Session 5B Discussant Comments

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"Is Secondary Prevention of Alzheimer's Disease Possible?
A Discussion of Studies in the Alzheimer's Disease Field"
Heather M. Snyder, Dean Hartley, Keith N. Fargo and Maria C. Carillo

There is no question that the rise in human longevity came with a very heavy price. I doubt humanity would have done anything different had we known the rise of Alzheimer's disease and a suite of other fatal and disabling conditions was the price to pay for our extended lives, so we should neither be surprised nor disappointed at the fate we brought upon ourselves. That said, now that we know the prevalence of Alzheimer's disease will rise dramatically in the coming decades, there is justifiable fear among people of all ages: Genetic tests for risk factors are creating a new set of ethical problems in the absence of treatments, challenges to the economy will be severe, and the health community and family members of people with Alzheimer's disease are going to face a set of challenges unprecedented in history.

Snyder et al. ask a thought-provoking question: Since there is a time between onset and symptoms of Alzheimer's when people are asymptomatic, is it possible to intervene at this critical juncture to delay progression long enough to reduce the incidence, prevalence and severity of the disease? The authors describe various clinical trials underway designed to do just this. The clinical trials speak for themselves, and there is little doubt that justification exists to probe into whatever intervention pathways present themselves.

What I would like us to do is think outside the box. Several years ago, my colleagues and I published an article titled "If Humans Were Built to Last" where we "redesigned" the human body to avoid many of the problems of aging. That paper was focused strictly on morphology. Several years later, we published a follow-up where we went inside the body for additional redesign, and one of the areas we addressed was the aging brain. John Trojanowski wrote that piece, and he suggested it would be worthwhile to examine protein folding as a method of finding a way to destroy unwanted proteins and drastically reduce the propensity for aggregation. It is my understanding that humans are the only species known to experience Alzheimer's naturally, so what is it exactly about the human brain that sets us apart from other species? A bowhead whale can live for 210 years; it's a mammal with a very large brain, and yet there is no evidence of Alzheimer's in any of these older animals. Can we learn about aging brains from other species, or, perhaps more importantly, what can

we learn from older humans that show no symptoms of Alzheimer's? Or what can be learned from variation in pathology within the brains of Alzheimer's patients?

There are many pathways between normal brain function and Alzheimer's, perhaps even a line of progression from early onset to symptoms. Interfering with any of these pathways or temporal events may yield the magic bullet, so what Snyder and colleagues are promoting is a critical step in developing an intervention for one of the most feared of all of the diseases of aging. My encouragement, once again, is to make sure we don't forget about underlying causes, which means that fundamental aging processes within and across species may yield clues about how to intervene in ways that might not seem obvious to those now working in the trenches.