

# Report: Gene therapy for Usher syndrome, type IC

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Harvard Medical School





# Model for Ush1c.216G>A (Acadian mutation)



Jennifer Lentz



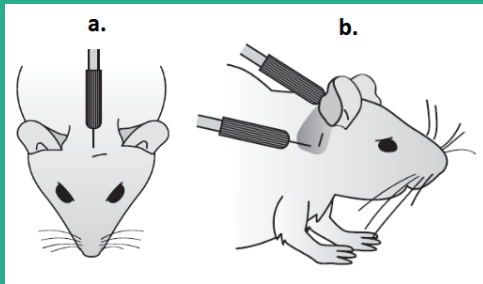
Characterization of the model  
(Hearing, Balance, Histology and Physiology)



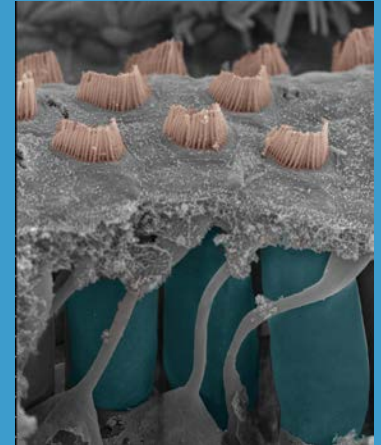
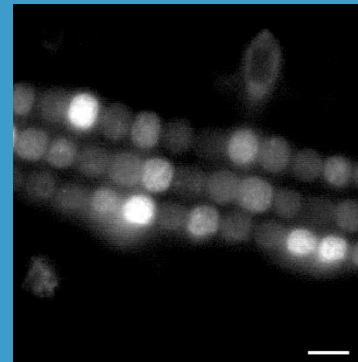
Development of gene therapy vectors  
Specific for the 216 G>A mutation

