LEADING ALZHEIMER'S DISEASE RESEARCHERS RECOGNIZED WITH METLIFE FOUNDATION AWARDS

(New York, NY, May 15, 2014) – MetLife Foundation today announced the recipients of the 2014 MetLife Foundation Awards for Medical Research: Riqiang Yan, Ph.D., vice chair of the Department of Neurosciences, Lerner Research Institute, Cleveland Clinic; and Lary C. Walker, Ph.D., research professor of neuropharmacology and neurologic diseases and associate professor of neurology, Yerkes National Primate Research Center, Emory University (Atlanta, GA) and Mathias Jucker, Ph.D., full professor, Hertie Institute for Clinical Brain Research and German Center for Neurodegenerative Diseases (Tübingen, Germany), who were given the award jointly. Jie Shen, Ph.D., professor of neurology, Harvard Medical School Center for Neurological Diseases, Brigham and Women’s Hospital Center for Neurologic Diseases (Boston, MA), was given the Promising Research in Alzheimer’s Disease Award.

Dr. Yan is co-discoverer of the protein BACE1, an enzyme that cleaves the amyloid-β precursor protein (APP) to form amyloid-beta (Aβ), a protein that is the main component of amyloid plaques. Aβ deposits in the brains of people with Alzheimer’s disease, damaging their brain cells (neurons). BACE1 is seen as an important drug target for Alzheimer’s therapy based on trying to decrease amyloid deposition.

Working collaboratively, Drs. Jucker and Walker pioneered a unifying principle for the onset and evolution of late-life brain disorders such as Alzheimer’s and Parkinson’s diseases, based on similarities with rare, fatal disorders known as prion diseases. They have amassed compelling experimental evidence that small aggregates of the basic proteins in these diseases act as “seeds” that start a domino-like chain reaction that causes similar proteins to aggregate and spread the disease throughout the brain.

Using a combination of research techniques, Dr. Shen elucidated the normal function of the presenilin gene in the developing, adult and aging brain. Her work revealed the importance of presenilins in memory, synaptic function and age-related survival of neurons. Presenilins, a family of proteins, have been implicated in several early onset forms of familial Alzheimer’s disease.

The winners were recognized at a scientific briefing and awards ceremony today in New York.

“MetLife Foundation is proud to present the awards to recognize the work of these leading scientists, whose research helps bring us closer to finding a cure for Alzheimer’s disease,” said A. Dennis White, president and chief executive officer, MetLife Foundation. “They have made significant contributions that have helped us better understand this devastating illness, and have laid the groundwork for effective treatments.”
About the Awards

Now in their 28th year, the awards provide outstanding researchers with an opportunity to freely pursue new ideas. At the heart of the program is a belief in research as the road to understanding and ultimately treating this devastating disease. This year, $600,000 in awards has been given. The major award carries a $200,000 institutional grant and a personal prize of $50,000. The Promising Research in Alzheimer’s Disease Award recipient receives a $100,000 institutional grant to further his or her work in Alzheimer’s disease. MetLife Foundation established the awards in 1986 to recognize and reward scientists demonstrating significant contributions to the understanding of Alzheimer’s disease.

The MetLife Foundation Awards for Medical Research are managed by the American Federation for Aging Research (AFAR). Founded in 1981, AFAR has championed the cause and supported the funding of science in healthier aging and age-related medicine.

“These four individuals have done groundbreaking work, and the awards will help them further their pioneering research efforts,” said David M. Holtzman, M.D., chair of the MetLife Foundation Awards for Medical Research Advisory Committee, which selected the winners. “We desperately need new Alzheimer’s disease treatments, and these researchers are bringing us closer to that goal.”

Dr. Holtzman, who is the Andrew B. and Gretchen P. Jones Professor and chairman, Department of Neurology, Washington University School of Medicine, is a previous recipient of the MetLife Foundation Award.

According to recent estimates, without the development of treatments that either delay its onset or slow its progression, by 2050 well over 100 million and possibly as many as 200 million people worldwide will be living with Alzheimer’s disease. The time spent caring for people with Alzheimer’s disease will be measured in billions of hours, and the cost will be trillions of dollars.

