

Pancreatic ductal fluid and HCO_3^- secretion is reduced in the absence of Na^+/H^+ exchanger regulatory factor-1 in mice

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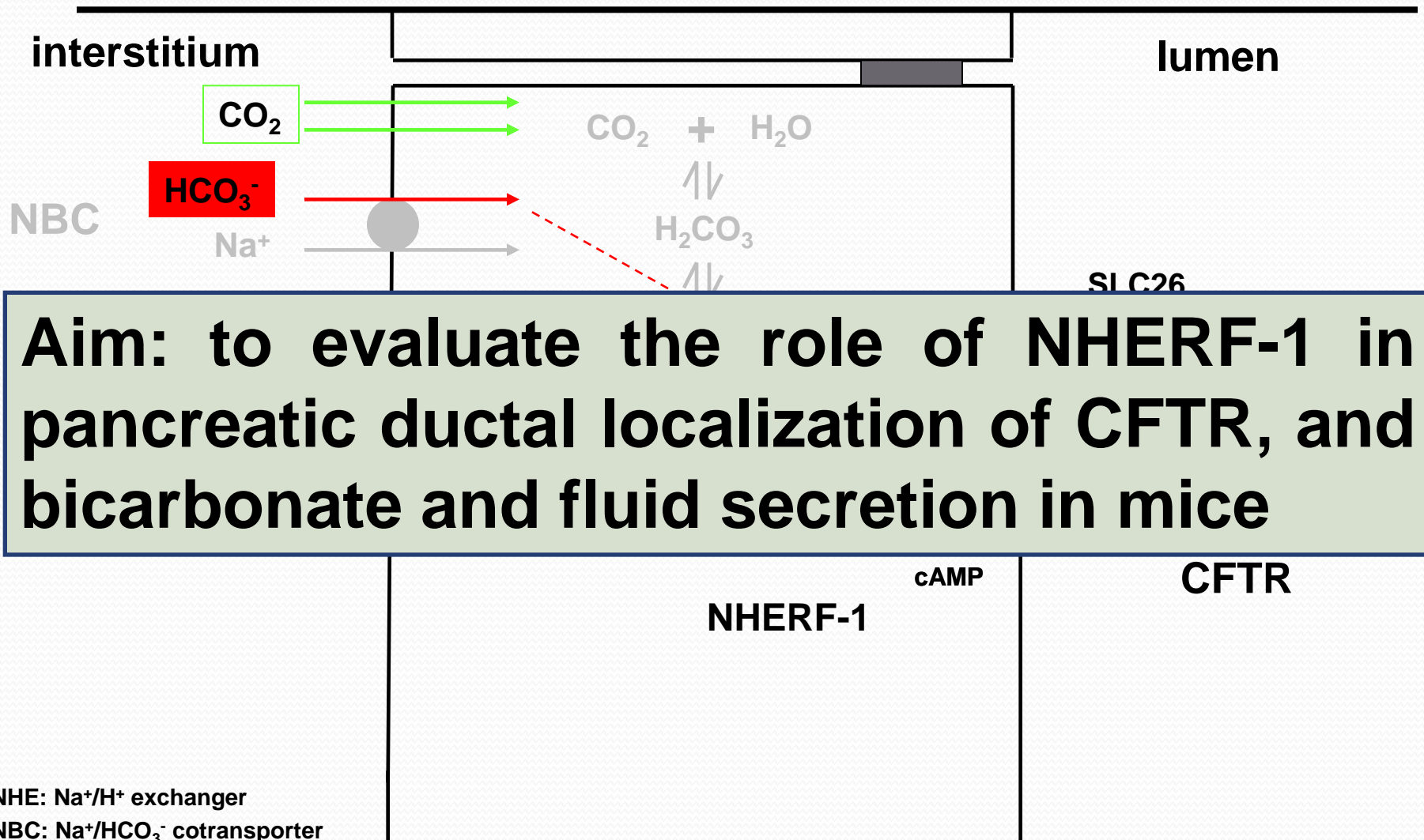
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Mechanism of HCO_3^- secretion of pancreatic ductal epithelial cells



Aim: to evaluate the role of NHERF-1 in pancreatic ductal localization of CFTR, and bicarbonate and fluid secretion in mice

