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LENNART MUCKE RECOGNIZED WITH AWARD FROM METLIFE FOUNDATION FOR RESEARCH IN ALZHEIMER'S DISEASE

Lennart Mucke, MD, director of the Gladstone Institute of Neurological Disease, received MetLife Foundation's *Award for Medical Research* for his contributions to Alzheimer's disease (AD) research on January 13th in Washington, DC.

As part of the award, Dr. Mucke received a \$100,000 institutional grant from MetLife Foundation to continue his research on mechanisms of AD-related neurodegeneration and cognitive decline.

"I am thrilled to receive this award," said Mucke, who is also professor of neurology and neuroscience at UCSF. "Any award reflects the participation of many, and I consider all my associates, collaborators and former mentors important contributors. We all share this award together."

Dennis Selkoe, MD, professor of neurology and neurosciences at Harvard Medical School, nominated Mucke for the award. Selkoe said, "The receipt of the MetLife award is a wonderful recognition of Lennart's strong contributions to unraveling the earliest mechanisms of neurodegeneration, particularly in AD. He has pioneered the study of both APP and apoE in the pathogenesis of this complex disorder. He has made major insights into how apoE is important for brain health in general."

As many as 10 percent of those over the age of 65 may show signs of AD, according to the Alzheimer's Association. Unless a cure or prevention is found, 14 million Americans will likely suffer from AD by 2050.

APP, or amyloid protein precursor, is the source of amyloid- β peptides (A β), which accumulate to abnormally high levels in the brains of AD patients.

A leader in the study of neurodegeneration and AD, Mucke has developed transgenic models of AD that have mutant forms of human APP, similar to those known to cause aggressive forms of inherited AD. Used by several research institutes and universities around the world, these models are extremely useful tools in the study of AD.

Mucke has used these and other transgenic models his group developed to study the role of molecules that either inhibit or augment the detrimental effects of A β on brain

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function. Differences in the activity of these molecules may help explain why different people get AD earlier, later, or not at all.

One of these molecules is the lipid carrier apolipoprotein E, or apoE for short, which comes in three main variants, E2, E3 and E4. People with E4 are at greater risk for developing AD. About 40 to 60 percent of all AD patients have at least one E4 gene. Work in Mucke's laboratory has shown that transgenic models expressing human APP together with E4 developed AD-like neurodegeneration and memory deficits at earlier ages than those expressing APP with E3.

Mucke's research into how E4 increases susceptibility to neurodegeneration is ongoing. One interesting finding is that E3 seems to protect against the neuronal damage inflicted by A β . Another finding shows that androgens, such as testosterone, reversed the learning and memory impairments seen in female transgenic mice expressing human E4. Both findings could lead to better treatments and prevention strategies.

In several other studies, Mucke's research team has shown that A β can impair the function of brain cells and their communication with each other well before it aggregates into clumps of protein, called plaques, commonly thought to be the culprit in causing AD. Together with collaborators at the Gladstone and other institutions, the investigators are now trying to find ways to block this type of early A β toxicity.

Mucke is the third Gladstone investigator to be honored by MetLife Foundation. Robert Mahley, MD, PhD, president of the J. David Gladstone Institutes, and Karl Weisgraber, PhD, deputy director of the Gladstone Institute of Cardiovascular Disease, each won MetLife awards in 1995.

"I feel honored and humbled by the outstanding cadre of scientists who have won this award before me," Mucke said. "I hope that additional members of the Gladstone Institute of Neurological Disease will become part of this group in the near future."

Some recipients of this prestigious annual award have gone on to win the Nobel Prize for physiology or medicine, including Paul Greengard, PhD, of Rockefeller University and Stanley B. Prusiner, MD, of the University of California, San Francisco.

The MetLife Foundation *Award for Medical Research* recognizes scientists whose work has significantly contributed to understanding AD. The program's unrestricted grants enable scientists to liberally pursue their creative ideas as they relate to AD research. A total of \$8.5 million has been awarded since the inception of the program in 1986. A committee of leading experts in neurology, neuroscience, gerontology and AD selects the award recipients.

Mucke received his MD from the Georg-August-University in Göttingen, Germany. After completing his thesis research in neurophysiology and neuroanatomy with Otto Creutzfeldt at the Max-Planck-Institute for Biophysical Chemistry, he trained in internal medicine at the Cleveland Clinic and in neurology at the Massachusetts General Hospital and Harvard Medical School. After his residency, he did a postdoctoral fellowship in neuroimmunology and neurovirology with Michael Oldstone at the Scripps Research Institute where he was subsequently appointed to the faculty.

In 1996, Mucke was recruited to head a new program in molecular neurobiology at the Gladstone Institutes and UCSF. The progress made by this program resulted in the establishment of

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the Gladstone Institute of Neurological Disease, which Mucke has directed since its inauguration in 1998. Mucke is the first holder of the Joseph B. Martin Distinguished Professorship in Neuroscience at UCSF where he has joint appointments in the department of neurology, the neuroscience program, the biomedical sciences program, and the program in pharmaceutical sciences and pharmacogenomics. He also serves as an attending physician in neurology at San Francisco General Hospital Medical Center and UCSF's Memory and Aging Center.

The Gladstone Institute of Neurological Disease is one of three research institutes that comprise The J. David Gladstone Institutes, a private nonprofit biomedical research institution affiliated with UCSF. The institute is named for a prominent real estate developer who died in 1971. His will created a testamentary trust that reflects his long-standing interest in medical education and research.

MetLife Foundation, established in 1976 by MetLife, supports health, education, civic and cultural programs throughout the United States.

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For more information about the Foundation, visit the website at www.metlife.org or contact Jennie Morgan at jmorgan3@metlife.com