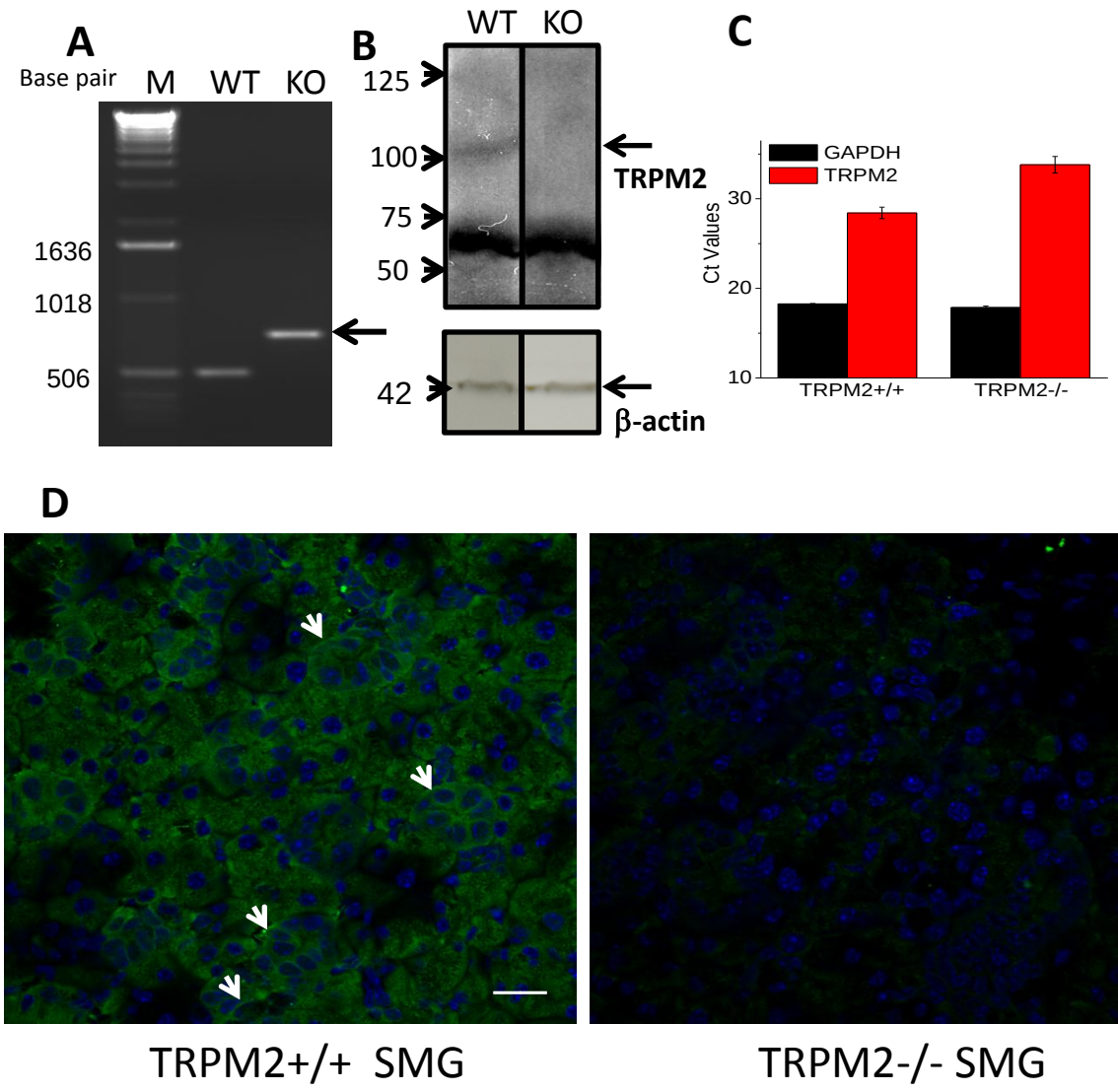
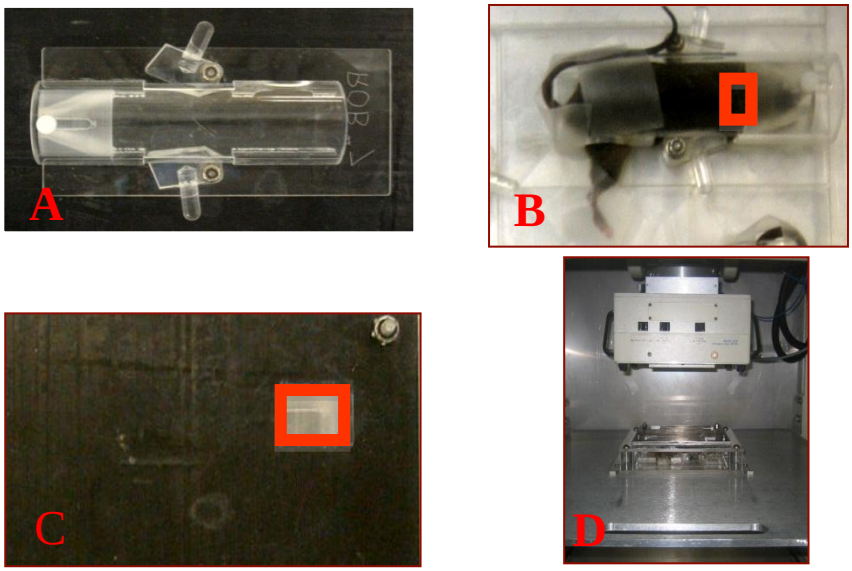
Supplementary Figure S1