# Evaluation of the therapeutic benefit

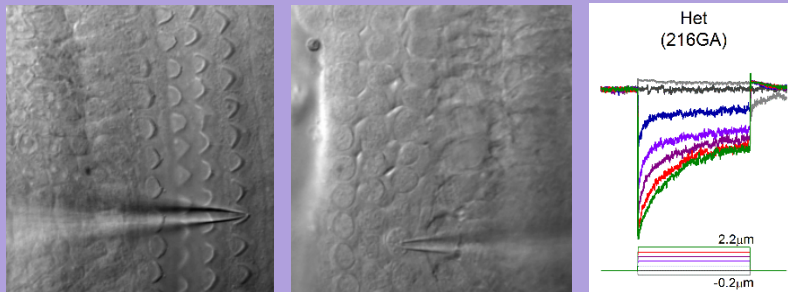
## Auditory and Balance Testing



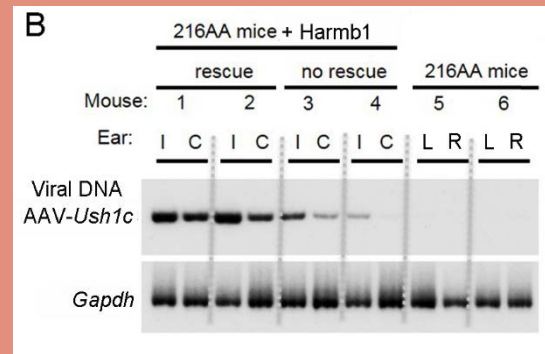
## Imaging



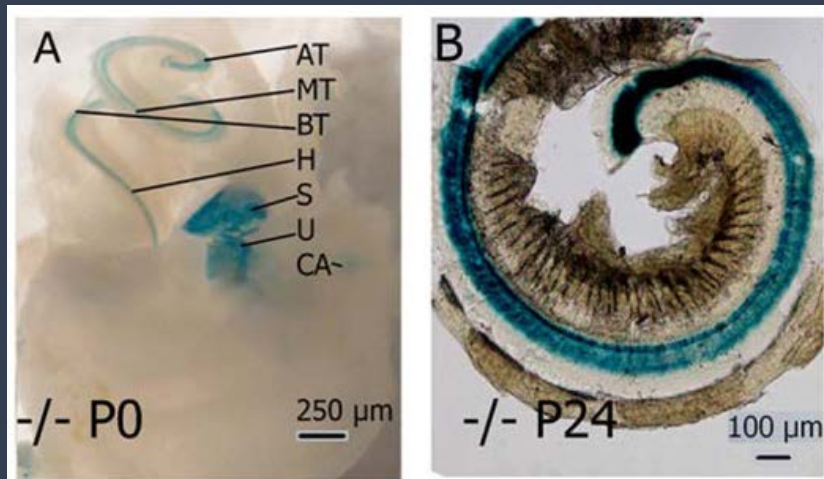
## Cellular physiology



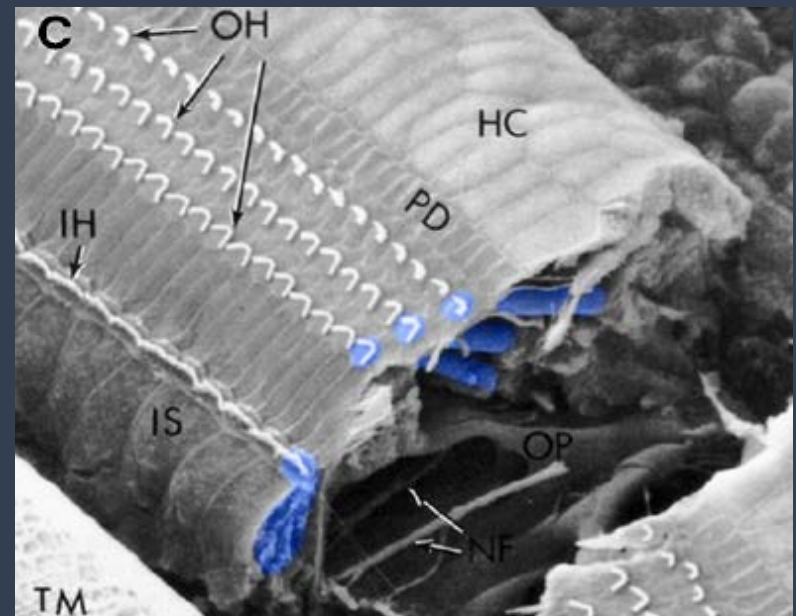
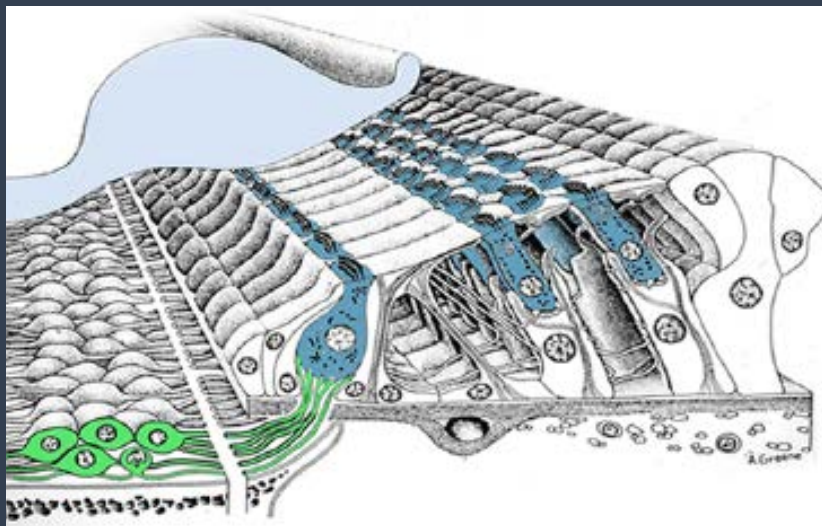
## Molecular work



# Development of gene therapy vectors Specific for the 216 G>A mutation

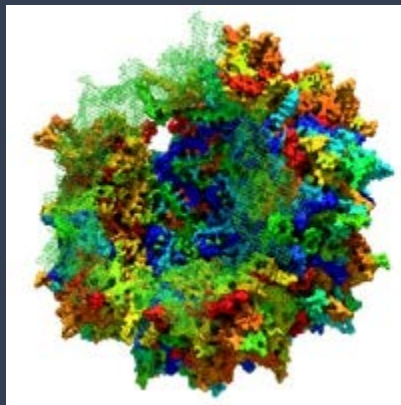
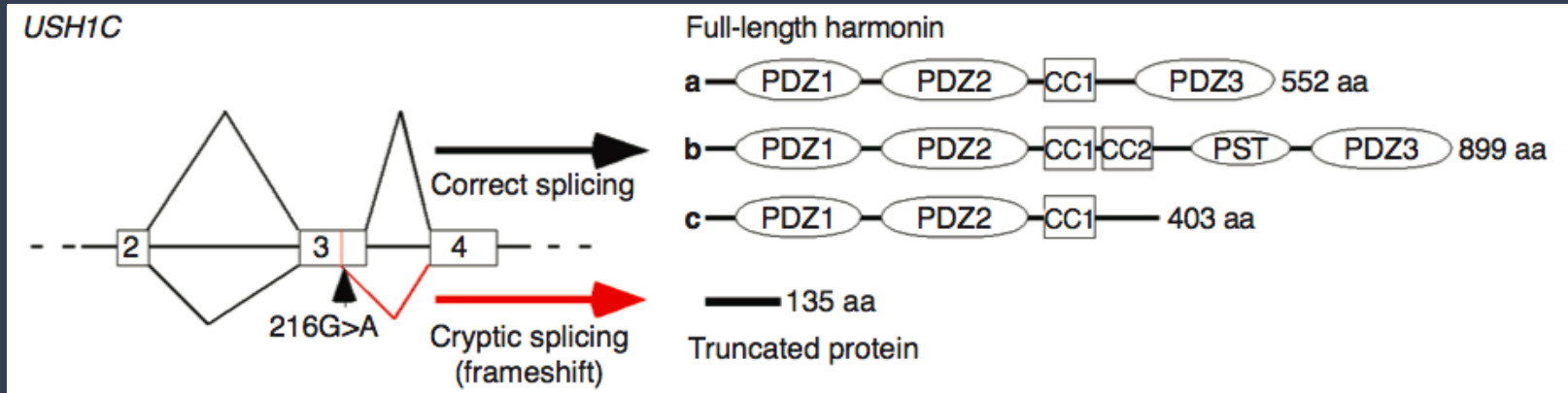


