

The Signal

Monthly newsletter of the W. M. Keck Center for Behavioral Biology
at North Carolina State University
January, 2017, vol. 18, no. 5

The Signal Wishes All Its Readers a Happy New Year!



Speakers at the First Annual Keck Center Faculty Research Symposium. Left panel, seated first row from left: Michael Cowley, Robert Anholt, Trudy Mackay, Troy Ghashghaei; standing from left: Brian Langerhans, Santosh Mishra, Coby Schal, Heather Patisaul, John Meitzen, Will Kimler, David Tarpy, Lisa McGraw, Reade Roberts, Russell Borski, John Godwin, David Aylor; Right top panel from left: Leslie Sombers, Fred Gould, Helen Huang. The lower right panel shows Keck Center faculty, who were not able to speak at the symposium, clockwise: Max Scott, Patricia Estes, Rob Dunn and Mary Anna Carbone. All wish you a Happy New Year! A synopsis of the symposium is presented by Leslie Wilson and Jaime Willett on page 2.

From the Director

The Keck Center has had a successful 2016, which culminated in the first Annual Faculty Research Symposium, described on page 2 of this issue of *The Signal*. I want to thank all faculty, students, postdocs and research staff for their enthusiastic participation in last year's Keck Center activities.

In 2017, we will see changes in the Keck Center governance with Drs. Fred Gould, Coby Schal and John Godwin rotating off the Executive Committee at the end of June. Fred Gould and Coby Schal are founding members of the Center and their nearly two-decade long service is immensely appreciated. Drs. John Meitzen and Brian Langerhans will join the Executive Committee along with two graduate students and a postdoc.

The new year will feature a professional development publication workshop jointly organized with the Comparative Medicine Institute, which will feature several editors of major journals, in February; our traditional student/postdoc symposium; another faculty research symposium; an excellent slate of distinguished seminar speakers; social evening discussions, and a variety of outreach activities in coordination with other programs through the NC Museum of Natural Sciences, including Darwin Day, Brain Day and Bug Fest. I am looking forward to seeing all of you at our many activities in 2017! Happy New Year!



The First Annual Faculty Research Symposium of the W.M. Keck Center for Behavioral Biology

by Leslie Wilson and Jaime Willett

The 1st annual Faculty Research Symposium of the W.M. Keck Center for Behavioral Biology was held on Friday, December 2nd in the Stanley Stephens Room at NC State. The Symposium consisted of 20 faculty research talks, broken up into 4 sessions, from 7 departments and 5 colleges across NC State. The symposium was held to promote discussion and interaction among members of the Keck Center and to help build the community of behavioral biologists at NC State. For these reasons, the faculty presentations were focused on new and unpublished work. It was an extremely diverse day of presentations, ranging in topics such as neuronal control of artificial limbs, to the plasticity of the reproductive potential in honey bees. The event was a huge success and another one will be planned for next year.

Welcoming remarks were given by Keck Center Director, Dr. Robert Anholt, in which he introduced the symposium and thanked the attendees for their participation. Session 1 was moderated by Dr. Coby Schal. The first session was mostly genetic-based topics with a diverse range in application topics, from invasive species eradication to monogamy in mammals. The first presentation of the day was given by Dr. Will Kimler. Dr. Kimler gave a historical view of evolution and behavior. He presented on how evolution is a branching descent through natural selection, which was described by Darwin in the 1860s. He then touched on how adaptive evolution does only occur through the physical characteristics of a species, but also the behavioral ones. He stated that the new molecular tools, developed over the last 30 years, have greatly expanded the capability for evolutionary and genetic studies. After Kimler, Dr. Trudy Mackay introduced quantitative trait genetics, describing the genetic variation of traits and what evolutionary forces are responsible for these variations. Dr. Marcé Lorenzen described her work uncovering a *Medea* (Maternal Effect Dominant Embryonic Arrest) gene within red flower beetles. In species that have a *Medea* gene, only the offspring who inherit *Medea* will survive, providing a tool for genetic pest control. Lorenzen has been using newly developed biological tools to determine which specific gene sequence is responsible for the *Medea* traits within these

beetles. After Lorenzen, Dr. John Godwin talked about methods to eradicate invasive mice on islands. Godwin explores how to implement genetic biocontrol of mice on islands as an alternative to killing with bait. The last speaker of the session was Dr. Lisa McGraw, who studies the neurogenetic architecture of monogamy. McGraw uses a model species of prairie voles, who are one of the few species known to form pair bonds with their partners. She studies individual variations in the propensity of these voles to be monogamous and if this has an effect on other behavioral characteristics. At the end of session 1 there was a coffee and tea break followed by open discussion and questions for the speakers.

