

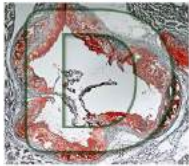
Biomed Highlights

DEPARTMENT of
BIOMEDICAL SCIENCES

Quillen College of Medicine

EAST TENNESSEE STATE UNIVERSITY

*T J Neal—Editor
Vol. 8 May 2016*



MESSAGE FROM...

THE CHAIR

**THEO HAGG, MD, PhD, PROFESSOR
DEPARTMENT OF BIOMEDICAL SCIENCES**



Dear Colleagues

We had another excellent semester of teaching our students. Teaching is indeed the most important mission of our Quillen College of Medicine and we are proud to be an integral and essential part of it. I continue to be impressed by the Faculty and Support Staff who help to maintain our excellence. We can all celebrate together with those who were honored by the medical students and Dean Means at the Caduceus and Medicine Commencement ceremonies. A special note of congratulations to Ben Hilton and Jessica Slade for successfully defending their dissertations and, of course, their supervisors, Drs. Zou and Schoborg.

Over the last five months since the last Newsletter, we welcomed Assistant Professor Qian Xie, as well as Staff member Kim Johnson, who jumped right in to support several of our courses. We also are in the midst of interviewing and recruiting two new Faculty members, one in the cardiovascular physiology and one in the cancer/gene regulation field. I am grateful to the hard work of the Committee as well as the many other departmental members who have participated in many ways in the interviews. All in all, we are making strides in increasing our Research productivity. I am particularly pleased to see several new and exciting collaborations that have materialized.

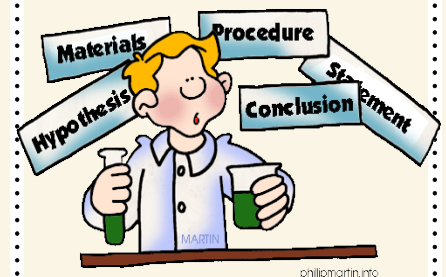
Dr. Schambra retired after more than two decades at the Quillen College of Medicine and we wish her well in this new phase of life as an Emerita. We also are saying a bitter-sweet good-bye to Research Assistant Professors, Katalin and Attila Szebeni, who are retiring and moving back to Mississippi after many years of excellent contributions to Dr. Ordway's laboratory and the Department. We were saddened by the sudden death of Dr. Joyner, but it was very good to see so many of our Biomedical Sciences team attend the uplifting celebration of his life.

Wishing everyone a pleasant summer and looking forward to continue working with everyone to keep the positive developments going.

INSIDE THIS EDITION

- ▶ Publications
- ▶ Grant Awards
- ▶ Presentations
- ▶ Faculty News
- ▶ Student News
- ▶ Staff News
- ▶ Seminar Information
- ▶ Abstracts

*Please submit news to
TJ Neal - neal@etsu.edu*



Employees and students are encouraged to occasionally check the departmental web site for updates and changes. Please contact Tonya Ward (439-2001) if you have questions regarding the site.

www.etsu.edu/com/dbms.



FUNDING— CONGRATULATIONS!

Dr. Valentin Yakubenko, Assistant Professor, received continuation of his NIH R01 award (R01DK102020-03) in the amount of \$222,000. Title of project is “Role of B2 integrins in macrophage retention and egress during inflammation.”

Dr. Qian Xie, Assistant Professor, received a continuing award from the Stephen M. Coffman Charitable trust of \$100,000 per year, “Identifying molecular determinants and biomarkers for MET-targeted therapy in glioblastoma” and an award from the Van Andel Research Institute in the amount of \$10,539 in support of her research.

Travel Awards

Dr. Qian Xie, Assistant Professor, received a travel award in the amount of \$1,200 from the American Brain Tumor Association.

Dr. Sanjay Singh, Research Assistant Professor, was awarded a travel grant of \$1,200 to attend the “Immunology 2016” meeting sponsored by the American Association of Immunologists. The meeting was held in Seattle, WA, May 13-17, 2016.

Donald Ngwa, Master’s graduate student in the laboratory of Dr. Alok Agrawal, was awarded a travel grant of \$500 to attend the “Immunology 2016” meeting sponsored by the American Association of Immunologists. The meeting was held in Seattle, WA, May 13-17, 2016.