Tian et al. 2010

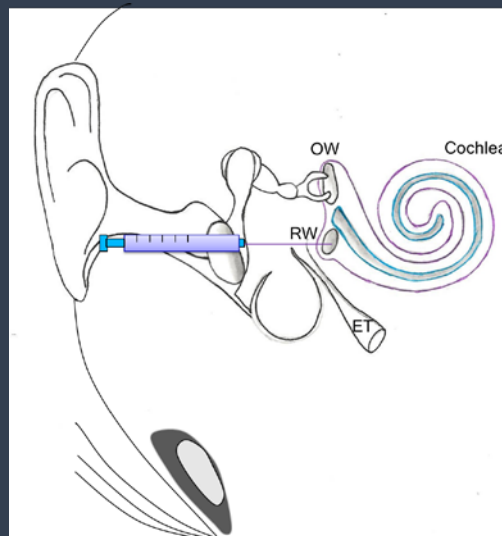


Geleoc and Holt, 2014

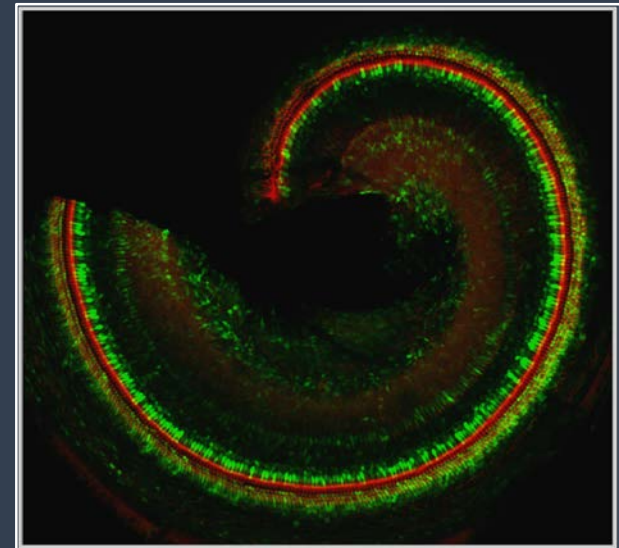
# Development of gene therapy vectors Specific for the 216 G>A mutation



Vector with  
gene fragment



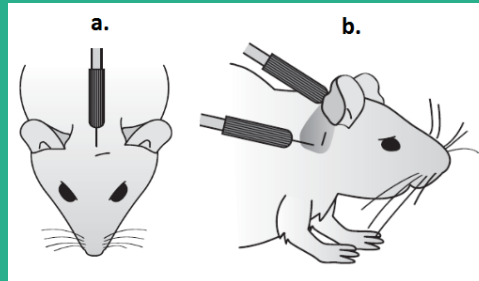
Round Window  
Membrane Injection



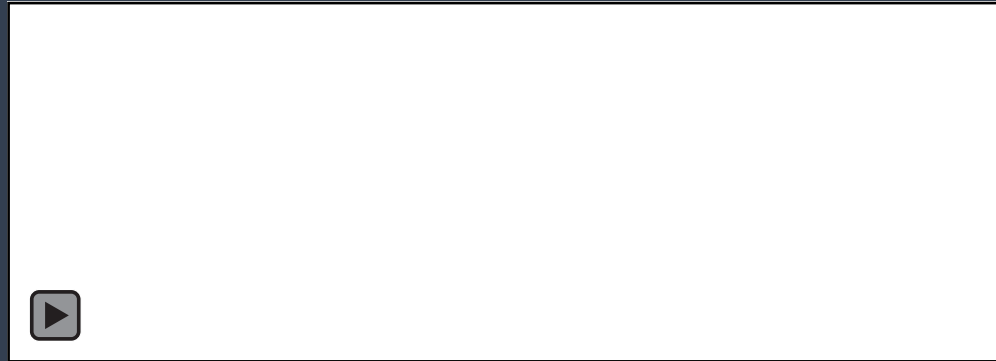
AAV vector (Green)

