

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF OTORHINOLARYNGOLOGY

Robert K. Duncan, Ph.D., assistant professor of otorhinolaryngology, Department of Otorhinolaryngology, Medical School, is recommended for promotion to associate professor of otorhinolaryngology, with tenure, Department of Otorhinolaryngology, Medical School.

Academic Degrees:

Ph.D.	1999	University of Pennsylvania
M.S.	1993	Virginia Polytechnic Institute and State University
B.S.	1992	Virginia Polytechnic Institute and State University

Professional Record:

2003-present	Assistant Professor of Otorhinolaryngology, University of Michigan
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Summary of Evaluation:

Teaching: Dr. Duncan is a gifted and enthusiastic teacher who is a lecturer and course director for two graduate level courses (20-25 students) in the Neuroscience Program: Neuroscience 602/614, The Neuroscience of Hearing, and Neuroscience 601/611, Excitable Membranes. These courses integrate knowledge of how cells signal in the peripheral and central nervous system. Since 2009 he also has given lectures in PHYS577, Membrane and Cell Physiology (15+ students). His student evaluations are among the best in the department and frequently comment upon the infectious enthusiasm he generates and how he incites students to want to learn more. Dr. Duncan has been highly innovative in his approach to revamping these courses. When Dr. Duncan took over as course director he did something that is very difficult for an assistant professor; he asked the lecturers to shift away from topics on their own work to the core information the students actually need to cover. Dr. Duncan also recognized that office hours are inefficient for both faculty and students, so he developed an innovative and highly effective method to make student-professor interaction fun and efficient. He set up evening Skype sessions where he sits at his computer at home and students gather in a study room. Dr. Duncan also teaches extensively in the laboratory where he mentors postdoctoral fellows, graduate students, medical students and undergraduate students. The excellence of his teaching comes through at every level. The Program in Biomedical Sciences (PIBS) program recently videotaped his lecture as a student recruitment tool. Additionally, he was selected as the outstanding UROP mentor in 2005. He is clearly one of our finest instructors.

Research: Dr. Duncan investigates the development of hearing and mechanisms of repair and regeneration in the auditory periphery. He brings specialized expertise in two divergent and rarely combined technological methodologies, single cell electrophysiology studies using patch clamping and molecular biology approaches to investigate ion channels and activity in auditory

cells. Dr. Duncan's research on voltage-gated potassium channels is technologically demanding. His is one of only five labs in the world that have successfully used this difficult methodology to study the ear, and his lab is the only one of these to sustain a reproducible and productive enterprise using these techniques to study the auditory periphery. In his first R01 to investigate the electrophysiology of development of hearing, he proposed the novel and intriguing hypothesis that potassium channels and their subunit selection is distributed systematically along the cochlea. This work demonstrated that alternative splicing rather than subunit selection was the developmental drive turning immature cells into high-fidelity sound transducing devices. In collaboration with Dr. Sally Camper, he identified alternative splicing of channel proteins as critical factor in hypothyroidism-induced deafness. This led to a successful collaboration and a joint R01 with Dr. Michele Jacobs (Tufts University) reflecting the strong national reputation that Dr. Duncan has developed in this field. He is the "go to guy" for expertise in ion channel physiology in the auditory periphery. In addition, Dr. Duncan has a very important role in the nascent stem cell research initiative that is developing within the Kresge Hearing Research Institute to deliver nanofibers seeded with stem cells as a bioengineered next-generation cochlear implant. Dr. Duncan's ideas and expertise in physiology, molecular biology and engineering are incorporated in a collaborative proposal submitted to NSF in September 2010. Dr. Duncan has developed a strong upward trajectory as exemplified by recent significant high impact publications. His seminal paper in the *Journal of Neuroscience* demonstrated that the mechanism of deafness in hypothyroidism is due to long-term ionic imbalance secondary to developmental failure of potassium channels normally driven by thyroid hormone. The 2010 *Journal of Comparative Neurology* paper from Dr. Duncan's lab is the follow-up to his original hypothesis on the role of BK potassium channel plasticity in development. This builds on his discovery that splice variation drives channel maturation during development and links this mechanism to subcellular trafficking. The results from this paper showing variant-dependent clustering of channels was combined with his data in another publication to implicate a role for lipid rafts in regulating ion channel function. This concept is novel, directly links lipid metabolism to channel function, and provides insight into hearing problems associated with lipid metabolism disorders. These papers all point to a central theme of research in the Duncan Laboratory, namely an investigation into the proteins, ligands, and membrane structures that govern channel behavior in the ear. Finally, in his 2010 *American Journal of Physiology* paper, Dr. Duncan establishes his expertise in the physiology of stem cell-derived neurons. This paper reports the rapid induction of electrical behavior in embryonic stem cells that have been turned into neurons. Action potentials were generated in these cells after only 72 hours of expressing the gene *Neurog1*. These data can be used to explore the downstream effects of *Neurog1* expression, which is a key event in sensory development. In addition, these cells are excellent candidates for use in peripheral nerve repair. Current projects launched by this paper involve collaborations within KHRI, the Center for Organogenesis, Neurology, and Bioengineering. Dr. Duncan is asked to serve as an expert reviewer for international grants including the Wellcome Trust and the Manitoba Health Research Council attesting to his growing prominence in his field. Nationally, he serves as a reviewer for the National Organization for Hearing Research and as a reviewer for multiple high profile journals. He is an invited session moderator for the Association for Research in Otolaryngology and has been invited to speak on his research at other institutions commensurate with the increasing appreciation of his recent research.

