Like Clockwork

Dartmouth's Life Sciences Symposium

by Soon Hyouk Lee '01

On Tuesday, October 17th, Dartmouth held its seventh annual life sciences symposium in Spaulding auditorium. Traditionally organized by the medical school's department of biochemistry, this year's symposium was organized by the department of genetics. The focus was on biological clocks, the endogenous temporal control systems that exist in almost all eukaryotic organisms.

The Past:

The history of biological clocks had its beginnings in 1729 when French astronomer Jean Jacques d'Ortous deMairan conducted experiments using a heliotrope plant. The leaves of the plant opened during the day and folded at night, yet when he put the plant in total darkness, the rhythm was not disrupted by the absence of daylight.

Progress in circadian clock research took off in the mid-eighties, when the first clock gene was cloned by Michael Young, now at Rockefeller University, Michael Rosbash, now at Brandeis, and Jeff Hall, also at Brandeis. The second clock gene was cloned in 1989, and dozens have been cloned since then.

Why biological clock research?

What is the significance of biological clocks? Biological clocks affect many cellular and organismal processes. Cardiovascular, urinary, and endocrine function as well as drug tolerance and effectiveness can be affected by the biological clock. In addition, the clock is important in human work-rest cycles and the jet lag phenomenon. There have even been associations between clock malfunction and common forms of manic depression as well as insomnia. Animals that rely and celestial

2000 Dartmouth Life Science Speakers

Rae Silver, Ph.D.
Columbia University
Professor Silver was the first to show that transplants of brain's clock in the suprachiasmatic nucleus (SCN) from one animal to another could restore circadian rhythmicity in SCN ablated animals

Susan S. Golden, Ph.D.
Texas A&M University
Using cyanobacteria as a model, Professor Golden focuses on the identification of the cellular and molecular components of the circadian clock and clock-regulated genes.

Steven M. Reppert, M.D.
Harvard Medical School/
Massachusetts General Hospital
Professor Reppert focuses on cellular and molecular mechanisms of circadian clocks

C. Robertson McClung, Ph.D.
Dartmouth College
Using *Arabidopsis thaliana* as a model, Professor McClung is investigating the genetic and molecular components of circadian rhythmicity.

Jay Dunlap, Ph.D.
Dartmouth Medical School
Professor Dunlap focuses on the mechanism by which eukaryotic organisms keep time on a daily basis and how this is used to regulate metabolism and development using *Neurospora* as a model.

William J. Schwartz, M.D.
University of Massachusetts Medical School
Professor Schwartz focuses on neural regulation of circadian rhythms in mammals.

navigation and flowers that depend on seasonal breeding times all rely on biological clocks.

The Symposium at Dartmouth

The biological life sciences symposium traditionally has had two speakers from Dartmouth and four from the international scientific community. This year, the two Dartmouth professors were Professor Robert McClung in the biology Department and Professor Jay Dunlap in the Genetics Department.

Attendees included undergraduate and graduate students from upstate New York, Massachusetts, Maine, Connecticut, and New Hampshire. Undergraduates, graduate students, postdoctorate fellows, and faculty from throughout the biology department and the medical school were in attendance.

There are conferences held worldwide on circadian rhythms. For example, the Society for Research on Biological Rhythms holds a conference every other year. The Society for Chronobiology also holds regular meetings with the international community. ❖

Resources regarding biological clocks

http://www.epub.org.br/cm/n04/mente/recritmos_i.htm
An outline of internet resources focusing on biological clocks

http://www.cbt.Virginia.edu/
The National Science Foundation Center for Biological Timing

http://www.med.harvard.edu/publications/Focus/complete_texts/Apr28_1995_complete.html
An article on biological clocks

http://www.geocities.com/Area51/Dimension/8211/JSS/00002.htm
An article on some of the genetic mechanisms of clock function

http://www.the-scientist.com/yr1999/oct/hot_991025.html
A scientific review of some biological clock research publications

The Research

Professor Robertson McClung in the biology department uses the plant *Arabidopsis thaliana* to study circadian rhythms. Using an array of molecular biology techniques, his laboratory studies periodicity of expression of certain genes.

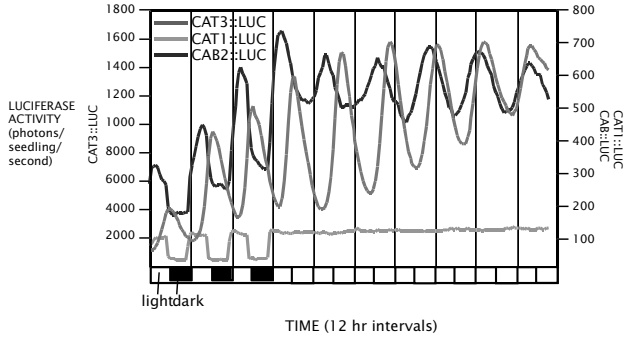

FIGURE 1

This figure shows three yfg (yellow fluorescent protein)::luc (luciferase) fusions, CAT3, CAT1, and CAB2. CAB2 is a chlorophyll a/b binding protein that anchors clorophyll molecules to the thylakoid membrane (the internal membrane system in the chloroplast). CAT1 and CAT3 are two catalase genes. Catalase breaks down hydrogen peroxide to water and oxygen and plays a critical role in cellular protection against oxidative stresses. This figure shows that cycling occurs in CAT3 and CAB2 even when periodicity of light source is eliminated by exposure of plants to constant light. CAT1 on the other hand, only shows periodicity during light cycling.

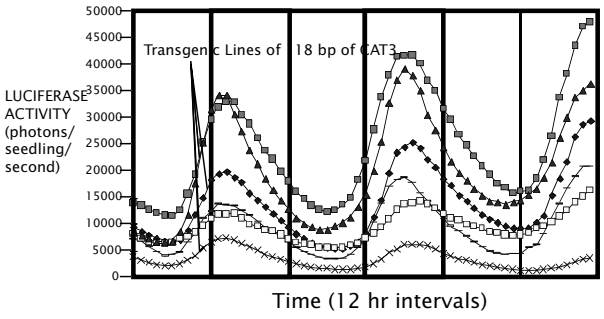

FIGURE 2

This figure demonstrates that 118 bp of the CAT3 promoter region is sufficient to confer circadian transcription on the luciferase reporter. Shown are 6 lines. Each line corresponds to an independent transgenic line (although 12 seedlings were monitored from each line and the line represents an average for those 12 seedlings). These seedlings started out in a light/dark cycle and after three days were released into continuous light (white boxes = light). The figure only shows the luciferase production after release into continuous light. The luciferase activity varies among the lines. This is an example of "position effect." That is, integration of the transgene at different chromosomal locations affects overall expression. But, note that the circadian parameters (period length and phase, or timing, of the peak) are constant among the lines.