NHE: Na^+/H^+ exchanger

NBC: $\text{Na}^+/\text{HCO}_3^-$ cotransporter

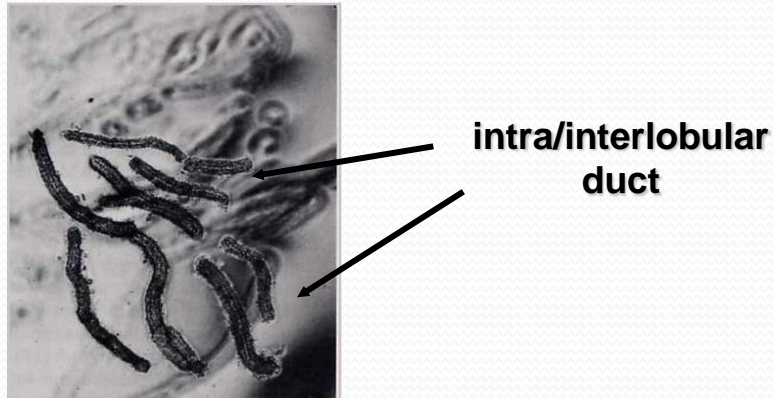
CFTR: cystic fibrosis transmembrane conductance regulator

NHERF-1: Na^+/H^+ exchanger regulatory factor 1

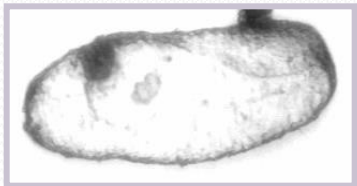
Methods

I. Wilde type (WT) and NHERF-1 knock-out (KO) mice

II. Isolation of intra/interlobular ducts



overnight incubation at 37 °C



III. Real-time PCR

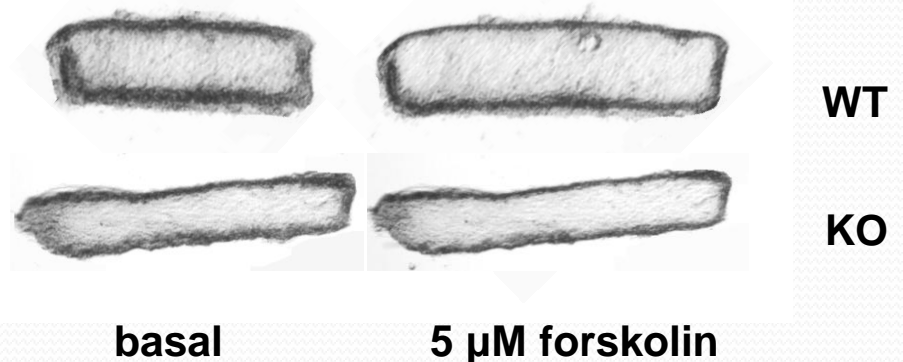
mRNA expression

IV. Immunohistochemistry

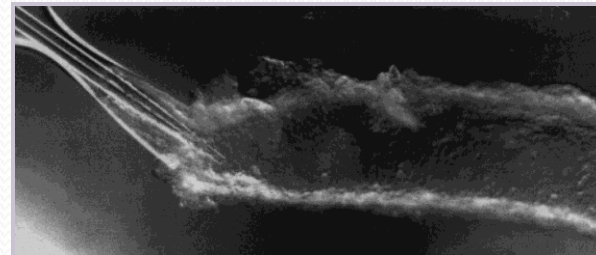
Localization of NHERF-1 and CFTR in pancreatic tissue