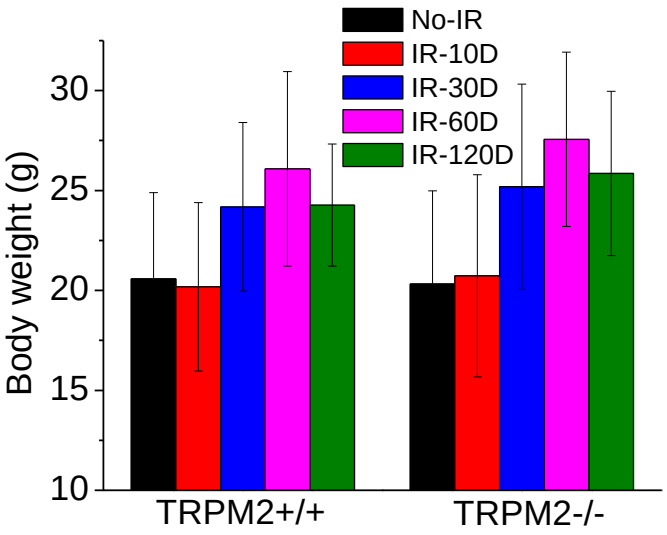
Supplementary Figure S1: Detection of TRPM2 channel in TRPM2+/+ and TRPM2-/- mice. A. Genotyping of TRPM2+/+ and TRPM2-/- mice. The 740 bp band (indicated by arrow in the third lane) confirms that the DNA sample originated from TRPM2-/- mice (see Methods for details regarding primers etc.). **B**. Western blot showing presence of TRPM2 in submandibular gland lysates from TRPM2+/+ mice but not in those from TRPM2-/- mice. Actin (lower blot) was probed as a control which remains unchanged. **C.** qPCR measurements of TRPM2 transcript levels in control HSG cells and cells treated with siTRPM2 (n=4). Data are expressed as mean±standard error. D. Immunofluorescence detection of TRPM2 in TRPM2+/+ submandibular gland sections (indicated by white arrows). There was low, relatively undetectable, signal in samples from TRPM2-/- mice, the scale bar for 10 µm.

