Phosphodiesterases (PDEs) and insulin signaling networks in the inner ear

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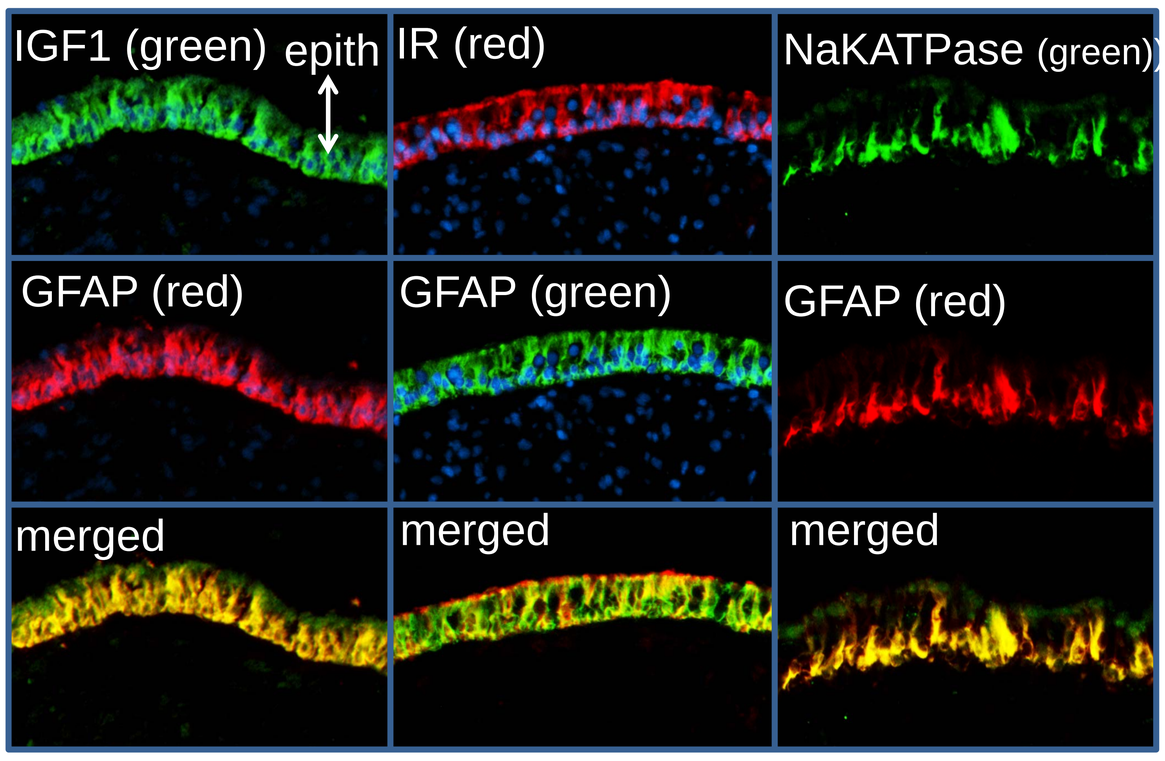
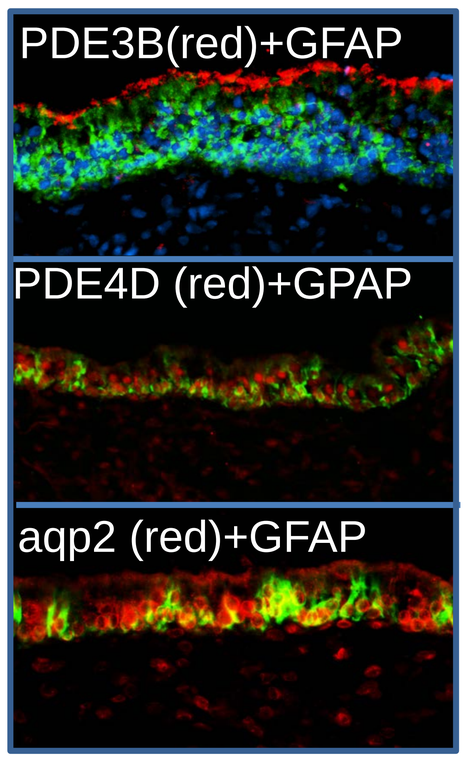
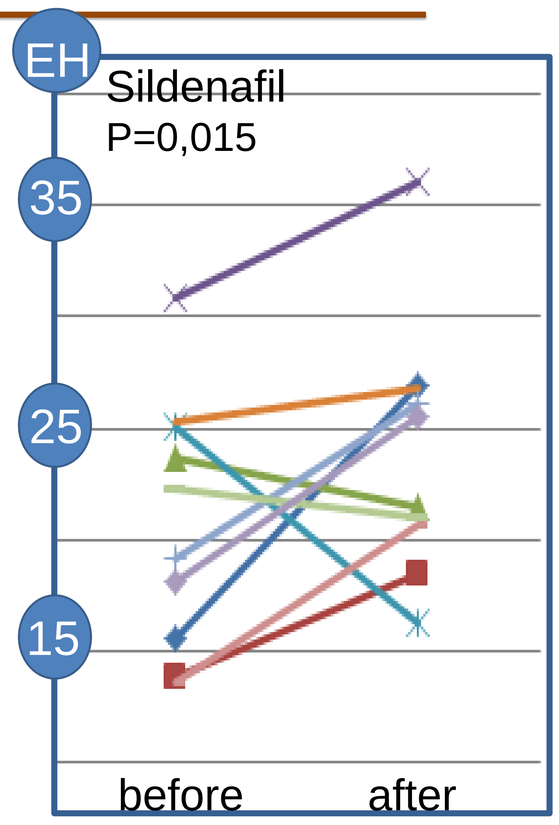
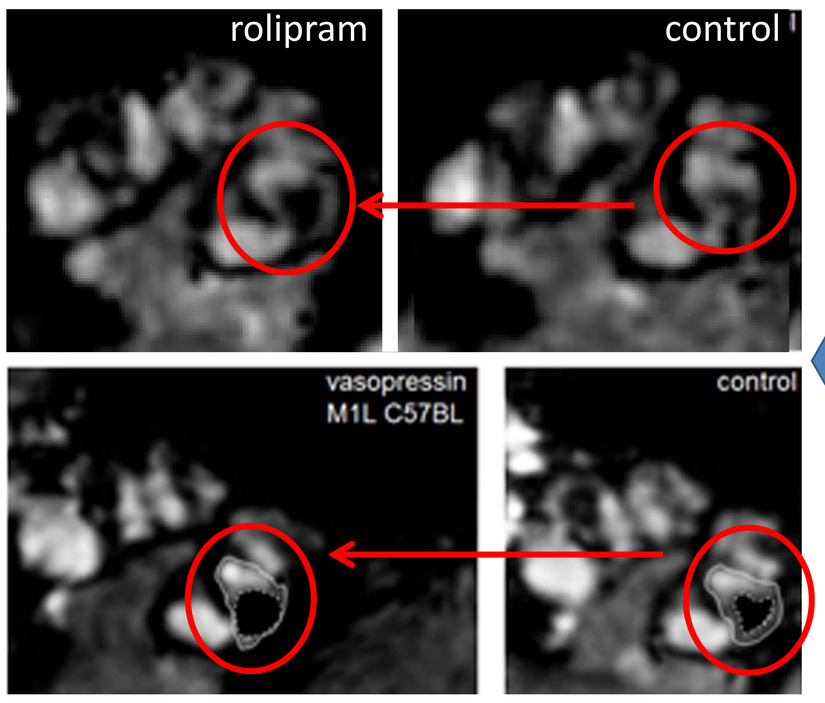
THE AIM is to [**1**] continue our work to map insulin and cAMP/PDE signaling networks in the inner ear using IHC and [**2**] to test the effect of PDE3/4/5 inhibitors on inner ear fluid homeostasis using MR as read-out. The **RESULTS** show that [**1**] a number of insulin related components and PDEs are expressed in human saccule and that [**2**] selected PDE inhibitors, with or without vasopressin, induce endolymphatic hydrops in mouse inner ear. **IN CONCLUSION** we have generated data of relevance for the association between diabetes and inner ear dysfunction reported on in literature and of relevance for Menieres disease. Thus, selective PDE3/4/5 inhibitors induced endolymphatic hydrops indicating important roles for selected cAMP and cGMP pools and associated insulin and other signaling networks.