VI. Collection of pancreatic juice *in vivo*

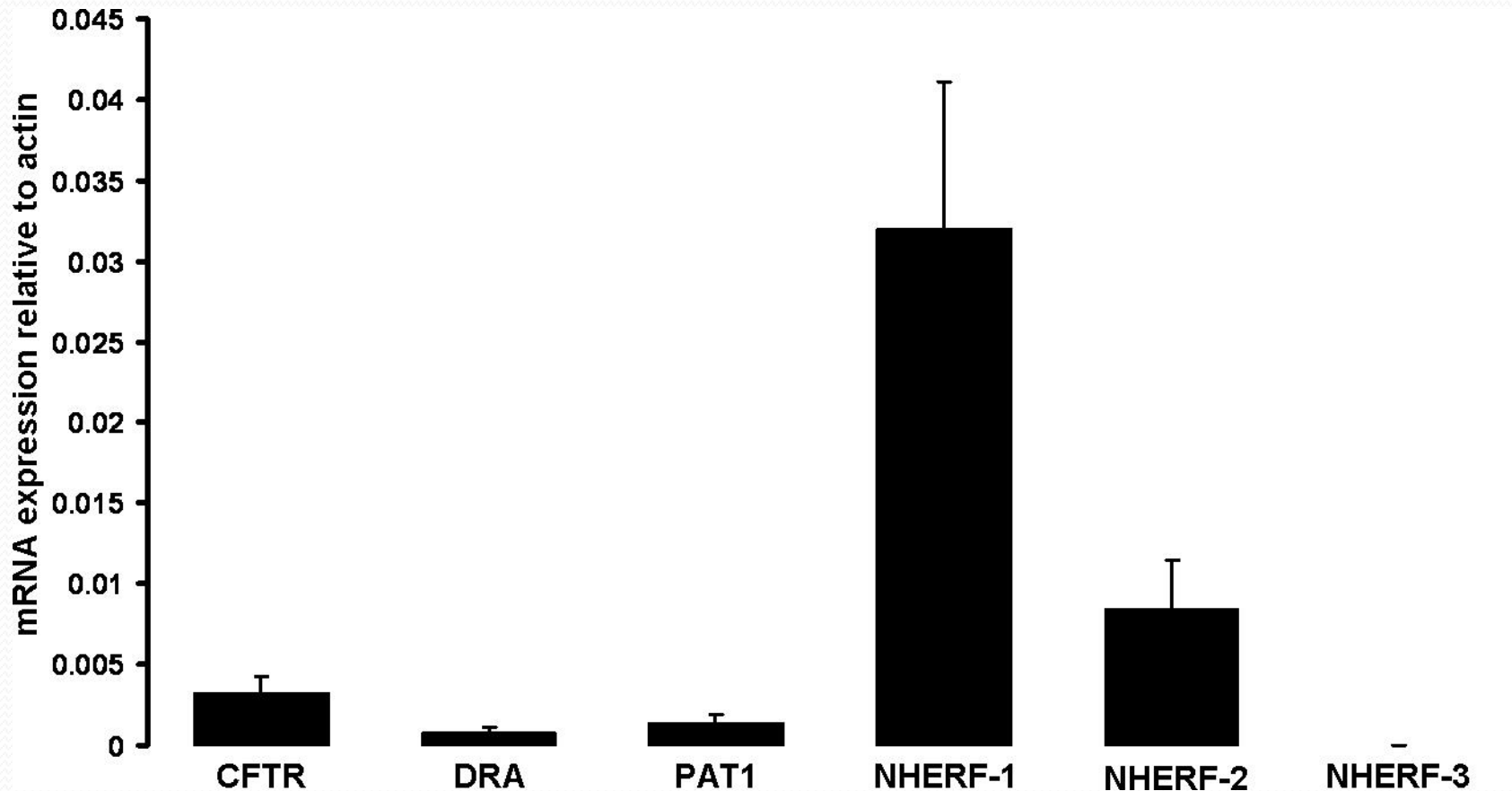
V. Video microscopy – „swelling technic”



VII. Microfluorometry, microperfusion



Expression of CFTR, DRA, PAT1 and NHERF-1-3 mRNA in WT mouse pancreatic ducts



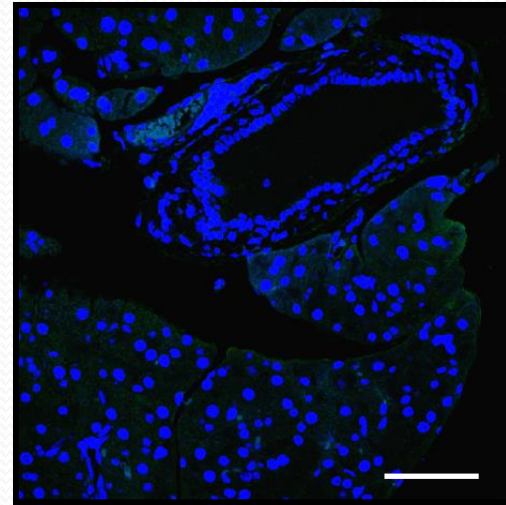
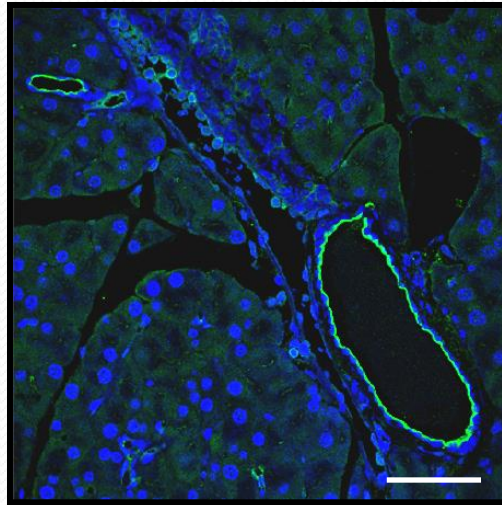
DRA: down regulated in adenoma, Slc26a3