Recent and Significant Publications:

Tong MT, Hernandez JL, Purcell EK, Altschuler RA, Duncan RK: The intrinsic electrophysiological properties of neurons derived from mouse embryonic stem cells overexpressing Neurogenin-1. *American Journal of Physiology-Cell Physiology* in press.

Kim J-M, Beyer R, Morales MM, Chen S, Liu L, Duncan RK: Expression of BK-type calcium-activated potassium channel splice variants during chick cochlear development. *Journal of Comparative Neurology* 518:2554-2569, 2010.

Mustapha-Chaib M, Fang Q, Gong TW, Dolan D, Raphael Y, Camper SA, Duncan RK: Deafness and permanently reduced potassium channel gene expression and function in hypothyroid *Pit1^{dw}* mutants. *Journal of Neuroscience* 29:1212-1223, 2009.

Crumling MA, Tong M, Aschenbach KL, Liu LQ, Pipitone CM, Duncan RK: P2X antagonists inhibit styryl dye entry into hair cells. *Neuroscience* 161:1144-1153, 2009.

Tong M, Duncan RK: Tamoxifen inhibits BK channels in chick cochlea without alterations in voltage-dependent activation. *American Journal of Physiology-Cell Physiology* 297:C75-85, 2009.

Service: Dr. Duncan is considered by his peers to be a solid citizen who takes his involvement in service very seriously and he always performs in an outstanding manner. He has served on several committees for the Neuroscience Program, including admissions, executive, and curriculum committees. He has chaired admissions for the Hearing and Chemical Sciences graduate program for many years, and has served on the internal review committee of the Kresge Hearing Research Institute. He is also very active in community organizations and brings much to our community and university.

External Review:

Reviewer A: "...Keith has hit his stride and is fulfilling the promise that he undoubtedly demonstrated in having received his first NIH R01 on BK channel regulation in auditory hair cells in 2005. His most recent publications in 2009 and 2010 are quite impressive; including excellent work published in high-quality journals including the *Journal of Neuroscience* and the *Journal of Comparative Neurology*."

Reviewer B: "...Keith has shown exemplary professional development in research, teaching and service. He has reached a stage where he has established a significant research program with productive independent and collaborative lines of research. He is respected for his expertise in the difficult but important area of ion channel regulation in sensory cells and neurons of the inner ear...He has mentored a large number of trainees at multiple levels, and his service record has been recognized by the University as outstanding."

Reviewer C: "Using quantitative PCR and immunohistochemistry, he has also provided...a detailed description of the alternatively-spliced variants in chick cochlea and their changes with

development. An important conclusion from this paper is that surface expression of the channels is not limited by translation but by protein synthesis and trafficking; i.e. the mRNA appears well before the presence of protein...Dr. Duncan's work...represents a significant contribution in the right direction and I hope he continues such research....He has clearly invested substantial effort in student training and, on a national level, is involved in the organization of the Association for Research in Otolaryngology."

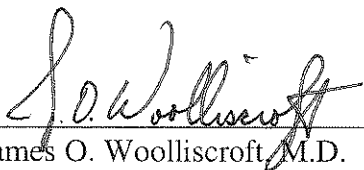
Reviewer D: "Dr. Duncan's scholarship has influenced the auditory field especially by his work on the molecular mechanisms of hypothyroidism, that showed hypothyroidism in late adulthood could be a contributing factor of presbycusis. In addition, his work on the splicing of the BK channels during chick development was first to identify the pivotal molecular changes that occur at the onset of hearing....all of Dr. Duncan's papers are scientifically challenging and first-rate."

Reviewer E: "...he is on an upward trajectory, having now built his lab and developed collaborations at both Michigan and with other institutions....the recent increase in publications suggests that the work that he has done is now bearing fruit.... his research is excellent and well respected...the work itself is scholarly and has translational implications."

Reviewer F: "His academic accomplishments, including many scholarly works that are published in high profile journals, are broadly recognized and highly regarded in the academic community. Dr. Duncan is widely known for his capacity to undertake and successfully pursue challenging scientific questions requiring creative and technically demanding solutions, an attribute that has led to any number of important and provocative findings. In my view, Dr. Duncan would be promoted to this rank in the most elite of academic settings..."

Summary of Recommendation:

Dr. Duncan has unique skills in electrophysiology and molecular biology and truly superior teaching skills in the classroom and the laboratory. His creative research ideas, innovative techniques and unique skill set are highly valued by colleagues in his department and others in the medical school and university. I am pleased to recommend him for promotion to associate professor, with tenure.



James O. Woolliscroft, M.D.
Dean
Lyle C. Roll Professor of Medicine

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