The American Otological Society

CLINICIAN SCIENTIST AWARD 2008 - 2010

"Molecular Mechanisms of Noise-Induced Delayed Primary Auditory Neuropathy"

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AMOUNT AWARDED BY AOS: $120,000

ONGOING FUNDING: The AOS award helped me get the K08 award from NIH titled, "Understanding Noise-Induced Delayed Primary Degeneration of the Auditory Nerve".

Miniature Intracochlear Imaging Probe Based on Micro Optical Coherence Tomography for Cellular-Level Diagnosis and Therapy of Hearing Loss (2021-2024); $1,077,882; Endomicroscope for diagnosis and therapy of hearing loss; WayVector, Inc; (2019-2024) $1,535,519; Preclinical Validation of Photobiomodulation Therapy for Sensorineural Hearing Loss (2019-2024); Uniformed Services University Medical Research HU00011920056; $788,845; Human Ear Cellular Atlas (2023-2028) NIH U24DC020857 $3,193,023; Targeting HMGB1 to improve hearing and enhance therapy for NF2 Vestibular Schwannomas (2024-2028) NIH R01DC020724 $749,476

PUBLICATIONS: Publications directly related to noise-induced primary auditory neuropathy.

Jensen JB, Lysaght AC, Liberman MC, Qvortrup K, Stankovic KM. Immediate and delayed cochlear neuropathy after noise exposure in pubescent mice. PLoS One. 2015 May 8;10 (5):e0125160. doi: 10.1371/journal.pone.0125160. PMID: 25955832; PMCID: PMC4425526.

Yang X, Pu Y, Hsieh CL, Ong CA, Psaltis D, Stankovic KM. Two-photon microscopy of the mouse cochlea in situ for cellular diagnosis. J Biomed Opt. 2013 Mar;18(3):31104. doi: 10.1117/1.JBO.18.3.031104. PMID: 23165736.

Groth JB, Kao SY, Briët MC, Stankovic KM. Hepatocyte nuclear factor-4 alpha in noise-induced cochlear neuropathy. Dev Neurobiol. 2016 Dec;76 (12):1374-1386. doi: 10.1002/dneu.22399. Epub 2016 May 9. PMID: 27112738.

Landegger LD, Vasilijic S, Fujita T, Soares VY, Seist R, Xu L, Stankovic KM. Cytokine Levels in Inner Ear Fluid of Young and Aged Mice as Molecular Biomarkers of Noise-Induced Hearing Loss. Front Neurol. 2019 Sep 11;10:977. doi: 10.3389/fneur.2019.00977. PMID: 31632328; PMCID: PMC6749100.

Seist R, Tong M, Landegger LD, Vasilijic S, Hyakusoku H, Katsumi S, McKenna CE, Edge ASB, Stankovic KM. Regeneration of Cochlear Synapses by Systemic Administration of a Bisphosphonate. Front Mol Neurosci. 2020 Jul 14;13:87. doi: 10.3389/fnmol.2020.00087. PMID: 32765216; PMCID: PMC7381223.

Seist R, Landegger LD, Robertson NG, Vasilijic S, Morton CC, Stankovic KM. Cochlin Deficiency Protects Against Noise-Induced Hearing Loss. Front Mol Neurosci. 2021 May 24;14:670013. doi: 10.3389/fnmol.2021.670013. PMID: 34108864; PMCID: PMC8180578.

Iyer JS, Yin B, Stankovic KM, Tearney GJ. Endomicroscopy of the human cochlea using a micro-optical coherence tomography catheter. Sci Rep. 2021 Sep 9;11(1):17932. doi: 10.1038/s41598-021-95991-8. PMID: 34504113; PMCID: PMC8429662.

Natarajan N, Batts S, Stankovic KM. Noise-Induced Hearing Loss. J Clin Med. 2023 Mar 17;12(6):2347. doi: 10.3390/jcm12062347. Erratum in: J Clin Med. 2024 Feb 07;13(4): PMID: 36983347; PMCID: PMC10059082.

Fujita T, Seist R, Kao SY, Soares V, Panano L, Khetani RS, Landegger LD, Batts S, Stankovic KM. miR-431 secreted by human vestibular schwannomas increases the mammalian inner ear's vulnerability to noise trauma. Front Neurol. 2023 Oct 9;14:1268359. doi: 10.3389/fneur.2023.1268359. PMID: 37885485; PMCID: PMC10598552.

RESEARCH SUMMARY: Moderate acoustic overexposure in adult rodents is known to cause acute loss of synapses on sensory inner hair cells (IHCs) and delayed degeneration of the auditory nerve, despite the completely reversible temporary threshold shift (TTS) and morphologically intact hair cells. We demonstrated that a cochlear synaptopathy followed by neuropathy occurs after noise exposure in pubescence, and that there is a fine line between neuropathic and non-neuropathic noise levels associated with TTS in the pubescent cochlea. Furthermore, we identified molecular pathways involved in this synaptopathy and demonstrated that their targeting can be therapeutic.

OUTCOMES: Definition of neuropathic versus non-neuropathic noise levels associated with temporary threshold shift in pubescent mice; 2) K08 award following AOS award

FURTHER FUNDING HAS ENABLED US TO EXPAND OUR RESEARCH TO: 1) Cellular-level imaging of the human inner ear to establish precise diagnosis and guide therapy; 2) Drug repurposing for sensorineural hearing loss; 3) Molecular mechanisms of Vestibular schwannoma-induced hearing loss; 4) Human induced pluripotent stem cell-derived models of hearing loss 5) Novel devices for inner ear stimulation and monitoring

LAY SUMMARY OF FINDINGS AND IMPLICATIONS OF THIS RESEARCH: Disabling hearing loss presently affects nearly half a billion people in the world. This figure is expected to increase to 2.5 billion people by 2050, with the associated economic cost estimated currently at approximately $800 billion. Despite these staggering statistics, the cellular basis of the most common type of hearing loss, called sensorineural hearing loss (SNHL), is unclear in living people. Consequently, available therapies are severely limited and there are no drugs FDA approved for the treatment of SNHL. Our research addresses these unmet medical needs through domain-specific customization and fusion of tools from molecular biology, bioinformatics, systems neuroscience, biotechnology, and otologic surgery.