PAT-1: putative anion transporter-1, Slc26a6

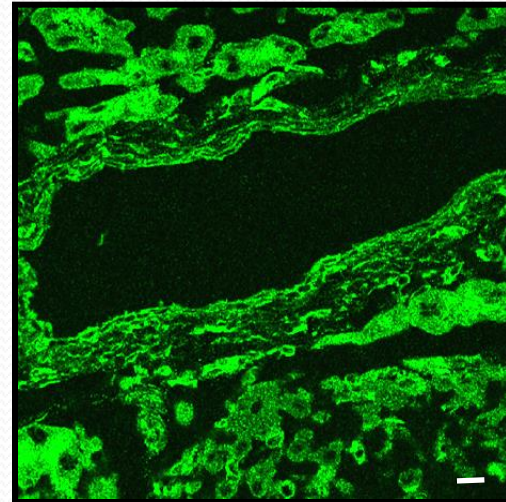
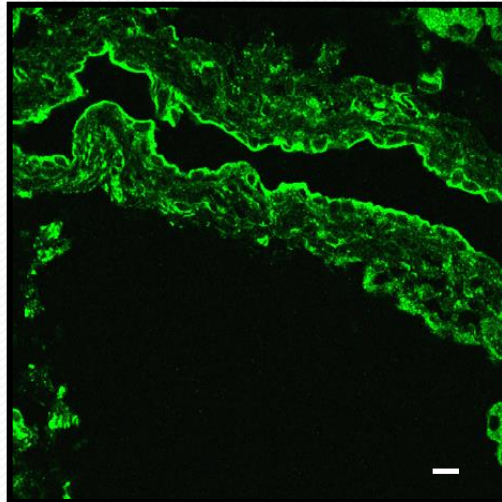
n=6

