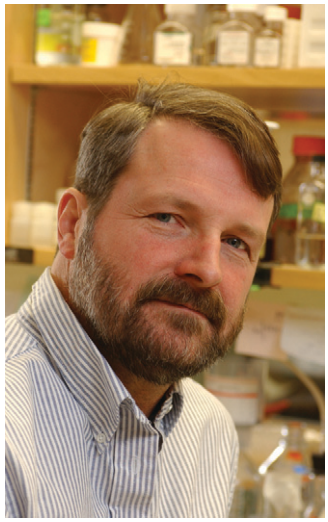

Jay C. Dunlap

The 2009 George W. Beadle Award

Jay C. Dunlap

THE 2009 George W. Beadle Medal for outstanding contributions to the genetics community is awarded to Jay C. Dunlap. This award is a tribute to Jay's pioneering studies on the circadian clock and the *Neurospora crassa frequency* (*frq*) gene—the first microbial clock gene to be cloned (McClung *et al.* 1989). Jay's work on the genetics of circadian rhythms came at a time when the field of chronobiology was still in its infancy and when the research focused primarily on the physiology and anatomy of the clock. It was widely believed that genetic approaches to understanding the clock were intractable and that clocks evolved independently in different organisms (Pittendrigh 1993). Thus, it was thought that studying the clock in fungi or other microbes would not reveal the mechanism used by the mammalian clock. In spite of this research climate, Jay persevered in studying the Neurospora clock and in the end proved the relevance of this system to mammalian chronobiology.

As Jay has pointed out, he happened upon daily (circadian) rhythms by chance after applying to Harvard's graduate program "on a whim" (Dunlap 2008). He was accepted and studied with J. W. (Woody) Hastings. He focused on bioluminescence in the marine organism Gonyaulax and determined the structure of luciferin (Dunlap and Hastings 1981a). The observation that Gonyaulax produces luciferin only during the night, when the light produced can be seen, made biological sense and launched Jay on the path to investigating the circadian clock that regulates daily rhythms in bioluminescence (Dunlap and Hastings 1981b; Hastings *et al.* 1981). He quickly realized that understanding the biochemical mechanism of the clock would also require a genetics approach, and this insight led him to the genetically tractable organism Neurospora, for which circadian clock regulation of development had been well established (Pittendrigh *et al.* 1959; Sargent and Briggs 1967). Jay moved to the University of California at Santa Cruz and joined Jerry Feldman's group. Feldman was the leading Neurospora geneticist studying the biological clock. He and his colleagues had isolated mutant strains with altered circadian periods in the developmental rhythm (Feldman and Hoyle 1973). Jay's arrival coincided with the newly emerging recombinant DNA techniques being developed for Neurospora (Case *et al.* 1979; Kinnaird and Fincham 1983; Schechtman and Yanofsky 1983). It was his goal to learn the tools of molecular and Neurospora biology, with the hopes of cloning the clock genes. Jay ultimately succeeded in cloning a clock gene after taking a position as an assistant professor of biochemistry at Dartmouth Medical School. His group cloned the *frq* gene using a chromosome walk and showed that the cloned DNA complemented the arrhythmic phenotype of a *frq* mutant allele (McClung *et al.* 1989).

During his time at Dartmouth Medical School, Jay has opened up the field of circadian molecular biology and biochemistry and developed the tools and intellectual framework for approaching mechanistic questions that relate to three key observations of the clock: (1) the ability of the clock to free-run with a period of about a day in constant conditions; (2) the phenomenon of clock resetting by environmental cues; and (3) the capacity for the clock to run with a similar period when the organism is placed in different temperatures, a property called temperature compensation. His work has provided answers to each of these questions and led to an often-cited molecular model for this microbial FRQ-based circadian oscillator that has formed much of the basis for our understanding of the mammalian clock (Dunlap 1999).

