

FSU Biomed

Florida State University College of Medicine

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Student News



From how we meet for seminars to how we get involved in outreach, COVID-19 has changed a lot of the ways we do things. In this case, the changes have opened up new opportunities!

In response to a call for videos for the “Lights on Afterschool Science Expo” sponsored by the local group “STEMS4GIRLS,” **Marisa Tillery** from the **Megraw Lab** created a short video with the help of the COM’s Instructional Design and Media Production Team. Now, the Biomed SGSA’s banana DNA extraction outreach activity can reach a wider audience!

<https://www.youtube.com/watch?v=jmZFY9aVJbc>

Upcoming Events

November 18

Seminar Series: **Elise Wight**

November 25-29

University Closed/Holiday

December 4

Lad Day of Fall Classes

December 9

Seminar Series: **Gloria Lee**

December 16

Seminar Series: Brad Grueter

December 21 – Jan. 1

University Closed/Holiday

BSGCA Update:

The Biomedical Sciences Graduate Student Association would like to say "THANK YOU!" to all 2019-2020 BSGSA members for the hard work and efforts put into making all the 2020 events a big success. An especial "THANK YOU!" to our former president **Jennifer Warnock** for the incredible work and leadership.

The BSGSA has now new E-board members for the 2020-2021 year:

President: **Maicon Landim Vieira**

Vice President: **Delaney Sherwin**

Treasurer: **Michelle Rodriguez Garcia**

Secretary: **Leanne Duke**

Outreach Coordinator: **Marisa Tillery**

Social Media Chair/CODI Representative: **Nella Delva**

MSC Representative: **Monica Abou Harb**

COGS Representative: **Chris Hagemeyer**

Wellness Committee Representative: **Sandra Zivkovic**

Congratulations to new E-board members, and good luck everyone!



Maicon Landim-Vieira

Third Annual 5MR Competition

This past September, the Office of Postdoctoral Affairs sponsored the Third Annual Five-Minute Research Competition in conjunction with the annual National Postdoctoral Appreciation Week. In previous years, this competition was held live, but due to the need to adhere to COVID requirements, this year's competition was held virtually via Zoom. In total, ten postdoctoral researchers from numerous departments and colleges across FSU shared their research with peers and a panel of judges.

Dr. Jacob Caldwell, with the **Delp Lab** was awarded 1st place for his presentation entitled "A Look at the Impact of Exercise Training on Cardiac Function in Adiponectin Knockout Mice" in a two-way tie with Dr. Vishnu Murali. Congratulations Dr. Caldwell!

News from the Blaber Lab

Trefoil Therapeutics was voted the People's Choice Award winner at the recent Eyecelerator 2020 Conference. Eyecelerator 2020 provides entrepreneurs the chance to showcase their technology and clinical advancements in front of mission-driven investors and business leaders eager to accelerate advancements in eye health. Trefoil's regenerative technology for corneal dystrophy, licensed from the **Blaber Lab** and currently in phase I/II clinical trials, was selected as the People's Choice winner from an impressive group of 27 innovative companies presenting. Trefoil's presentation can be viewed at: <https://bit.ly/35hRBkt>

Funding News



Drs. **Jose Pinto** and Ken Taylor (IMB) were awarded a 2-year NIH R21 grant in the amount of \$362,170 to determine the high-resolution structure of the vertebrate skeletal muscle thick filament using cryo-electron microscopy.

Below is the project summary:

"The long term goal of this research project is to understand the molecular mechanism of force production through 3-D visualization of myosin molecular motors in their natural environment. This research project focuses on extending methods used and results obtained in structural studies of muscle filaments isolated from the large waterbug *Lethocerus* sp. to vertebrate striated muscle, specifically skeletal muscles obtained from rabbits, *Oryctolagus cuniculus*. We have obtained a near atomic resolution 3-D image of thick filaments from *Lethocerus* flight muscle, which have a helical structure with 4-fold rotational symmetry. No coiled-coil protein of the size of myosin had been imaged previously at the resolution we have achieved (4.2Å) in the backbone of the myosin filament. There is now more known about the 3-D structure of *Lethocerus* thick filaments than those from any other animal. Recent advancements in detector technology, robotic electron microscopes and high throughput data collection, have made this possible. We now propose to extend these methods to the much more difficult vertebrate skeletal muscle thick filament, which is not a helical assembly and has only 3-fold rotational symmetry. The high-resolution structure of *Lethocerus* thick filaments suggests that studies of invertebrate thick filaments can inform familial muscle diseases caused by myosin rod mutations. About 40% of disease-causing myosin mutations occur in the myosin coiled-coil domain. However, how well invertebrate thick filaments can inform human disease depends on how similar their filament backbones are structured like those of vertebrates. In the current funding period, we have obtained unprecedented resolution and detail of the relaxed state of thick filaments from *Lethocerus* flight muscle. This advance provides opportunity to investigate the mechanism whereby myosin rod mutations can affect muscle