APS Fellowship Award

Dustin Gilmer, Undergraduate Student working in the laboratory of Dr. Theo Hagg, has received an APS Fellowship. Congratulations to Dustin. His project is under the supervision of **Dr. Jia Cuihong**.

RDC GRANT AWARDS

Dr. Tom Ecay. Project Title: Molecular analysis of nutrient transport pathways in amniote embryos. Awarded FY ‘16: \$10,000.

Dr. Jennifer Hall. Project Title: Does estrogen and/or progesterone alter Chlamydia trachomatis development through the Wnt/B-catenin signaling pathway. Awarded FY ‘16: \$10,000.

Dr. Russ Hayman. The induction of integrin signaling by microsporidia adherence to host cells. Awarded FY ‘16: \$8,000.

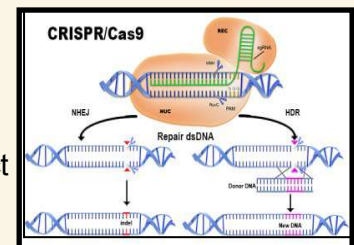
Dr. Rob Schoborg. Project Title: How does chlamydia genital tract infection protect from subsequent herpes virus challenge? Awarded FY ‘16: \$10,000.

STUDENT FACULTY COLLABORATIVE GRANT AWARD

Vlad Razskazovski received the Student Faculty Collaborative Grant Award (\$1,190).

This award comes from the ETSU Honors College Undergraduate Research & Creative Activities. The project is under the supervision of **Dr.**

Matt Keasey, Research Associate in the laboratory of Dr. Theo Hagg. They are using CRISPR gene editing technology. CRISPR technology may lead to breakthrough for such diseases as cancer and autism. Congratulations to Vlad and Matt.





JOURNAL PUBLICATIONS

- Archer T, **Kostrzewa RM** (2015) Physical exercise alleviates health defects, symptoms, and biomarkers in schizophrenia spectrum disorder *Neurotox Res.* Oct;28 (3):268-80. [Epub ahead of print] Jul 15 PMID: 26174041.
- Archer T, **Kostrzewa RM** (2016) Neuroteratology and Animal Modeling of Brain Disorders. *Curr Top Behav Neurosci.* Feb 9. [Epub ahead of print] PMID 26857462.
- Archer T, **Kostrzewa RM.** (2016) Exercise and Nutritional Benefits in PD: Rodent Models and Clinical Settings. *Curr Top Behav Neurosci* Jan 5. [Epub ahead of print] PMID 26728168.
- Beaumont E, Wright GL, Southerland EM,** Li Y, Chui R, KenKnight BH, Armour JA, Ardell JL (2016) Vagus nerve stimulation mitigates intrinsic cardiac neuronal remodeling and cardiac hypertrophy induced by chronic pressure overload in guinea pig. *Am J Physiol Heart Circ Physiol.* May 15;310(10):H1349-59. PMID 26993230.
- Biswas S, Xin L, Panigrahi S, Zimman A, Wang H, **Yakubenko V,** Byzova TV, Salomon RG Podrez EA (2016) Novel phosphatidylethanolamine derivatives accumulate in circulation in hyperlipidemic ApoE^{-/-} mice and activate platelets via TLR2 *Blood* Mar 25. pii: blood-2015-08-664300 PMID: 27015965 [Epub ahead of print]
- Borel N, Leonard C, Slade J, **Schoborg R** (2016) Chlamydial Antibiotic Resistance and Treatment Failure in Veterinary and Human Medicine. *Current Clinical Microbiology Reports*, March Volume 3, Issue 1, pp 10-18.
- Crawford JD, Chandley, MJ, **Szebeni K, Szebeni A,** Waters B, **Ordway GA** (2015) Elevated GFAP Protein in Anterior Cingulate Cortical White Matter in Males With Autism Spectrum Disorder. *Autism Res* Dec; 8(6):649-57. [Epub ahead of print] PMID: 25846779.
- Danysz W, Flik G, McCreary A, Tober C, Dimpfel W, Bizot JC, **Kostrzewa R, Brown RW,** Jatzke CC, Greco S, Jenssen AK, Parsons CG (2015) Effects of sarizotan in animal models of ADHD: Challenging pharmacokinetic-pharmacodynamic relationships, *J Neural Transm* (Vienna) Sep;122 (9):1221-38. [Epub ahead of print] Mar 22, PMID: 25796190.
- Downs AM, Jalloh HB, Prater KJ, Fregoso SP, Bond CE, Hampton TG, **Hoover DB** (2016) Deletion of neurturin impairs development of cholinergic nerves and heart rate control in postnatal mouse hearts. *Physiol Rep* May;4(9). pii: e12779. PMID 27162260.
- Ewan EE, **Hagg T** (2016) Intrathecal Acetyl-L-Carnitine Protects Tissue and Improves Function after a Mild Contusive Spinal Cord Injury in Rats. *J Neurotrauma.* Feb 1;33(3):269-77. PMID 26415041.



