Application number/Title: 40951 - GWAS of tinnitus and hearing loss in the general population with emphasis on noise exposure and aging

Applicant PI: Dr Royce Clifford

Application Institution: University of California, San Diego, USA

Keywords provided by the Applicant PI to describe the research project:

GWAS, genome wide association study, hearing loss, tinnitus, twins

Application Lay Summary:

Tinnitus, or ringing in the ears with no outside sound, is reported in 19.6% of UK Biobank participants, and is associated with hearing loss in 90% of tinnitus sufferers. Tinnitus is associated with sleep disorders, mental health diagnoses such as depression, and cognitive issues. The economic cost to society is enormous, including health care, alternative medicine, productivity, and personal costs. Yet, it has no specific objective test nor any cure.

Given the same exposure to noise, some people will sustain tinnitus, and some will not. Thus, there is a genetic component to this syndrome. Our goal is to identify genes that contain single nucleotide polymorphisms (SNPs), defined as small anomalies in a person's DNA that individually would otherwise not be harmful, but in aggregate, can lead to chronic disease.

Many diseases are polygenic, i.e., made up of large numbers of these SNPs; adult-onset diabetes is an example. We feel that tinnitus may be a polygenic syndrome, and that these SNPs may lead to a vulnerability to tinnitus, given the exposure of chronic noise in industry, sudden noise, such as blast, or just the natural process of aging. Using unidentified data, we will compare individual DNA sequencing from the UK Biobank to questionnaires, hearing tests, and demographic information, in order to identify genes associated with ringing in the ears, to perform GWAS.

We are currently studying other populations, including a US Marine cohort of 3000 young men and a Vietnam Era Twin Study of 1200 twins and have tentatively identified several genes in the smaller male population, however,

finding significant genes requires larger populations. The UK Biobank provides an opportunity to study a large civilian population and includes both genders with a good range of ages, allowing generalization of any findings. It is anticipated that multiple genes will be identified, including those associated with aging, repair of nerves after injury, and others.

Our work will aid in identification of a polygenic risk score to distinguish those that might be more vulnerable to environmental exposure of noise. In addition, comparison of findings to other polygenic diseases will identify similar cellular pathways that might aid in the understanding of why some people have tinnitus and some do not.

We anticipate that this study will take about three years, including analysis and comparison with other populations. It will provide direction towards further research into diagnosis and treatment of this pervasive syndrome.