The Signal

Monthly newsletter of the W. M. Keck Center for Behavioral Biology
at North Carolina State University
May, 2006, vol. 7, no. 9

The Signal Volume 8 Goes Electronic

When the next edition of The Signal appears in September, 2006, the first issue of volume 8, readers will receive an electronic version. All members of the W. M. Keck Center for Behavioral Biology and all current recipients of The Signal will receive a monthly e-mail with a pdf attachment instead of a hard copy of the newsletter. Display copies with color illustrations will still be distributed in paper format to university administrators, and foundation and granting agency officials.

Distribution of The Signal electronically is cost-effective, allows for broader distribution, is easy to post each month on the Keck Center's website, and will enable each reader to view illustrations in color. Readers are encouraged to print their own hard copy of the newsletter. The format of The Signal will remain the same and, as in the past, the newsletter will be distributed from September through May of the academic year.

The Executive Committee of the W. M. Keck Center for Behavioral Biology would like to thank all of our Keck Center friends and colleagues for their continued enthusiastic participation in the Center's activities and their many contributed articles to The Signal. We wish you all a productive summer recess.

Keck Center Plans Exciting Seminar Series for 2006

The W. M. Keck Center distinguished seminar series for the fall semester of 2006 promises a range of diverse and outstanding speakers. Leading off in September will be Susan Fahrbach from Wake Forest University, followed by Cathy Rankin from the University of British Columbia, Bert Holldoebler from the University of Arizona, and Hopi Hoekstra from the University of California at San Diego. Seminar topics will range from social behaviors in honey bees and ants to somatosensory behaviors in nematodes, and evolutionary genetics of adaptive behaviors in wild mice.

"It will be an eclectic and exciting series," says Keck Center Director, Dr. Robert Anholt, "These are also great people for our students and postdocs to interact with."

As always, seminars will be announced in The Signal. Mark your calendars!

BASF Pledges Renewed Keck Center Support

For the third straight year BASF Corporation has pledged support for the seminar series of the W. M. Keck Center for Behavioral Biology. "Private funds are extremely important for the operation of the Keck Center," says Center Director Dr. Robert Anholt, " such funds have great flexibility as they are not subject to the same restrictions as State allocated funds. BASF has been a generous sponsor of the Keck Center for several years and we greatly value and appreciate their support."

Out and About

As graduation approaches and the summer recess looms, many members of the Keck Center are looking forward to spending the summer at their field sites. Studies of animals in their natural habitat and the effects of environmental changes on populations provide an important dimension to the scope of the W. M. Keck Center for Behavioral Biology. Keck Center faculty are involved with numerous projects in behavioral ecology that involve distant field sites, including Belize, Mexico, the Virgin Islands, Peru, Trinidad and field sites in North Carolina and other locations within the United States.

We wish our colleagues in the field a productive and successful summer and are looking forward to seeing you back at NC State in September.

The Sweet Smell of Sex

by Harland Patch

On April 6, Dr. Frank Zufall, a professor in the Department of Anatomy and Neurobiology at the University of Maryland School of Medicine delivered yet another stimulating W. M. Keck Center distinguished seminar, entitled "Encoding Immune System Signals by the Mammalian Nose: The Scent of Genetic Compatibility." Dr. Zufall received his Ph.D. from the Technical University of Munich in 1990 and has lived in the United States since 1992 when he moved to the Yale University School of Medicine to continue his early work on the mammalian olfactory system. For Zufall the mouse offers a particularly good experimental model for the study of olfaction because a great deal is known about its cellular physiology, genetic manipulations are fairly straightforward, and mice have robust behaviors that can be easy scored.

Zufall's most recent research focuses on pheromone sensing by the mouse's "second nose," known as the vomeronasal organ (VNO). In rodents and other mammals, this olfactory organ is prominent and appears dedicated to the detection of pheromones, but in humans and our nearest primate cousins it is vestigial and presumed non-functional.

The VNO is a distinct and separate system from the main olfactory organ, which detects general olfactory compounds in mammals. Zufall and colleagues have used electrophysiological recording and calcium imaging to identify which neurons in the VNO epithelium respond to a group of putative pheromones, molecules that were previously shown to elicit responses in behavioral assays. The authors were able to show that single VNO neurons are highly sensitive and narrowly tuned to specific pheromones. Furthermore, these distinct neurons form non-overlapping subsets which map to distinct regions in the epithelium

Unlike other olfactory neurons, the neurons in the VNO are selective and do not show broadening of their tuning curves with increased concentrations of pheromones. Later research in collaboration with Peter Mombaerts using deficiency mutants indicated that the V1R superfamily of seven transmembrane receptors, one of two superfamilies of candidate pheromone receptors in the mouse, is expressed in the apical or "superficial" zone of the VNO epithelium and plays a principal role in the detection of urine-derived volatile pheromones. A tour-de-force study published in 2004, revealed that neurons which express the other receptor type, the V2R receptors, in the basal or "deep"epithelium respond to peptide ligands of the major histocompatibility (MHC) complex.

