



2018 Wyoming SBC Newsletter

December 29, 2018

Director's Message

Achieved milestones for COBRE mission. SBC center activities have centered on our core mission: to foster and conduct high-quality scientific research that advances the understanding of our sensory systems and disorders related to them. After the center was established on September 2017, we have continued to support 4 junior project leaders and promote their success, we have grown our center in size via new hires and pilot projects, we have continued to build the infrastructure to enable *cutting edge research*, and finally we have already made great progress on research fronts. Overall, we have achieved all the milestones outlined in our SBC COBRE proposal.

New Hires and Pilot Projects. SBC welcomes two new faculty members, Drs. Yun Li from National Institute on Drug Abuse (NIDA) and Karen Mruk, from Stanford University. Dr. Li will use miniature microscopes to study large-scale in vivo neural calcium imaging from freely behaving mice, to understand neural basis underlying social behavior. Dr. Mruk will use zebrafish model to understand neural circuit regeneration following spinal cord injury. SBC welcomes Dr. Michael Taylor from Chemistry department, Dr. Guanglong He from School of Pharmacy and Dr. John Oakey from Department of Chemical Engineering College of Engineering and Applied Science, as our pilot project leaders.

Core facility. Established and expanded the Integrated Microscopy Core facility (IMCore). IMCore space has been doubled, two newly renovated labs (1800 ft²) now

provides better service to the entire campus. We acquired a major instrument: a multi-photon microscope (Neurolabware), molecular imaging devices (Zeiss and ThermoFisher) and a number of services (equipment share etc). Via communication with NIGMS and our EAC board and based on changes in our research needs, we have reorganized our core facility services. The IMCore now provides service to 49 labs across 4 colleges and 14 departments.

Research and grants. During the 16 months of funding, SBC members published 19 peer-reviewed articles and one patent filed. Highlights and a full-list of publications are show in page 2 & 3, respectively. 12 grants were submitted and 3 from federal agencies (NIH 2 and NSF 1) were funded. During last year, SBC center hosted our Inaugural National Sensory Biology Symposium in Grand Teton AMK Ranch and our distinguished seminar speaker, Dr. Zach Hall.

HIGHLIGHTS

Major miles stones achieved in year 1.5 of COBRE funding cycle

- **Two new faculty** members were hired. A **third faculty** line was recently approved.
- **Three new pilot projects** (\$50K annual budget for each project) were selected and funded.
- Participating faculty members have increased to 15.
- The IMCore facility is up and running, it provides services for 49 labs across campus.
- 20 publications, 3 external grants and one patent filed.
- Inaugural National Sensory Biology Symposium in Grand Teton AMK ranch.

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Core facility (IMCore) highlights

Building on the existing Jenkins Microscopy Core Facility, SBC continues to help expand the service and instrumentations housed in the microscopy core.

- A new multi-photon microscope (Neurolabware) has been built and is has been recently launched to provide service. This equipment will enable multiple groups to collaborate on the use of genetically encoded calcium indicators to decipher the neural code underlying sensory processing.
- Other Instrumentations recently purchased include iBright FL1000, QS3 0.1ML QPCR SYSTEM, a SomnoSuite Low-Flow Digital Vaporizer, a fully motorized Carl Zeiss Axio Zoom V16 High Resolution Zoom Microscope, Milli-Q purified water systems. Med Associate Mouse home cage running wheels.
- In addition, SBC continues to service existing equipment that are vital for our research.



Core director, Dr. Zhang, is installing a PMT, which is a critical part of the two-photon microscope.

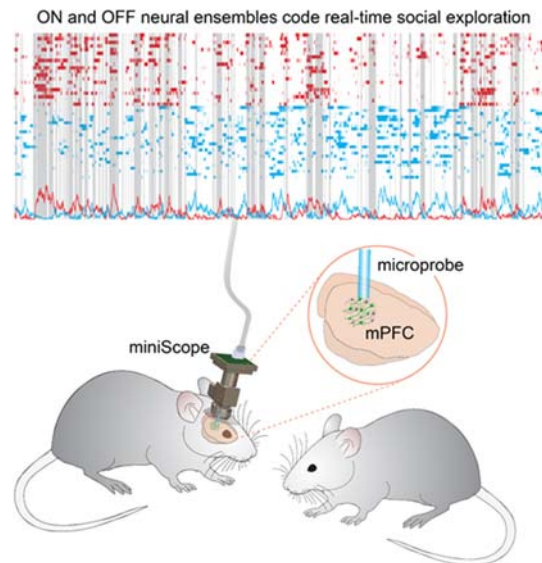
Research highlights

Project leader Dr. Kara Pratt and Stephen Santoro's group collaborated in a recent research entitled "Presenilin Regulates Retinotectal Synapse Formation through EphB2 Receptor Processing". In this research, they discovered that proper formation of excitatory synapses requires presenilin-dependent processing of EphB2 receptors, and concomitant recruitment of NMDA receptors to nascent synapses. This research is exciting because, presenilin, a protein studied mainly in the context of Alzheimer's disease, is now showing important role in early formation of the nervous system. Results are published in *Developmental Neurobiology*.



