The American Otological Society

CLINICIAN SCIENTIST AWARD 2006-2008

"ErbB Regulation of Vestibular Schwannoma Tumorigenesis"

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AMOUNT AWARDED BY AOS: $160,000

ONGOING FUNDING: $1.8M NIDCD K08 grant for further vestibular schwannoma molecular studies and $1.3M Department of Defense grant for NF2 clinical drug trial using RAD001 for growing NF2-related vestibular schwannoma.

PUBLICATIONS:

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Ahmad Z, Brown C, Patel AK, Ryan AF, Ongkeko RW, Doherty JK. Merlin knockdown in human Schwann cells: clues to vestibular schwanoma tumorigenesis. *Otol Neuroto.l* 31(3):460-6, 2010. PMID: 20195187.

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Yi D, Kuo SZ, Zheng H, Abhold EL, Brown CM, Doherty JK, Wang-Rodriguez J, Harris JP, Ongkeko WM. Activation of PDGFR and EGFR Promotes the Acquisition of a Stem Cell-like Phenotype in Schwannomas. *Otol Neurotol*. 33(9):1640-7, 2012. PMID: 22935817.

Toren A, Reichardt JK, Andalibi A Hsu NY, Doherty J, Slattery W, Mehrian-Shaw R. Novel age dependent targets in vestibular schwannoma. *Hum Genomics.* 8;10, 2014. PMID 24980480.

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RESEARCH SUMMARY: I studied both sporadic and neurofibromatosis 2-related vestibular schwannoma tumors at the molecular level to determine erb-b2 family receptor and ligand (i.e., growth factor) expression patterns and differences between the two tumor types. We further analyzed estrogen and progesterone receptor involvement. The goal of this research was to determine molecular targets for therapy to control tumor growth.

OUTCOMES: Based on my research, many clinical trials were initiated to treat NF2-related vestibular schwannomas using erbB family receptor inhibitors and RAD001. Some of these studies have been promising.

LAY SUMMARY OF FINDINGS AND IMPLICATIONS OF THIS RESEARCH: RAD001 reduced vestibular schwannoma tumor growth rate in 25% of patients enrolled. In one-third of Neurofibromatosis 2 patients enrolled, growth rate was stabilized.