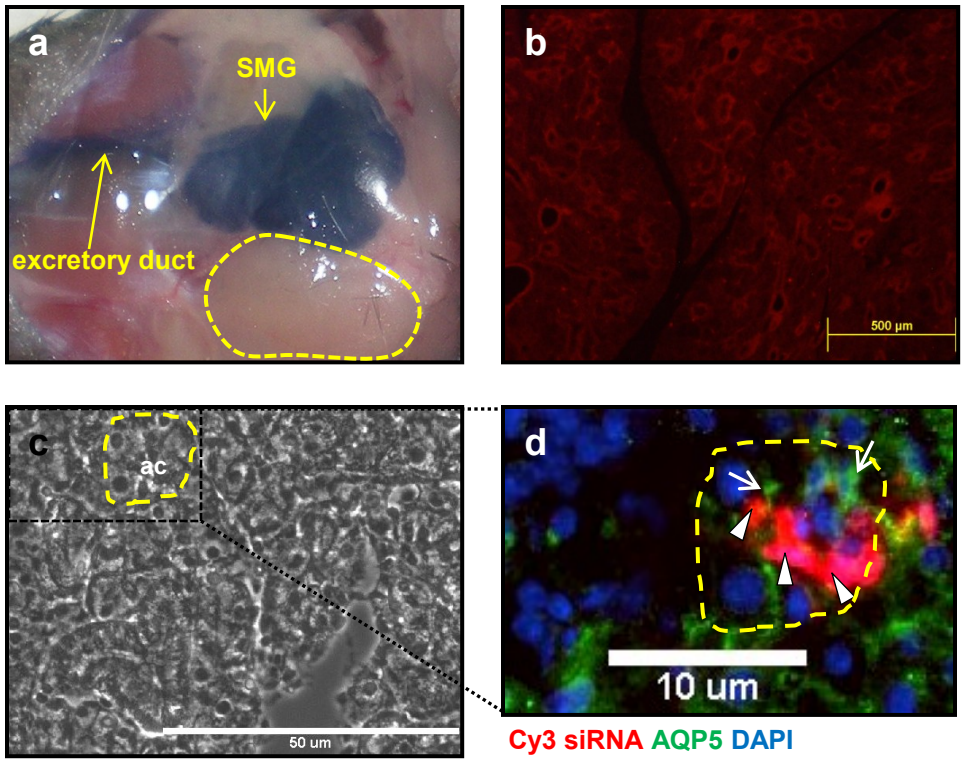
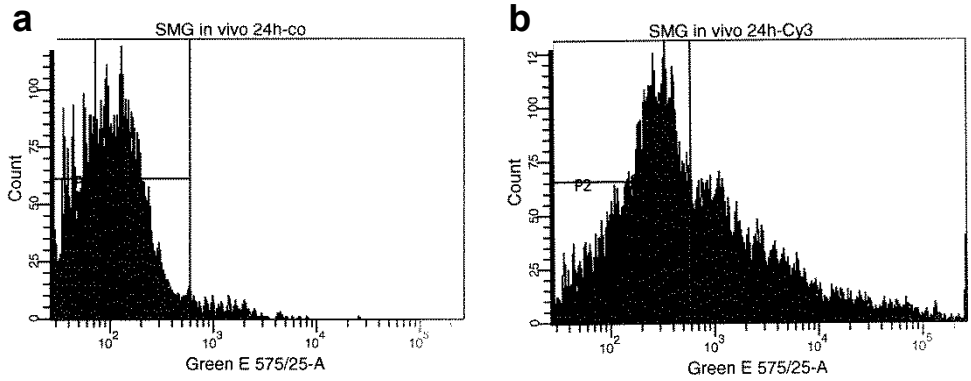
Supplementary figure 1