# Evaluation of the therapeutic benefit

## Auditory and Balance Testing

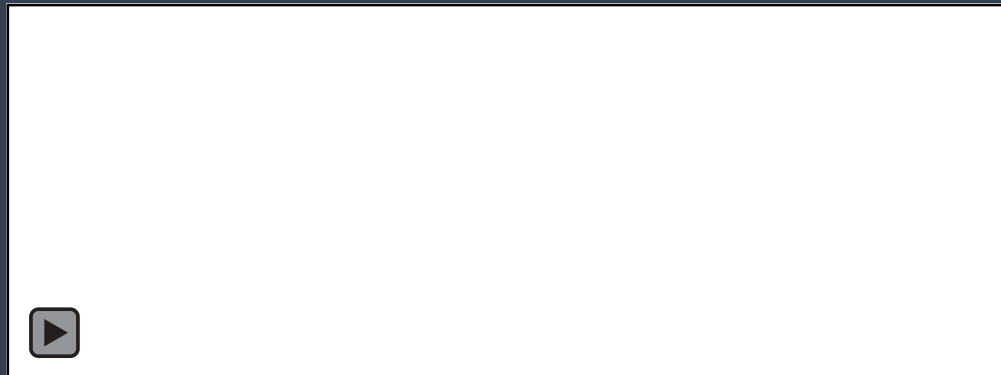


# Open Field Behavior



Mutant

Control

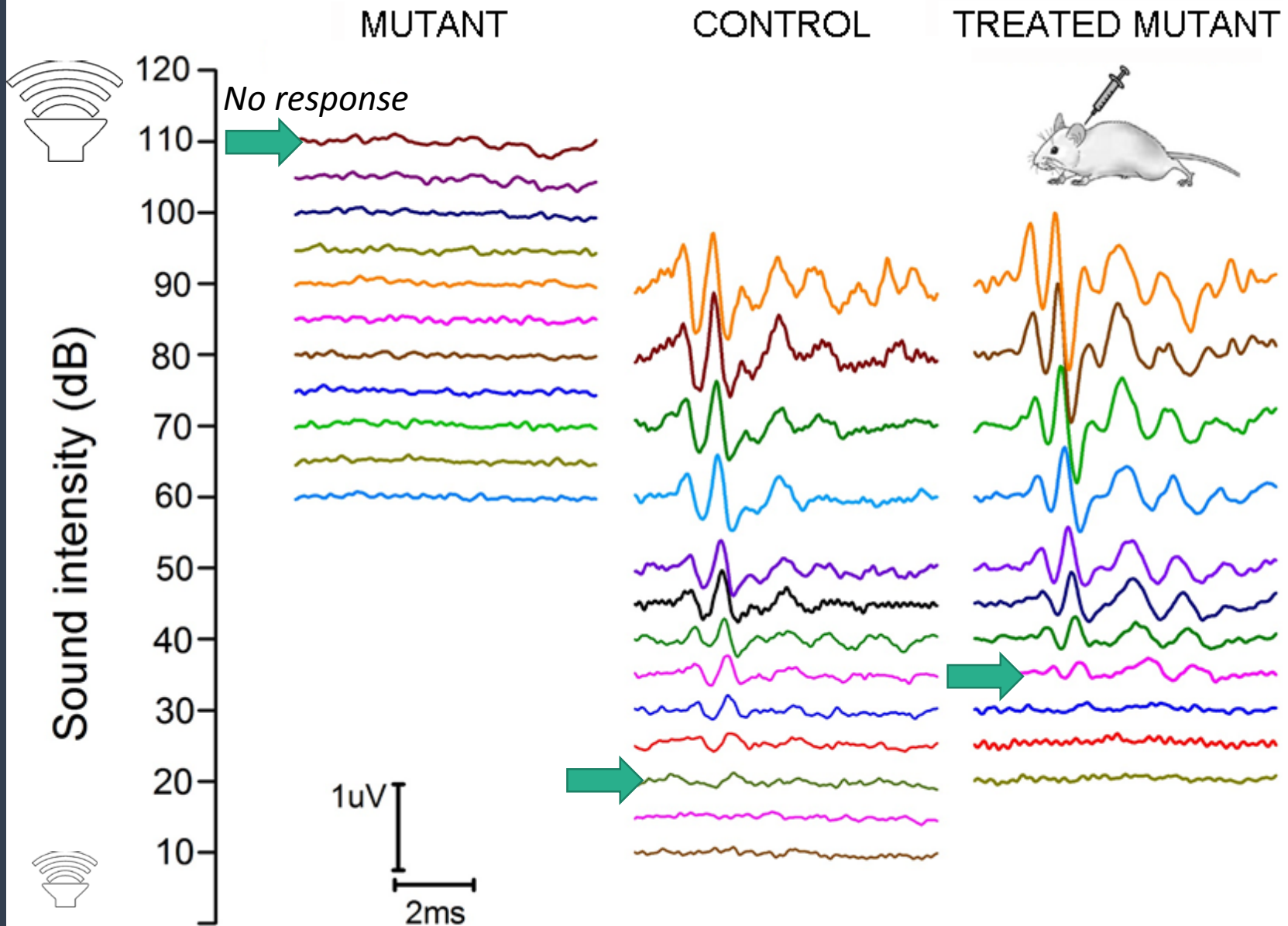


Mutant after treatment



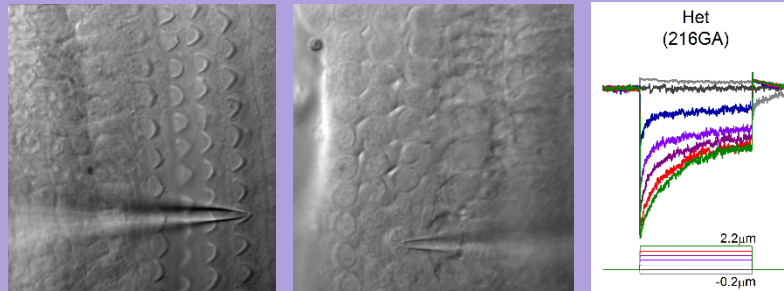


# Auditory Brainstem Responses



# Evaluation of the therapeutic benefit

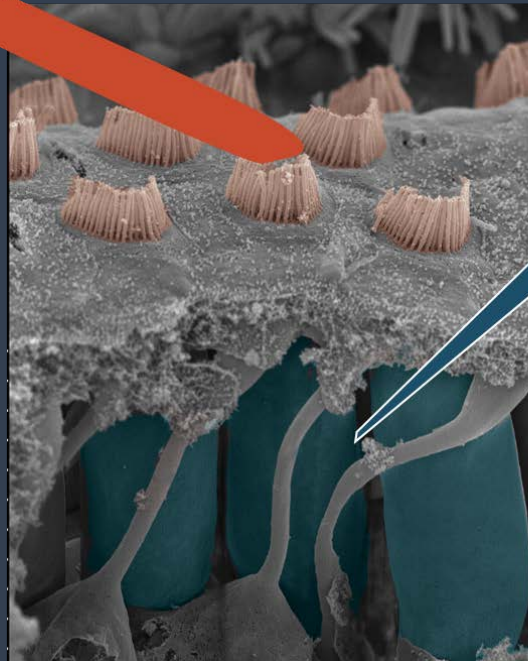