NHERF-1 and CFTR staining in pancreatic ducts reduced in NHERF-1 KO mice

NHERF-1



CFTR

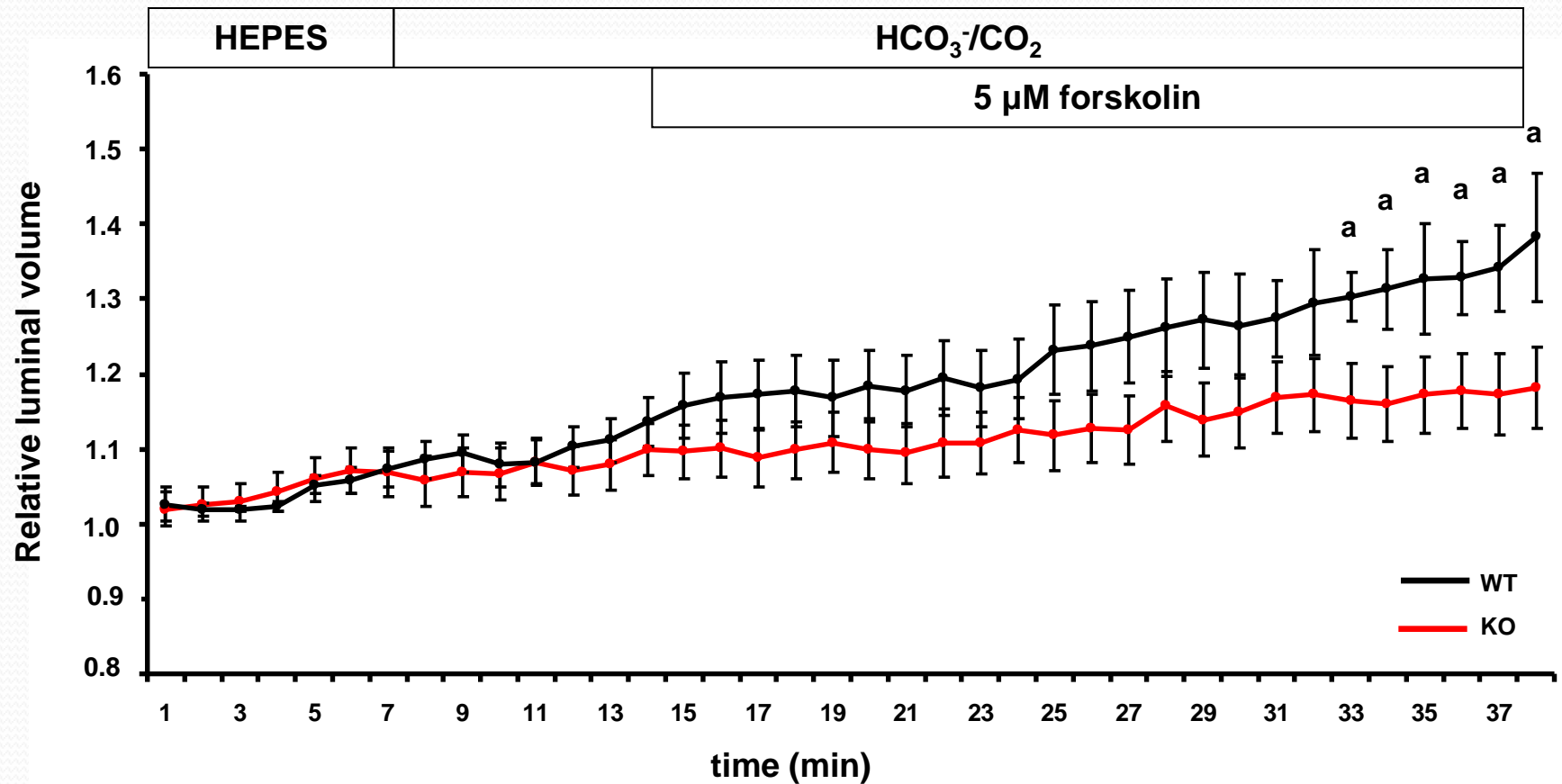


WT

NHERF-1 KO

Scale bar: 50µm

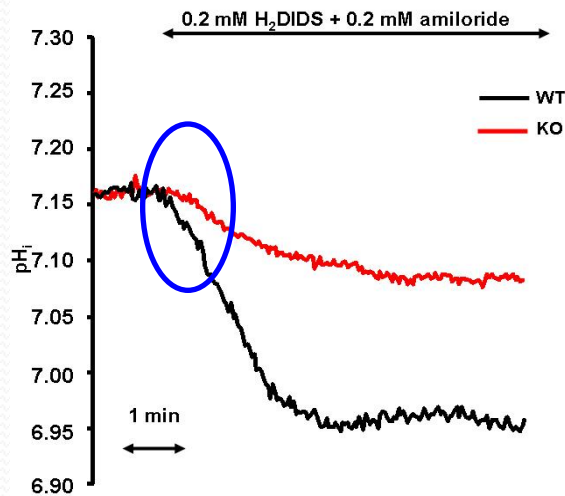
Forskolin-stimulated ductal fluid secretion is reduced in NHERF-1 KO mice