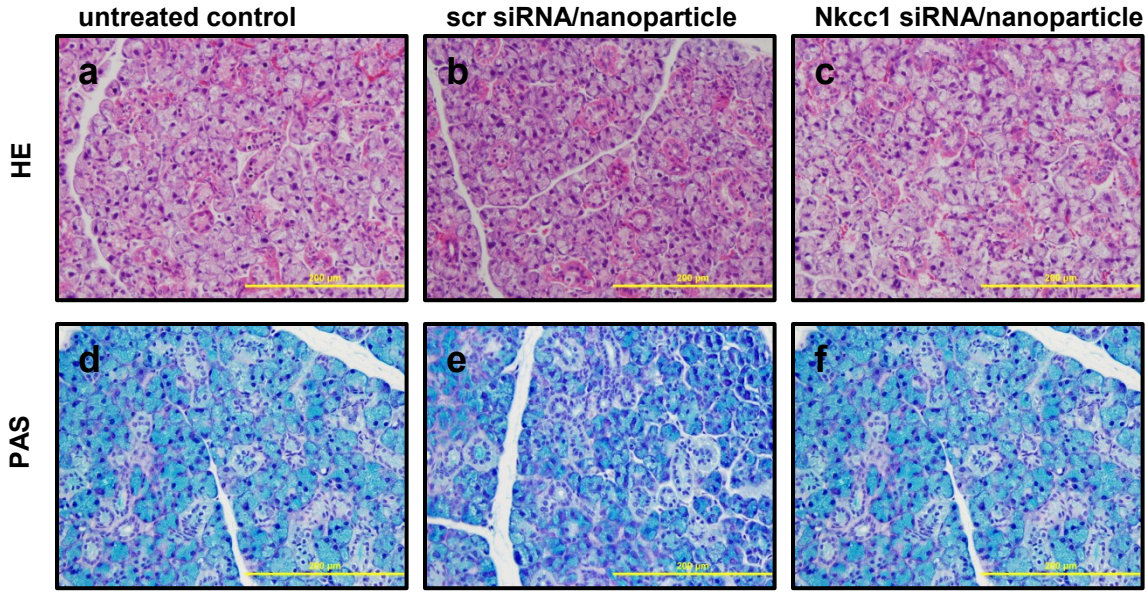
Retroductal injection into mouse SMG. **(a)** Photo documents delivery of Toluidine blue into the SMG. The dye fills the left SMG and Wharton's duct (arrows) immediately after retroductal injection. (Right SMG serving as control is encircled by dotted line.) **(b)** Fluorescent image of SMG section isolated following retroductal injection of naked Cy3-labeled siRNA in vivo. **(c)** Phase contrast photomicrograph of SMG parenchyma 6hr after Cy3 siRNA-nanoparticle injection (bar = 50 µm). **(d)** Inset from c. SMG section was stained with antibody to acinar cell membrane-specific marker aquaporin 5 (AQP5; green). AQP5-labeled acinar cell membranes (arrows) co-localize with cells carrying Cy3-labeled siRNA-nanoparticle conjugates (red; arrowheads). Nuclei labeled with DAPI. (bar = 10 µm; ac, acinus; du, ductal cells)