Supplementary Figure S2



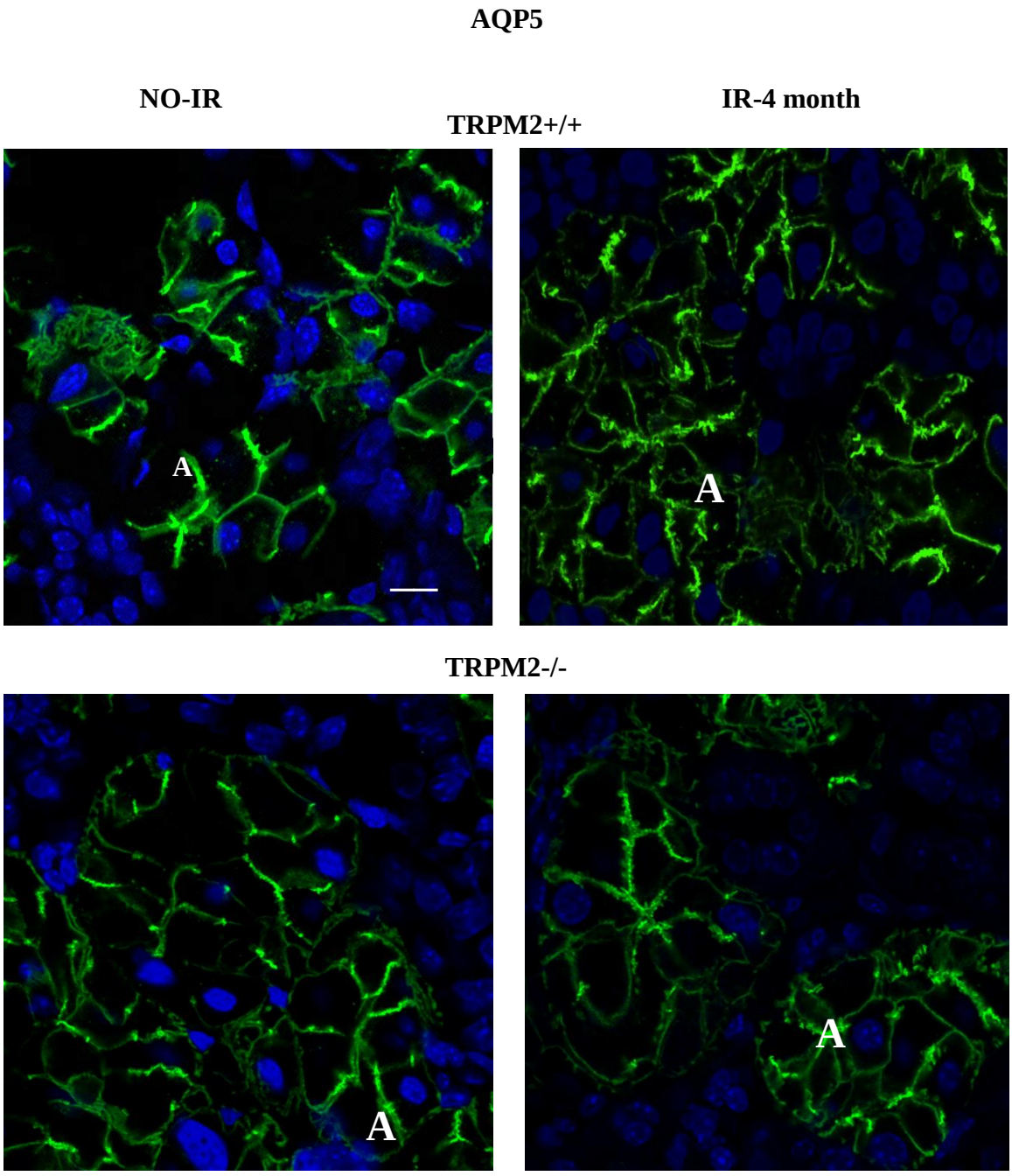
Supplementary Figure S2. Irradiation set up. As shown in figure B, animals are placed in to the lucite jig (shown in A), and immobilized. A lead shield (shown in figure C) with an opening in the field where the salivary glands are located (shown in red) is placed on top of the jig allowing irradiation to be delivered only to this specific area [48].