JOURNAL PUBLICATIONS

Habecker BA, Anderson ME, Birren SJ, Fukuda K, Herring N, **Hoover DB**, Kanazawa H, Paterson DJ, Ripplinger CM (2016) Molecular and cellular neurocardiology: Development, cellular and molecular adaptations to heart disease. *J Physiol.* Apr 6. [Epub ahead of print] PMID 27060296.

Harrison TA, He Z, Boggs K, Thuret G, Liu HX, **Defoe DM** (2016) Corneal endothelial cells possess an elaborate multipolar shape to maximize the basolateral to apical membrane area. *Mol Vis.* 2016 Jan 16;22:31-9. PMID 27081293.

Keasey MP, Lemos RR, **Hagg T**, Oliveira (2016) Vitamin-D receptor agonist calcitriol reduces calcification *in vitro* through selective upregulation of SLC20A2 but not SLC20A1 or XPR1. *cientific Reports* 6, Article 25802, May 17, srep25802, PMID 27184385.

Kostrzewska RM, Kostrzewska RA, Kostrzewska JP (2015) Botulinum neurotoxin: Progress in negating its neurotoxicity; and in extending its therapeutic utility via molecular engineering. Mini Review. *Peptides* Oct; 72:80-87. Review Jul 17 [Epub ahead of print] PMID: 26192475.

Kostrzewska RM, Nowak P, Brus R, **Brown RW** (2016) Perinatal treatments with the dopamine D₂-receptor agonist quinpirole produces permanent D₂-receptor supersensitization: A model of schizophrenia. *Neurochem Res* 41(1,2) 183-192. [Epub Ahead of Print] Nov 7; PMID: 26547196.

Kostrzewska RM (2015) Perinatal Lesioning and lifelong Effects of the Noradrenergic *Neurotoxin* 6-Hydroxydopa. *Curr Top Behav Neurosci.* 2015 Dec 12. [Epub ahead of print] PMID 26660536.

Olive KE, **Kwasigroch TE**, Wooten DJ, Lybrand C, Peeples CR (2016). A Career Exploration Program: An Effective Alternative to the Traditional Use of Faculty Advisors. *Acad Med.* May 3. [Epub ahead of print] PMID 27144992.

Raza MU, Tufan T, Wang Y, Hill C, **Zhu MY** (2016) DNA Damage in Major Psychiatric Diseases. *Neurotox Res.* 2016 Apr 28. [Epub ahead of print] PMID 27126805.

Scofield SL, Amin P, **Singh M, Singh K** (2015) Extracellular Ubiquitin: Role in Myocyte Apoptosis and Myocardial Remodeling. *Compr Physiol.* Dec 15;6(1):527-60. PMID 26756642.

She X, Calderone R, **Kruppa M**, Lowman D, Williams D, Zhang L, Gao Y, Khamooshi K, Liu W, Li D (2016) Cell Wall N-Linked annoprotein Biosynthesis Requires Goa1p, a Putative Regulator of Mitochondrial Complex I in *Candida albicans*. *PLoS One.* Jan 25;11(1):e0147175. PMID: 26809064.

Slade J, Hall JV, Kintner J, **Schoborg RV** (2016) Chlamydial Pre-infection Protects from Subsequent Herpes Simplex Virus-2 Challenge in a Murine Vaginal Co-infection Model. *PLOS One*, Jan 4;11(1):e0146186.

SCIENTIFIC MEETINGS/INVITED PRESENTATIONS

Dr. Alok Agrawal, Professor, was invited to give a lecture in the Rheumatology Grand Rounds, Division of Clinical Immunology and Rheumatology, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, on March 3, 2016. The title of the lecture was "C-reactive protein in inflammation."

