Spotlight on Science

Identifying Mutations that Impact Human Aging and Disease

Gregory Tranah, Ph.D
Senior Scientist
California Pacific Medical Center
University of California
San Francisco

Dr. Tranah is a Professor at the California Pacific Medical Center (CPMC) Research Institute and an Adjunct Professor in the Department of Epidemiology and Biostatistics at the University of California, San Francisco. Dr. Tranah's current research program is focused on identifying inherited and acquired genetic factors that impact aging and disease with the goal of revolutionizing risk assessment and identifying widely applicable and inexpensive genomic tests that identify persons who would benefit from specific pharmacologic and behavioral treatments to prevent disability and disease.

What is the key focus of your research project?

My current research initiative is intertwined with several longitudinal studies focused on human aging. I am working collaboratively with investigators from the Study of Osteoporotic Fractures (SOF), the Study of Osteoporosis in Men (MrOS) and the Health, Aging and Body Composition Study. These long-term studies have spanned decades and are comprised of thousands of participants, resulting in a wealth of clinically relevant information about the trajectory of aging for each individual. In my research, I have been focusing specifically on the analysis of mitochondrial DNA (mtDNA) from these samples to better understand how mtDNA mutations are implicated in the aging process. It is known that acquired mtDNA mutations present at high levels cause severe neurological disorders, encephalopathy, deafness, myopathy, diabetes and a number of other diseases. We also know that mtDNA mutates as we age, but it is not known how lower mutation levels impact aging.

Why focus on mtDNA?

Many overlook mitochondrial data and are not spending time thinking about it. I believe there is value in focusing on that data. Age is the strongest risk factor for all diseases.

What tools are you using to study mtDNA?

Using custom targeted sequencing of mtDNA, I have been studying how gene variants contribute to cognitive function and dementia. Further mining of sequencing data could aid in understanding the contribution of gene variants to aging and whether a mitochondrial mutation can affect multiple measures of age phenotypes, such as cognitive function in combination with movement. It would also be interesting to identify mitochondrial mutations that affect multiple diseases - like spokes on a wheel with a mitochondrial hub. Once a dataset is available, I can apply it to other diseases as well. I am one of the few doing this work presently.

How has NuGEN enabled your research?

The DNA samples I received from my collaborators were of poor quality and low concentration, making them suboptimal for sequencing. I was able to use a customized version of the Ovation Target Enrichment System to prepare the poor quality samples and proceed with sequencing. NuGEN's sales and technical support staff were very helpful throughout the process and have continued to provide bioinformatics support to advance the study.

And the final goal of this study?

I think about the end game in terms of extending healthspan as opposed to expanding lifespan. Healthy aging impacts everyone. Identifying subsets of disease allows us to use personalized medicine to direct treatment in the most effective manner. If we can diagnose mitochondrial dysfunction and identify interventions that extend the cognitive and physical healthspan as long as possible, we can improve the quality of life that people experience as they age.