Precision Genetic Medicines for Inner Ear Disorders

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Disclosure:

Yes, within the last 12 months, I have/had a financial arrangement or affiliation with commercial interests related to the content of this continuing education activity that requires disclosure.

I receive a salary from and hold equity in Akouos, Inc.
Gene Augmentation
Gene Knockdown
Genome Editing

Potential for one-time delivery to restore normal protein function or selectively regenerate the hearing circuit
Monogenic Hearing Disorders
- >150 genes implicated
- Millions of families affected

Acquired / Environmental Hearing Loss
- Increasing understanding of underlying biology & pathophysiology
- >900 million affected by 2050
2017

First FDA-approved *in vivo* gene therapy – treatment of rare inherited retinal disorder
FDA-approved AAV gene therapy for infants with spinal muscular atrophy
Over 70 Gene Therapies Currently in Clinical Trials

Newly Initiated AAV Gene Therapy Trials

- 2009: Phase I (3), Phase II (2), Phase III (1)
- 2010: Phase I (3), Phase II (2), Phase III (2)
- 2011: Phase I (2), Phase II (2), Phase III (1)
- 2012: Phase I (2), Phase II (2), Phase III (1)
- 2013: Phase I (2), Phase II (2), Phase III (1)
- 2014: Phase I (2), Phase II (2), Phase III (1)
- 2015: Phase I (2), Phase II (2), Phase III (1)
- 2016: Phase I (2), Phase II (2), Phase III (1)
- 2017: Phase I (2), Phase II (2), Phase III (1)
- 2018: Phase I (2), Phase II (2), Phase III (1)

Primary Tissue Target:
- Eye
- Brain / CNS
- Liver
- Muscle
- Bone
- Heart
- Others

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Enclosed compartments → opportunity for local, targeted delivery
Reduced immune surveillance → lower levels of pre-existing neutralizing antibodies
Non-dividing target cells → potential for one-time delivery to provide life-long benefit
Unique Challenges of the Ear

Outer hair cells

Inner hair cell

Outer hair cells
Novel AAV Vector Platform

Minimally-Invasive Surgical Delivery
The Adeno-associated Viral Anc80 Vector Efficiently Transduces Hair Cells in Cynomolgus macaques (M. fascicularis): ... Darcy for the dissection of 2 of the 6 NHP cochleae, and Jen Wellman and Eva Andres-Mateos for helpful revisions.
Trans-RWM Delivery in the NHP (Cynomolgus macaque)
Opportunity to Target Multiple Cell Types Previously Thought to be Inaccessible