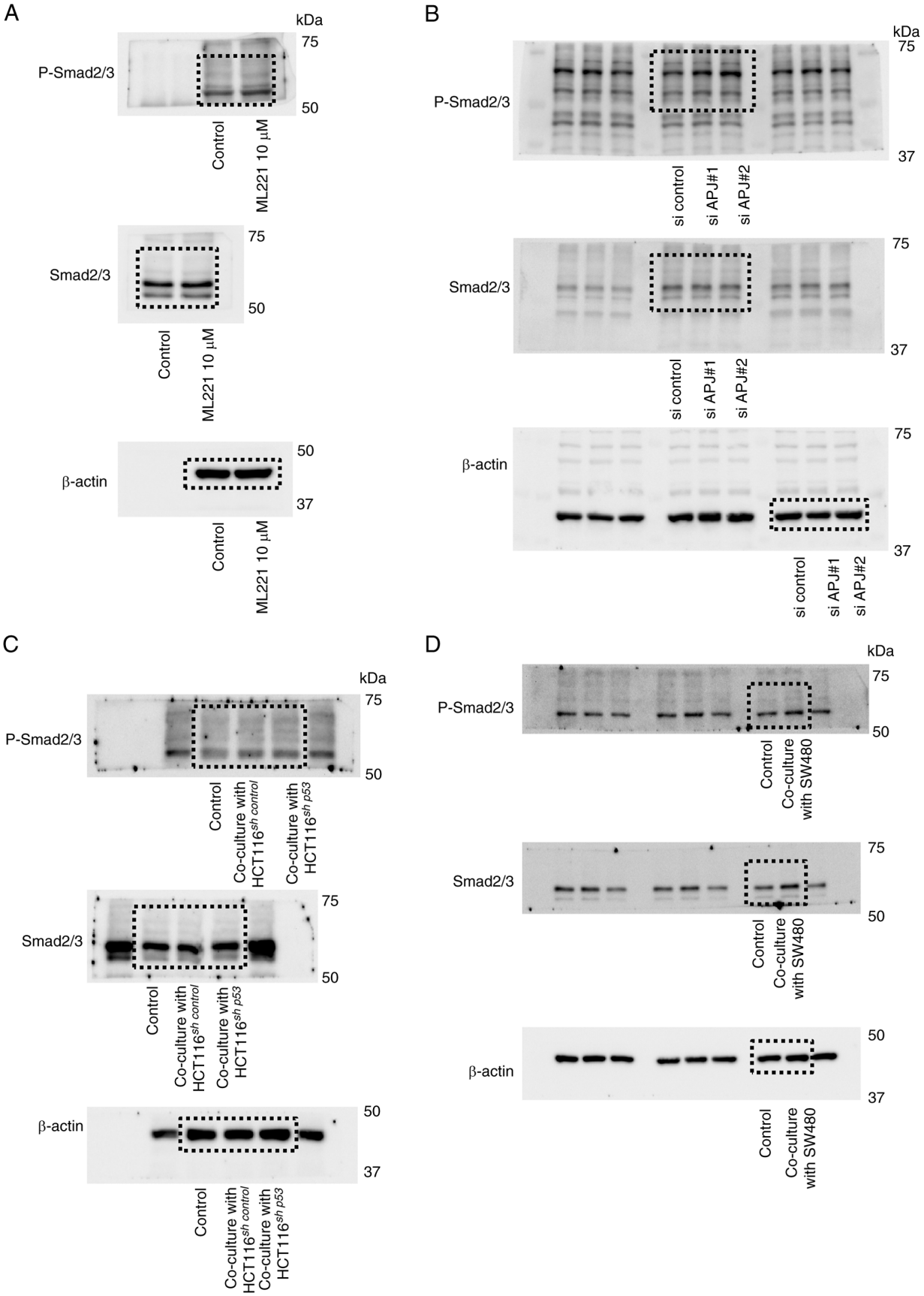

Figure S6. Full-length images of the immunoblots in Figure 5. Black dot line boxes indicate the cropped images used in Fig. 5. Western blot analysis was performed to assess exosomal specific markers ALIX, CD63 and CD9 and exosome-negative proteins calnexin and EEA-1 using cell lysates or isolated pellets from HCT116$^{sh\ control}$ or HCT116$^{sh\ p53}$ cells. ALIX, ALG-2 interacting protein X; EEA-1, early endosome antigen 1; CD63, cluster of differentiation 63; CD9, cluster of differentiation 9; shRNA, short hairpin RNA.

