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John O'Keefe

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GRUBER PRIZE CELEBRATES "PLACE CELL" PIONEER

John O'Keefe is Honored Speaker at Society for Neuroscience Annual Meeting

November 14, 2008, New York, NY -- It was a winding path John O'Keefe followed to one of the most dramatic discoveries about the brain and, on November 16, his success will lead him to the podium at the Society for Neuroscience's Annual Meeting in Washington, D.C. where he will receive the \$500,000 Gruber Foundation Neuroscience Prize for 2008.

O'Keefe's research on how specific brain cells enable an animal to determine, to map, and to remember a location, helped launch an entire subfield of study about the neural basis of thinking and behavior and has influenced some of the most recent research on memory loss and Alzheimer's disease.

"We are delighted to honor Prof. O'Keefe for his amazing achievements advancing our knowledge of the brain and the thinking process," said Patricia Gruber, president of the Peter and Patricia Gruber Foundation. Following the presentation, O'Keefe will deliver the annual Gruber Lecture at the SfN meeting on the topic "The Role of Theta Oscillations in Spatial Processing in the Hippocampal Formation."

Well before he found himself in a scientific laboratory, O'Keefe had explored several other fields of human endeavor, including philosophy, psychology, music, engineering, filmmaking and the ancient classics. The son of Irish immigrants who, he says, landed in New York "just in time to meet the Depression," O'Keefe had a classics high school education in Latin and Greek and spent several years studying engineering at New York University before running out of money. He moved to the City College of New York to take advantage of what was then a free college education. Along the way he also garnered varied work experience, including working on a film set, making aircraft on Long Island and driving a New York yellow cab. By the time he got to CCNY he had decided to study brain and behavior, and in preparation, he set out to equip himself with a broad background in the arts and sciences.

"It was like a wonderland" at CCNY, he says. "They had a very liberal registration system" that would allow a student to get into advanced courses without the normal prerequisites and to monitor courses without registering for them, so he was able to sample a smorgasbord of subjects. Finally the college officials ran out of patience and forced him to choose a major. "They said, 'You have to go,'" he recalls with a laugh. He settled on psychology for his undergraduate degree and then went on to McGill University in Montreal where he earned a doctorate in physiological psychology. At the time McGill was already a major center of brain and behavior research, home to such giants as Donald Hebb, Wilder Penfield, Brenda Milner and Ron Melzack. In 1967 O'Keefe moved to University College London, where he continues to carry out research and teaches cognitive research.

He credits his diverse education and work experience with preparing him for what became his life's work. "There were a lot of different strands at work that were active," he says. They all came together to afford him an understanding of the significance of what he was seeing when he began experimenting with rodents in the 1970s. "I was fortunate in my research directors Ronald Melzack and later Pat Wall at UCL who both let me follow my instincts and develop my own research pathway."

His method was unusual at the time. Instead of studying the brain of an anesthetized mammal, O'Keefe observed free-moving rats with tiny permanent implants in their brains, which, he explains, gave him "a window onto the activity

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of the brain" as the animals ate, slept, ran, explored their environments, and generally went about their daily business. His Eureka moment came when he realized that what are now called "place cells" in the brain's hippocampus region were activated not by any given behavior but rather by the animal's physical location in its box. "I realized we were looking at the brain's spatial map," he recalls. Further studies showed the predicted correlation between damage in the hippocampal region and loss of spatial memory.

In 1978, with Lynn Nadel, O'Keefe co-authored *The Hippocampus as a Cognitive Map*, which became a virtual textbook on the brain, cognition and behavior and ensured him an important place in the history of cognitive neuroscience. The book was just a "for openers" achievement for O'Keefe whose insatiable curiosity continues to drive his own research and inspire others.

"What started as a purely intellectual pursuit," he says "now has medical application." Many researchers, including O'Keefe himself, have zeroed in on the hippocampus to learn more about dementia, Alzheimer's disease and general memory loss. A UCL colleague is currently developing spatial memory tests for humans aimed at very early detection.

In contrast to his radical success in the lab, O'Keefe describes himself as personally conventional, spending most of his adult life in the same apartment, working at the same institution, and married to the same woman, Eileen O'Keefe, whom he met more than 46 years ago in a philosophy class at CCNY. She is a professor of public health; they have two grown sons, Kieron and Riley, and continue to share a love of philosophy.

"You can see different lives you could have had," O'Keefe says, reminiscing on a summer he spent on a film set during the shooting of Chekov's play *Uncle Vanka*. "At some point my wife Eileen and I will write a play. Or a musical comedy more likely."

The idea carries no hint of regret that he took the wrong direction, however. For O'Keefe, "the relationship between the mind and the brain is the big question in neuroscience." And it hasn't been answered – yet.

Additional Information

The Gruber Prize Program honors contemporary individuals in the fields of Cosmology, Genetics, Neuroscience, Justice and Women's Rights whose groundbreaking work provides new models that inspire and enable fundamental shifts in knowledge and culture. The Selection Advisory Boards choose individuals whose contributions in their respective fields advance our knowledge, potentially have a profound impact on our lives, and demonstrate courage and commitment in the face of significant obstacles.

The Society for Neuroscience nominates the members of the Neuroscience Prize Selection Advisory Board. Current members are: Carol A. Barnes, University of Arizona; Colin Blakemore, University of Oxford; Linda S. Buck, Fred Hutchinson Cancer Research Center; Sten Grillner, Karolinska Institute; H. Robert Horvitz, Massachusetts Institute of Technology; Donald Price, Johns Hopkins University School of Medicine; Li-Huei Tsai, Massachusetts Institute of Technology.

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The Peter and Patricia Gruber Foundation honors and encourages educational excellence, social justice and scientific achievements that better the human condition. For more information about Foundation guidelines and priorities, please visit www.gruberprizes.org

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