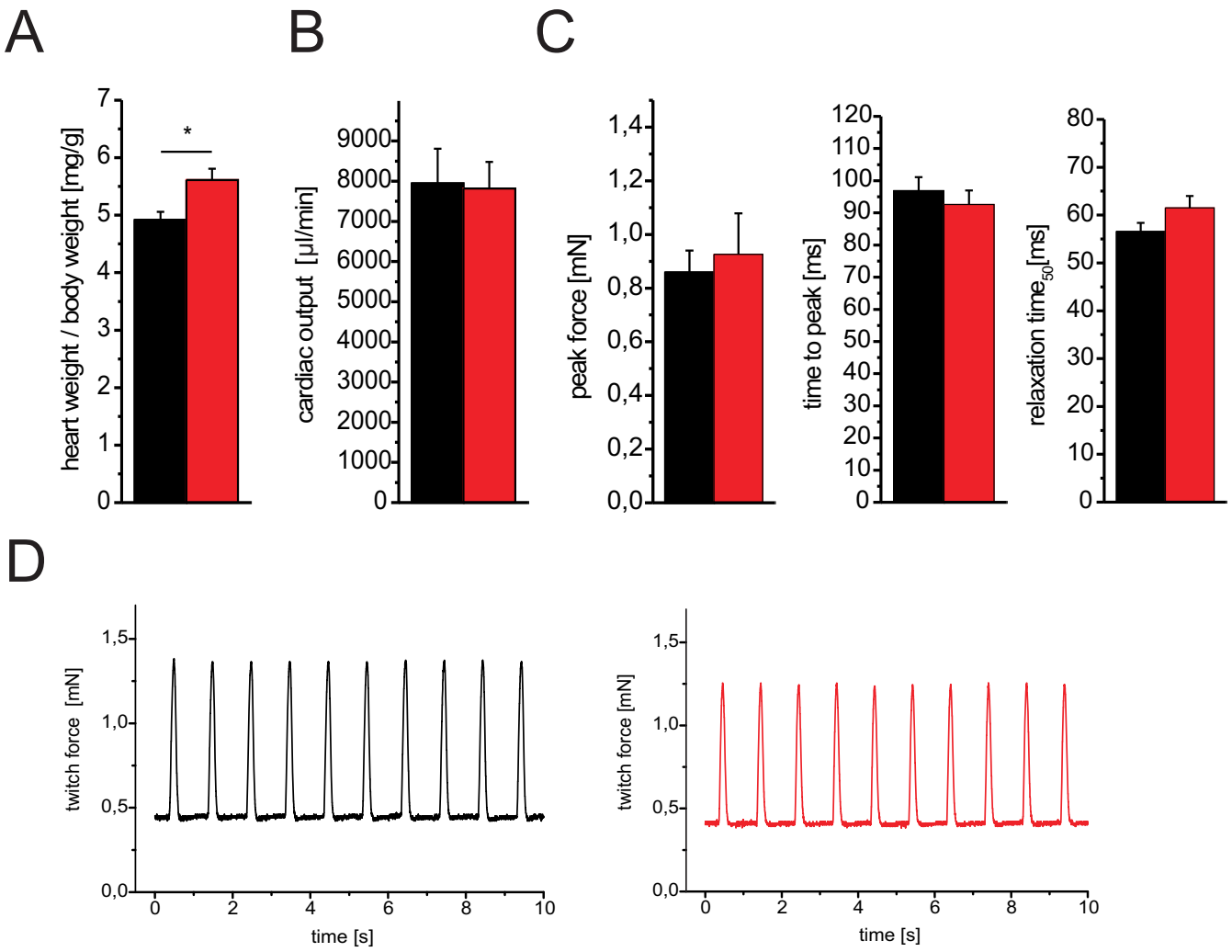
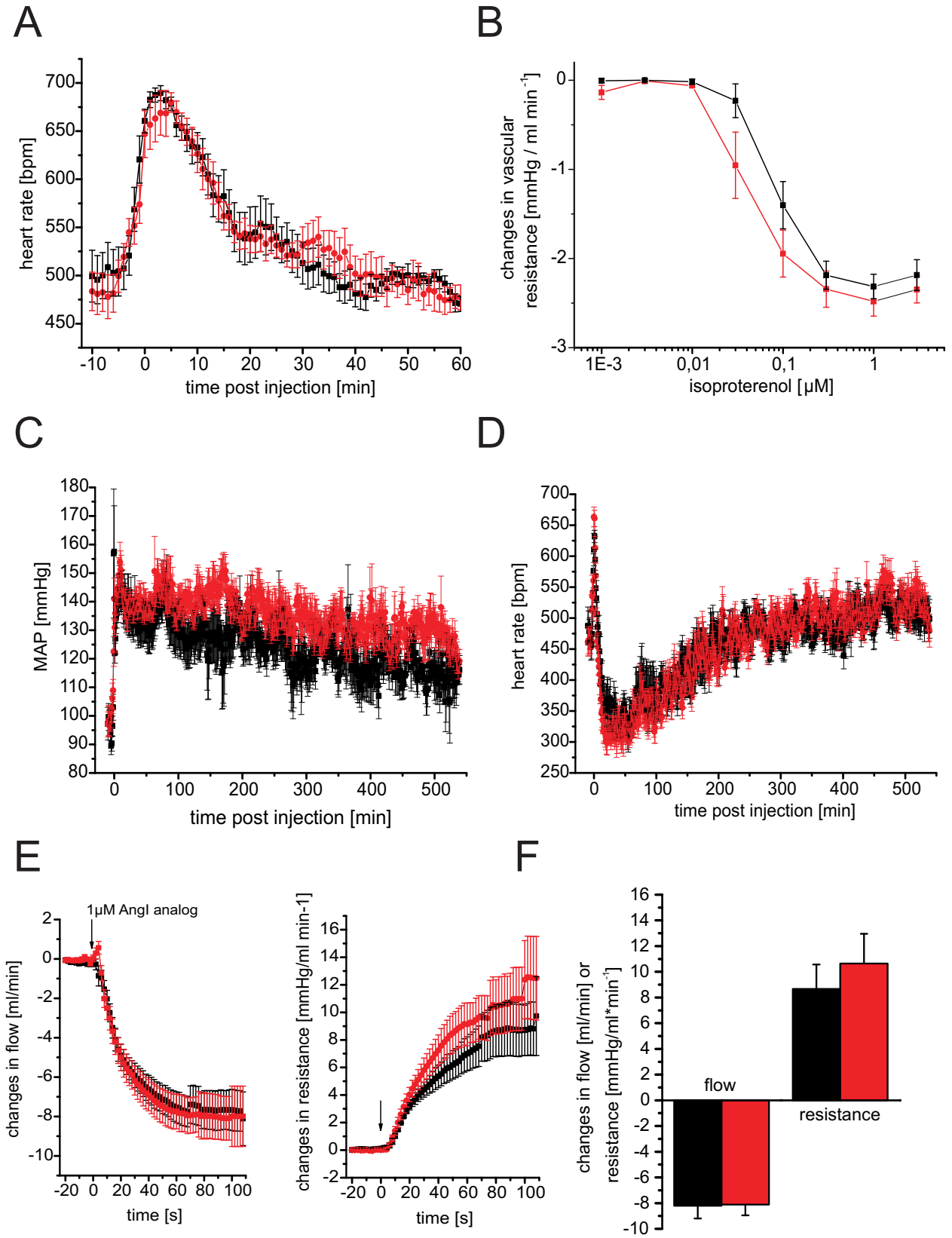
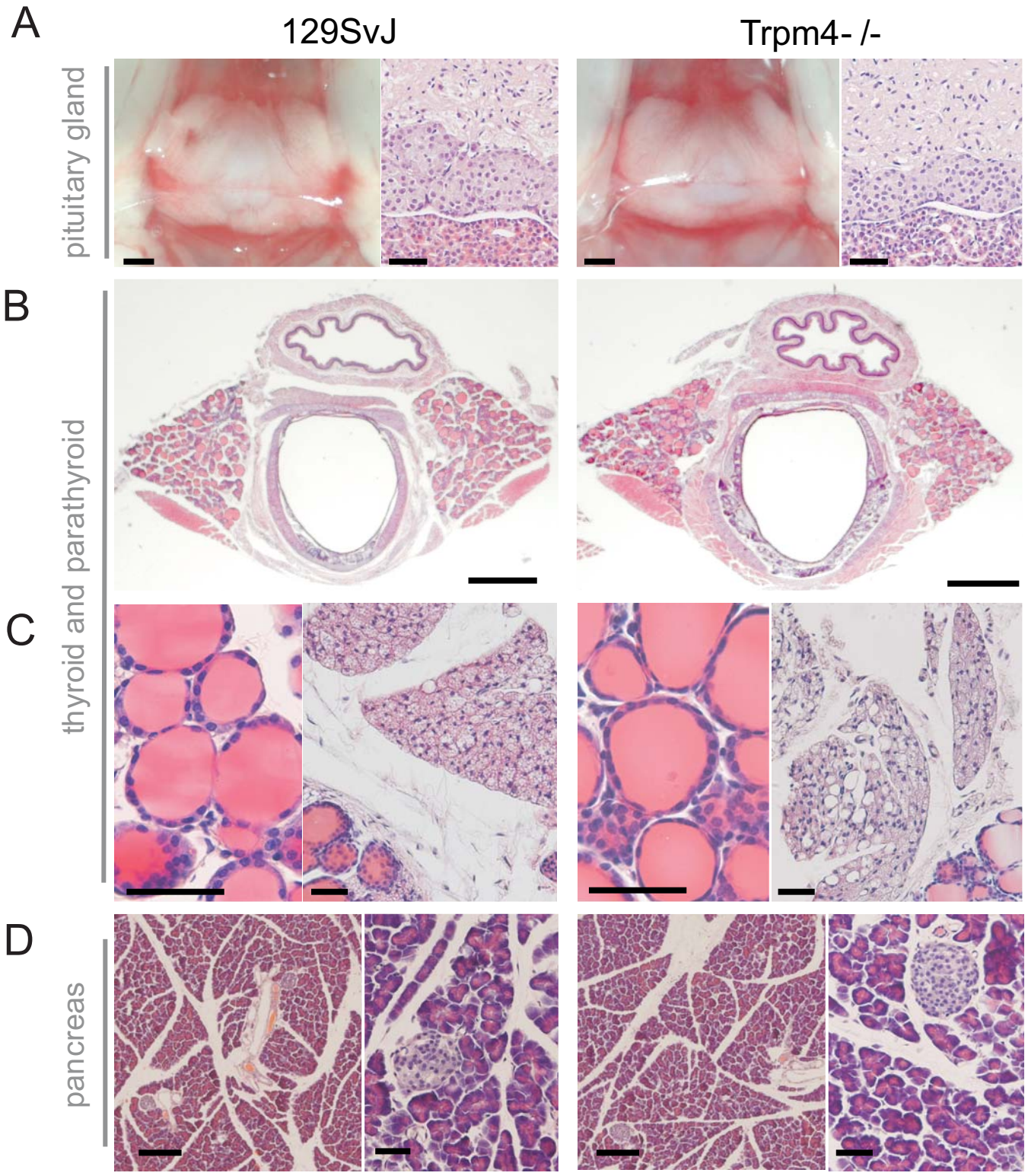


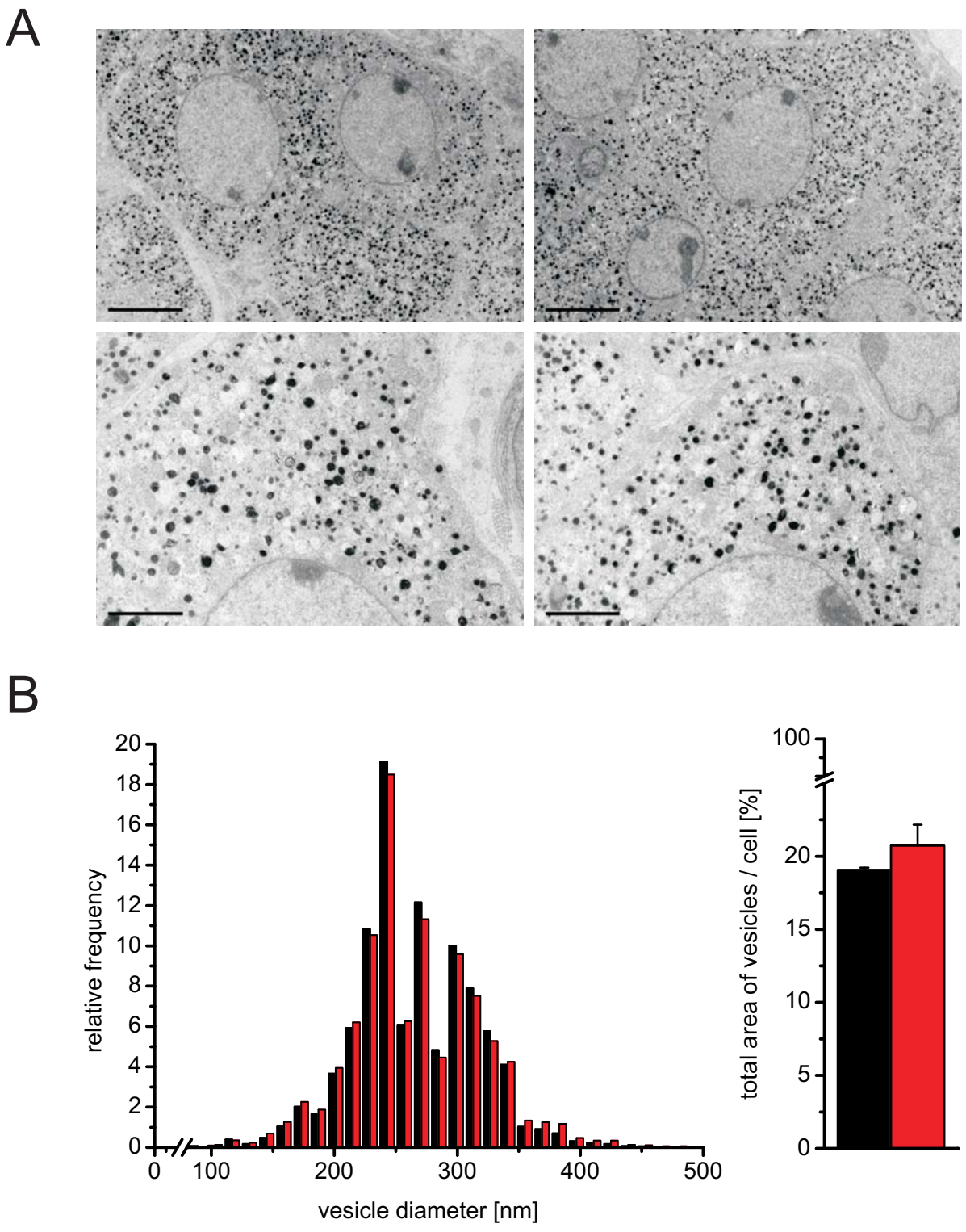

**Supplementary Figure 1: Moderate cardiac hypertrophy and normal contractility of isolated papillary muscles in TRPM4-deficient mice. (A)** Heart to body weight ratio of 6 to 8 months old wild-type (n=17, black) and *Trpm4* $^{-/-}$ mice (n=25, red); * p<0.05. **(B)** Cardiac output from anesthesized wild-type (n=13, black) and *Trpm4* $^{-/-}$ mice (n=14, red) **(C)** Twitch tension, time to peak and relaxation time of isolated papillary muscles from WT (black, n=8) and *Trpm4* $^{-/-}$ (red, n=7) mice. **(D)** Original trace of basal contractility in wild-type (black) or *Trpm4* $^{-/-}$ (red) papillary muscle.




