

# Innovation and Research Week

## שבוע חדשנות ומחקר

### Novel Approach to the Unmet Medical Need of Inner-Ear Injury: Application of Clinical-Grade $\alpha$ 1-Antitrypsin

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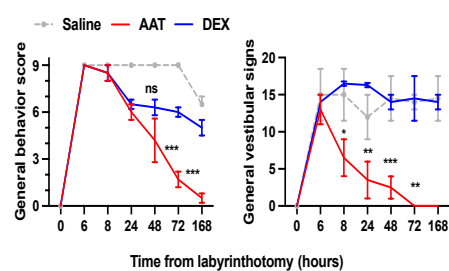
**Background** Alpha1-antitrypsin (AAT) is a circulating tissue-protective molecule that is elevated during inflammatory conditions; AAT insufficiency in human perilymph correlates with hearing loss severity; concomitantly, transgenic mice overexpressing AAT restore vestibular function after inner ear trauma. Locally applied AAT, however, has yet to be examined in this context, nor has it been directly compared to standard corticosteroid treatment.

**Aim** To characterize functional cochlear recovery in a mouse model of surgical and medication-related inner ear injury under local AAT and dexamethasone treatments.

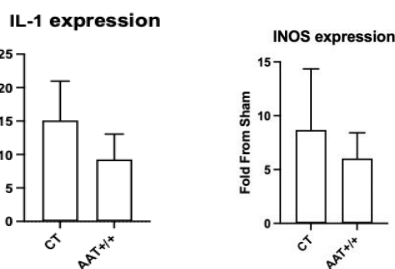
**Methods** **A. Wild-type mice** underwent inner ear injury. 9  $\mu$ L of either saline, clinical-grade AAT (180 mg/kg), dexamethasone (4 mg/kg) or both were applied to the middle ear on days 0,1 and 2 (n=5/group). Vestibular function was evaluated serially. **B. Wild-type mice** (n = 6/group) were injected with gentamicin (100 mg/kg, i.p., daily) and treated with local I.T. h-AAT; the control group was left untreated. On day 9, a BERA exam was performed, and the cochlea was excised for gene analysis by RT-PCR. **C. In vitro, an** epithelial gap closure assay was performed in the presence of AAT, dexamethasone, or both.

## Results

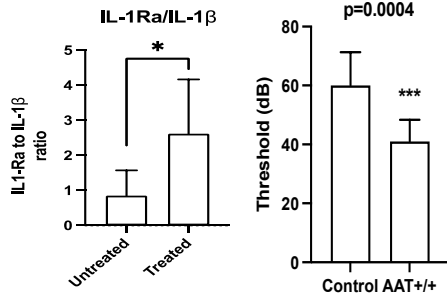
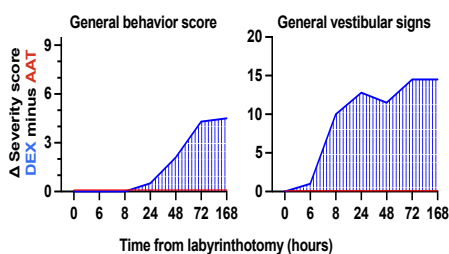
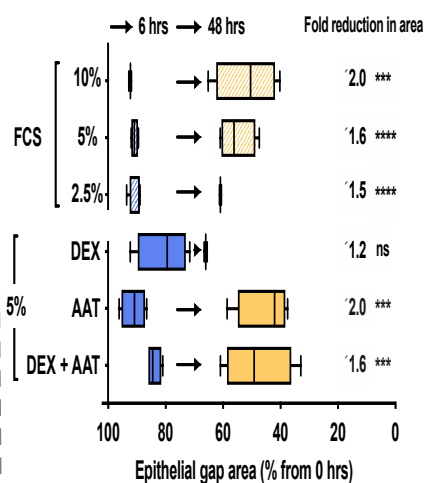
### Vestibular sings DEX versus AAT



### BERA&PCR



### Epithelial gap closure assay (DEX versus AAT)



## Conclusion

Locally applied AAT is superior to locally applied dexamethasone treatment in promoting post-traumatic vestibular recovery in vivo as well as providing cochlear protection against gentamicin-induced inner ear injury in mice.