Session 2 was moderated by Trudy Mackay and started with Dr. Brian Langerhans, who gave a talk on the phenotypic differences that occur within mosquitofish in the Bahamas with and without predator threats. Specifically, he analyzes differences in mating success and courtship of these fish. After Langerhans, Dr. Reade Roberts presented a new story on the genetic makeup of people with smelly armpits and wet earwax *versus* people with dry earwax and non-smelly armpits. Roberts has been collaborating with multiple laboratories and sampled 70+ people to analyze genetic trends in these fragrant data. At the end of his talk he presented data suggesting that bacteria found in your armpit may make you more or less susceptible to be bitten by a mosquito. This intriguing presentation was followed by many questions and discussion from the audience. After Roberts, Dr. Russell Borski described the relation between leptin and glucocorticoid levels in tilapia fish with stress responses. As lunchtime was approaching, the pleasant aroma of pizza was complemented with a presentation given by Dr. Coby Schal on bedbugs. Schal has been studying alternative methods to address bedbug infestations. The current methods involve heat, fumigation, and do-it-yourself methods; however, these are either very expensive or ineffective. Schal is studying the components necessary to develop proper baits for bedbug infestations based on the behavioral responses from the bedbugs towards certain compounds. Dr. David Tarpy finished up session 2 with a presentation on the plasticity of caste determination in honey bees. Tarpy has been

experimenting with varying the diets of honey bee larva to make intermediate castes of honey bees.

Session 3 of the symposium was introduced and moderated by Dr. Fred Gould. Dr. John Meitzen opened the session with a talk overviewing his lab's ongoing investigation of the intersecting roles of estradiol and biological sex on the function of striatal neurons. The Meitzen lab has identified sub-region specific sex differences in striatal neuron electrophysiological properties in pre-pubertal rats and is currently investigating the persistence of these differences into adulthood as well as the modulatory effects of unstable neuroendocrine state. Dr. Helen Huang then discussed her lab's progress in improving human-machine symbiotic systems through development of bidirectional neural-machine interfaces to better translate neural will into artificial limb action in her talk Towards Bionic Limbs: Neural Control of Artificial Limbs. Dr. Leslie Sombers presented electroanalytical approaches developed and expanded upon in her lab, which enable for monitoring neuroenergetic and neurochemical dynamics in living brain tissue and intact brain tissue in behaving animals - providing examples from research conducted in her lab in which the neurochemical dynamics underlying specific behaviors can be analyzed using these techniques. Dr. Santosh Mishra shared recent findings in his ongoing work elucidating the neurocircuitry underlying chronic allergic itch sensation that implicate periostin and the ITGB3 integrin receptor as a novel ligand and receptor, respectively, acting within the itch pathway, which may serve as potential new targets for anti-chronic allergic itch therapies. Dr. Troy Ghashghaei concluded the third session with a talk about his lab's work investigating how hedonic olfactory learning is developmentally regulated in the mouse forebrain using DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) to target olfactory bulb neurons born at different times during development. Ghashghaei's research indicates that the neural pathways involved in different olfactory behaviors are organized at different developmental time points.

The final session 4 was moderated by Dr. John Godwin. Dr. Heather Patisaul described her lab's findings on the bioaccumulation and endocrine disrupting effects of the flame retardant chemical Firemaster 550 and introduced the placenta as a new frontier for neuroendocrine disruption research. Dr. Fred Gould followed with a talk entitled "Can genes drive safely?", in which he discussed the potential for and limitations of using

gene drive systems to generate transgenic pests as a new form of pest control. Dr. David Aylor presented his lab's research using a genetic reference population of mice, the Collaborative Cross, to investigate the genetics of susceptibility to exposure to diethylstilbestrol (DES). Exposure to DES, a drug prescribed to women who had suffered a prior miscarriage, has been linked to infertility and cancer. The Aylor lab is working to identify genetic susceptibilities, such as a pre-cancerous gene profile using the Collaborative Cross mice. Dr. Michael Cowley discussed his lab's research on the interaction of the environment and the epigenome. Specifically, how exposure to a maternal high-fat diet during early life can increase the risk of hepatic steatosis in offspring. Finally, Dr. Robert Anholt concluded the fourth and final session with a talk entitled "Functional reconstruction of the evolution of chemoreceptor gene clusters in Drosophila" in which he discussed his lab's approach using CRISPR to systematically and functionally characterize different gene clusters and their individual constituents for chemosensation-related phenotypes through interrogation of these phenotypes after excision of gene clusters and systematic reinsertion of gene cluster constituents.