## Cellular physiology



# Hair Cell Physiology



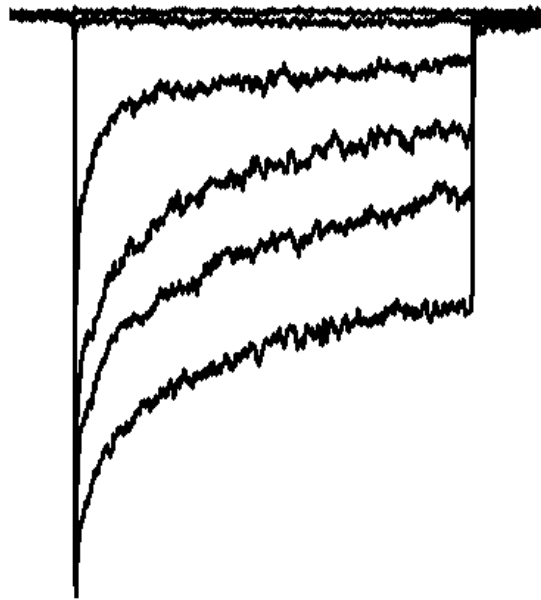
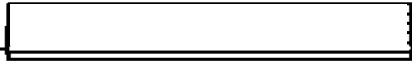
Stimulus pipette



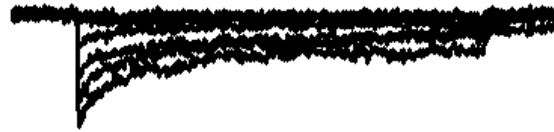
Recording electrode

# Recovery of mechano-sensitivity

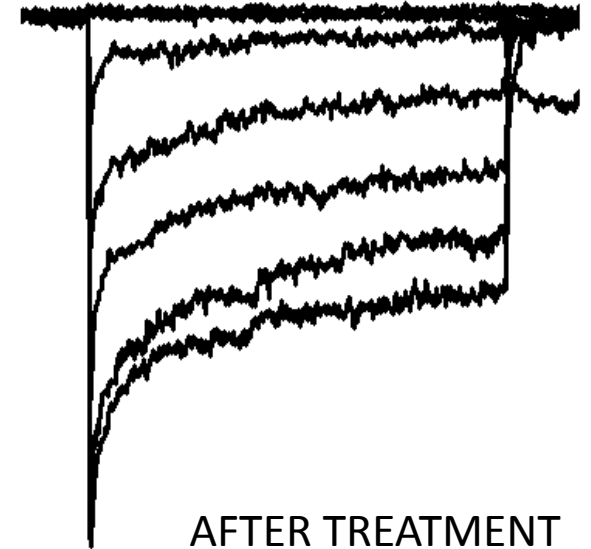
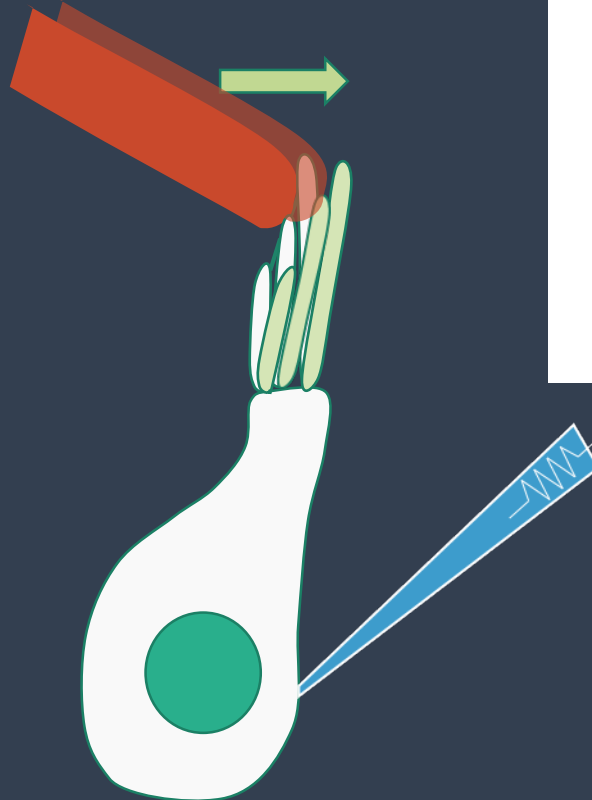
STIMULUS