With this study Zufall and his collaborators showed for the first time that molecules known to be integral to the immune system also act as sensory stimuli and impart information about genetic individuality. They tested this assertion by exploiting selective pregnancy block, known as the Bruce effect, which occurs when a female mouse which has been inseminated by one male spontaneously aborts the pregnancy when exposed to the urine of another unrelated male. When pregnant females were exposed to MHC peptides of strange males, pregnancy was effectively blocked indicating that the MHC peptides functioned as pheromones capable of influencing mating and perhaps mate selection.

This story, however, is not so simple. Dr. Zufall presented other results that showed that neurons in the main olfactory system also respond to nonvolatile immune system derived peptides, which raises the possibility that MHC peptides could play an olfactory role in mammals that lack a functional VNO. Perhaps our nose knows our mate choices better than our eyes.

For further reading on this interesting topic, see:

Del Punta, K. *et al.* (2002) Deficient pheromone responses in mice lacking a cluster of vomeronasal receptor genes. *Nature* **419:** 70-74.

Leinders-Zufall, T. *et al.* (2004) MHC class I peptides as chemosensory signals in the vomeronasal organ. *Science* **306:** 1033-1037.

Leinders-Zufall, T. *et al.* (2000) Ultrasensitive pheromone detection by mammalian vomeronasal neurons. *Nature* **405:** 792-796.

Spehr, M. *et al.* (2006) Essential role of the main olfactory system in social recognition of major histocompatibility complex peptide ligands. *J. Neurosci.* **26:** 1961-1970.

Keck Center Students to Visit Atlanta's CBN

Once again students from the W. M. Keck Center for Behavioral Biology will participate in our longstanding exchange program with the Center for Behavioral Neuroscience in Atlanta. This year Deepa Sambandan and Scott Dobrin will represent NC State's Keck Center and present posters during the May 20th annual research symposium at the CBN. We are looking forward to a report of their experience in the September issue of The Signal.

Insights From Comparative Genomics

by Julien Ayroles

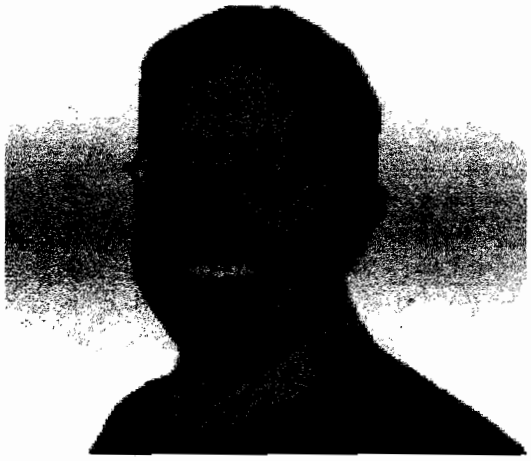
This month the Keck Center's social event hosted by Trudy Mackay and Robert Anholt welcomed UNC professor, Dr Corbin Jones, for a lively discussion on the usefulness of comparative genomics in addressing phenotypic and behavioral evolution. The same day Dr. Jones presented our weekly genetics seminar on "The evolution of genome content: early insights from the genome of *drosophila simulans* and its close relatives."

Dr. Jones did his Ph. D. at the University of Rochester with Dr. H. Allen Orr, where he studied the genetics of natural adaptation using *Drosophila sechellia*. He did his postdoctoral training at the University of California at Davis under Dr. David Begun, where he investigated the evolutionary genetics of *Drosophila* reproduction and the origin and evolution of "novel" *Drosophila* genes.

Presently at UNC, his lab uses a multidisciplinary approach including bioinformatics, gene mapping, population genetics and functional genomics to ask questions related to the molecular basis of adaptive evolution. He studies species-specific adaptations in *D. sechellia* and *D. morinda* as well as the emergence of new genes in *Drosophila*. His general interests are broad; he studies a variety of issues ranging from speciation to genome structure.

That evening, a large number of people gathered for the Keck Center's social event to discuss how comparative genomics has and will help us better understand the molecular processes underlying evolution. The number of sequences poured daily into databases around the world is growing exponentially. We now have sequenced the entire genome of several of the main branches of the tree of life but the challenge in this genomic era is to sort through this plethora of data and gain a better understanding of how these genomes have evolved. In other words, how do we explain the heterogeneity in terms of gene number, mutation rate, and recombination rate?

The discussion wandered around these central questions: What can we do with all of these sequence data, how far can we take the results from comparative genomics, and will these data allow us to say anything about behavior? We addressed the use of bioinformatics in assigning a gene with a functional annotation, including its limitations and the absolute need to confirm these annotations experimentally. We also discussed the diversity of odorant binding proteins and the extent of variation in the type and number of chemosensory genes identified in a variety of sequenced organisms.