Supplementary Figure S3



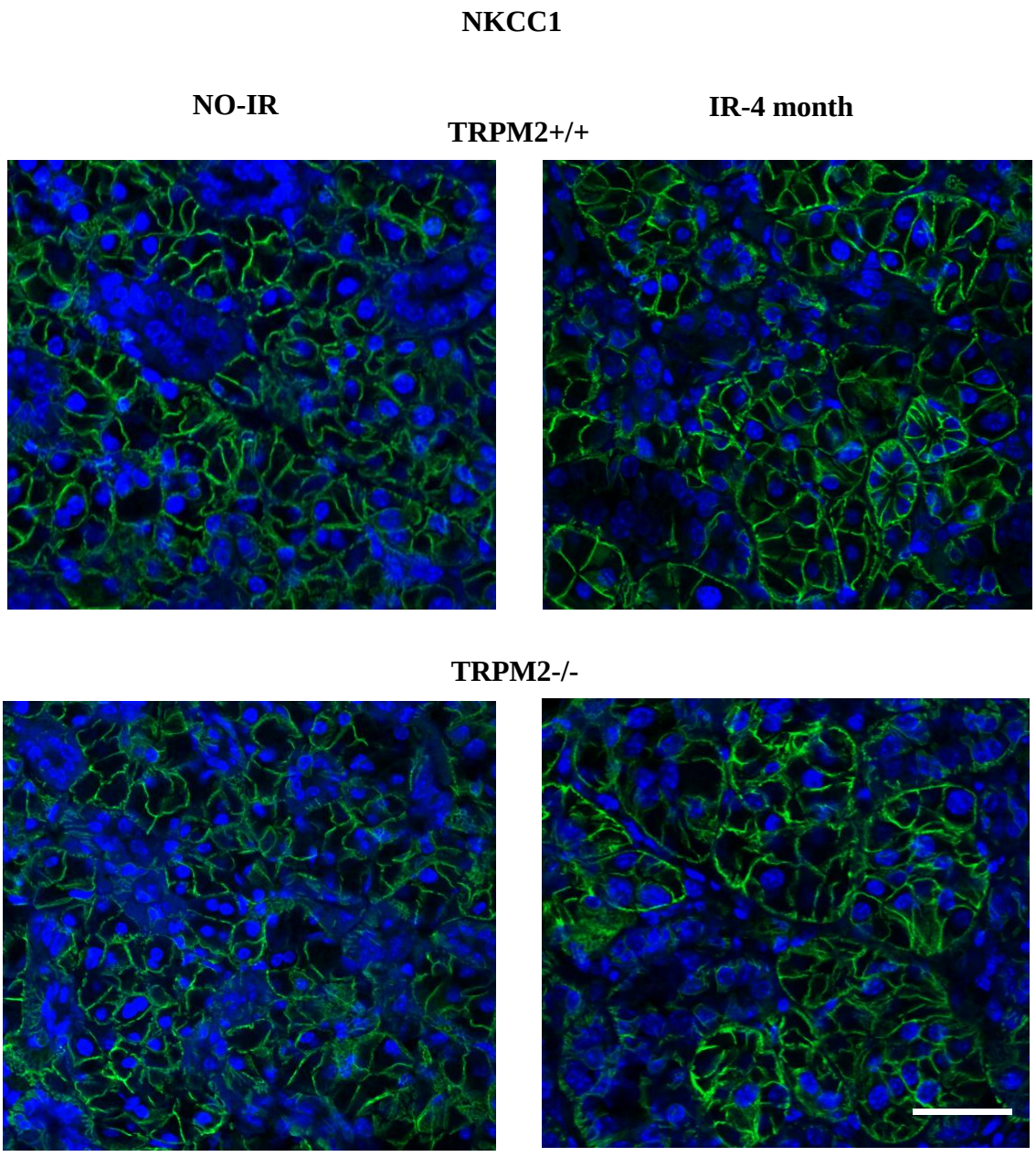
Supplementary Figure S3: The body weights of non-IR and 15 Gy IR in TRPM2+/+ and TRPM2-/- mice. The body weights of non-IR and in 15 Gy IR TRPM2+/+ and TRPM2-/- mice monitored from 10 to 120 day post IR period as indicated. Age and sex were matched for these two groups and numbers of mice were between 10 to 24. Both sets of mice did not lose weight within 10 days of IR and gained weight between 10 days after radiation upto 60 days after IR (the age of the animals is 4 months at this time). Control non-IR mice show similar changes in body weight. Data are expressed as mean±standard error.