CONTROL



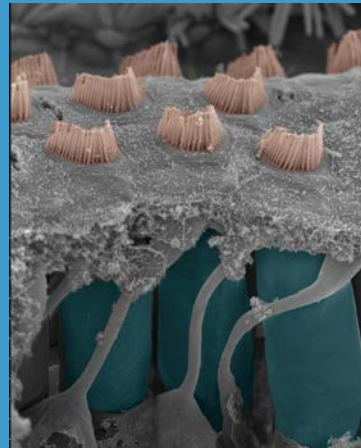
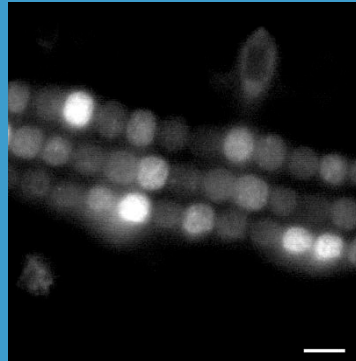
MUTANT



AFTER TREATMENT

# Evaluation of the therapeutic benefit

## Imaging



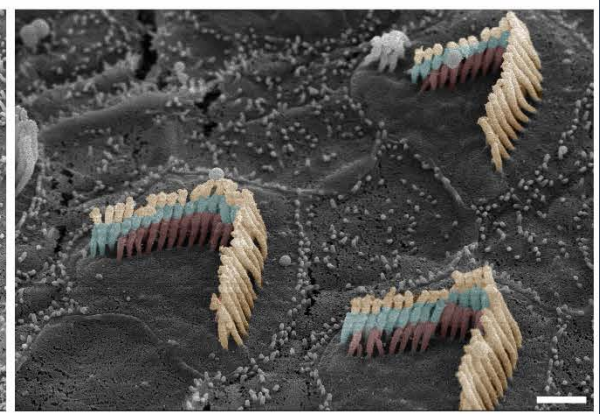
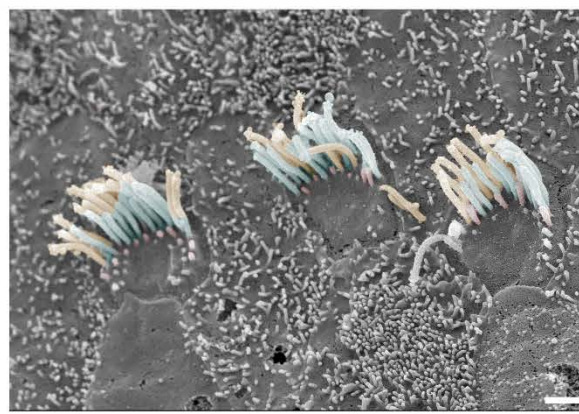
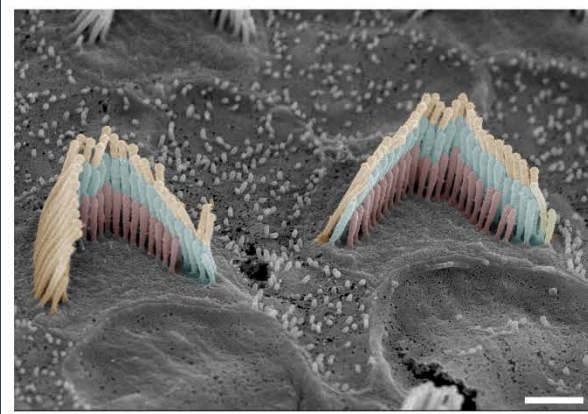
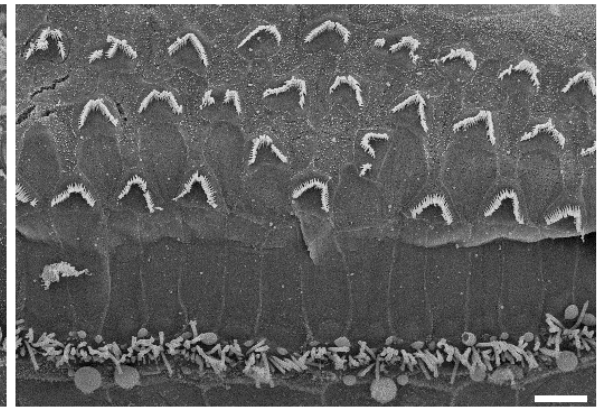
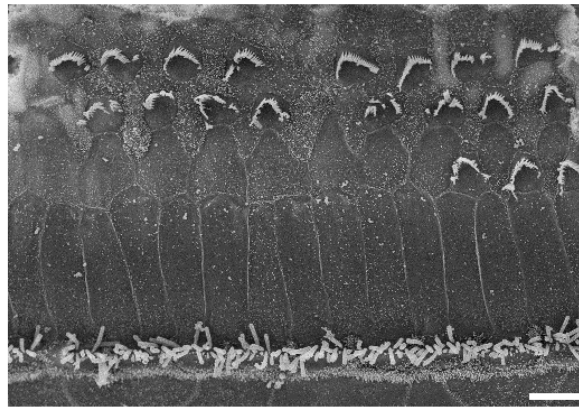
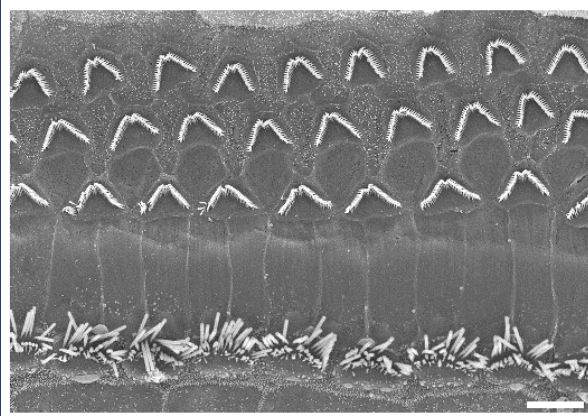
# Hair bundles recovery



