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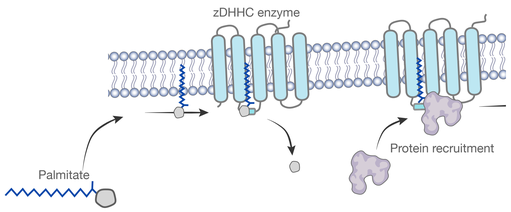
PALMITOYLATION AFFECTS THE FORMATION OF HAIR CELLS IN THE ZEBRAFISH INNER EAR

INTRO

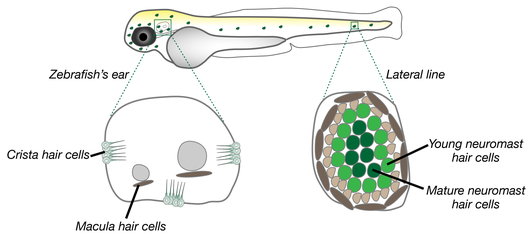
Palmitoylation:

- Adds palmitate to the protein
- Drives protein re-localisation in the cell
- Performed by a family of 23 enzymes (zDHHCs)



Hair cells:

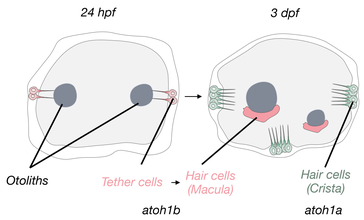
- Primary (immotile) cilia cells
- Sense sound/movement and transmit in to neurones
- Located in the zebrafish inner ear and lateral line



Hypothesis: Palmitoylating Enzymes are Involved in Hair Cell Formation

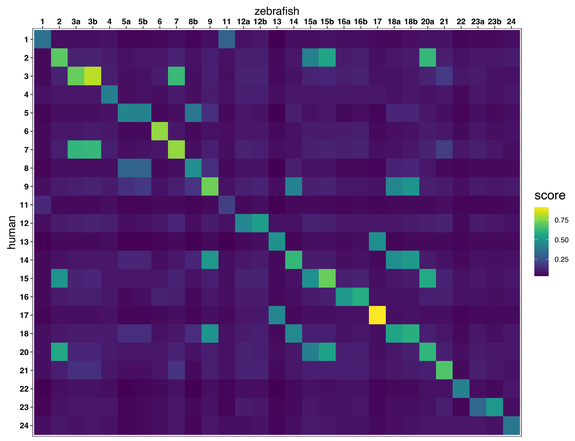
Inner ear:

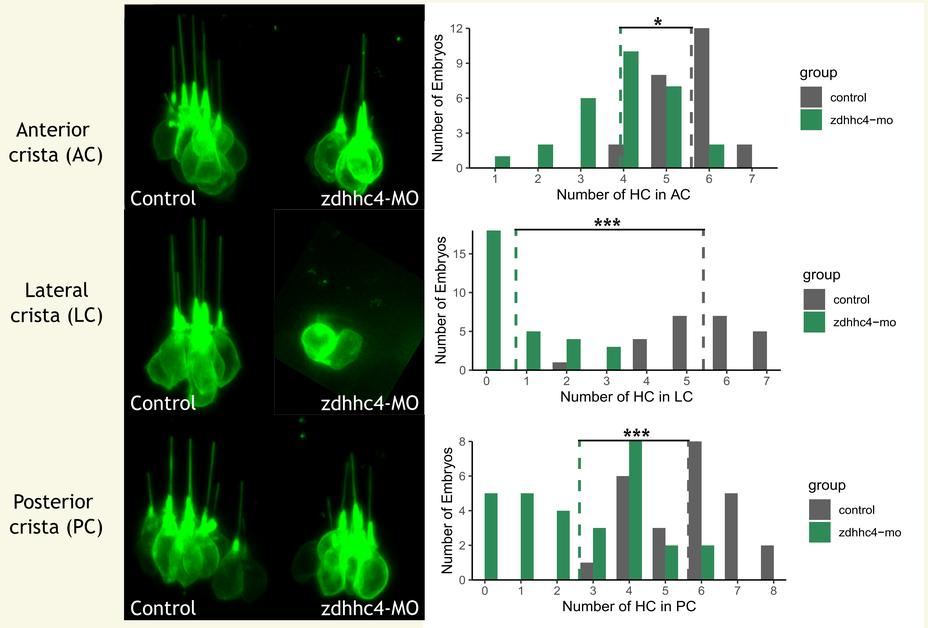
- Contains two different hair cell types
- Macula hair cells arise from tether cells (*atoh1b*)
- Crista hair cells appear at 3dpf (*atoh1a*)



zDHHC palmitoylating enzymes:

