

The Signal

Monthly newsletter of the W. M. Keck Center for Behavioral Biology
at North Carolina State University
May, 2013, vol. 14, no.9.

Two Keck Center Founding Members Receive Awards

In April, two founding members of the W. M. Keck center for Behavioral Biology received prestigious awards, William Neal Reynolds Distinguished Professor of Entomology Fred Gould and Professor Emeritus John G. Vandenberg.

Fred Gould has been awarded the 2013 Borlaug Service to Society and Environment Award. The award is named in honor of the late Dr. Norman E. Borlaug, Nobel Laureate and father of the Green Revolution. The award recognizes exemplary service to the environment and society in academics, research or service through enhancing global practices, new technologies, impact on students or global communities. The award is intended to recognize accomplishments and encourages future work.

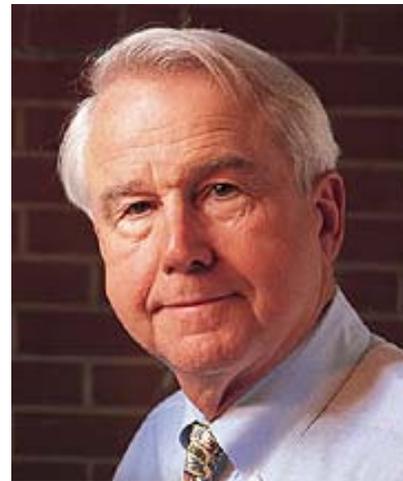
Vandenberg received the William C. Friday Award for Distinguished Service in Retirement. The award is named after William C. Friday (1920-2012), an education icon who provided extraordinary vision in leading the University of North Carolina from 1956 to 1986, three decades marked both by great challenges and impressive change. His dedication to the improvement of the human condition is reflected in the superb family of public universities in North Carolina he helped to build and in his distinguished record of public service to the nation.

Following in Friday's footsteps, Vandenberg has not slowed down after retiring. He continues to provide extensive service to the scientific community, serving on numerous committees and maintaining a keen interest in animal welfare regulations and effects of environmental toxins.

Congratulations to Fred and John!



Fred Gould



John Vandenberg

***The Signal* will not be published during the summer recess. The next issue of *The Signal* will appear in September, 2013.**

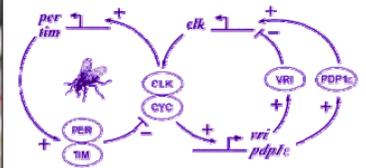
Period, Timeless and Night Owls: Is It Time To Wake Up Already?

by Rebecca Linger

This semester's final installment of the W. M. Keck Center distinguished seminar series showcased Dr. Michael W. Young from the Rockefeller University in New York, NY. Dr. Young discussed his fascinating work on "Genes Controlling Sleep and Circadian Rhythms in *Drosophila*." A pioneer in circadian clock research, Young began his scientific career with a Ph.D. in genetics from the University of Texas, Austin, followed by a postdoctoral research position in biochemistry at Stanford University. He then accepted an assistant professorship at Rockefeller University, where he progressed to full professor. Following a stint at the Howard Hughes Medical Institute, Young returned to Rockefeller, where he eventually became the University's Vice President for Academic Affairs. Young has received numerous awards for his many contributions to the field of neuroscience, including the 2009 Neuroscience Prize of the Peter and Patricia Gruber Foundation and most recently, the 2013 Wiley Prize in Biomedical Science.

Young began the seminar by reviewing the early discoveries in circadian rhythm research that began nearly 30 years ago. Microarray data of RNA isolated from heads of *Drosophila* exposed to light/dark cycles revealed waves of gene activity. Mutations in genes later identified as period (*per*), timeless (*tim*), and Clock abrogated these patterns. When *tim* and *per* were explored further, it was found that their expression is cyclic, their expression cycles align with one another, and mutation of one gene affects the rhythm of expression of the other. It was later found that the cyclic expression levels of *tim* and *per* are the result of their physical, functional, and regulatory interaction. During daylight hours, expression of *per* and *tim* is constitutive and both proteins localize to the cytoplasm; however, *Per* is phosphorylated and targeted for degradation. During hours of darkness, *Tim* levels increase, as *Tim*'s negative regulator, cryptochrome, is absent. Immunofluorescent colocalization and fluorescence energy transfer experiments revealed that when *Tim* accumulates to a sufficient level, *Tim* complexes with *Per*, saving *Per* from degradation. *Tim* and *Per* together translocate to the nucleus, where *Per* represses expression of *Tim* and itself. In response to daylight, *Tim* is degraded and *Per* is once again vulnerable to degradation as well, completing the cycle.