Corbin Jones

What can comparative genomics tell us about how animals can regulate the perception of different olfactory stimuli in their environment? It appears that different strategies are in place to detect or regulate the reaction to a given stimulus; we wondered how much of this regulation was due to sequence variation and regulation of gene expression.

Some species (such as *D. sechellia)* live on a plant host that is toxic to most other arthropods. Other species of *Drosophila* recognize the distinctive smell of this plant and avoid it. We wondered what adaptive mechanisms are in place in *D. sechellia* to allow this fly to ignore this smell; did it lose the gene coding for the receptor, or is it simply ignoring the signal? In the light of the sequence data currently available and what we have learned from it, a different kind of sampling strategy is needed to gather more information from genomes. Now that we are beginning to have a better idea of the picture of between species variation, a great deal of information may be gained by sequencing variation within species. An effort is underway at UC Davis where Charles Langley and colleagues are using an Affymetrix platform to re-sequence 50 lines of *Drosophila melanogaster*, coming from our very own Raleigh Farmer's market.

All in all, the take home message was that every genome has a very unique story to tell, and right now, comparative genomics is a major way to unveil that story. But as Corbin stated, "Take what you can from the genome sequences, but remember that in the end you'll have to do an experiment."

Adolescence and Alcoholism - Twin Trouble

by Deepa Sambandan

The last W. M. Keck Center distinguished seminar for the spring 2006 semester was held on April 24th. The speaker was Dr. Matthew McGue from the University of Minnesota whose talk on "Adolescent Substance Use and Abuse: Emerging Evidence for Gene-Environment Interplay' was remarkable. During lunch with the speaker the graduate students and post-docs of the Keck Center had a wonderful opportunity to discuss at great length issues on substance abuse including cross-cultural practices and international policies on alcoholism.

Dr. McGue is biostatician transformed into a behavioral geneticist whose studies, according to him, are based on the "messiest species - the human adolescent." He chose to study this stage in human development as early adolescence is the critical period in adult development. Thus, to really understand what drives individuals to alcoholism, adolescence appears to be the most important phase.

McGue started the Minnesota State Twin Family Study in the early 1990s to look at gene-by-environment interactions on alcoholism. Two cohorts of twins were studied, one starting at age 11 and the other starting at age 17. A nation-wide survey indicates that the earlier is the onset of drinking (especially before 15-years of age), the higher is the risk for developing adult alcoholism. There is also a significant association between early drinking and incidence of other problematic behaviors such as drug abuse and antisocial behavior. The questions that arises are: what are the mechanisms that underlie this correlation? and, are genes that lead to these conditions expressed early in adolescence? Heritability analyses in adults show that depression and anxiety are correlated with alcoholism. The genes involved appear to be the same in both sexes that lead to "dis-inhibitory psychopathology."

In Dr. McGue's opinion, parents are not the principal environmental role model that influence behavior of adolescent children. Rather, it is the older siblings that serve as role models for disinhibitory disorders.

McGue presented an interesting example of gene-by-environment interaction. The ALDH2 gene product encodes aldehyde dehydrogenase, which performs the rate limiting step in the conversion of alcohol to acetate. The dysphoria experienced after alcohol intake (hangover) is due to excess acetaldehyde. There is a naturally occurring mutation in the ALDH2 gene, which occurs in 50% of the East Asian population. As they have low alcohol tolerance, these people avoid drinking alcohol and incidence of alcoholism is relatively low in these populations. Whereas this protective allele has increased in frequency in the population over years, its frequency is not high enough to completely eliminate alcoholism in these populations. Studies on Asian-American adopted youth indicate that the protective ALDH2 allele actually does not diminish alcoholism. Thus, the mutated allele influences, but does not determine behavior, reflecting cultural modulations of genetic predisposition. Furthermore, there was no correlation the mutant ALDH2 allele and other adolescent problematic behaviors. McGue addressed the issue that sources of environmental effect are still being underappreciated. His studies show that genes influence behavior, but can and are modulated by culture and environment.

Science in Bloomington at the CISAB Conference

by Nicole Benda

Spring is beautiful, but it goes by so quickly! So it was nice to travel back in seasonal time to Bloomington, Indiana, where the dogwoods and tulips were still in full force. Alexis Edwards and I traveled there in mid-April to attend the 13th Annual Indiana University Animal Behavior Conference, sponsored by The Center for the Integrative Study of Animal Behavior (CISAB). Similar to NC State's W. M. Keck Center's annual symposium, this event provides students of CISAB the opportunity to share their findings in a semi-formal environment. Talks and posters were presented by researchers (both students and faculty) from more than 10 different institutions. Alexis presented her work on the "Genomic response to artificial selection on aggression in Drosophila". I reported on the "Fitness consequences of non-host oviposition to a specialized herbivore". There were many excellent presentations! Here are a few:

Bob Brodman of Saint Joseph's College described the "weird" ecology and natural history of the western lesser siren. This two-legged salamander is paedogenic and spends its entire life in water. Its distribution is unusual in that it seems to be delineated by water resources (watersheds of the Mississippi and Lake Michigan basins) instead of temperature zones. It survives drying habitats by

burrowing into the mud and entering estivation.