Supplementary figure 2



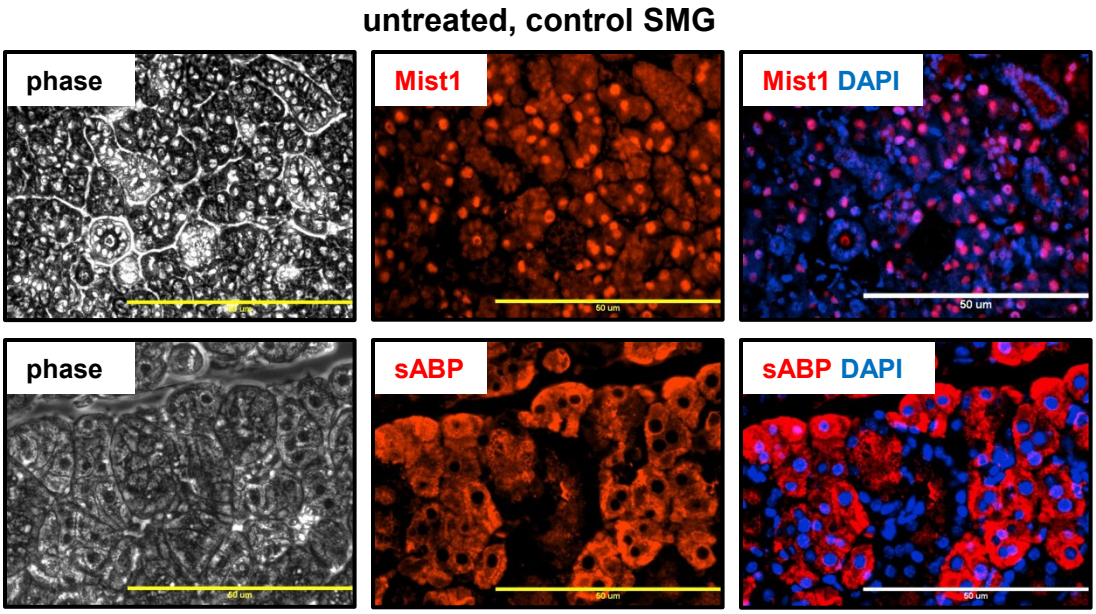
Cellular uptake of siRNA-nanoparticle complexes is confirmed by FACs analysis. **(a)** The flow cytometric analysis profile of a cell preparation isolated from the SMG of an uninjected animal is compared to **(b)** the profile generated from cells isolated from SMG at 24hr after retroductal injection of Cy3-tagged siRNA-nanoparticle complexes. The extended shoulder in **(b)** is due to the presence of Cy3-positive cells, indicating uptake of the fluorescently-tagged siRNA-nanoparticle complexes.

Supplementary figure 3



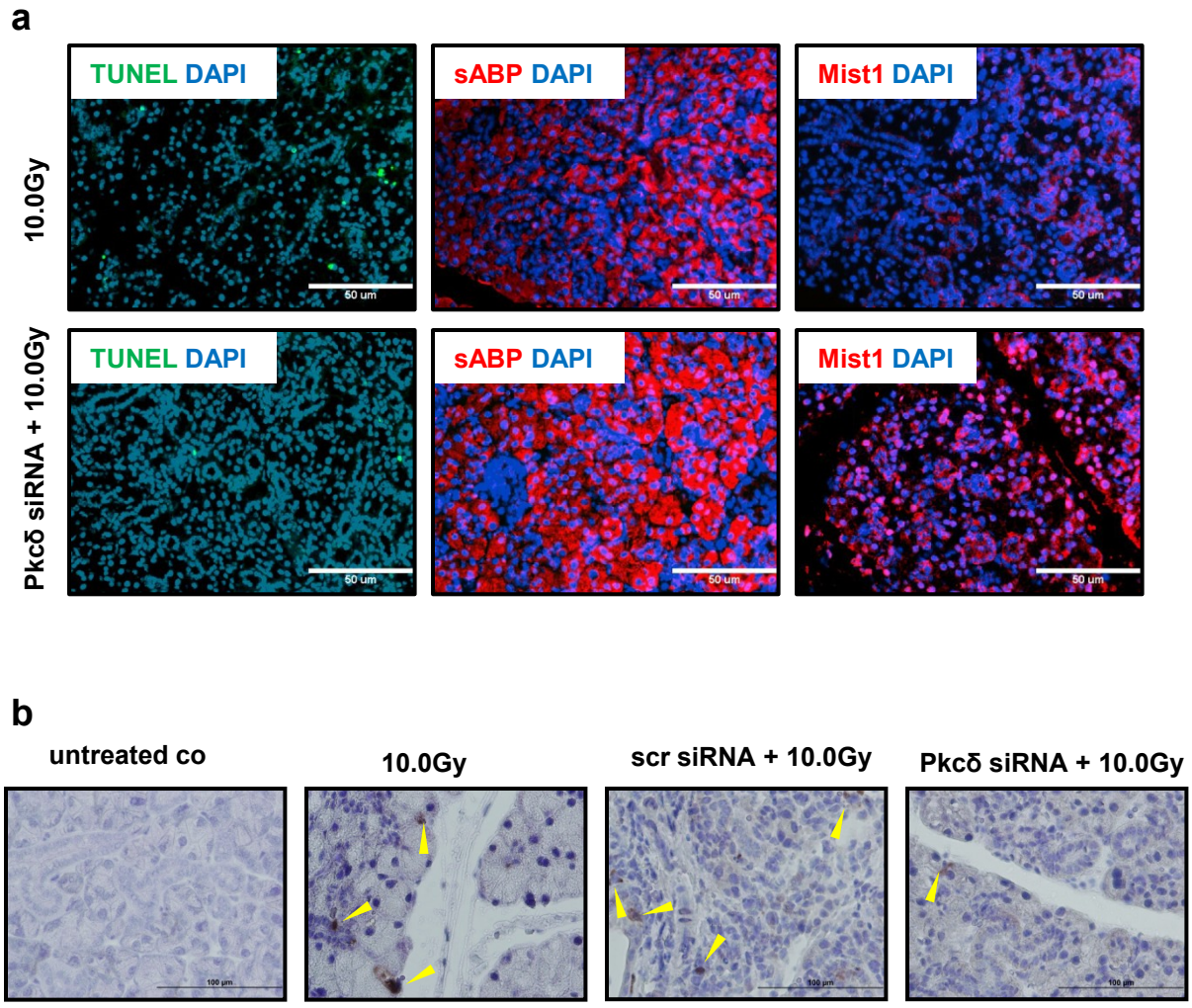
Histology of SMG is not altered following siRNA-nanoparticle injections. Sections of SMG were isolated from untreated control **(a, d)**, scrambled siRNA-nanoparticle injected **(b, e)**, and **(c, f)** Nkcc1 siRNA-nanoparticle injected animals at 1 week post injection. Hematoxylin/Eosin (HE) and Alcian Blue/Periodic acid-Schiff (PAS) staining revealed no alterations in histology as a result of siRNA-nanoparticle injections. (bars = 200 µm)

