Biomarkers used to predict chronological and physiological age

November 19 2008

Scientists at the Buck Institute for Age Research have identified for the first time biomarkers of aging which are highly predictive of both chronological and physiological age. Biomarkers are biochemical features that can be used to measure the progress of disease or the effects of treatment.

The research involves nematode worms, microarrays which measure changes in gene expression, and complex computer algorithms. This is the first step toward identifying similar biomarkers in humans which would provide a means of scientifically validating anti-aging therapies. The research is due to appear in the November 20, 2008 online edition of *Aging Cell*.

Chronological and physiological age are rarely in sync. Determining chronological age in both worms and humans is easy – count forward from birth. Determining physiological age remains subjective – based on how someone looks or functions. Some 70 year old humans function at the level of those in their 50's, others become frail elderly sooner than would be expected. C. elegans, the nematode worm, is a similar creature. With an average lifespan of three weeks, some nematodes remain spry much longer than then their similarly-aged brethren, while others show signs of premature aging (lack of symmetrical appearance, uncoordinated motion, and the need to be prodded into movement). Buck researchers were able to predict the age of the worms by doing whole-genome expression profiles of 104 individual wild-type worms covering the entire nematode lifespan and correlating that profiling with

age-related behavior and survival. The study revealed a suite of genes that are actively involved in the aging process. The research was the largest study of aging utilizing gene profiling to date.

"This is the first evidence that physiological age can be predicted non-subjectively," said Simon Melov, PhD, Buck faculty member and lead author of the study. "This is a first step; our results were not perfect, but we were able to predict the ages of the animals 70% of the time, which is far better than anything that has been done before."

The findings have major implications for age research in humans. Examining biomarkers over time would provide a scientific baseline for clinical trials of anti-aging medicines, which is currently impossible to determine given the lengthy lifetime of human beings. The technology would also provide a means of determining whether an individual is aging faster or slower than would normally be expected.

Melov and his Buck Institute colleagues are considering several options for further studies. The next step is to do a larger study involving wild-type nematodes to see if the same suite of genes remains active in the aging process and to see if the predictive rate can be increased. Scientists are also considering comparing biomarkers in wild-type worms with mutant long-lived strains of the worms. Mouse studies may focus on gene expression profiling in different types of body tissue – for example, does heart muscle age faster than liver tissue given a certain set of environmental or nutritional factors. Melov also plans on utilizing this biomarker technology in studies involving humans who undertake various forms of exercise over a set length of time. Melov published a study in 2007 showing that regular strength training reversed aspects of aging in skeletal muscle in healthy seniors.

"I am optimistic that we will be able to pursue this line of research further," said Melov. "Research into the biology of aging in humans has

been hampered by the lack of irrefutable biomarkers that correlate with the aging process". He added, "I am confident that at some point there will be a non-subjective method of determining how old someone is with a high level of confidence."

Source: Buck Institute for Age Research