CONTROL

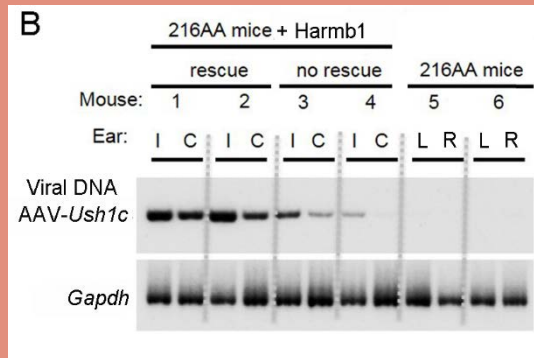
MUTANT

MUTANT AFTER TREATMENT

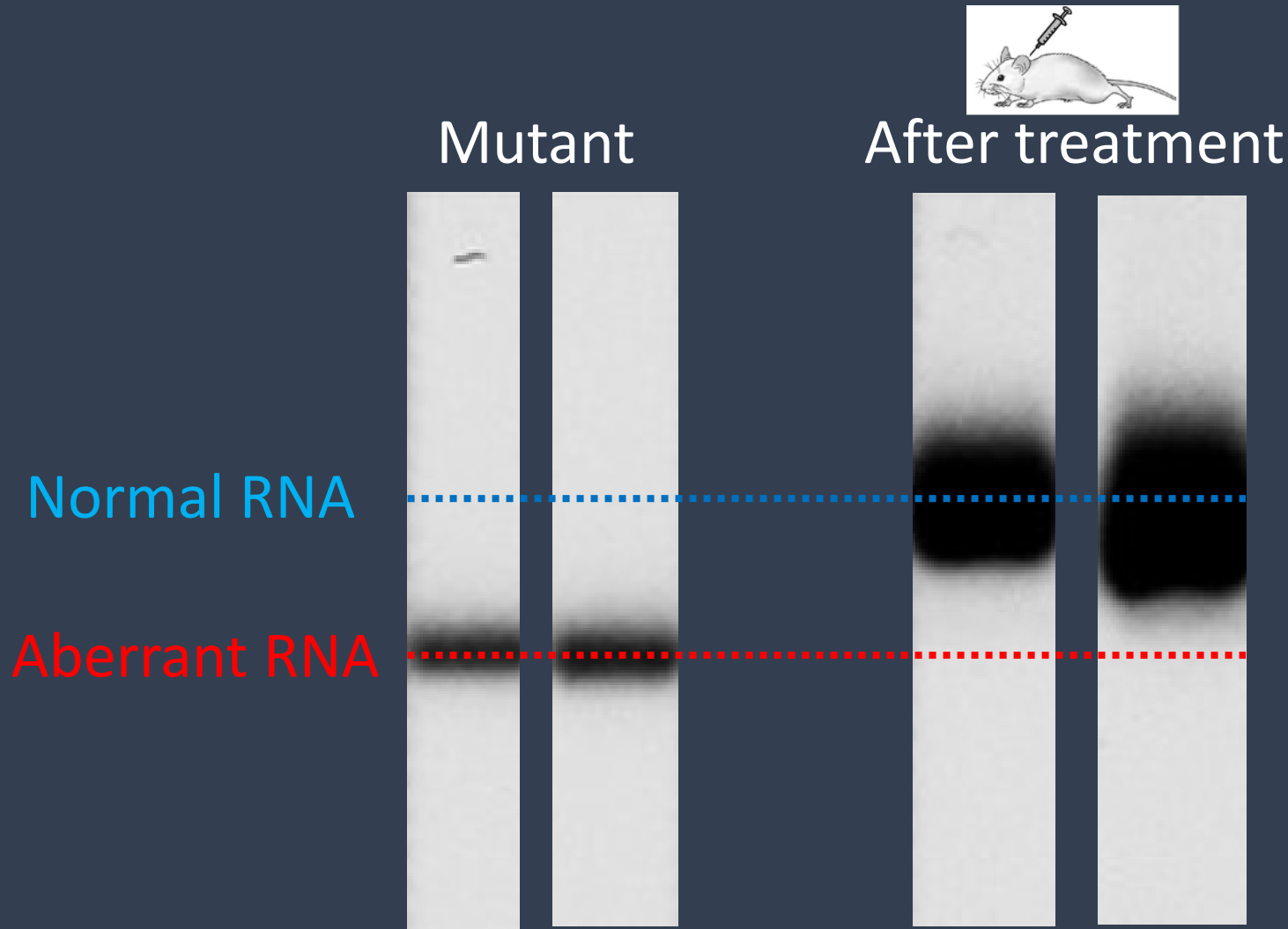


# Evaluation of the therapeutic benefit

## Molecular work

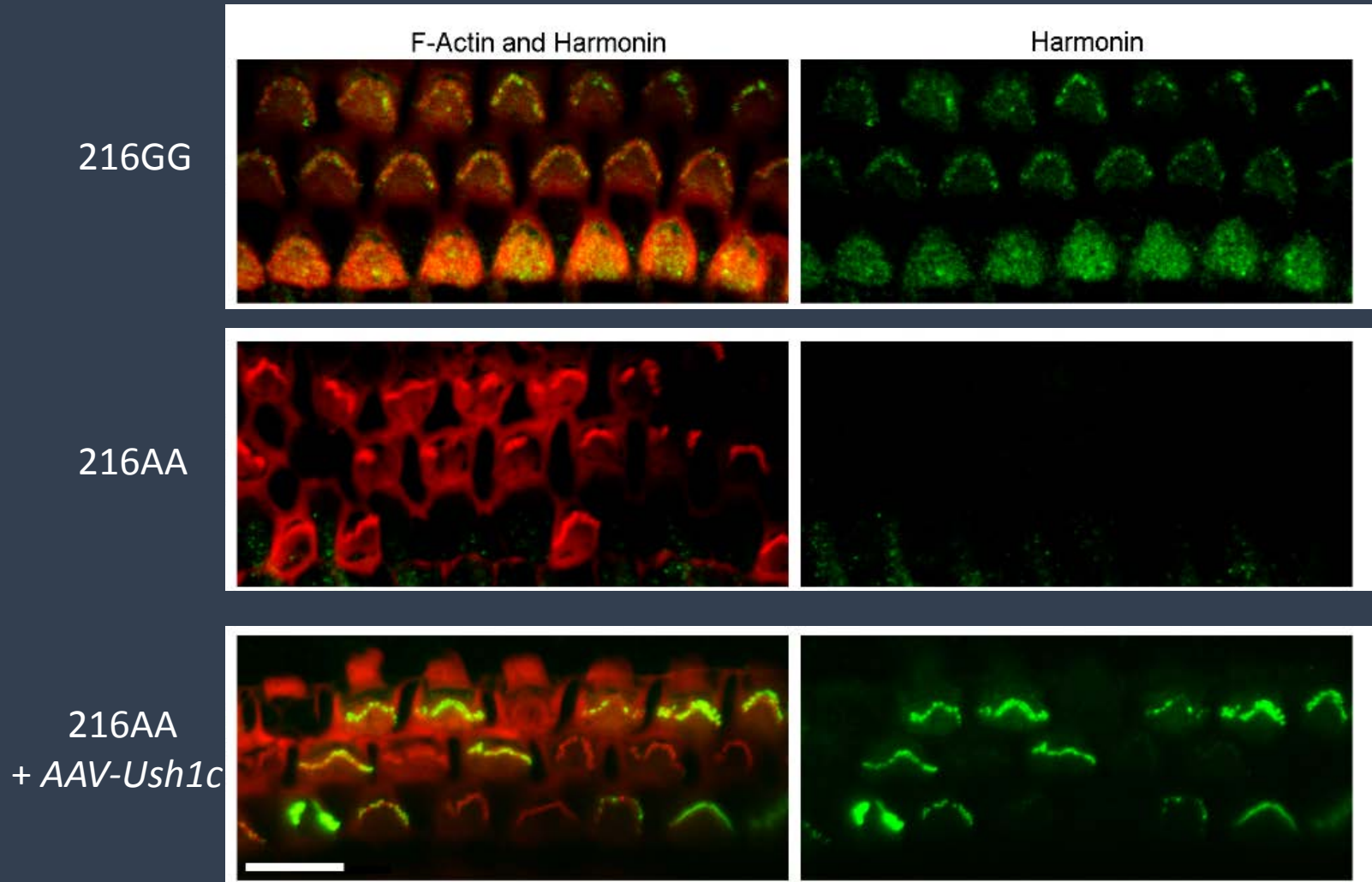


# Correct genetic message (RNA) is detected In mice that have received the vector





# Protein is detected in recovered subjects



# Summary



We have developed gene therapy vectors specific for the 216 G>A *Ush1c* mutation

Rescue of Auditory and balance function

Survival of sensory hair cells and recovery of hair bundle morphology

Sensory hair cells maintain mechanosensation

Normal RNA and protein

# THANKS TO OUR SPONSORS!

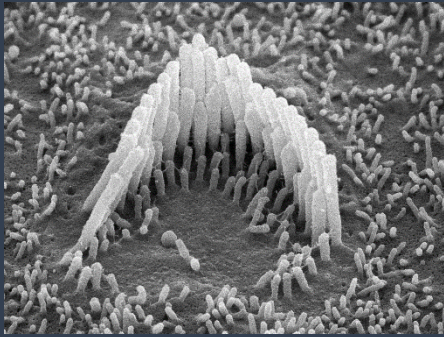


**Boston Children's Hospital**  
Manton Center for Orphan Disease Research



**FOUNDATION  
FIGHTING  
BLINDNESS**

**fb** **fondation  
bertarelli**



# THANKS!

## Boston Children's Hospital

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