The symposium concluded with a lively discussion amongst attendees regarding the future of the Keck Center for Behavioral Biology. Anholt cited the conclusions of the 2013 5-year review and invited suggestions from attendees on what changes could be implemented to optimize the Center. Attendees were invited to respond to the following questions: Should the Keck Center continue to exist? What should we do differently to reinvigorate the Center? Should the director of the Keck Center be replaced with new leadership? To what extent should governance for the Center change? There was an enthusiastic affirmation across attendees of the symposium that the Keck Center should continue to exist. Attendees responded positively to the suggestion of reviving the Keck Center training grant program as well as involving students in the leadership and governance of the Center. Overall, the discussion concluded with a general consensus that collaboration and communication within the Keck Center needs to be further consolidated and student leadership roles created to boost student involvement. To adjourn the first annual Keck Center Faculty Research Symposium, Anholt thanked all presenters and attendees for participating and invited all speakers to gather for dinner at Château MacAnholt.

The Variation of Monogamy

by Andrea Vogel

On December 8th, Dr. Steve Phelps from the University of Texas at Austin gave the W. M. Keck Center seminar entitled “Caught in peculiar positions: Variation in the mechanisms of monogamy”. Phelps began his seminar by talking about his field of social behavioral neuroscience, which includes how animals use social information to inform their decisions. Many neuroscience studies use lab mice and rats, and try to extrapolate findings from these rodents to humans. However, it can be difficult to extrapolate because the evolutionary history is needed, but not well known for most lab animals, because inbred lines were created from pet strains. Furthermore, Phelps discussed his interest in individual variation, for which inbred lines are not the best option. Individual variation can be found in many traits, such as alternate mating strategies, personality, resilience, neurodiversity, and personalized genomics. This leads to the main question of Phelps’ research: Can we identify adaptive variation in the social brain?

To answer this question, Phelps uses the prairie vole (*Microtus ochrogaster*) as his animal model. Prairie voles are small rodents that are socially monogamous and practice biparental care. Previous research has shown that vasopressin, working as a neuropeptide in the brain, is important for many aspects of social behavior. Vasopressin is critical in males for expression of pair bonding, aggression, social memory, and vocalizations. The bed nucleus of the stria terminalis (BNST), the ventral pallidum (VP), and the retrosplenial cortex (RSC) are all brain regions where vasopressin receptors are present in males and these areas belong to the social brain network. Examining vasopressin receptors in the RSC is where Phelps focused the rest of his talk.

The RSC is important for spatial memory, and is in a circuit with the hippocampus and the thalamus. It contains vasopressin receptors, with lots of individual variation. This leads to the question of: Has selection in space use and sexual fidelity prompted variation within the vasopressin receptors of the RSC? To answer this question, Phelps examined space use patterns and paternity analysis in a semi-naturalistic setting, and then looked at the vasopressin receptor of the RSC. Male prairie voles were separated into two groups after paternity analysis of their offspring. One group were males who had been successfully



Dr. Steve Phelps

mated with a female that was not the male’s partner, called extra-pair fertilizations (EPF); while the other group were males who only successfully mated with their partners, called in-pair fertilizations (IPF). The males who were in the EPF group had larger territories, were more likely to intrude into other males’ territories, and were more likely to be intruded by other males. This points to a trade-off between mate guarding and EPF, as the males who left their territories to have EPF were more likely to have their territories intruded upon. Interestingly, males with a higher density of vasopressin receptors in their RSC were IPF males, while males with a lower density of vasopressin receptors in their RSC were EPF males. This suggests that males in the IPF group had greater access to social information than EPF males. When the RSC was lesioned, there was no change in rates of aggression or mating, but the males did not display preference towards a partner. Taken together, the results from the lesion RSC and the space use analysis indicated that males with high density of vasopressin receptors were efficient at mate guarding, while males with low density of vasopressin receptors tended towards a scramble competition mating strategy.