The Inaugural Sensory Biology Symposium attendee group photo. Experts and trainees from 16 labs spent two days in AMK ranch, brainstormed cutting-edge research.

Research highlights, continued



Dr. Yun Li led a study entitled "Distinct and dynamic ON and OFF neural ensembles in the prefrontal cortex code social exploration". They used a custom developed miniature fluorescence microscope (miniScope) to record calcium activities from hundreds of excitatory neurons in the medial prefrontal cortex (mPFC) when mice engage social interactions with other mice. Computational analysis demonstrated that mPFC excitatory neurons formed two non-overlapping ensembles displaying opposing calcium activities (ON and OFF ensembles) to code real-time behavioral information. Their approach could be applied to other mouse models of psychiatric disorders such as schizophrenia and autism spectrum disorders, paving the way for future studies of neural circuit dysfunctions in psychiatric disorders. Their research is published in *Neuron*.

Publications from SBC investigators

(Manuscripts authored by SBC investigators may not be directly supported by COBRE funding).

1. **Taylor MT**, Nelson JE, Suero MG, Gaunt MJ. 2018, “A Protein Functionalization Platform Based on Selective Reactions at Methionine Residues.” *Nature*. 562, 563-568.
 2. Liang B, Zhang L, Barbera G, Fang W, Zhang J, Chen X, Chen R, **Li Y***, Lin DT*. 2018. Distinct and dynamic ON and OFF neural ensembles in the prefrontal cortex code social exploration. *Neuron* 100, 700-714 (***Co-corresponding authors, #Lead Contact**)
 3. Liang B, Zhang L, Moffitt C, Li Y, and Lin DT. 2018. An open-source automated surgical instrument for microendoscope implantation. *J Neurosci Methods* 311(1): 83-88.
 4. Zhang L, Liang B, Barbera G, Hawes S, Zhang Y, Stump K, Baum I, Yang Y, **Li Y**, and Lin DT. 2018. Miniscope GRIN lens system for calcium imaging of neuronal activity from deep brain structures in behaving animals. *Curr Protoc Neurosci*. e56. doi: 10.1002/cpns.56
 5. Baskaran P, Covington K, Bennis J, Mohandass A, Lehmann T, **Thyagarajan B**. 2018 Binding Efficacy and Thermogenic Efficiency of Pungent and Nonpungent Analogs of Capsaicin. *Molecules*. 23(12). pii: E3198. doi: 10.3390/molecules23123198. PMID: 30518154
 6. Liu, Z., Thakar, A., Santoro, S.W., **Pratt, K.G.** (2018) Presenilin regulates retinotectal synapse formation through EphB2 receptor processing. *Dev Neurobiol*. doi: 10.1002/dneu.22638.
 7. Liu, Z., Donnelly, K.B., **Pratt, K.G.** (2018) Preparations and protocols for whole cell patch clamp recording of *Xenopus laevis* tectal neurons. *J. Vis. Exp.* 133 doi: 10.3791
 8. Van der Linden, C., Jakob, S., Gupta, P., Dulac, C., and **Santoro, S.W.** 2018 Sex separation induces differences in the olfactory sensory receptor repertoires of male and female mice. *Nat. Commun.* 9(1):5081. doi: 10.1038/s41467-018-07120-1.
 9. **Santoro, S.W.** and Jakob, S. Gene expression profiling of the olfactory tissues of sex-separated and sex-combined female and male mice. *Scientific Data*, 2018 Dec 4;5:180260. doi: 10.1038/sdata.2018.260.
 10. Xu G, Han S, Huo, C, Chin KH, Chou SH, **Gomelsky M**, Qian G, Liu F. 2018. Signaling specificity in the c-di-GMP-dependent network regulating antibiotic synthesis in *Lysobacter*. *Nucl Acids Res* gky803.
 11. Zhang J, Chen T, Yang Y., Du J, Li H, Troxell B, He M, Carrasco S, **Gomelsky M**, Yang XF. 2018. Positive and negative regulation of glycerol utilization by the c-di-GMP binding protein PlzA in *Borrelia burgdorferi*. *J Bacteriol* pii: JB.00243-18.
 12. Bjarnsholt T, Buhlin K, Dufrêne YF, **Gomelsky M**, Moroni A, Ramstedt M, Rumbaugh KP, Schulte T, Sun L, Åkerlund B, Römling U. 2018. Biofilm formation – What we can learn from recent developments. *J Intern Med* 284:332-345.
 13. Latanova AA, Petkov S, Kilpelainen A, Jansons J, Latyshev O, Kuzmenko Y, Hinkula J, Abakumov M, Valuev-Elliston V, **Gomelsky M**, Karpov V, Chiodi F, Wahren B, Logunov
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- D, Starodubova E, Isaguliants M. 2018. Codon optimization and improved delivery/immunization regimen enhance the immune response against wild-type and drug-resistant HIV-1 reverse transcriptase, preserving its Th2-polarity. *Sci Rep* 8:8078.
14. Elbakush AM, Miller KW, **Gomelsky M**. 2018. CodY-mediated c-di-GMP-dependent inhibition of mammalian cell invasion in *Listeria monocytogenes*. *J Bacteriol* 200:e00457-17.
 15. Hwang S, **Mruk K**, Rahighi S, Raub AG, Chen CH, Dorn LE, Horikoshi N, Wakatsuki S, Chen JK, Mochly-Rosen D. Correcting glucose-6-phosphate dehydrogenase deficiency with a small-molecule activator. *Nat Commun*. 2018 Oct 2;9(1):4045. doi: 10.1038/s41467-018-06447-z.
 16. Qin X, Peterson MR, Haller SE, Cao L, Thomas DP, **He G**. Caspase recruitment domain-containing protein 9 (CARD9) knockout reduces regional ischemia/reperfusion injury through an attenuated inflammatory response. *PLoS One*. 2018 Jun 25;13(6):e0199711. doi: 10.1371/journal.pone.0199711. eCollection 2018
 17. Ghnenis AB, Czaikowski RE, Zhang ZJ, **Bushman JS**. 2018. Toluidine Blue Staining of Resin-Embedded Sections for Evaluation of Peripheral Nerve Morphology. *J Vis Exp*. 2018 Jul 3;(137). doi: 10.3791/58031.
 18. Yang W, **Sun QQ**. 2018. Circuit-specific and neuronal subcellular-wide E-I balance in cortical pyramidal cells. *Sci Rep*. 8(1):3971. doi: 10.1038/s41598-018-22314-9.
 19. Wu GY, Liu SL, Yao J, Sun L, Wu B, Yang Y, Li X, **Sun QQ**, Feng H, Sui JF. 2018. Medial Prefrontal Cortex-Pontine Nuclei Projections Modulate Suboptimal Cue-Induced Associative Motor Learning. *Cereb Cortex*. 28(3):880-893. doi: 10.1093/cercor/bhw410.
 20. Agrawal S, Fox J, Thyagarajan B, **Fox JH**. 2018. Brain mitochondrial iron accumulates in Huntington's disease, mediates mitochondrial dysfunction, and can be removed pharmacologically. *Free Radic Biol Med*. 120:317-329.