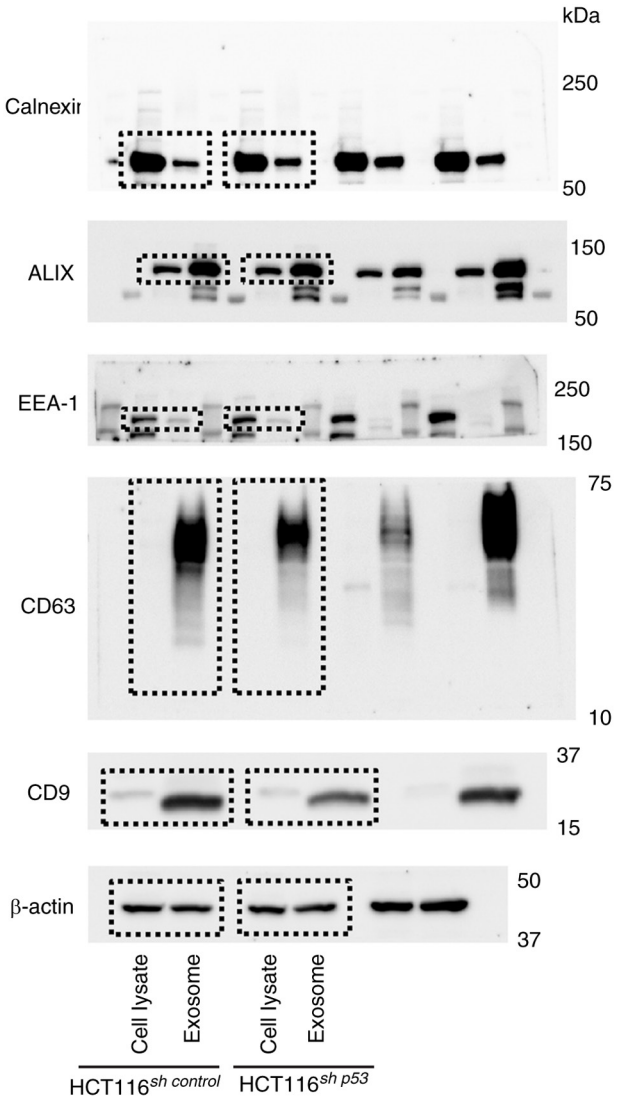

Figure S7. Full-length images of the immunoblots in Fig. 5. Black dot line boxes indicate the cropped images used in Fig. 5. (A) Western blotting analysis of APJ in CCD-18Co cells treated with HCT116$^{sh\ control}$ or HCT116$^{sh\ p53}$ cell-derived exosomes. (B) Western blotting analysis of APJ in CCD-18Co cells treated with SW480 cell-derived exosomes. (C) Western blotting analysis was performed for APJ in CCD-18Co cells co-cultured with SW480 cells with or without siRNA against RAB27A. shRNA, short hairpin RNA; APJ, apelin receptor; Exo, exosome; siRNA, short interfering RNA.