function. The head folding of myosin II produces a head conformation called the interacting heads motif that sequesters the myosin heads from interaction with the thin filament. In filaments of smooth and non-muscle myosin, the head folding leads to filament instability and formation of a soluble conformation, called 10S, incapable of polymerizing. This phenomenon has been hypothesized to be due to changes in the rod structure brought on by the head folding. Put simply, the structure of the myosin rod and the myosin heads are coupled in some way. Recent muscle research has pointed to the possibility that tension applied either internally by myosin heads or externally by a stretch, can affect the structure of the thick filament. Thus, the thick filament may function as a tension transducer, but the molecular mechanism by which this occurs is unknown. We hypothesize that tension applied to the thick filament affects the structure of the myosin heads and vice versa, that the myosin heads affect the structure of the myosin tails. This hypothesis can be tested using cryoEM by comparing a naturally formed super-relaxed filament to one with the myosin heads disordered."

Publications



Maicon Landim-Vieira and **Dr. Jose Pinto** had a paper published in *Journal of Muscle Research and Cell Motility* entitled: “*A Comprehensive Guide to Genetic Variants and Post-Translational Modifications of Cardiac Troponin C*”. This project was done in collaboration with Dr. Bryant Chase of FSU's Biology Dept., Dr. Andrew Landstrom of Duke University, and Dr. Hanna Tadros of University of Florida.

Abstract: Cardiomyopathy is a disease that affects the structure and function in the heart and has an extreme range of phenotypes. Among the millions of individuals affected by this disease, patients with hypertrophic (HCM), dilated (DCM), and left ventricular non-compaction (LVNC) cardiomyopathies can experience morphologic changes in the heart, which in the most detrimental cases, lead to sudden death. Presented here is a discussion of the mechanisms of variants and post-translational modifications (PTM) in cardiac troponin C (cTnC) and how such variants produce genetic variation TNNC1. Using UniProt, PhosphoSitePlus, ClinVar and published literature, compilation of all identified variants and PTMs in cTnC to date was accomplished. Additionally, using a recent cryo-EM structure of the cardiac thin filament regulatory unit, the localization of each post-translational modification (acetylation, glycation, s-nitrosylation, phosphorylation) and functionally studied variant amino acid residue in the sequence of cTnC was illustrated. The mapped variant amino acids and PTMs are distributed throughout the cTnC protein, although it appears as if there are many cardiomyopathy-associated variants that localize in α -helical regions of cTnC but this is not statistically significant $\chi^2 (1, N=27) = 0.124, p=0.72$. Furthermore, exploring the roles of variants in TNNC1, the gene for cTnC, through discussion of their cardiomyopathy association and potential non-canonical roles help clarify the many facets of TNNC1 as a cardiomyopathic gene. doi: [10.1007/s10974-020-09592-5](https://doi.org/10.1007/s10974-020-09592-5)

A *trifecta* of publications from the Kumar Lab



Beesley S, Sullenberger T, Kumar SS (2020), The GluN3 subunit regulates ion selectivity within native N-methyl-D-aspartate receptors. *IBRO Reports* 9:147-156.

Abstract: Glutamatergic N-methyl-d-aspartate receptors (NMDARs) are heterotetrameric proteins whose subunits are derived from three gene families, GRIN1 (codes for GluN1), GRIN2 (GluN2) and GRIN3 (GluN3). In addition to providing binding sites for glutamate and the co-agonist glycine, these subunits in their di (d-) and tri (t-) heteromeric configurations regulate various aspects of receptor function in the brain. For example, the decay kinetics of NMDAR-mediated synaptic currents depend on the type of GluN2 subunit (GluN2A-GluN2D) in the receptor subunit composition. While much is known about the contributions of GluN1 and GluN2 to d-NMDAR function, we know comparatively little about how GluN3 influences the function of t-NMDARs composed of one or more subunits from each of the three gene families. We report here that in addition to altering kinetics and voltage-dependent properties, the GluN3 subunit endows these receptors with ion selectivity wherein influx of Ca^{2+} is preferred over Na^{+} . This became apparent in the process of assessing Ca^{2+} permeability through these receptors and is of significance given that NMDARs are generally believed to be nonselective to cations and increased selectivity can lead to enhanced permeability. This was true of two independent brain regions where t-NMDARs are expressed, the somatosensory cortex, where both receptor subtypes are expressed at separate inputs onto single neurons, and the entorhinal cortex, where they are co-expressed at individual synaptic inputs. Based on this data and the sequence of amino acids lining selectivity filters within these subunits, we propose GluN3 to be a regulatory subunit for ion selectivity in t-NMDARs.