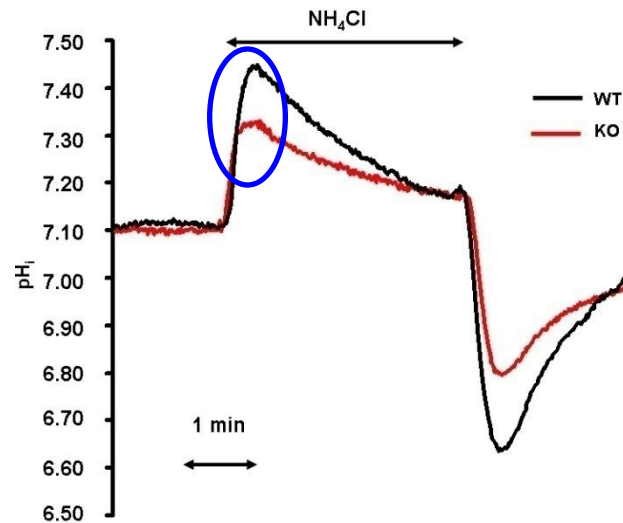
a: p<0.05 vs. KO n = 10

HCO₃⁻ secretion is reduced in NHERF-1 KO mice

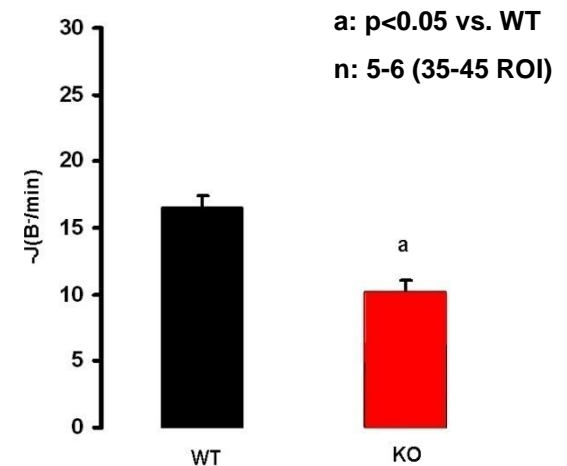
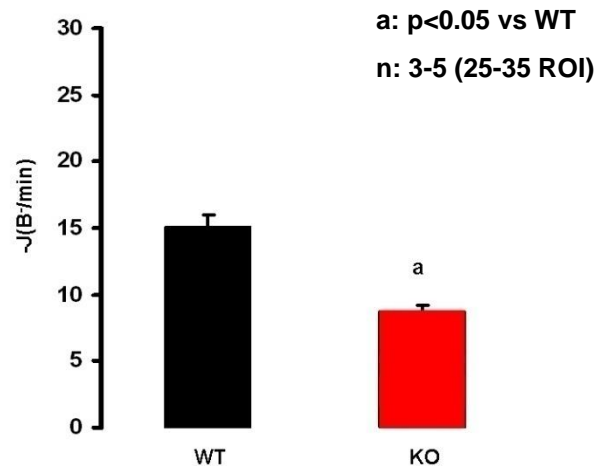
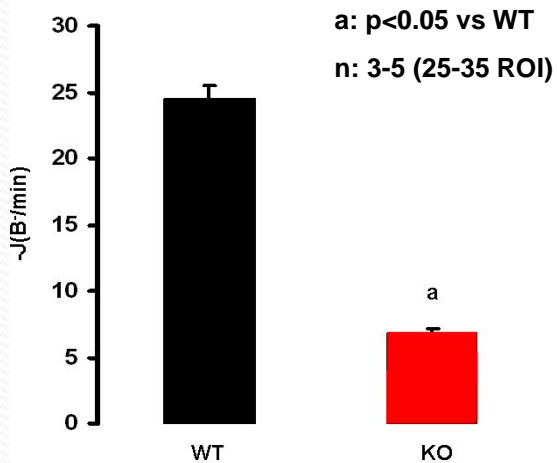
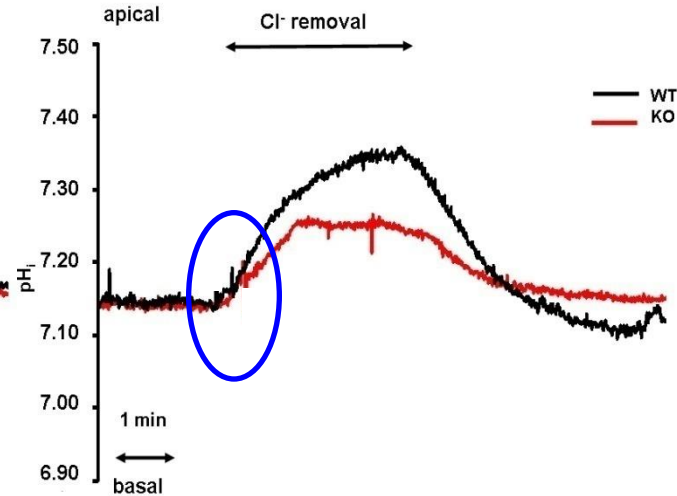
Inhibitory stop method



Regeneration from alkalosis



Luminal Cl⁻ removal



ROI: region of interests

Conclusions

- NHERF-1 is required for the localization of CFTR on the apical membrane of pancreatic ductal cells
- NHERF-1 is involved in both pancreatic HCO_3^- and fluid secretion

THANK YOU FOR YOUR ATTENTION!

NEW

SZÉCHENYI PLAN



HUNGARY'S RENEWAL



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