Elizabeth Lehman of Indiana University found that tetrodotoxin (TTX) may act as a maternally-endowed defense against egg predation in the rough-skinned newt. However, TTX was not toxic to caddisfly larvae, a common predator of newt eggs. In fact, it appears that caddisfly larvae in habitats where newts are present may use TTX as a predator signal, whereas caddisfly larvae in habitats where newts are absent do not respond to the neurotoxin as a predator cue.

Melissa Scotti of Indiana University investigated seasonal aggression in female Siberian hamsters. She found that females housed under short-day photoperiods were more aggressive to intruder females than those housed under long-day photoperiods. Interestingly, aggressive behavior did not seem to be mediated by gonadal steroids. Although little is known regarding the natural mating system of these hamsters, Scotti hypothesized that increased aggression during the winter months may be due to a need to vigorously defend resources during this time.

Katheryn Lenz of Indiana University described the effect of maternal licking of pup's perineal regions on dendritic development of the spinal nucleus of the bulbocavernosus (SNB) in male rat pups. The SNB is a sexually dimorphic motor neuron that controls penile reflexes involved in copulation, and arborizations grow to a maximum at postnatal day (P) 28 and then reduce to a normal amount by P49. Maternal licking normally ends at ~P14. Reduced maternal licking did not have an effect on maximum arborization (on P28) but by P49, dendritic arborizations had shrunk back much further (23%) in male pups with reduced maternal licking. The reduction was pronounced in the rostral end of the SNB.

In addition to these and many other interesting talks, there were also many posters. Two were especially interesting:

Idelle Cooper is investigating female mimicry of male coloration in damselflies. Several damselfly species have a color dimorphism in females in which one female morph looks like the male. In some Hawaiian species, females can be green (the typical female color) or red (male color). Based on an elevational gradient in morph frequency and lab experiments, Cooper hypothesizes that this coloration is not related to sexual signaling, but is being used for protection from high levels of solar radiation. The red coloration displayed by males may also protect females from the harsh conditions at high elevations

Helena Sownoini presented her group's findings on the seasonal variation in volatile profiles in the preen gland secretions of dark-eyed juncos. Along with differences between seasons, sex differences were also found. Many compounds were long-chain aldehydes and alcohols, similar to pheromones in mammals and insects. The behavioral and biological relevance of these compounds is still being explored.

The conference was capped off with a talk by plenary speaker Lauren Riters of the University of Wisconsin. Dr. Riters investigates why European starlings sing. During the breeding season, when testosterone is high, possession of a nesting cavity and presence of a female are both an impetus for a male starling to sing. However, during the non-breeding season, when testosterone is low, presence of females does not affect males, though males do sing throughout the year. Dr. Riters found that, when these cues are in place, dopamine stimulates song and opioids inhibit song, and that this is in part regulated by brain regions involved in sexual motivation and reward. Females prefer longer bursts of song, and Riters also found that the density of opioids in motivation and reward brain regions is higher in longer singers.

We were warmly welcomed to this beautiful college town, treated to delicious ethnic dinners (one at the Snow Lion, owned by the Dalai Lama's brother) and tours of the castle-like campus and the biology department's natural history display and greenhouses. At the evening of the conference, a lovely reception was hosted by faculty members Laura Hurley and Troy Smith. The reception featured tasty desserts and allowed us to learn more about the people behind the day's presentations.

Alexis and I were very happy to be able to attend the CISAB animal behavior conference. It was great to make new friends, meet again with students that have attended past Keck Center symposia, and to meet so many researchers with a broad range of interests regarding the study of animal behavior.

Grants and Contracts

Philip Awadalla received a two-year $75,000 grant from the National Academies Keck Futures Initiative to study human-malaria co-evolution.

Publications

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

Groot, A.T., Horovitz, J. L., Hamilton, J., Santangelo, R. G., Schal, C. and Gould, F. (2006) Experimental evidence for interspecific directional selection on moth pheromone communication. *Proc. Natl. Acad. Sci. USA* **103:** 5858-5863.

Of note...

Philip Awadalla presented seminars at Brown University and at the Departments of Genetics and Medicine at Yale University on the evolutionary genomics of haplotype variation in malaria.

Alexis Edwards and **Nicole Benda** attended the annual animal behavior conference at the Center for the Study of Animal Behavior at Indiana University.

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