Supplementary figure 4



Immunohistochemistry to detect expression of acinar cell-specific markers in SMGs. Sections of untreated control SMG were stained with antibody to the acinar cell-specific markers, Mist1 (nuclear) and sABP (cytoplasmic). DAPI was used to label all nuclei. The phase contrast, fluorescent antibody and merged DAPI/antibody images are shown. (bars = 50 µm)

Supplementary figure 5



Radiation-induced apoptosis and secretory cell impairment is attenuated after Pkcδ knockdown in irradiated SMG compared to irradiated controls. (**a)** Apoptotic cells are visualized by TUNEL (green) assay in paraffin sections prepared from irradiated and Pkcδ siRNA-pretreated irradiated SMGs. Immunostaining demonstrates Mist1- or sABP-expressing cells (red) at 3 months following irradiation. Nuclei stained with DAPI. (bars = 50µm). **(b)** Radiation-induced apoptosis was detected at 2 days after radiation by staining for active caspase-3 (brown, marked by arrowheads) in normal control SMG, in irradiated SMG, as well as in irradiated, scrambled or Pkcδ siRNA injected SMG. Hematoxylin counterstain, bars = 100µm.

Supplementary Table 1.

Quantitative PCR primer sequences

Genes		**Forward (5'- 3')**	**Reverse (5'- 3')**
Reference genes	UBC	AAGCCCCTCAATCTCTGGACGC	TCTCAATGGTGTCACTGGGCTCG
	GAPDH	TGTGTCCGTCGTGGATCTGA	TTGCTGTTGAAGTCGCAGGAG
	18S	ACGGAGGATGAGGTGGAGCGAGT	AAGTGGCCAGCCCTCTATGGG
SMG targets	NKCC1	TCCTTCTCGGTGGACTGGTGGT	AAGAGCTCGTCCTCATCGTCGC
	Pkcδ	CCGGGTGGCAGCTGACATGTTT	GTAGAAGAGGGCAACCACGCGG
Immune response	Oas1	TTTCAGCTAGGCTGGGAGACCC	GCTGGGATGCTCCTGAGTCCG
genes	Mx1	AGGAGAAGGTGCGGCCCTGT	GGGCCAGGTCCTGCTCCAC
	IFIT1	GAGAGCAGAGAGTCAAGGCAGGT	AAGGTGGTAGCTGTTCTCTGGGT
	STAT1	CCCACTTGGGACACTGCTGAGCG	GGCTCTCACTCACTCACTGCACGC