**Supplementary Figure 2: Cardiovascular reactivity in TRPM4-deficient mice.**
**(A)** Heart rate response after intraperitoneal application of isoproterenol (2µg/kg BW, WT n=7, black, and *Trpm4* $^{-/-}$ n=9, red). **(B)** Changes in vascular resistance after bolus injections (200 µl) of increasing isoproterenol concentrations (WT, n=6; *Trpm4*$^{-/-}$, n=7). **(C, D)** Response of MAP **(C)** and heart rate **(D)** after intraperitoneal application of L-NAME (25mg/kg; WT, n=7; *Trpm4*$^{-/-}$, n=9). **(E)** Averaged change in perfusate flow and vascular resistance for the first 60 seconds after switching to a perfusate containing 1µM of the chymase substrate [Pro11, DAla12] Ang I (n=5 per genotype). **(F)** Peak flow and peak vascular resistance calculated from experiments shown in E.




**Supplementary Figure 3: *Trpm4* $^{-/-}$ mice show normal morphology of tissues frequently affected in multiple endocrine neoplasia (MEN). (A)** Dorsal view on pituitary glands from wildtype and *Trpm4* $^{-/-}$ mice photographed in situ; scale bar 500 µm (left panels). HE stained sections of the pituitary glands; from up to down: pars distalis, pars intermedia, pars nervosa; scale bar 50 µm (right). **(B)** HE stained transverse section through the thyroid trachea block of wildtype and *Trpm4* $^{-/-}$ mice; scale bar 500 µm. **(C)** Higher magnification shows no apparent morphological difference thyroid follicles (left panels, scale bar 50 µm) or in the parathyroid glands (right panels); scale bar 200 µm. **(D)** HE stained pancreas sections from wildtype and *Trpm4* $^{-/-}$ mice, scale bar 200 µm; (left panels) and 50 µm (right panels).




**Supplementary Figure 4: Ultrastructural analysis reveal no difference in size or density of dense core vesicles in chromaffin cells of *Trpm4* $^{-/-}$ mice . (A)** Representative electron micrographs of chromaffin cells in low (upper panel, scale bar 5µm) and high (lower panel, scale bar 2µm) magnification from wildtype (left) and *Trpm4* $^{-/-}$ (right) mice. **(B)** Quantitative analysis of dense core vesicle size performed on 10-23 cells per mouse (black, wildtype; red, *Trpm4* $^{-/-}$ mice; n=3 mice/genotype) reveals no difference in the size-dependent distribution of vesicles (left) or total area of vesicles per cell (right).