Supplementary Figure S4



Supplementary Figure S4: **AQP5 detection in TRPM2+/+ and TRPM2-/- mice SMG**. Immunofluorescence detection of AQP5 in acinar cells from TRPM2+/+ and TRPM2-/- mice before and 4 months after IR with the scale bar of 10 μm.

Supplementary Figure S5

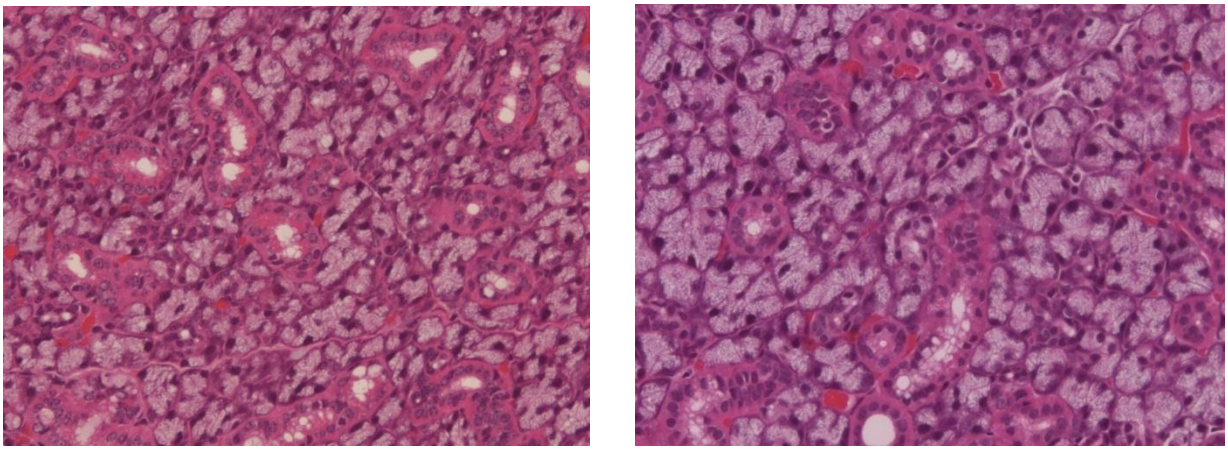


Supplementary Figure S5: NKCC1 staining in TRPM2+/+ and TRPM2-/- mice SMG. Immunofluorescence detection of NKCC1 in acinar cells from TRPM2+/+ and TRPM2-/- mice before and 4 months after IR with the scale bar of 50 µm.