From here, Phelps discussed how genetic variation is translated into phenotypic variation, and how selection maintains that variation. Approximately 8kb of the vasopressin receptor gene (*avpr1a*) was sequenced, and 4 single nucleotide polymorphisms (SNPs) were found to predict the density of the vasopressin receptor in the RSC. The allelic differences reflect epigenetic regulation of the vasopressin receptor. To examine how the variation was maintained, breeding lines for high (HI) or low (LO) density of vasopressin receptor in the RSC were established, and then crossed, to produce heterozygous offspring. Then the heterozygous offspring were crossed, so each family produced HI/HI, HI/LO, and LO/LO offspring. When looking at relative fitness with IPF males, the high allele was favored, while when

looking at relative fitness with EPF males, the low allele was favored. One of the SNPs was found to be a G/T polymorphism that altered the presence of a CpG site, and was linked to a cluster of CpG polymorphisms within the enhancer sequence. CpG sites are common targets for DNA methylation, so the CpG polymorphisms changed the number of CpG sites available for methylation. HI/HI animals had less enhancer methylation than LO/LO animals, which implies that methylation could be impacting the density of the vasopressin receptors in the RSC. Overall, the differences in density are mirrored by differences in spatial memory and space use by male prairie voles. Phelps concluded that polymorphisms in CpG sites may underlie gene by environment interactions that affect social behavior.

Seminars

On **January 26**, 3:30 pm, Dr. John McGann from the Psychology Department at Rutgers University will present a seminar, titled “Beyond bottom-up sensory processing: learning and expectation can shape sensory input to the mouse brain.”

The seminar will be in 101 David Clark Laboratories.

On **February 9**, 3:30 pm, Dr. Karen Carleton from the Department of Biology at the University of Maryland, College Park, will present a seminar, titled “QTL and gene regulatory networks for seeing through the eyes of a fish.”

The seminar will be in 3503 Thomas Hall.

Grants

Troy Ghashghaei, together with K. Adler, received a five year \$1,626,055 grant from the National Institute for Neurological Disorders and Stroke to study the role of ependyma in forebrain homeostasis.

Troy Ghashghaei, together with Ninomiya-Tsuji, received a \$1,466,970 grant from the National Institute of General Medical Sciences to study Tak1 regulation of metabolism.

Troy Ghashghaei, together with Haider and Meitzen, received a \$30,000 NC State Research Innovation Seed Fund grant for discovery and modeling of clonality in forebrain stem cells during gliogenesis.

Publications

Dwyer, N. D., Chen, B., Chou, S. J., Hippenmeyer, S., Nguyen, L. and Ghashghaei, H. T. (2016) Neural stem cells to cerebral cortex: emerging mechanisms regulating progenitor behavior and productivity. *J. Neurosci.* **36**: 11394-11401.

Muthusamy, N., Zhang, X., Johnson, C. A., Yadav, P. N. and Ghashghaei, H. T. (2017) Developmentally defined forebrain circuits regulate appetitive and aversive olfactory learning. *Nat. Neurosci.* **20**: 20-23. (cover story).

Hosseini, S. A., van Wijk, M., Ke, G., Goldansaz, S. H., Schal, C. and Groot, A.T. (2016) Experimental evidence for chemical mate guarding in a moth. *Sci. Rep.* **6**: 38567.

Balvín, O., Bartonička, T., Pilařová, K., DeVries, Z. and Schal, C. (2017) Discrimination between lineage-specific shelters by bat- and human-associated bed bugs does not constitute a stable reproductive barrier. *Parasitol. Res.* **116**: 237-242.

DeVries, Z. C., Mick, R. and Schal, C. (2016) Feel the heat: activation, orientation and feeding responses of bed bugs to targets at different temperatures. *J. Exp. Biol.* **219(Pt 23)**: 3773-3780.

Of note...

Huriyyah Chaudhry, a high school research intern in the Anholt Lab, received Spotlight on Students: An Award for Outstanding Achievement from the Wake County Public School System.

Hongmei Li-Byarlay produced a new episode for the Nature and Nurture Podcast focused on

wasps, ants, and termites as special edition for the IUSSI-NAS 2016 meeting.

(<https://soundcloud.com/nnpodcast/episode-5-iussi-special-edition-wasps-ants-and-termites>).

Troy Ghashghaei was named a University Faculty Scholar. He also chaired a minisymposium at the Society for Neuroscience annual meeting in San Diego and served on an NIH study section, which he will join as a permanent member in the Emerging Technologies and Training in Neurosciences (ETTN) Integrated Review Group.

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 Biological Sciences, Box 7614, North Carolina State University, Raleigh, NC 27695-7614, tel. (919) 515-1173, anholt@ncsu.edu.

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The W. M. Keck Center for Behavioral Biology gratefully acknowledges generous support from our corporate sponsors.