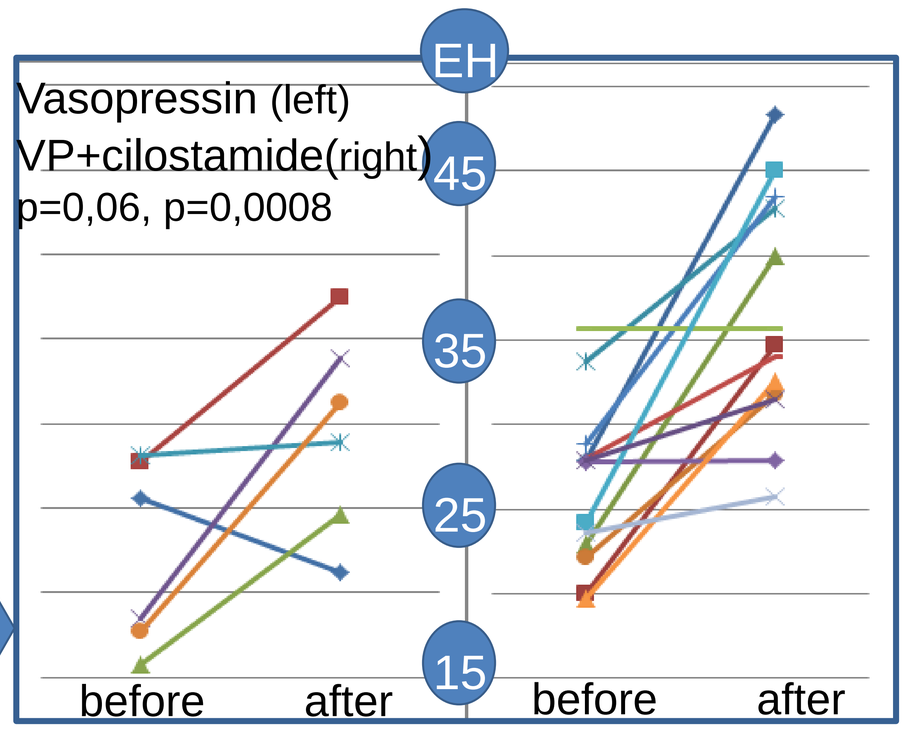
IHC of human saccule-some examples, for summary see bottom left

