endpoints in the trial Targeting Aging with MEtformin (TAME). Through these examples we will explore issues related to effect sizes and statistical challenges related to composite endpoints. Finally, we will discuss the role existing and emerging biomarkers of aging in clinical trials in geroscience and summarize evidence linking biomarkers to clinically meaningful outcomes.

### UNBIASED PROTEOMICS AND TARGETED BIOMARKERS ASSOCIATED WITH EXCEPTIONAL LONGEVITY AND MULTIMORBIDITY IN HUMANS

Michelle Odden, *Stanford University, Stanford, California, United States*

Biomarkers ideal for geroscience trials could be those simultaneously identified using targeted and discovery assays and which strongly associate with complementary disease (multimorbidity) and longevity (exceptional survival) outcomes. To identify a tractable set of biomarkers for use in geroscience trials, we used the Cardiovascular Health Study (CHS), whose participant makeup closely aligns with the Targeting Aging with MEtformin (TAME) trial. In ~4800 CHS participants, quantitative assays of nine a priori-identified biomarkers were used to construct a biomarker index which strongly associated with the TAME primary outcome of mortality and multimorbidity over 6 and 10 years of follow-up. In ~3000 CHS participants, 1300 proteins were measured with unbiased aptamer proteomics and associated with survival to age 90 over 25 years of follow-up. Proteins in the biomarker index were identified as some of the strongest associated with survival to 90. This convergent evidence suggests these biomarkers may be well-suited for geroscience trials.

### CHRONIC INFLAMMATION AND THE ACCELERATION OF CHRONIC DISEASE STATES

Jeremy Walston, *Johns Hopkins University School of Medicine, Baltimore, Maryland, United States*

The chronic activation of the immune system is commonly observed in older adults, and is highly associated with multiple chronic disease states and Geriatric syndromes including physical frailty, sarcopenia and mild cognitive impairment. Chronic inflammation is multifactorial, and the individual inflammatory mediators that drive the development and propagation of disease states impact normal tissue homeostasis as well as stem cell vitality. This session will discuss age-related etiologies of chronic inflammation and specific inflammatory mediators and their measurement, including Tumor Necrosis Factor (TNF) alpha and its receptors. Inflammation-driven molecular pathways that most impact relevant chronic disease states such as the tryptophan degradation pathway, and its relationship to pathophysiological changes, will also be considered. Finally, discussion of potential treatment modalities, including several emerging from Geroscience research, will be described as will their impact on chronic disease states.

### IMMUNOMETABOLIC STRESS AND KETONE BODIES IN DISORDERS OF THE AGING BRAIN

John Newman, *Buck Institute for Research on Aging, Novato, California, United States*

Delirium is an acute confusional state that is a common complication of acute illness in older adults, and is associated with increased risk of death, disability, and dementia. Delirium in older adults is an example of a geriatric syndrome, with multifactorial, multi-system causes that include existing aging-related physiological changes as well as external acute stressors. Its pathophysiology delirium is not well understood but may include glycolytic energy deficits associated with acute inflammation in the brain. The endogenous ketogenic system provides ketone bodies as a lipid-derived alternative to glucose for cellular energy, and ketone bodies are increasingly understood to have immunomodulatory effects particularly on innate immune cells. We used a mouse model of acute inflammation-associated behavioral change to investigate how age-related differences in energy utilization in the brain affect delirium-like phenotypes, focusing on energy metabolism and innate immune activation in the brain as an example of immunometabolic approaches to geriatric syndromes.

## Session 3340 (Symposium)

### BEHAVIORAL HEALTH, SOCIAL ENGAGEMENT, AND LONG-TERM CARE SERVICES USE AMONG COMMUNITY OLDER ADULTS: USA VS. TAIWAN

Chair: Su-I Hou
Co-Chair: Chien-Ching Li
Discussant: Darren Liu

As healthcare advances, older adults are living longer. While 90% of older adults prefer aging in their own homes and communities, it is important to examine key factors influencing healthy aging-in-community and community-based long-term care (LTC) services available in different countries. This symposium examines behavioral health, social engagement, and LTC services utilization among community-dwelling older adults in the USA and Taiwan. Lessons learned from older adults across countries will provide insights for tailored community-based LTC services and program development. Dr. Hou from The University of Central Florida (UCF) will highlight similarities and differences in behavioral health profiles and the topics that most interest community-dwelling older Americans participating in three aging-in-community programs in Central Florida. Dr. Wang from Case Western Reserve University will examine the impact of neighborhood social cohesion on mobility among community-dwelling older Americans aged 65 and older from the national Health and Retirement Study. Dr. Liu from National Cheng-Kung University in Taiwan will share results of healthy lifestyle on quality of life among community-dwelling older adults in southern Taiwan. Dr. Young from State University of New York at Albany will compare long-term care use among community-dwelling older adults with and without dementia in Central Taiwan. Finally, Drs. Cao and Hou from UCF will analyze home and community-based services in the USA versus Taiwan. This symposium will further discuss similarities and differences of key factors related to healthy aging-in-community, along with practical recommendations and lessons learned across countries and cultural environments to improve community-based long-term care services and programs.