Summer Student Research Program
Project Description

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PROJECT TITLE (200 Characters max):

Image analysis of epithelial migration of the tympanic membrane and ear canal

HYPOTHESIS:
Computer-based image analysis of endoscopic photographs of the tympanic membrane and ear canal can reveal directional patterns and force vectors of epithelial migration in normal and pathologically or surgically altered ears.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

Design: This study will be a retrospective analysis of existing endoscopic photographs, all of which are restricted to the ear canal and ear drum and therefore do not reveal any patient's identity.

Methods: High definition endoscopic photographs of the tympanic membrane and ear canal are taken in the routine care of patients in Dr. Jyung's practice, to document the clinical findings and to educate patients about their disease. These photographs potentially contain important data relevant to our understanding of epithelial migration and its possible role in the pathogenesis of cholesteatoma formation.

Data collection: These photographs exist as digital files which will be analyzed using Image J (formerly known as NIH Image) software, focusing on the wrinkles of the stratum corneum which reliably develop in a perpendicular orientation to the direction of epithelial migration. Initial analysis will consist of applying the convolve filter to the base image files, in order to highlight the wrinkles. The majority of the tympanic membrane consists of the pars tensa, which will be divided into quadrants using the convention of clinic examination (antero-superior, antero-inferior, postero-inferior, and postero-superior, based on the manubrium of the malleus as the vertical dividing line and a horizontal line drawn perpendicular to the vertical line at its mid-point) and the number of wrinkles as well as the length of individual wrinkles will be counted. A fifth "quadrant" will consist of the pars flaccida, which is the most superior portion of the tympanic membrane and usually the most prone to forming retraction pockets. Therefore, each case/photograph will generate 5 data sets. If possible, features of the wrinkles such as thickness or the amount of light reflectance will be measured, which may serve as a proxy for the prominence of individual wrinkles. In addition, the overall pattern of a series of adjacent wrinkles (parallel, diverging, or converging lengths) will be measured, using a "best fit" approach. A bioengineering consultant will advise on the mathematical basis for determining the appropriate vector for each series of wrinkles, with the vector direction generally oriented towards the diverging end. The proximity of any series of wrinkles to any potential obstacle for epithelial migration (bony edge known as the scutum, retraction pocket, tympanic membrane perforation, granulation tissue, foreign body, etc.) will be noted and measured. Experimental cases will consist of any patient with the diagnosis of a cholesteatoma or any patient with deformation of the tympanic membrane due to retraction or any of pathology that would be expected to impair epithelial migration. Control cases would include any cases where epithelial migration would be expected to occur normally, such as in otosclerosis or small tumors of the middle ear. Post-operative cases will be analyzed as experimental or control

cases depending on the quality of healing: cases with relatively flat, smooth surfaces will be included as controls while cases with surface defects or projecting edges would be considered

experimental. Quadrants that are occupied by gross pathology such as the mouth of a cholesteatoma, granulation tissue polyp, or any other material that does not allow a direct image of the tympanic membrane will not be included in the wrinkle analysis. In addition, we will record pertinent medical history that would affect epithelial migration, such as radiation therapy with fields involving the ear.

Data analysis: A statistics consultant from the statistics department at Rutgers will be utilized for all data analysis. The data from each tympanic membrane quadrant will be compared to the other quadrants within a particular case but data for each quadrant (antero-superior, antero-inferior, postero-inferior, postero-superior, and pars flaccida) will be averaged and compared across cases.

Interpretation of data: Attention will be paid to the relationship between the proximity of obstacles to epithelial migration and wrinkle formation, if any exists. Careful comparison of the 5 "quadrants" will be necessary to determine if the pars flaccida and the postero-superior quadrant of the pars tensa demonstrate a greater degree of wrinkle formation compared to other quadrants, since these two locations are the classic sites of primary acquired cholesteatoma formation. If force vectors can be generated, these will be directly compared to the known patterns of epithelial migration of the human tympanic membrane.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

Fang CH, Chung SY, Blake DM, Vazquez A, Li CR, Carey JP, Francis HW, and **Jyung RW**. "Prevalence of Cochlear-Facial Dehiscence in a Study of 1,020 Temporal Bone Specimens." Otol Neurotol. 2016 Aug;37(7):967-72.

Blake DM, Vazquez A, Tomovic S, **Jyung RW**. "Tympanic membrane perforation with squamous epithelial ingrowth." Ear Nose Throat J. 2014 Aug;93(8):E31-2.

Blake DM, Vazquez A, Tomovic S, and **Jyung RW**. "Auto-mastoidectomy" Ear Nose Throat J. 2014 Jun;93(6):E53-4.

Blake DM, Vazquez A, **Jyung RW**. Bilateral external auditory canal cholesteatomas. Ear Nose Throat J. 2014 Mar;93(3):92-6.

Blake, Danielle M., Senja Tomovic, and **Jyung RW**. "Congenital Cholesteatoma." Ear Nose Throat J. Ear Nose Throat J. 2013 Apr-May;92(4-5):189-90.

Jyung RW and Wacharasindhu, C. Quantification of angiogenesis in otoslcerosis. Laryngoscope, 115(5), 811-816, 2005.

IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS?

Yes ☐ or No X☐

(IF YES, PLEASE SUPPLY THE GRANTING AGENCY'S NAME)

THIS PROJECT IS: X☐Clinical ☐Laboratory ☐ Behavioral ☐ Other

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THIS PROJECT IS CANCER-RELATED ☐NO
Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED ☐NO
Please explain Heart, Lung, Blood relevance

THIS PROJECT EMPLOYS RADIOISOTOPES ☐NO

THIS PROJECT INVOLVES THE USE OF ANIMALS ☐NO
PENDING ☐ APPROVED ☐ IACUC PROTOCOL #

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS ☐NO
PENDING ☐ APPROVED ☐ IRB PROTOCOL # M

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS	☐	ENTERING FRESHMAN	☐
SOPHMORES	☐	ALL STUDENTS	☐**YES**

THIS PROJECT IS WORK-STUDY: Yes ☐ or No ☐NO

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR
FOR INTERESTED VOLUNTEERS: Yes ☐X or No ☐

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
The student will learn how to use image analysis software including Image J. In doing so, the student will gain valuable experience using this powerful software, which is widely used in biomedical research. In addition, the student will learn about the basics of endoscopic photography of the ear. Therefore, the student will be exposed to an exciting area of research, where image analysis of medical images plays a role in studying and diagnosing disease. Most importantly, however, the student will learn about the potentially fundamental role that normal epithelial migration plays in the genesis of a common destructive disease of the human ear called cholesteatoma. Given the number of differing theories about the pathogenesis of this disease, this project has the potential to provide strong supporting evidence for a clear, unified, and accurate pathogenic mechanism for this long recognized but poorly understood entity.