The American Otological Society

CLINICIAN SCIENTIST AWARD 2008-2010

"Differentiation of Inner Ear Stem Cells"

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AMOUNT AWARDED BY AOS: $160,000

ONGOING FUNDING: RNID/Cystic fibrosis foundation 2022-25, NIH/NIDCD RO1, K08, R21, U24/

PUBLICATIONS: (*most impactful five*)

Chai R, Kuo B, Wang T, Liaw EJ, Xia A, Jan TA, Liu Z, Taketo MM, Oghalai JS, Nusse R, Zuo J, Cheng AG. (2012) Wnt signaling induces proliferation of sensory precursors in the postnatal mouse cochlea. Proc Natl Acad Sci USA, 109(21):8167-72, 10.1073/pnas.1202774109.

Jan TA, Chai R, Sayyid ZN, van Amerongen R, Xia A, Wang T, Sinkkonen ST, Levin JR, Zheng Y, Heller S, Nusse R*, Cheng AG*. (2013) Tympanic border cells are Wnt-responsive and act as progenitors for the postnatal mouse cochlear cells. Development 140(6):1196-1206, DOI: 10.1242/dev.087528.

Cox BC, Chai R, Lenoir A, Liu Z, Zhang LL, Nguyen DH, Chalasani K, Steigelman KA, Fang J, Rubel EW, Cheng AG*, Zuo J*. (2014) Spontaneous hair cell regeneration in the neonatal mouse cochlea in vivo. Development 141(4): 816-829 doi:10.1242/dev.103036.

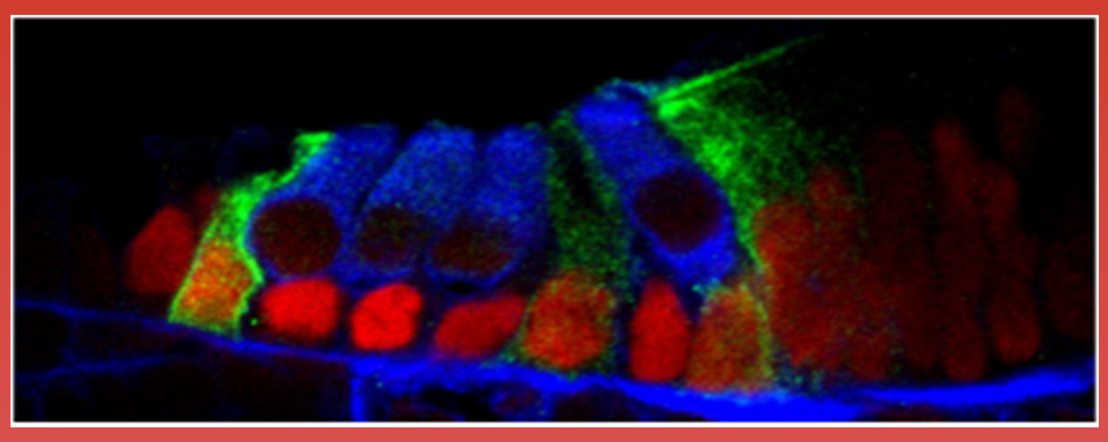
Atkinson P, Dong Y, Gu S, Liu W, Huarcaya Najarro E, Udagawa T, Cheng AG. (2018) Sox2 haploinsufficiency primes regeneration in the mouse cochlea. J Clin Invest. Apr 2;128(4):1641-1656. doi: 10.1172/JCI97248.

Udagawa T, Atkinson PJ, Milon B, Abitbol JM, Song Y, Sperber M, Huarcaya-Najarro E, Scheibinger M, Elton R, Hertzano R, Cheng AG. Lineage-tracing and translatomic analysis of damage inducible mitotic cochlear progenitors identifies candidate genes regulating regeneration. (2021) PLoS Biol Nov 10;19(11):e3001445. doi: 10.1371/journal.pbio.3001445.

RESEARCH SUMMARY: The mammalian cochlea harbors endogenous hair cell and supporting cell progenitors particularly in the neonatal mouse period.

OUTCOMES: This has led to a new line of research where additional pathways are being evaluated to enhance hair cell regeneration.

Lgr5 marks regenerative supporting cells in the neonatal mouse cochlea.



FURTHER FUNDING HAS ENBLED US TO EXPAND OUR RESEARCH TO: Examine dynamic gene expression during hair cell and supporting cell regeneration; examine pathways that enhance maturation of regenerated hair cells; characterize vestibular hair cell regeneration

LAY SUMMARY OF FINDINGS AND IMPLICATIONS OF THIS RESEARCH: Hair cell regeneration underlies most forms of hearing loss, since it is a final common pathway of genetic, noise, and drug-induced hearing loss. As mammals do not regenerate hair cells, therapeutics leading to hair cell regeneration can be therapeutic. Our long-term goal is to restore hearing via cell regeneration.