



# GRUBER FOUNDATION

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FOR IMMEDIATE RELEASE

## HALL, ROSBASH, AND YOUNG SHARE \$500,000 GRUBER NEUROSCIENCE PRIZE FOR THEIR PIONEERING WORK IN UNCOVERING THE MOLECULAR BASIS OF CIRCADIAN RHYTHMS IN THE NERVOUS SYSTEM

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Jeffrey Hall



Michael Rosbash



Michael Young

July 1, 2009, New York, NY – The 2009 Neuroscience Prize of The Peter and Patricia Gruber Foundation is being awarded to **Jeffrey Hall**, professor of neurogenetics at the University of Maine; **Michael Rosbash**, professor and director of the National Center for Behavioral Genomics at Brandeis University; and **Michael Young**, professor and head of the Laboratory of Genetics at Rockefeller University. On October 18, at the annual meeting of the Society for Neuroscience in Chicago, Illinois, these three distinguished scientists will receive this prestigious international award for their groundbreaking discoveries of the molecular mechanisms that control circadian (daily) rhythms in the nervous system. Their research was the first to establish a simple relationship between single genes and a complex behavior.

“The combined discoveries of Jeffrey Hall, Michael Rosbash and Michael Young are stunning in their creativity, breadth and significance. These researchers began with a complicated animal behavior, established that single genes can define specific aspects of this behavior and determined mechanistically how such genes act,” says H. Robert Horvitz, David H. Koch Professor of Biology at MIT. “Hall, Rosbash and Young have not only defined the genetic, molecular and biochemical bases of a complex animal behavior but have also established a paradigm for how such analyses should be done.”

Before Hall, Rosbash, and Young published their seminal studies on the molecular underpinnings of the circadian rhythms of the fruit fly, *Drosophila melanogaster*, many people questioned whether a compelling relationship between genes and behavior could be established. By the early 1970s, the first fruit fly mutants with altered circadian rest/active cycles had been identified—making a case for the genetic control of behavior—but the mechanism behind the phenomenon remained unknown. What was running the internal biological clock in *Drosophila*?

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In 1984 came the first breakthrough. That year Hall and Rosbash, working at Brandeis University, and Young, working at Rockefeller University, simultaneously cloned the *period (per)* gene of *Drosophila*. That pivotal discovery led to subsequent studies from all three labs that eventually unmasked the general molecular mechanism for circadian clocks: a transcriptional feedback loop that oscillates during the 24-hour cycle.

Hall and Rosbash demonstrated, for example, that *per* gene products exhibit oscillations for their concentrations and that during a daily cycle the *per* protein represses transcription of the very gene that specifies that “final” product. (Transcription is a gene’s ability to copy its DNA sequence into messenger RNA, a necessary step for translating the gene into a protein that performs a specialized function in the cell). Young identified *per*’s partner gene, *timeless (tim)*, and then showed that when these two genes’ protein products (PER and TIM) reach certain levels, they bind together in the cell’s cytoplasm and are transported back into the nucleus, where primarily PER shuts down the genes that made them. After a few hours, the proteins degrade, the genes start up again—and the cycle begins anew.

As Hall, Rosbash, and Young continued their research, the fundamental workings of this complex feedback system came into even sharper focus. They discovered other genes and protein products that play critical roles in regulating the loop. They found that mutations affecting any of these genes had effects on *Drosophila*’s molecular rhythms—and on its behavior. They also identified how certain stimuli, most notably the light-dark cycle, help regulate the feedback loop in order to reset the clock everyday to operate in synch with natural environmental cycles (a key and universal feature of daily rhythms).

When other researchers investigated the clock mechanisms in mammals, they found them to be strongly analogous to what Hall, Rosbash, and Young had found in *Drosophila*. Thus, the uncovering of the mechanism in the fruit fly—a tour de force of genetics and molecular biology—has paved the way for the study of human circadian genetics.

“Practically all biological creatures thus display a circadian rhythm, whether fruit fly or man, as some species are active during night and others during daytime. This astounding ability depends on an intricate molecular mechanism that, once developed, has been conserved throughout evolution,” says Sten Grillner, Director of the Nobel Institute for Neurophysiology at the Karolinska Institutet. “To reset the biological clock takes many days, as all intercontinental travelers are forced to experience - for shift-workers it is more serious, it creates stress and fatigue that over many years can lead to harmful medical conditions.”

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## Additional Information

The official citation reads:

*The Peter and Patricia Gruber Foundation proudly presents the 2009 Neuroscience Prize to Jeffrey Hall, Michael Rosbash, and Michael Young for their pioneering discoveries of molecular mechanisms that control circadian rhythms in the nervous system.*

*These investigators established that in the fruit fly *Drosophila melanogaster* circadian rhythms are driven by a transcriptional feedback loop that controls the expression of the period gene. They discovered a set of interacting genes that control this process, including the light-sensing protein that establishes circadian rhythms in response to the day-night light cycle.*

*Subsequent work by others demonstrated that these findings apply broadly to both invertebrates and vertebrates and that a mutation in the human counterpart of the period gene causes a human circadian sleep disorder. These discoveries reveal a striking solution to the problem of how genes control a higher-order behavior.*

## Laureates of the Gruber Neuroscience Prize:

**2008: John O'Keefe**, for discovering place cells, which led to important findings in cognitive neuroscience

**2007: Shigetada Nakanishi**, for pioneering research into communication between nerve cells in the brain

**2006: Masao Ito** and **Roger Nicoll**, for work on the molecular and cellular bases of memory and learning

**2005: Masakazu Konishi** and **Eric Knudsen**, for work on the neural basis of sound localization

**2004: Seymour Benzer**, for applying the tools of molecular biology and genetics to the fruit fly, *Drosophila*, and linking individual genes to their behavioral phenotypes

The Prize recipients are chosen by the Neuroscience Selection Advisory Board. Its members are:

**Carol A. Barnes**, University of Arizona; **Linda S. Buck**, Fred Hutchinson Cancer Research Center; **Sten Grillner**, Karolinska Institutet; **H. Robert Horvitz**, Massachusetts Institute of Technology; **Masao Ito**, RIKEN Brain Science Institute; **Donald Price**, Johns Hopkins University School of Medicine; and **Li-Huei Tsai**, Massachusetts Institute of Technology.

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The Gruber International Prize Program honors contemporary individuals in the fields of Cosmology, Genetics, Neuroscience, Justice and Women's Rights, whose ground-breaking 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, in the case of the Justice and Women's Rights Prizes, demonstrate courage and commitment in the face of significant obstacles.

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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](http://www.gruberprizes.org).

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Media materials and additional background information on the Gruber Prizes can be found at our online newsroom: [www.gruberprizes.org/Press.php](http://www.gruberprizes.org/Press.php)

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