

UC SANTA BARBARA

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UC Santa Barbara Awarded \$2 Million for Alzheimer's Research

The University of California, Santa Barbara has been awarded nearly \$2 million from the Larry L. Hillblom Foundation for innovative research in Alzheimer's disease. The grant will support research on the neurofibrillary tangles that, in addition to amyloid plaque, are a hallmark of the disease.

The research effort will be led by Kenneth Kosik, co-director of UCSB's Neuroscience Research Institute and Harriman Professor of molecular, cellular, and developmental biology. He will head the Larry L. Hillblom Center for Neurodegeneration Research at UC Santa Barbara, which will exist for the duration of the four-year, \$1,970,291 project.

Kosik has spent most of his career studying the neurofibrillary tangles of Alzheimer's disease. His research group at Harvard University, where he was previously a faculty member, was one of the first to discover that "tau" is the protein involved in the tangles. Recent discoveries in his lab at UCSB helped to attract the foundation's attention.

The new research is highly interdisciplinary in its approach; a team with a wide range of specialties will carry out the research. Said UCSB Chancellor Henry T. Yang: "We are extremely grateful for this generous support from the Larry L. Hillblom Foundation, which will enable us to launch a truly novel research network directed toward the neurofibrillary pathology of Alzheimer's disease and frontotemporal

dementia. Our campus is very proud of the pioneering contributions and interdisciplinary approach of Professor Ken Kosik and the entire research team, all of whom are renowned leaders in their fields."

Kosik explained that the grant proposal was submitted to the Hillblom Foundation because the foundation recognizes not just the importance of interdisciplinary research, but also its challenge. He said that the foundational biology in this research project that is the basis for biomedical advances is increasingly choked off in the current funding atmosphere in which research is evaluated for its immediate "translational value" -- meaning quick clinical applications and medications.

"A firm foundation is needed before we can do the translation," said Kosik. "The basic underlying biological foundation must be understood first, but right now the pendulum has swung far to the application side. The Hillblom Foundation is providing a major service by laying the basis for translational research."

Tau, the protein, is normally found in brain cells, but scientists don't know why it clumps into tangles. "The goal of the grant is to understand this process better," said Kosik.

The research project is built on the hypothesis that the accumulation of tau protein is due to a failure of the protein degradation machinery. "To survive, all cells need to be able to remove damaged proteins," said Kosik. "There is no doubt that the protein that is collecting into tangles is damaged. We don't know why it doesn't get removed; we do know that the cells are trying to remove it."

He explained that cells normally use an enzyme to chop up and remove the damaged protein. "But it is not getting chopped down, degraded, as it should," said Kosik. "Also, it is sequestered in one place, pushed to one place. More and more of it then fills up the cell."

Kosik said that it is possible the cell can't handle it and pushes it aside -- or maybe tau is toxic in this form. He also said that since the relationship between amyloid plaques and neurofibrillary tangles is unknown, it is possible that the protein in the plaque is fundamental to triggering the disease. It may initiate the tangles, he explained.

Members of the diverse team and their research strengths include:

- Kenneth Kosik, cell biological and neurobiological expertise
- Stuart Feinstein, co-director of the Neuroscience Research Institute, biochemical expertise
- Omar Saleh, assistant professor of materials, physics and single molecule expertise
- Frank Doyle, professor of chemical engineering, systems engineering expertise and experience at modeling data mathematically
- Linda Petzold, professor of mechanical engineering, computational expertise and mathematical perspectives

A number of graduate students and postdoctoral scholars are also participating.

With the support of the Hillblom Foundation, the Kosik research team may thus elucidate an important piece of the puzzle of this disease that affects five million Americans.

Based in Petaluma, California, the Larry L. Hillblom Foundation is funded through a bequest from Larry L. Hillblom, a respected international businessman who was one of the three founders of DHL Worldwide Express. Hillblom designated that the foundation's funding should be used to support medical research with particular attention to research programs conducted by the University of California.

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