



# Andrew Dillin

Howard Hughes Medical Institute Investigator  
Associate Professor, Molecular and Cell Biology Laboratory

**“Aging is the single biggest risk factor for most human diseases, ranging from arthritis and cancer to diabetes and neurodegenerative disease. Our goal is to unravel the basic molecular mechanisms that drive the aging process, which will allow us to promote healthy aging for humankind.”**

Beyond age 65, the number of people with Alzheimer’s disease doubles every five years. Centenarians, however, seem to escape most common age-related diseases, including the ravages of Alzheimer’s. One of the telltale signs of Alzheimer’s disease is the buildup of toxic clumps of beta amyloid plaques in the brain. Beta amyloid production probably occurs in all brains, but healthy cells clear away excess amounts. Brains of people with Alzheimer’s disease, by contrast, are unable to control beta amyloid accumulation. The same is true for Alzheimer’s mouse models, which are genetically engineered to overproduce beta amyloid.

To determine whether modulating the aging process could influence the onset of Alzheimer’s, a team of investigators in Dillin’s lab slowed the aging process in an Alzheimer’s mouse model by lowering the activity of the IGF-1 signaling pathway—a highly conserved pathway that plays a crucial role in regulating lifespan and youthfulness across many species and is linked to extreme longevity in humans. Mice with reduced IGF-1 signaling live up to 35 percent longer than normal mice, and some very long-lived humans carry mutations in components of the IGF-1 pathway.

Dillin’s group then employed a battery of behavioral tests to find out whether it was simply the passage of time or aging per se that determined the onset of the disease. Chronologically old but biologically young animals appeared nearly normal in the tests long after age-matched, normal-aging Alzheimer’s mice exhibited severe impairments. When Dillin and his team looked at their brains, however, they found that those of the long-lived mice were riddled with highly compacted plaques.

These results clearly support the emerging theme that the plaques have a protective function and that as mice age, they become less efficient at stashing toxic beta amyloid fibrils in tightly packed aggregates. This work validates the hypothesis that genetic and pharmacologic changes to create a healthy lifespan can greatly reduce the onset of some of the most devastating diseases afflicting mankind.

For more information, please visit  
[salk.edu/faculty/dillin.html](http://salk.edu/faculty/dillin.html)

#### Left to right:

*Back row:* Thomas Heimbucher, Daniel De Magalhaes Filho, Erik Kapernick, Juan Valenzuela, Derek Joyce, Nate Baird, Will Mair, Ian Nicastro, Siler Panowski, David Vilchez, Pete Douglas

*Front row:* Hyun-Eui Kim, Deepti Wilkinson, Jenni Durieux, Nessa Morantte, Virginia Butel-Murillo, Rebecca Taylor, Kristen Berendzen, Celine Riera, Gina Artale

*Front row:* Andy Dillin