In vivo experiments in which mutated proteins are "seeded" into cells confirm the importance of the interaction between *Tim* and *Per* and their turnover. The "per long" mutation delays nuclear transfer of *Per* in neurons and results in a 29h cycle, while a *Tim*



Dr. Michael Young

protein that lacks its nuclear localization sequence or resists degradation slows the cycle to 35h. Mutations that abrogate *Tim* phosphorylation sites that are important for degradation lengthen the cycle, while mutations that mimic phosphorylation shorten the cycle.

Young then outlined some fascinating studies on human sleep disorders that utilized parallels between prolonged nighttime rest periods in insects and sleep in humans. Evidence shows that during rest periods insects have an elevated threshold for arousal, show brain activity changes, and exhibit responses to pharmacological manipulation similar to those of sleep in humans. RNAi was used to identify potential genes important in homeostatic control of rest using *Drosophila* locomotion as the output. Researchers found that mutation of the gene encoding Regulator of Cyclin A1 decreased overall rest time, length of sleep bouts, recovery from sleep deprivation and longevity. In addition, flies displayed increased sleep latency.

Lastly, Young discussed current research on Delayed Sleep Phase Disorder (DSPD) in humans. DSPD is the most common sleep disorder and affects 2% of the human population. Patients have difficulty falling asleep until 2-3am and rising before late morning, and frequently have trouble conforming to temporal social norms for work and activities. Interestingly, skin fibroblasts from patients in culture exhibit oscillations in luciferase levels under the control of the Clock gene promoter. In the family of one DSPD patient, the disorder was shown to be heritable and associated with a cryptochrome (*Cry1*) mutation resulting in a truncated *Cry1* protein that becomes enriched in the nucleus, resists interaction with its repressor, and may have a dominant negative effect on wild type *Cry1* activity. This discovery is likely only a small piece of a complicated puzzle that regulates sleep genes and behavior.

The 54th Drosophila Research Conference

by Wen Huang

The 54th Drosophila Research Conference (commonly known as the “Fly meeting”) took place in Washington D.C. on April 3-7, 2013. More than 1,500 Drosophila researchers from 40 states in the U.S. and 32 countries participated in this meeting, where Keck Center faculty, students, postdocs, and alumni were extremely well represented. The conference featured a wide variety of topics, all using Drosophila as a model.

The meeting opened Wednesday night with the presentation of the Larry Sandler Award, given to the best dissertation work of the previous year. Dr. Weizhe Hong, a former graduate student trained in the Liqun Luo lab at Stanford University was the recipient of this year’s award. Dr. Hong spoke about a series of elegant genetics experiments to understand the specific pairing between olfactory receptor neurons (ORNs) and projection neurons (PNs). Using genetic screening, Dr. Hong first identified a transmembrane protein called caps, which has specific expression patterns in different PNs, suggesting that caps may be a candidate gene involved in targeting of PNs. By manipulating caps expression, Dr. Hong was able to show that its proper expression is required for the targeting of PNs but not ORNs. Additionally, Dr. Hong found that two Teneurin proteins, Ten-m and Ten-a, can instruct the matching between neurons by homophilic interactions. Following the recognition of a rising star from the Drosophila community, Nobel Laureate Dr. Jules Hoffmann recounted the history of the discovery of the *Toll* gene in flies and a series of important experiments to understand innate immunity from flies to mammals. Dr. Hoffmann shared the 2011 Nobel Prize in Physiology or Medicine for “discoveries concerning the activation of innate immunity”. The first night’s opening session concluded with the presentation of the George W. Beadle Award to Dr. Scott Hawley from the Stowers Institute for Medical Research.