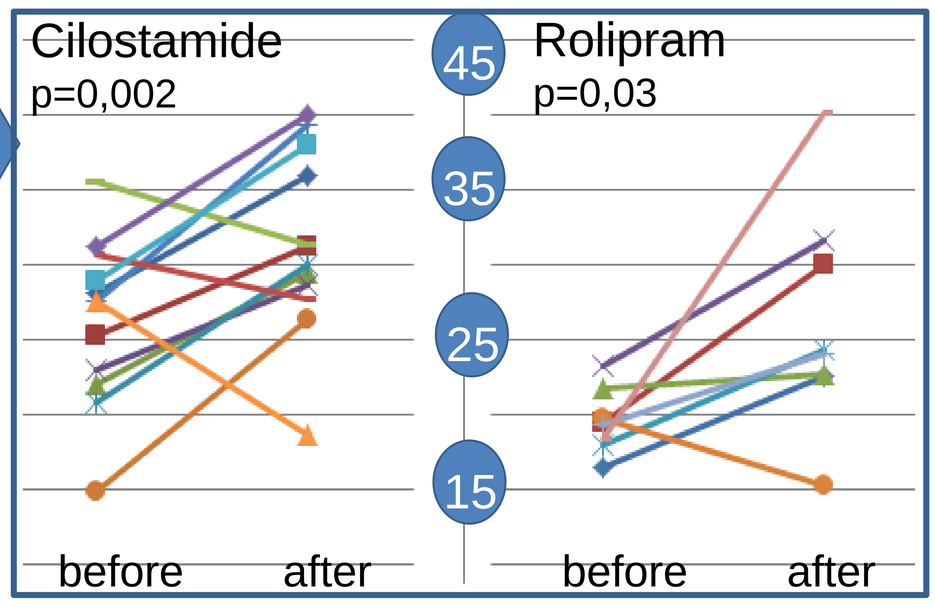
9.4T MRI of inner ear-examples using continous vassopressin and rolipram injections to induce EH in mice (ROI/red, endol./black)

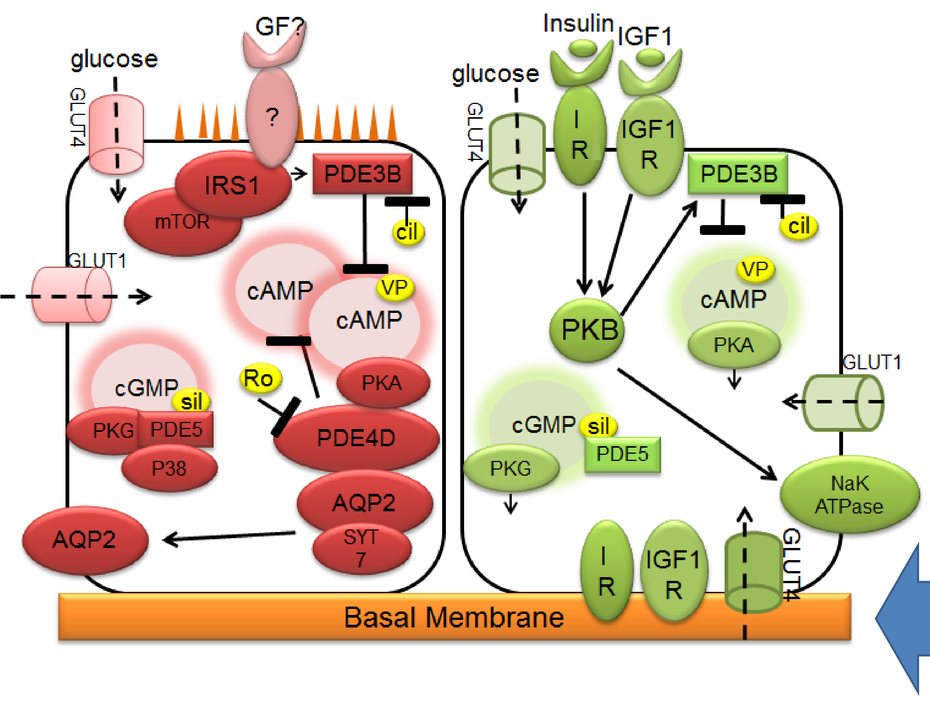
Analysis of images for EH as exemplified (left) before and after treatment with VP and VP+cil.

Analysis of images obtained as indicated up/left before and after treatment with rolipram and cilostamide (sildenafil top,right)

Schematic illustration of PDEs and insulin signaling networks in sensory epithelium, see also IHC.







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