- Conserved between human and zebrafish
- Zebrafish has orthologs for all human's zDHHCs



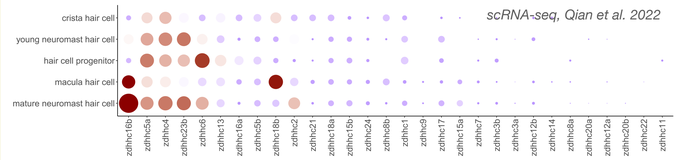


Downregulation of zDHHC4 palmitoylating enzyme results in fewer number of hair cells (pou4f3) in the cristae of the inner ear of 3dpf zebrafish larva

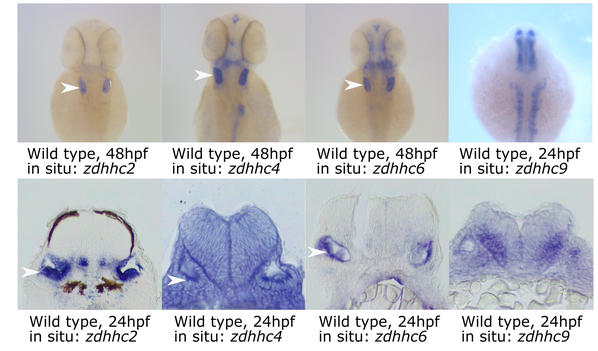
WHAT IS THE MECHANISM?

DATA

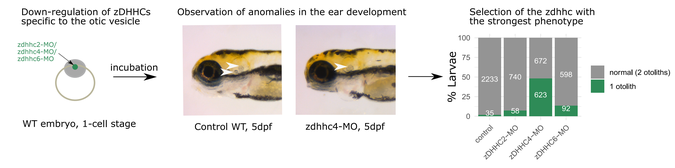
Are palmitoylating enzymes expressed in hair cells?

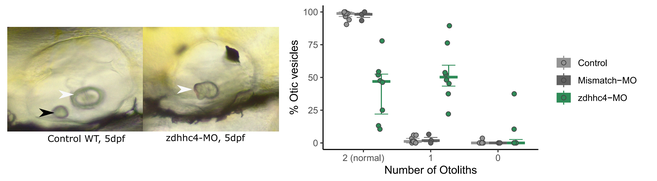


- zDHHCs 16b,5a,4,23b,6,18b,2 are expressed in ***hair cell types*** in scRNA-seq data
- zDHHCs expression was validated at the ***tissue level*** by in-situ hybridisation
- zDHHCs 2,4,5a,6,18a are expressed in ***the otic vesicle***

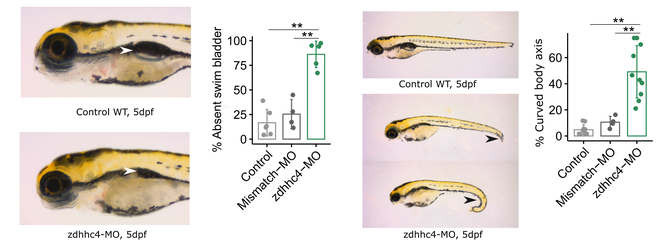


What happens if palmitoylating enzymes aren't there?

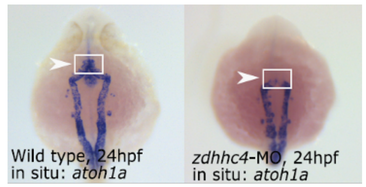




- ***Otolith fusion*** - signature phenotype of cilia mutants
- ***zDHHC4*** has ***the strongest*** otolith fusion ***phenotype***
- ***Absence of swim bladder*** and ***curved body axis*** are other observed phenotypes



How do palmitoylating enzymes regulate hair cell formation?



- zDHHC4 down-regulation results in ***misexpression of atoh1a***
- *Atoh1a* is responsible for ***crista hair cell formation***