The first plenary session took place on the morning of April 4. The Drosophila Image Awards were presented to “the most striking image that clearly conveys a point of important biological information”. Joanna Krzemien and Yufeng Pan won the still image and video awards for their stunning work of “a complex set of muscles underlying the body wall of third-stage Drosophila larva” (*Development* **139**: 75-83) and “motion input and activation of P1 neurons elicit courtship behaviors” (*Proc. Natl. Acad. Sci. USA* **109**: 10065-10070), respectively.

Dr. Marc Freeman from the University of Massachusetts Medical School and the Howard Hughes Medical Institute then told us about his identification of a gene required for proper axon degeneration. He performed EMS mutagenesis and screened thousands

of images to identify a loss-of-function mutation in the gene *dSarm* that blocks the normal degeneration of axons following axotomy. Furthermore, the mammalian ortholog of *dSarm* is also required for axon degeneration after injury *in vivo*, suggesting a conserved function of this gene in axon degeneration. Dr. Chris Jiggins from the University of Cambridge talked about his work on coloration in *Heliconius* butterflies. Jiggins started with the interesting observation of independent origin of mutations causing the same pattern of coloration in different butterfly species. His work identified regulatory variations in the gene *optix*, which drives convergent adaptation in multiple species and may explain mimicry. Using genetic and genomic tools, Jiggins further found that the gene *kinesin*, which is expressed earlier than *optix* during development, is also associated with coloration pattern. He proposed a model which involves both genes in a common pathway. Dr. Terry Orr-Weaver from the Whitehead Institute of MIT was the recipient of the FASEB Excellence in Science Award and gave a talk on her work on variation in cell cycle during development. Using genetic and biochemical approaches, Dr. Orr-Weaver showed that the proteins png, plu, and gnu form a complex, which regulates the translation of cyclin B. The protein complex achieves the regulation through inhibition of the pum gene, which binds to the 3’UTR of the cyclin B messages and de-adenylates and degrades mRNAs. Through this and other mechanisms, the png/plu/gnu complex ensures the proper expression and timing of cyclin B.

As always, this year’s conference featured emerging new technologies for Drosophila research. In the Techniques and Functional Genomics workshop, Dr. Dana Carroll from the University of Utah introduced the Transcription activator-like effector nuclease (TALEN) technique. TALEN is a nuclease that cuts specific DNA sequences based on the combination of its zinc finger DNA recognition domains. By designing specific recognition domains, TALEN can be engineered to introduce double strand breaks to DNA any arbitrary sequences, which can then be used to splice in an exogenous fragment of DNA through harnessing the homologous repair machinery of the cell. Dr. Carroll demonstrated the successful application of TALEN to introduce mutations in the Drosophila genome. Peter Combs, a graduate student from the University of California at Berkeley developed a novel technique to perform mRNA sequencing for cryo-sliced Drosophila embryos, which contain very little RNA. By combining these RNAs with RNAs from a distantly related sequence, the

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by Gunjan Arya

sequencing library preparation quality is dramatically improved. This allows them to obtain RNA sequence data with good quality and analyze the spatial distribution of gene expression during development.

The Evolution and Quantitative Genetics workshop contained many interesting and useful talks, including multiple talks using the *Drosophila melanogaster* Genetic Reference Panel (DGRP) developed in Keck Center faculty member Dr. Trudy Mackay's lab. Nandita Garud, a graduate student from Stanford University, developed a novel haplotype statistic to distinguish soft selective sweeps from hard selective sweeps, using population sequence data from the DGRP. Dr. Andrew Clark from Cornell University described his effort to sequence 92 lines from five geographical locations and characterize them. Dr. David Houle from Florida State University spoke about his multivariate approach for genome-wide association in the DGRP. Bin He, a graduate student from the University of Chicago sensitized flies by expression of a misfolded human protein. By crossing DGRP lines to this sensitized background, he then assessed the effect of natural variation on phenotypes in response to the sensitization.