Seminal Discoveries That Have Made a Significant Impact

Drs. Yan, Jucker, Walker and Shen have made major discoveries that have identified underlying mechanisms of Alzheimer’s disease and have led to promising directions for treatment.

Dr. Yan’s original BACE1 discovery was published in Nature in 1999; he has made additional major discoveries on the biology of BACE1 since this publication. For example, he discovered that BACE1 regulates myelination, the process in which a protective “sheath” is formed around neurons. He was the first to discover that mice without BACE1 develop spontaneous epileptic seizures – a discovery that was later verified by others. He also demonstrated that the BACE2 gene cleaves the amyloid-β precursor protein (APP) to prevent Aβ (amyloid-beta) formation, and his research suggests that targeting BACE2 activity is likely an alternative approach for reducing the accumulation of amyloid proteins.

His ongoing studies of BACE1 continue to provide important guidance for the safe development of therapeutic BACE1 inhibitors for patients with Alzheimer’s disease. Several drug candidates based on Dr. Yan’s discoveries are now in clinical trials.

Drs. Jucker and Walker have jointly published a number of seminal papers on the “seeding” concept in age-related brain diseases, beginning with a study in Science in 2006. Their accomplishments include finding that: protein-rich “seeds” of aggregated amyloid-beta (Aβ) underlie both the emergence and progression of Aβ abnormalities in the brains of animals; variations in the size and molecular structure of these seeds profoundly influence their disease-causing characteristics; and small, soluble collections of Aβ are especially potent seeds – and are key targets for therapeutic intervention and possibly also early biomarkers of Alzheimer’s disease in bodily fluids.

Their work has decisively established the “seeding” model as a comprehensive mechanistic explanation for the abnormal assembly of proteins and their spread through the brain (including Aβ plaques in Alzheimer’s) in many of the devastating, untreatable brain diseases that afflict humanity. Their “seeding” concept has had a huge impact on the field of neurodegenerative disease research in just a brief time: in the past five years, the seeded aggregation of specific proteins has been linked to a remarkable variety of brain disorders.
Over the last 15 years, Dr. Shen has been the leading researcher in the study of the role of presenilin function in the brain. Her work established that presenilin proteins perform a variety of functions that range from a role in cell-fate determination during brain development to a role in nerve impulse transmission in the mature adult brain. She also showed a molecular pathway by which presenilin mutations may cause the progressive loss of structure and function in neurons.

In the developing brain, presenilins play an important role in controlling the differentiation and size of the neural progenitor cell (cells that become neurons) population. Dr. Shen showed that presenilins promote re-entry of induced neural progenitor cells into the cell cycle by regulating a type of inter-cell signaling system known as “Notch signaling.” Dr. Shen also demonstrated that the loss of presenilins in the adult cerebral cortex causes memory impairment and synaptic dysfunction. Her genetic studies revealed that loss of presenilins causes an age-dependent reduction in brain signaling structures and neurons, changes in nerve cells known as “glia,” and that this loss plays a role in turning tau proteins (which play a role in Alzheimer's) on or off.

For additional background on the award recipients, visit: http://www.afar.org/research/MLF-awards

About MetLife Foundation - MetLife Foundation was established in 1976 by MetLife to carry on its long tradition of corporate contributions and community involvement. For over 25 years, MetLife and MetLife Foundation have invested more than $32 million for Alzheimer's research and public information programs, including over $17 million through the Awards for Medical Research in Alzheimer’s Disease program. The Foundation has also supported a number of major initiatives, including the PBS documentary The Forgetting: A Portrait of Alzheimer’s; short pocket films on Alzheimer's narrated by David Hyde-Pierce; an educational initiative with the National Institute on Aging’s Alzheimer’s Disease Centers; the film Alzheimer’s Disease: Facing the Facts; and initiatives that include caregiving videos, Alzheimer's toolkits and resources for the Hispanic community.