



July 29, 2021

To: Committee on Energy and Commerce, Subcommittee on Health

From: Global Down Syndrome Foundation

RE: Global Down Syndrome Foundation Statement/Hearing on “The Path Forward: Advancing Treatments and Cures for Neurodegenerative Diseases.”

The Global Down Syndrome Foundation welcomes the opportunity to discuss congressional work and the Administration’s efforts to address research gaps, specifically in the neurological space needed to improve the lives of the 400,000 plus Americans with Down syndrome in addition to the millions of Americans who suffer from diseases that may be unlocked or even cured by research on Down syndrome.

The Crnic Institute Human Trisome Project™, funded and co-organized by the Global Down Syndrome Foundation, led to the discovery that Down syndrome is an immune system disorder. It also confirmed that people with Down syndrome have a radically different disease spectrum. This means they are predisposed to or protected from major diseases that are the cause of death for over of 50% of Americans. Research in this field could lead to new treatments or cures of diseases that they and millions of others suffer from.

Improved medical care of individuals with Down syndrome over the past several decades has led to a dramatic increase in life expectancy to over the age of 60 years. In conjunction with this new aging population of adults with Down syndrome, there has been an increase in age-related co-occurring conditions including Alzheimer's disease (AD).

The scientific world now understands that 100 percent of people with Down syndrome have the “brain pathology” of Alzheimer’s disease. In other words, the plaques and tangles that present only in the brains of typical individuals when they have Alzheimer’s disease will be present in all people with Down syndrome by the time they are in their 30s or 40s.

We also know there is a causal relationship. Typical people with Alzheimer’s disease develop three copies of the Amyloid Precursor Protein gene (APP) instead of having just two. People with Down syndrome are born with three copies of chromosome 21 – the chromosome on which the APP gene resides.

Therefore, all people with Down syndrome have three copies of the APP gene and will develop the brain pathology of Alzheimer's disease over time.

However, although all those with Down syndrome have the brain pathology of Alzheimer's disease it is estimated that only 50-70 percent will get the actual symptoms of dementia associated with the disease. Clearly, answering the question why some people with Down syndrome, even with the triplication of the APP gene, do NOT get dementia demands exploration. In addition, following a population from the earliest age prior to developing the brain pathology of Alzheimer's disease is a promising path that should be followed.

Researchers have also found that the *entire* chromosome 21 is triplicated in the skin and nerve cells of typical people with Alzheimer's, reinforcing an even closer connection between the two conditions.

The Global Down Syndrome Foundation and Alzheimer's Association established a partnership almost 10 years ago to create the Down Syndrome-Alzheimer's Disease Investigator Program. The program has funded top national and international scientists working on the most promising research aiming to develop and devise treatments for Alzheimer's disease by studying individuals with Down syndrome. In 2021, the CU Alzheimer's and Cognition Center presented evidence that Sargramostim is the first drug to show improvement in Alzheimer's patients in a phase II clinical trial. These results published in *Alzheimer's & Dementia: Translational Research and Clinical Interventions* March 2021.

We also need to better understand how immune modulatory therapies slow down or even reverse Alzheimer's disease and other neurodegenerative diseases, another potential promising field of research that is just starting to accelerate.

Congress is making important strides in expanding the research opportunities in these critical spaces through the INCLUDE program at the National Institutes of Health, managed by the Office of the Director. We applaud your leadership today in ensuring that our federal agencies continue to prioritize research opportunities that will directly improve the lives of Americans with Down syndrome.