The *Drosophila* community has been very excited about large-scale efforts to produce high throughput data and identify functional elements in the genome. In the Future of *Drosophila* Genomics workshop, scientists from the modENCODE consortium updated the audience on the current status of their data production, analysis, release, and integration with FlyBase. Dr. Gerald Rubin from the HHMI Janelia Farm campus talked about an enormous effort to image the central nervous system of thousands of flies expressing a particular DNA element. Keck Center faculty Trudy Mackay updated the community on the status of the DGRP resource, noting the importance of overlaying natural variation on top of the static data produced by modENCODE. Mackay introduced several nice successful examples of using the resource in her laboratory and provided her perspectives on the future of *Drosophila* genomics.

The poster session of the meeting was a great success; more than 800 posters were displayed. Keck Center students and postdocs Bryn Gaertner, Chad Hunter, John Shorter, Lauren Dembeck and Wen Huang presented their work. Many former Keck Center students and postdocs continue to excel and presented their new discoveries at this meeting as well. The 54th *Drosophila* Conference came to a close on April 7. At this meeting, old colleagues and friends re-united, new collaborations were formed, and new ideas were inspired. We look forward to the next gathering of *Drosophila* researchers in San Diego next year.

The 35th AChemS (Association for Chemoreception Sciences) Annual Meeting was held at the Hyatt Regency, Huntington Beach, CA. The meeting started off with an awards ceremony honoring senior and junior scientists. Dr. Bill Hansson presented the keynote Givaudan lecture entitled "Non-Model Models in Olfaction". Hansson showed how desert ants use olfactory cues to identify their home nests. These remarkable rapidly moving creatures can cover the size of a football field during a foraging outing using the sense of smell to identify dead insects on which they feed. He also showed that primitive insects, such as silverfish and bristletails already have gustatory (*Gr*) and ionotropic (*Ir*) olfactory receptors, but that the family of *Or* receptors evolved later during a burst of rapid evolution that likely accompanied the development of flight.

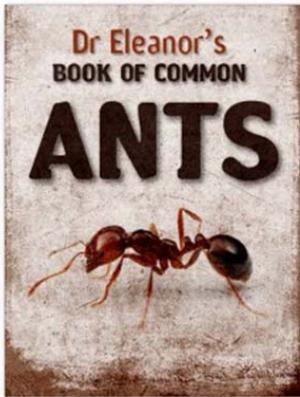
The conference was divided into concurrent platform and poster. The meeting this year predominantly had talks geared towards structural biology and biophysics. Most of the talks and posters were on research conducted on humans and rodents with few presentations from labs using *Drosophila* as their choice of model organism. A couple of talks from the Industry symposium: "Taste and smell in translation: applications from basic research" caught my attention. This was an interesting topic of discussion because it built a bridge of how we can use our basic research findings and apply it in the industry. Dr. Richard Mattes from Purdue University talked about individual differences in oral fat detection and their health implications. Dr. Timothy Gilbertson added to Dr. Mattes findings on fatty acid receptor function and the role of salivary lipase in fat detection. His talk on mechanisms of fat taste threw light on the function of CD36 and Trpm5 in fatty acid signal transduction. The first half of the industry symposium concentrated on taste reception and function while the second half had talks on olfaction. Dr. Joel Mainland from the Monell Chemical Senses Center talked about insights from olfactory receptor screening. Using a combined psychophysical and molecular approach, he aims to develop a predictive model relating molecular structure and olfactory perception. The other event that was especially interesting was the Presidential Symposium which included talks on gut peptide interaction between taste, feeding and reward. Of note was Dr. Carel le Roux's talk on the exceptional weight loss that results from Roux-en-Y gastric bypass (RYGB) that is accompanied by notable changes in circulating levels of gut peptides and postsurgical alterations in taste preferences, food reward, and caloric intake in both bariatric patients and rodent models.