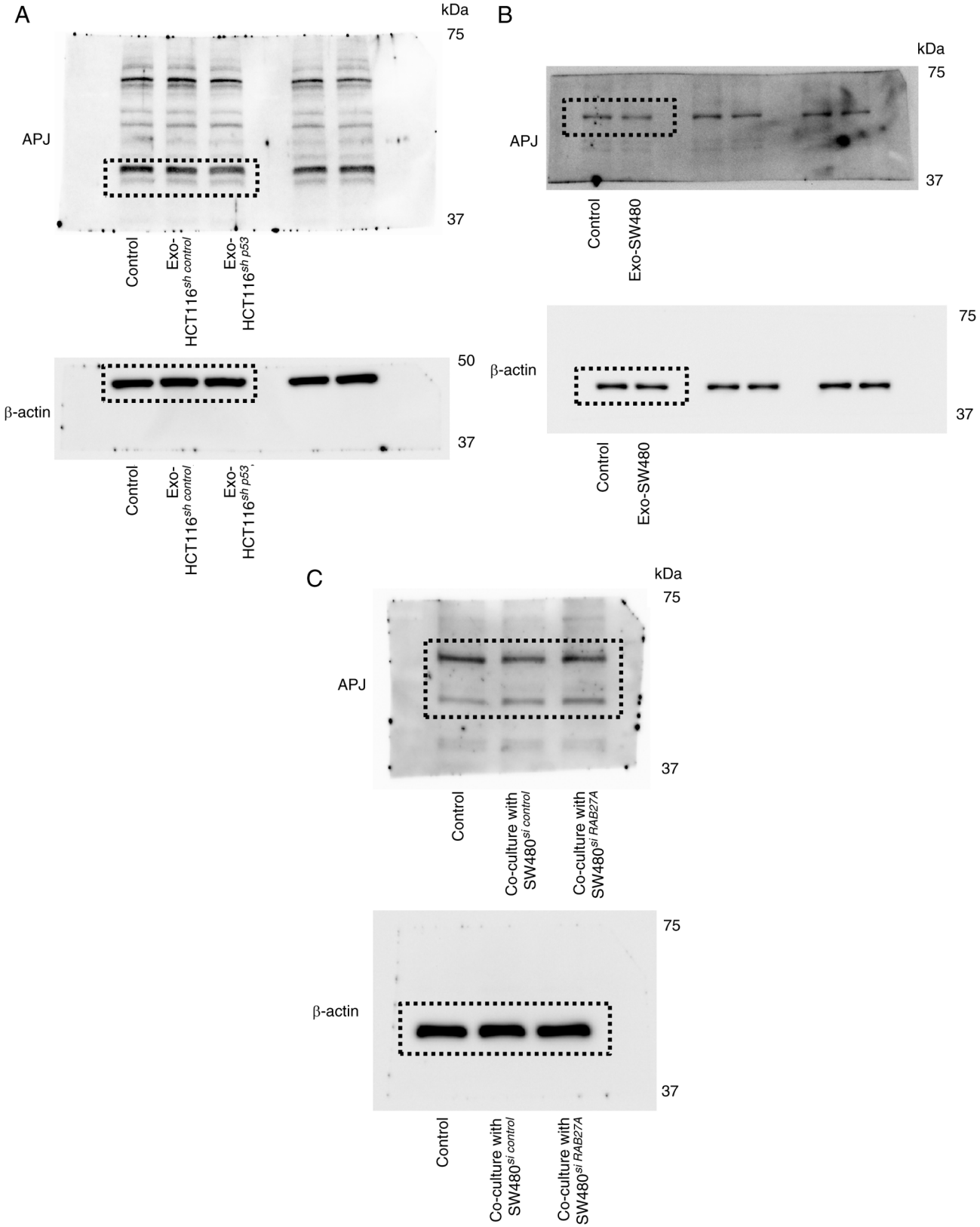

Figure S8. Full-length images of the immunoblots in Fig. 6. Black dot line boxes indicate the cropped images used in Fig. 6. (A) Western blotting analysis of APJ in CCD-18Co cells with miR-5703 mimic. (B) Western blot analysis of APJ in CCD-18Co cells treated with or without the miR-5703 inhibitor when co-cultured with SW480 cells. miR, microRNA; APJ, apelin receptor; N/C, negative control.