Beesley S, Sullenberger T, Crotty K, Ailani R, D'Orio C, Evans K, Ogunkunle EO, Roper MG, et al. (2020), D-serine mitigates cell loss associated with temporal lobe epilepsy. *Nature Communications* 11:4966.

Abstract: Temporal lobe epilepsy (TLE) is the most common type of drug-resistant epilepsy in adults, with an unknown etiology. A hallmark of TLE is the characteristic loss of layer 3 neurons in the medial entorhinal area (MEA) that underlies seizure development. One approach to intervention is preventing loss of these neurons through better understanding of underlying pathophysiological mechanisms. Here, we show that both neurons and glia together give rise to the pathology that is mitigated by the amino acid D-serine whose levels are potentially diminished under epileptic conditions. Focal administration of D-serine to the MEA attenuates neuronal loss in this region thereby preventing epileptogenesis in an animal model of TLE. Additionally, treatment with D-serine reduces astrocyte counts in the MEA, alters their reactive status, and attenuates proliferation

and/or infiltration of microglia to the region thereby curtailing the deleterious consequences of neuroinflammation. Given the paucity of compounds that reduce hyperexcitability and neuron loss, have anti-inflammatory properties, and are well tolerated by the brain, D-serine, an endogenous amino acid, offers new hope as a therapeutic agent for refractory TLE.

Beesley S, Sullenberger T, Kumar SS (2020), D-serine intervention in the medial entorhinal area alters TLE-related pathology in CA1 hippocampus via theTemporoammonic Pathway. Neuroscience (accepted for publication).

Abstract: Entrainment of the hippocampus by the medial entorhinal area (MEA) in Temporal Lobe Epilepsy (TLE), the most common type of drug-resistant epilepsy in adults, is believed to be mediated primarily through the perforant pathway (PP), which connects stellate cells in layer (L) II of the MEA with granule cells of the dentate gyrus (DG) to drive the hippocampal tri-synaptic circuit. Using immunohistochemistry, high-resolution confocal microscopy and the rat pilocarpine model of TLE, we show here that the lesser known temporoammonic pathway (TAP) plays a significant role in transferring MEA pathology to the CA1 region of the hippocampus independently of the PP. The pathology observed was region-specific and restricted primarily to the CA1c subfield of the hippocampus. As shown previously, daily intracranial infusion of D-serine (100 μ m), an antagonist of GluN3-containing triheteromeric N-Methyl D-aspartate receptors (t-NMDARs), into the MEA prevented loss of LIII neurons and epileptogenesis. This intervention in the MEA led to the rescue of hippocampal CA1 neurons that would have otherwise perished in the epileptic animals, and down regulation of the expression of astrocytes and microglia thereby mitigating the effects of neuroinflammation. Interestingly, these changes were not observed to a similar extent in other regions of vulnerability like the hilus, DG or CA3, suggesting that the pathology manifest in CA1 is driven predominantly through the TAP. This work highlights TAP's role in the entrainment of the hippocampus and identifies specific areas for therapeutic intervention in dealing with TLE.

Helping Children In Need

Deadline December 4, 2020



FSU College of Medicine students have been working with PAEC school-based clinics, and migrant summer school clinics for the last 13 years. COVID 19 has hit this underserved community especially hard, and many of these essential workers do not have luxury of quarantining for 10 days. If they do not work their families do not eat. These people are the frontline workers that enable our supermarkets to have fresh fruits and vegetables, yet somehow, they are invisible. It is our hope that we can make their holiday a little brighter this year with our annual holiday project. We are seeking new or used children clothes, toys, small books, and \$25.00 Walmart gift cards.

Donations can be dropped off at FSU College of Medicine, Tallahassee Campus located at 3331 Capital Oaks Drive, or at the Main Campus at Jan Beane's office of Human Resources.

Our regional campus is on the corner of Miccosukee Rd and Capital Oaks Drive, near Tallahassee Regional Medical Center, and Tallahassee Orthopedic Clinic. Online donations can be accepted <http://floridalearnsfoundation.org/>.

For more info: elaine.geissinger@med.fsu.edu or maria.pouncey@paed.org

Save the Date

Wednesday, Jan. 6th

Spring Semester Begins

Wednesday, Jan. 6th

Seminar Series: **Stephen Chelko**

Wednesday, Jan. 13th

Seminar Series: **Marisa Tillery**

Wednesday, Jan. 18th

MLK Holiday/University Closed

Wednesday, Jan. 20th

Seminar Series: **Cory Haluska**

Wednesday, Jan. 27th

Seminar Series: Weikang Ma

Do you have news you wish to share in the Biomed Newsletter? Contact Ryan Teston at:
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