

The Signal

Monthly newsletter of the W. M. Keck Center for Behavioral Biology
at North Carolina State University
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The Keck Center Welcomes Neurobiologist Elizabeth Lucas



In January of 2018 NC State welcomed the newest member of its neuroscience community, Dr. Elizabeth (Beth) Lucas. Dr. Lucas's doctoral and postdoctoral training has spanned almost every sub-discipline of neuroscience, from molecular to systems to behavioral. Her doctoral research was conducted in the laboratory of Dr. Rita Cowell in the Department of Psychiatry and Behavioral Neurobiology at the University of Alabama at Birmingham. She combined molecular biology with genetic approaches in mouse models to determine novel region- and cell-specific gene targets of a transcriptional coactivator implicated in neurodegenerative and neuropsychiatric illness. Her thesis was highlighted by the remarkable discovery that the transcriptional coactivator acts as a master regulator of gene programs necessary for the maturation and maintenance of cortical interneurons. Following her successful PhD work, Lucas joined the lab of Dr. Roger Clem as a postdoctoral fellow in the Fishberg Department of Neuroscience at the Icahn School of Medicine at Mount Sinai in New York City. Here she incorporated optogenetic approaches with *in vitro* slice electrophysiology to examine experience-dependent plasticity of neural circuits after emotional learning. The initial results of

this work were published in the journal *Neuron*, one of the premier journals in neuroscience. Beth found that emotional memory encoding results in persistent downregulation of inhibition in the amygdala, the emotional processing center of the brain, through extensive plasticity of local inhibitory interneurons. Lucas received numerous accolades during her doctoral and postdoctoral training, including "Outstanding Graduate Student of the Year in Behavioral Neuroscience" and a recent "Society for Neuroscience Professional Development Award".

After being recruited to NC State's College of Veterinary Medicine and Department of Molecular Biomedical Sciences, Lucas will establish a research program that is focused on elucidation of the neurobiological underpinnings of sex differences in susceptibility to mental illness. Women are twice as likely as men to be diagnosed with fear-, anxiety-, and mood-based psychiatric disorders, yet our progress in elucidating the neural circuits underlying susceptibility to mental illness in females has remained stagnant due to the exclusion of female subjects in preclinical research. Lucas's laboratory will utilize a multifaceted, systems-based approach that combines *in vivo*

behavioral manipulations with *ex vivo* electrophysiological, transcriptional, anatomical, and endocrinological analyses in mouse models to dissect the neurobiological mechanisms underlying sex differences in behavioral states relevant to mental illness at the levels of the cell and the circuit. This research seeks to expand upon previous research conducted by herself and others, in hopes of attaining novel, potentially sex-specific, therapeutic targets for devastating mental illnesses disproportionately experienced by women, for which there are currently limited effective treatments and no cures. As the National Institutes of Health recently prioritized inclusion of female subjects in all basic science research, Beth's research program is particularly timely.

At NC State, Lucas will investigate how early-life experiences alter brain function and shape our ability to cope with stressful or traumatic events later in life. She will initially focus on examining sex differences in the maturation of the inhibitory circuitry of the basolateral amygdala, a brain region critical for emotional processing. Because increased prevalence of most fear-, anxiety-, and mood-based disorders in women occurs only during childbearing years, puberty onset and circulating sex hormones have been hypothesized to confer women's susceptibility to such disorders.

However, little is known about the mechanisms by which puberty affects the development of specific brain circuits during adolescence. Lucas seeks to determine the causal relationship between puberty onset and inhibitory maturation in the amygdala as well as how peri-puberty stress may affect this maturational process and lead to sex differences in susceptibility versus resilience to fear-, anxiety- and depression-related behaviors later in life.