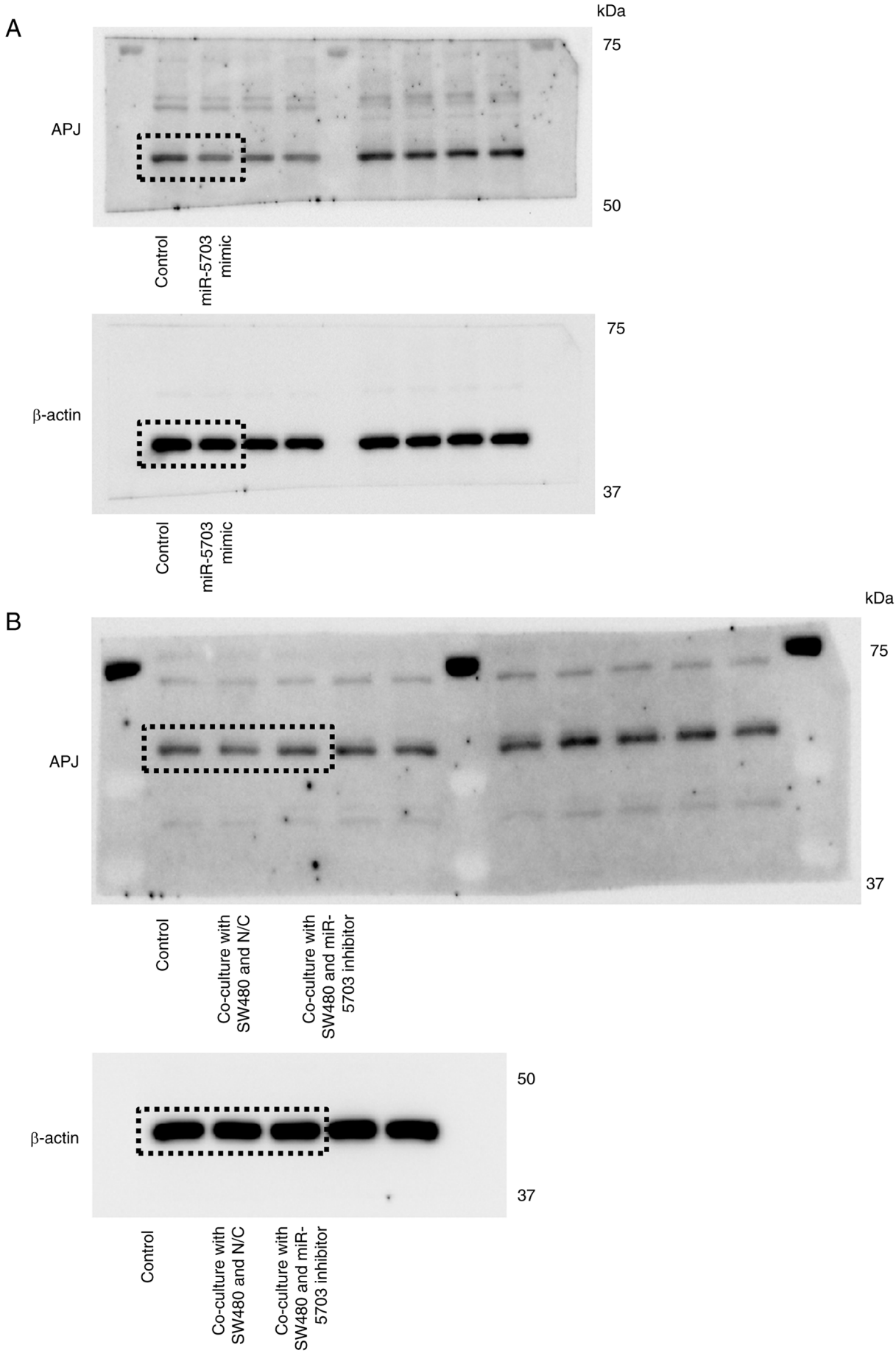

Figure S9. Interstitial fibroblast APJ score in the immunohistochemical staining. The interstitial fibroblast APJ score separately in the left colon (descending colon, sigmoid colon, rectum) and right colon (cecum, ascending colon, transverse colon). Data are presented as the mean ± SD. NS, not significant; APJ, apelin receptor.