Outreach

Reaching Out: Dr. Eleanor's iBook of Common Ants

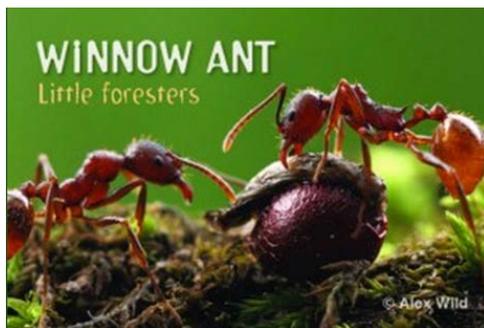
by Lea Shell and the Your Wild Life team

Myrmecologist Dr. Eleanor Spicer-Rice has been busy during April 2013 answering questions about ants at events such as talking to crowds at the Science Café at the Nature Research Center and in her new free iBook, Dr. Eleanor's Book of Common Ants. This past month, the Your Wild Life team has been busy sharing all things ANTS. The team also shared the availability of the free iBook with museum crowds during BEST Fest.



Dr. Eleanor's Book of Common Ants is now available for free on iTunes and on the yourwildlife.org website.

In the new iBook Dr. Eleanor shares stories about the 13 most common ants that we encounter in North America. The stories grace the (digital) pages alongside beautiful photos from Alex Wild with pages designed by Neil McCoy.



Stories of the Winnow Ant grace the pages of the iBook of Common Ants.

Head on over to iTunes or YourWildLife.org to download the free iBook!

For more information about our projects: check out our blog at YourWildLife.org and follow us on Twitter @YourWild_Life

Seminars

As part of the University Global Partnership Network (UGPN), the Keck Center organizes a **conference on "Genes and Behavior" on May 29 and May 30, 2013**. The UGPN includes the University of Surrey, UK; North Carolina State University, USA; and the University of São Paulo, Brazil. While these institutions have established bilateral relations for some years, the UGPN is designed to leverage mutual strengths in research and education to broaden collaborative endeavors. This conference will be attended by representatives from the University of Sussex and the University of São Paulo and is designed to showcase potential research areas at NCSU that could result in international collaborations, including international student exchange. Lunch will be provided.

The conference will be in 3503 Thomas Hall.

Publications

The following publication from the W. M. Keck Center for Behavioral Biology has appeared in print:

Meitzen, J., Perry, A. N., Westenbroek, C., Hedges, V. L., Becker, J. B. and Mermelstein, P. G. (2013) Enhanced striatal β 1-adrenergic receptor expression following hormone loss in adulthood is programmed by both early sexual differentiation and puberty: A study of humans and rats. *Endocrinol.* **154**: 1820-1831.

Of note...

Robert Anholt served on the program committee and the awards committee of the American Chemoreception Sciences annual meeting in Huntington Beach, CA.

Gunjan Arya and **Robert Anholt** presented a poster at the annual meeting of the American Chemoreception Sciences in Huntington Beach, CA.

Bryn Gaertner, **Chad Hunter**, **John Shorter**, **Lauren Dembeck** and **Wen Huang** presented posters at the 54th annual Drosophila Research Conference in Washington, DC.

Fred Gould gave the Alfred M. Boyce Lecture at the University of California at Riverside on "Two-locus models for applied entomologists." He has also been awarded the 2013 Borlaug Service to Society and Environment Award.

Jim Hunt presented a seminar in the Department of Entomology at the University of Arkansas.

Trudy Mackay gave a presentation on the *Drosophila melanogaster* Genetic Reference Panel at the 54th annual Drosophila Research Conference in Washington, DC.

John Meitzen became a member of the Corporation of the Marine Biological Laboratory at Woods Hole, MA.

Heather Patisaul's laboratory is featured in a documentary on early puberty called "Big Girl."

Leslie Sombers gave an invited talk on the voltammetric detection and characterization of met-enkephalin in brain tissue at the National Institute of Alcohol Abuse and Alcoholism.

John Vandenberg received the William C. Friday Award for Distinguished Service in Retirement.

To contribute to The Signal, to be placed on our mailing list or for information about the W. M. Keck Center for Behavioral Biology, visit our website <http://projects.cals.ncsu.edu/behavioralbiology/> or contact Dr. Robert Anholt, Department of Biology, Box 7617, North Carolina State University, Raleigh, NC 27695-7617, tel. (919) 515-1173, anholt@ncsu.edu.

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