As mentioned above, Jay was a pioneer in cloning clock genes. He conceived the criteria for identifying clock components and was the first to use experimental tests to establish the identity of a clock protein (FRQ) (Aronson *et al.* 1994). Jay was also the first to determine

the biochemical activities of the clock molecules WC-1 and WC-2 and to show that these heterodimeric transcription factors are central to circadian feedback loops that, along with FRQ, form a circadian oscillator (Crosthwaite *et al.* 1997). His lab led the way in the discovery of clock-regulated genes as central to circadian output, identifying the first *c*lock-*c*ontrolled *g*enes, and in so doing, inventing a term to describe them, ccg, now applied universally in the field of chronobiology (Loros *et al.* 1989). With close scientific collaborator (and spouse), Dartmouth Medical School Professor Jennifer Loros, Jay discovered the molecular basis for light resetting of the clock, a mechanism that is conserved in mammals (Crosthwaite *et al.* 1995). He undertook a molecular understanding of temperature effects on the clock, including the mechanism for temperature-induced clock resetting (Liu *et al.* 1997, 1998). Such investigations of temperature compensation of the clock—a problem that has been difficult to address experimentally—are a current research focus in his group (Dunlap *et al.* 2007).

To advance the science, Jay's group, frequently in collaboration with the Loros laboratory, developed numerous innovations for the Neurospora system. These include the use of heterologous regulatable promoters and targeted gene replacement strategies. Jay played an important role in early efforts to obtain funding for sequencing the Neurospora genome, and he spearheaded and is the principal investigator for a functional genomics project. In collaboration with one of us (K. Borkovich), Jay's group focused on developing a high-throughput gene knockout procedure for Neurospora (Colot *et al.* 2006). The knockout project is on schedule to mutate ~7500 of the ~10,000 Neurospora genes in early 2009. Jay's leadership of large-scale genetics- and genomics-based projects has made a major contribution to the pace of research with these organisms and has impact well beyond his own investigations of the circadian clock. The new technologies are now being extended to other filamentous fungi, for example, in the production of knockout mutants in the model fungus *Aspergillus nidulans*.

Not only has Jay forged new ground scientifically, he continues to be a role model and mentor for junior faculty, postdoctoral researchers, and graduate students. He is rigorous, yet gentle, in his critiques and actively promotes others. Jay has helped numerous postdocs from his group (including one of us, D. Bell-Pedersen) to start their own independent laboratories, with many of them continuing to work in the field of fungal circadian rhythms.

Jay has made significant contributions of his time and effort to the larger scientific community. He has served as the inaugural chair of the Department of Genetics at Dartmouth since 1999. Jay served on the National Advisory Council for the National Institute of General Medical Sciences, National Institutes of Health (NIH), and has been a member of several study sections for the NIH and the National Science Foundation. Jay is an editor for *Eukaryotic Cell* and a co-editor-in-chief for *Advances in Genetics* and has served as the President for the Society for Research on Biological Rhythms and as Chair of the Neurospora Policy Committee. Jay has been an invited speaker and has organized numerous symposia and scientific conferences. He received the prestigious Robert L. Metzenberg Award in recognition of his innovative contributions to our understanding of biology (in Neurospora and beyond) in 2005.

Jay is a master at describing the complexities of the fascinating biological phenomenon that is the circadian clock, and his research publications are at the same time enlightening and exciting. He was a major contributor and editor for a comprehensive book on chronobiology (Dunlap *et al.* 2004) that is a must-have for students and researchers in the field. Jay has authored more than 100 publications, several of which were chosen as cover articles or were highlighted by the journal editors. One article that reviews the molecular mechanism of the clock and emphasizes the similarities among the fungal, fly, and mouse clocks is the most highly cited article on circadian rhythms written in the past 25 years (Dunlap 1999).

George W. Beadle is best known for his Nobel-Prize-winning studies with the organism *N. crassa* that led to the "one-gene–one polypeptide" hypothesis. It is fitting that the larger genetics community is recognizing Jay Dunlap—the first Neurospora scientist to receive the George W. Beadle Medal—for his ground-breaking research toward understanding the molecular mechanism of the circadian clock, again using the *N. crassa* system. We congratulate Jay on his receipt of this award and look forward to many more years of illuminating research contributions from this talented scientist.

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