Lucas's lab provides students and post-graduate fellows at NC State and in particular students associated with the Keck Center a unique opportunity to receive training in cellular and molecular techniques to understand systems, endocrinological, and neurobiological mechanisms underlying sex differences in behavioral states relevant to psychiatric disorders. "Beth Lucas is an incredibly valuable addition to the W. M. Keck Center for Behavioral Biology", says Keck Center director Dr. Robert Anholt, "she provides enormous impetus to our growing presence in behavioral neuroscience." The NC State community is lucky to have her here, and we wish her the best of luck with setting up her new lab.

contributed by Troy Ghashghaei

Jamie Willett Receives Prestigious Grass Fellowship



Jaime Willett, a graduate student in the laboratory of Dr. John Meitzen, has been awarded a Grass Foundation Fellowship. Grass Fellowships support early career scientists to perform investigator-designed, independent research projects for 14 weeks at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. The fellowship targets promising new investigators that are at the "critical period", when the possibility of becoming their own PI during the summer will help to develop the self-confidence and drive to pursue an independent research career. This "critical period" usually takes place during the late postdoctoral years but the program is also appropriate for advanced graduate students and new Assistant Professors. Fellows function as an intellectual and social group within the MBL scientific community while sharing space in the Grass Laboratory. In a weekly private seminar series, eminent investigators at the MBL discuss their work with the Fellows. In addition, a yearly Forbes Lecturer will spend a portion of the summer in the Grass Laboratory interacting with Fellows. This provides a valuable opportunity to perform independent research for an early career scientist.



The Mystery of Monarch Migration



by James Withrow

Each year several generations of monarch butterflies (*Danaus plexippus*) slowly make their way north across the central and eastern United States and Canada until the final generation embarks on an epic 3,000 mile journey back to their overwintering grounds in central Mexico in what is both one of the most iconic animal migrations on Earth and the longest such journey undertaken by any insect. The length of this journey is remarkable, especially for such tiny creatures, but the real mystery has been over how they are able to accurately navigate throughout their migration to successfully arrive in the same area of forest each year.

At the University of Cincinnati, Dr. Patrick Guerra and his laboratory investigate the sensory cues animals utilize to determine their behaviors, including those used by monarchs to undertake their annual migration. Monarchs are a model organism for the study of the biological compasses animals use for orientation and navigation. Guerra recently shared his work on monarch butterflies in a W. M. Keck Center seminar entitled “There and back again: The compass mechanisms migratory monarch butterflies use to get to and return from Mexico”.

Guerra discussed how monarchs utilize a suite of navigational tools in concert to determine which way to fly. The first is a time-compensated bi-directional sun compass to guide their flights south in autumn and then, after recalibrating from cold temperatures, back north in the spring. The monarchs use their antennae to detect the sun and determine orientation in conjunction with light-entrained circadian clocks. Guerra’s work has demonstrated that only one (and either) antenna is sufficient for the butterflies to correctly entrain their circadian clocks and determine flight orientation, but that painting a single antenna black stops the light entrainment and disrupts their ability to orient. However, navigation ability is restored when the black-painted antenna is removed, even with the remaining antenna painted clear as a control. This indicates that, while a single antenna is sufficient for monarch sun compass to function, the information from both antennae is processed together and conflicting information between the two disrupts the entire process.

The sun is not always available over a months-long migration, however, yet the monarchs are still able to fly with the correct orientation even in the absence of directional cues from the sun. Guerra discussed how they also utilize a magnetic compass to orient based on the Earth’s magnetic field. Through indoor flight trials



Dr. Patrick Guerra

he has found that monarchs are able to sense the inclination of the Earth’s magnetic field and use this to fly southwards. Magnetosensors allow the butterflies to orient and, while the monarch magnetic compass does not depend on directional cues from the sun, it utilizes ultraviolet-A/blue light in the spectrum from 380 to 420 nm to function. Unlike many other species, however, monarchs do not use light polarity to determine directionality. Guerra’s work suggests that the magnetosensors are located in monarch antennae as individuals exhibited a significant decline in flight directionality after having their antennae painted black in contrast to control butterflies with clear-painted antennae.

Guerra concluded his talk by discussing potential threats to monarch butterflies from changes in the sensory information they utilize to complete their migration. In particular, he discussed threats from warming temperatures and light pollution. Cold winter temperatures are essential for triggering an orientation switch so that monarchs use solar cues to fly north instead of south in the spring. As of yet we have not determined the thresholds necessary for this switch and how likely it will be that warming temperatures disrupt monarch migrations. Similarly, light pollution from urbanization is a contemporary source of sensory disruption that could impact monarch navigation and is a topic that Guerra is beginning to investigate.

Seminars

On **February 19**, 1:30 pm, Dr. David Stern from the Janelia Research Campus will present a seminar titled “Neural changes underlying rapid fly song evolution.”

The seminar will be in 3503 Thomas Hall.