Funded New Grants from SBC investigators

1. NIH R21 AI135683-01. 01/2018-12/19. Interplay between c-di-GMP signaling, metabolism and virulence in *Listeria monocytogenes*. **Gomelsky M**, (PI). \$388,000.
2. NSF-CMI-1808507, Dutta (PI), **Taylor MT** (CO-PI), 08/01/2018-07/31/2021
Development of Sensitive Electrochemiluminescent Immunoassays through Electric Field Assisted Rapid Analyte Capture and Rational Design of the Reporter Catalyst/Reaction System. \$459,000.
3. 3P20GM121310-02S1. 8/1/2018-7/30/2019. Wyoming Sensory Biology COBRE Administrative supplements. NOTAG-18-008: Alzheimer's Disease and its related Dementias (AD/ADRD)-focused Administrative supplements for NIH grants that are not focused on Alzheimer's disease. **Sun QQ** (PI) and **Pratt K**. (CO-PI). \$299,573

Pending grants from SBC investigators.

1. NIH R21 CA238080-01. Remotely controlled listerial bactodrones for cancer immunotherapy. **Gomelsky M**, PI.
2. Illustrating Mechanisms for Upper Motor Neuron Degeneration in ALS, The Robert Packard Center for ALS Research at Johns Hopkins, \$60,000. PI. Yun Li.

3. 1R43DK117674-01A1 NIH NIDDK. Development and evaluation of a polymer coated proprietary cream formulation of Resiniferatoxin nanoparticles for the treatment of Diabetic Neuropathy. \$225,000. Thyagarajan B (Subaward consortium-PI).