Intracochlear delivery strategies for gene therapy in hearing loss

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OBJECTIVES

Inner ear delivery offers several advantages for gene therapy, including reduced viral titers, non-systemic administration, and improved transduction efficiency.
Delivery can be performed via the **round window** (RW), **posterior semi-circular canal** (PSCC), or **intra cochleostomy** (IC), each providing access to specific inner ear compartments.

PSCC injections target both endolymphatic & perilymphatic spaces, while RW and IC approaches primarily deliver into the perilymph in adult animals. These techniques are **technically challenging** due to the small size, delicate structure, and deep anatomical location of the inner ear, requiring **high surgical precision** and species-specific anatomical knowledge.

This poster highlights the cross-species application of these techniques, showcasing **successful delivery via PSCC injection in mice, intracochlear** (cochleostomy) **infusion in guinea pigs, and RW injection in swine.**

CONCLUSIONS

These results demonstrate the **effectiveness of inner ear injection techniques** for **gene therapy** across species, with access routes adapted to each model.

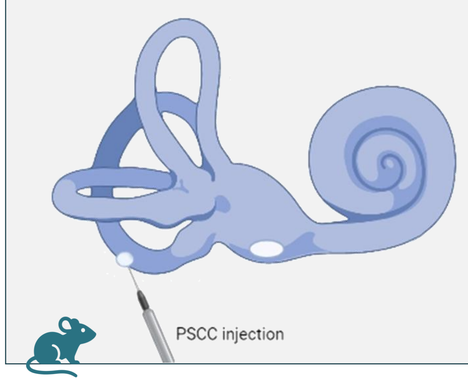
PSCC injection in mice, targeting the vestibular system, shows **no impact on hearing**. In contrast, approaches involving the cochlear base—such as **cochleostomy in guinea pigs**—result in **slight to moderate ABR threshold shifts**. In **swine**, the **round window** provides **reliable cochlear access, confirmed by imaging.**

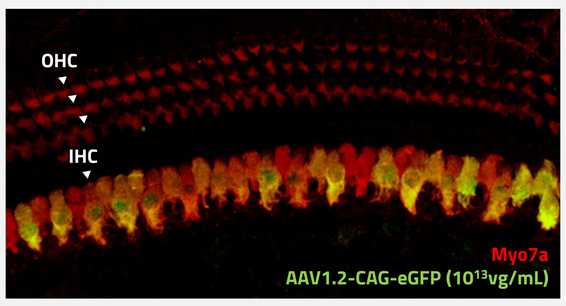
Together, these findings highlight the **importance of route selection by species** and **support the translational potential of these targeted delivery strategies.**

	RW	Cochleostomy	PSCC
Mouse	✓	✓	✓
Guinea pig	✓	✓	✓
Swine	✓	–	–

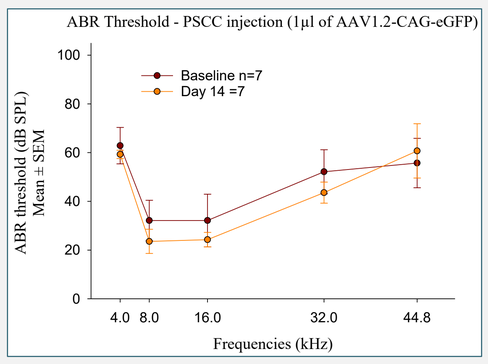
RESULTS & METHODS

FIGURE 1 - **Efficient Transduction of Inner Hair Cells Following PSCC Injection in Adult Mouse Cochlea Without Impact on Hearing**



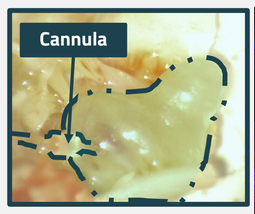


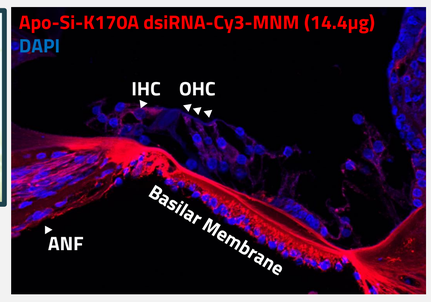
- GFP expression in AAV-transduced cells
- Decreasing GFP expression in inner hair cells (IHCs) from base to apex
  Limited vector diffusion
- Minimal expression in outer hair cells (OHCs)



- **No significant hearing loss** at any frequency 14 days post-injection
- Confirms the **safety of the PSCC injection method**

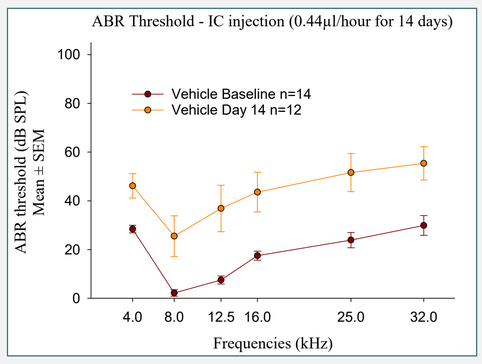
FIGURE 2 - **Efficient MNM-siRNA Delivery & Hearing Shift Following Intracochlear Infusion in Guinea Pig**





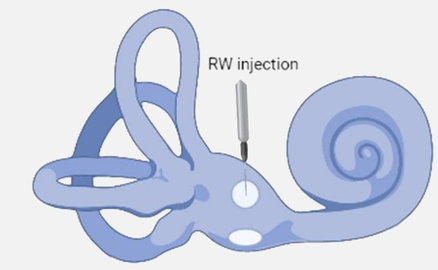
Penetration of dsiRNA in:
- Basilar membrane
- Auditory nerve fibers (ANFs)

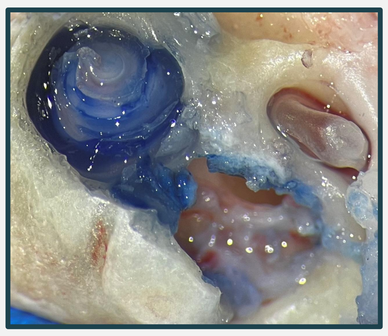
Minimal penetration in Inner and Outer Hair Cells (IHCs and OHCs)



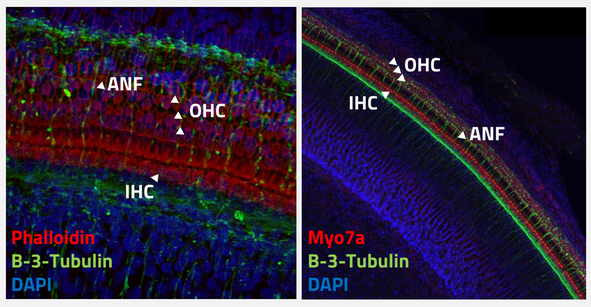
- **Mild hearing loss** in vehicle group due to surgery

FIGURE 3 - **Successful Round Window Injection and Delivery in Swine**





- Injection with Trypan Blue (50 µL)
- **Successful round window delivery** along the entire length of the cochlea.



- Subsequent **cochleogram staining**

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