Grants

Reade Roberts together with Margareta Thompson received a four-year \$499,000 grant from the National Institutes of Health Environmental Health Sciences to provide environmental health research experiences for teachers in high-poverty schools.

Publications

The following publications of the W. M. Keck Center for Behavioral Biology have appeared in print:

Gutzmann, N., Elsensohn, J. E., Barnes, J. C., Baltzegar, J., Jones, M. S. and Sudweeks, J. (2017) CRISPR-based gene drive in agriculture will face technical and governance challenges. *EMBO Rep.* **18**:1479-1480.

Wilson, L.R., Panda, S., Schmidt, A. C., and Sombers, L. A. (2018) Selective and mechanically robust sensors for electrochemical measurements of real-time hydrogen peroxide dynamics *in vivo*. *Anal. Chem.* **90**: 888-895.

Roberts, J. G. and Sombers, L. A. (2018) Fast-Scan Cyclic Voltammetry: Chemical sensing in the brain and beyond. *Anal. Chem.* **90**: 490-504.

Lstibůrek, M., Bittner, V., Hodge, G. R., Pícek, J. and Mackay, T. F. C. (2018) Estimating realized heritability in panmictic populations. *Genetics* **208**: 89-95.

Kuzma, J., Gould, F., Brown, Z., Collins, J., Delborne, J., Frow, E., Esvelt, K., Guston, D., Leitschuh, C., Oye, K. and Stauffer, S. (2018) A roadmap for gene drives: using institutional analysis and development to frame research needs and governance in a systems context. *J. Responsible Innovation* **5**:13-39.

Delborne, J., Kuzma, J., Gould, F., Frow, E., Caroline Leitschuh, C. and Sudweeks, J. (2018) Mapping research and governance needs for gene drives. *J. Responsible Innovation* **5**: 4-12.

Leitschuh, C. M., Kanavy, D., Backus, G. A., Valdez, R. X., Megan Serr, M., Pitts, E. A., Threadgill, D. and Godwin, J. (2018) Developing gene drive technologies to eradicate invasive rodents from islands. *J. Responsible Innovation* **5**: 121-138.

Facka, A. N., Lewis, J. C., Happe, P., Jenkins, K., Callas, R., and Powell, R. A. 2016. Timing of translocation influences birth rate and population dynamics in a forest carnivore. *Ecosphere* **7**: e01223.

Powell, R. A., Facka, A. N., Gabriel, M. W., Gilbert, J. H., Higley, M., LaPoint, S. D., McCann, N. P., Spencer W. and Thompson, C. M. (2017) The fisher as a model organism. In *Biology and Conservation of Wild Musteloids* (Macdonald, D. W., Harrington, L. and C. Newman, C., editors). Chapter 11, Pp. 299-313. Oxford University Press, London.

Powell, R. A., Ellwood, S., Kays R. and Maran, T. (2017) Stink or Swim: Techniques to meet the challenge for study and conservation of small critters that hide, swim, or climb, and may otherwise make themselves unpleasant. In *Biology and Conservation of Wild Musteloids* (Macdonald, D. W., Harrington, L. and C. Newman, C., editors). pp. 216-230. Oxford University Press, London.

Baldwin, K. R., Horman, B., Phillips, A. L., McRitchie, S. L., Watson, S., Deese-Spruill, J., Jima, D., Sumner, S., Stapleton, H. and Patisaul, H. (2018) EDC IMPACT: Molecular effects of developmental FM 550 exposure in Wistar rat placenta and fetal forebrain. *Endocr. Connect.* pii: EC-17-0373.

Vogel, A. R., Patisaul, H. B., Arambula, S. E., Tiezzi, F. and McGraw, L. A. (2018) Individual variation in social behaviours of male lab-reared prairie voles (*Microtus ochrogaster*) is non-heritable and weakly associated with V1aR density. *Sci Rep.* **8**:1396.

Of note...

Leslie Sombers gave a presentation at the Winter Conference on Brain Research on overlapping chemical systems that contribute to the control of dyskinetic movements in the rat during chronic l-DOPA treatment for Parkinson’s disease.

Robert Anholt and **Trudy Mackay** attended the National Institute on Drug Abuse Animal Models Consortium Meeting in Rockville, MD. **Trudy Mackay** gave a presentation and **Chad Highfill** and **Brandon Baker** presented posters at the meeting.

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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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