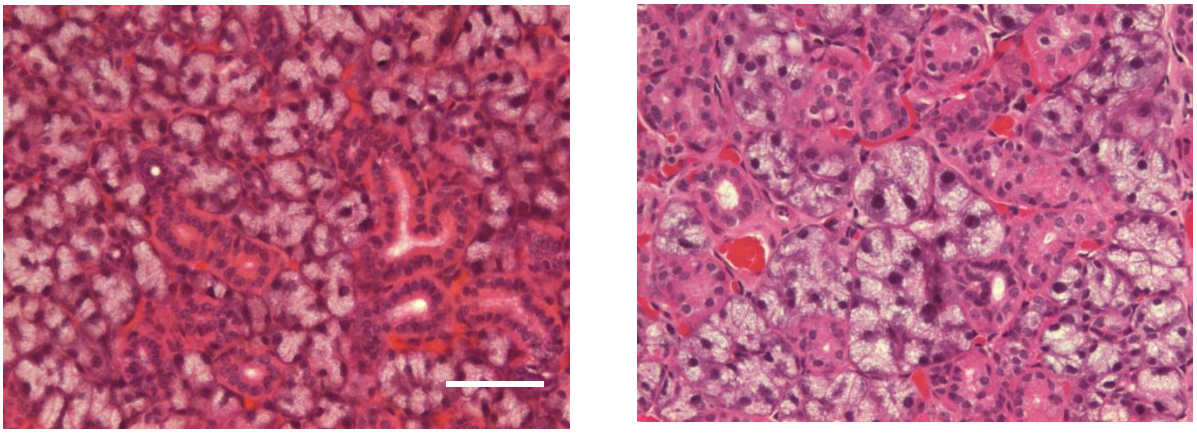
Supplementary Figure S6

NO-IR **IR-4 month**

TRPM2+/+

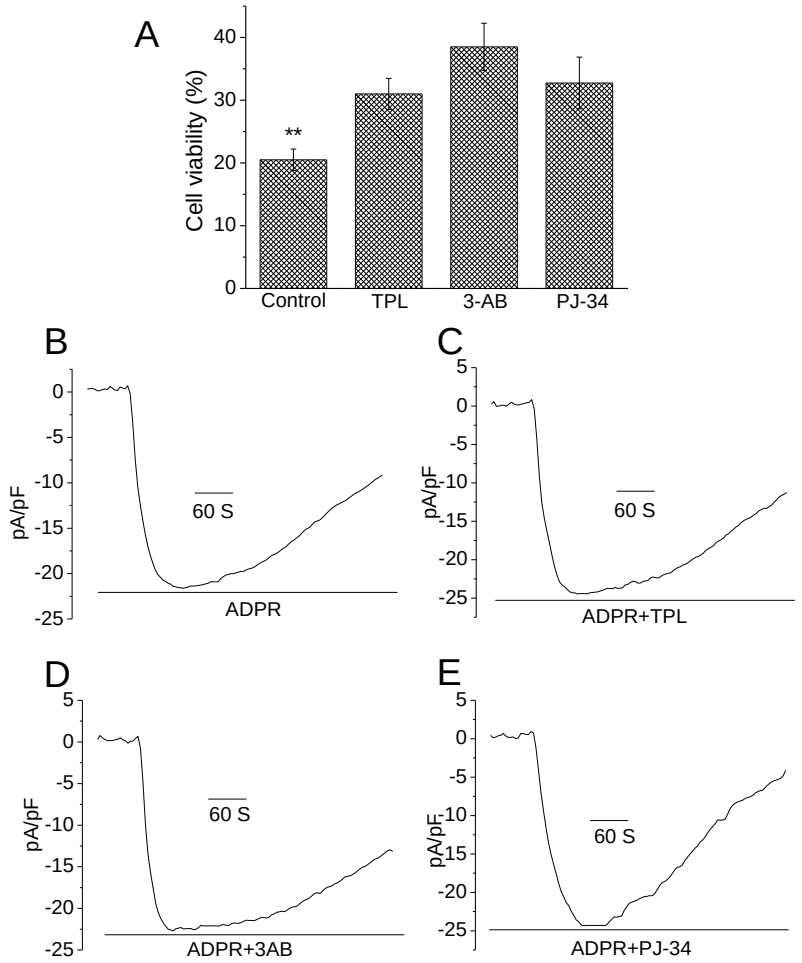


TRPM2-/-



Supplementary Figure S6: **Morphology of salivary glands in TRPM2+/+ and TRPM2-/- mice SMG**. Morphology of salivary glands from TRPM2+/+ and TRPM2-/- mice before and 4 months after IR. H and E staining pattern of salivary gland sections reveals no significant differences between these groups of animals with the scale bar of 50 µm.

Supplementary Figure S7



Supplementary Figure 7. Effects of TPL, 3-AB and PJ-34 on cell viability and TRPM2 channel activity. (A), Trypan blue exclusion in HSG **c**ells following 15 Gy IR. The indicated cells were pre-treated with TPL (10 mM), 3-AB (10 μM) or PJ-34 (1 μM) prior to IR. ** indicates values that are significantly different $p<0.01$ compared to the rest group from two different experiments (number of cells counted from 820 to 1260). Data are expressed as mean±standard error. ADPR-induced membrane current in HSG cells in TRPM2 currents activated by 1 mM ADPR (included in the patch pipette in control cell (B), cells pretreated with TPL (10 mM) (C); 3-AB (10 μM) (D), and PJ-34 (1 μM) (E). These traces were representative of data from 4 to 5 cells recordings in two to three different experiments.