Dr. Greg Ordway, Professor, was an Invited Guest speaker at "Out of Darkness Campaign" designed to raise awareness about suicide at Virginia Tech, Blacksburg, Virginia, Thursday March 17, 2016.

Dr. Greg Ordway, Professor, presented a paper, "Elevated DNA oxidation and DNA repair enzyme gene expression in brain white matter in major depressive disorder," at the Annual Meeting of the Society for Biological Psychiatry in Atlanta, GA on May 13th. The poster was co-authored by: Katalin Szebeni, Timothy P. DiPeri, Luke A. Johnson, Craig A. Stockmeier, Jessica D. Crawford, Michelle J. Chandley and Attila Szebeni.

REVIEW STUDY SECTIONS

Dr. Alok Agrawal, Professor, served on the "Innate Immunity and Inflammation" study section review committee, NIH, February 18-19, 2016, Arlington, VA.

Dr. Greg Ordway served on the Research Grants Committee for the American Foundation for Suicide Prevention in New York City on April 18-19th.



2016

35 Years

Phillip R. Musich

30 Years

Mitchell E. Robinson

25 Years

Diana Sue Toler

20 Years

Thomas Walter Ecay, Jr.

15 Years

Russell Wayne Brown

10 Years

Rolf B. Fritz

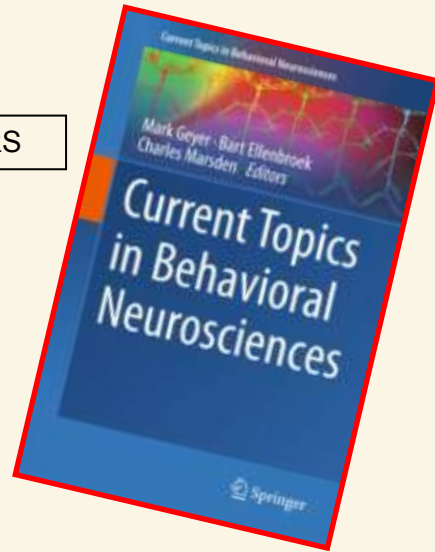
Gregory A. Ordway

Attila Szebeni

Katalin Szebeni



BOOK CHAPTERS



Congratulations to Dr. Richard Kostrzewa, Professor, on the publication of *Current Topics in Behavioral Neurosciences*. See book chapters listed below thus far with more forthcoming.

Kostrzewa RM, T Archer (co-Editors) (2016) Neurotoxin Modeling of Brain Disorders – Life-long Outcomes in Behavioral Teratology (working title), for *Current Topics in Behavioral Neurosciences* (CTBN) book series (Geyer M, C Marsden, B Ellenbroek, Editors) New York: Springer.

Kostrzewa RM (2016) Perinatal lesioning and lifelong effects of the norenergic neurotoxin 6-hydroxydopa. In Geyer M, C Marsden, B Ellenbroek (Eds.), *Curr Top Behav Neurosci* (pp. 1-8) New York: Springer. 2015 Dec 12 [Epub ahead of print] PMID: 26660536.

Kostrzewa JP, Kostrzewa RA, **Kostrzewa RM**, Brus R, Nowak P (2016) Perinatal 6-hydroxydopamine modeling of ADHD. In Geyer M, C Marsden, B Ellenbroek (Eds.) *Curr Top Behav Neurosci* (pp. 1-15) New York: Springer. 2015 Oct 17 [Epub ahead of print] PMID: 26475157.

Kostrzewa RM, Brus R (2016) Lifelong Rodent model of tardive dyskinesia-persistence after antipsychotic drug withdrawal. In Geyer M, C Marsden, B Ellenbroek (Eds.), *Curr Top Behav Neurosci* (pp. 1-10) New York: Springer. 2015 Oct 16 [Epub ahead of print] PMID: 26472552.

Archer T, **Kostrzewa RM** (2016) Exercise and nutritional benefits in PD: Rodent models and clinical settings. In Neurotoxin Modeling of Brain Disorders—Life-long Outcomes in Behavioral Teratology In Geyer M, C Marsden, B Ellenbroek (Eds.) *Curr Top Behav Neurosci* (pp. 1-19) New York: Springer. 2016 Jan 5 [Epub ahead of print] PMID: 26728168.

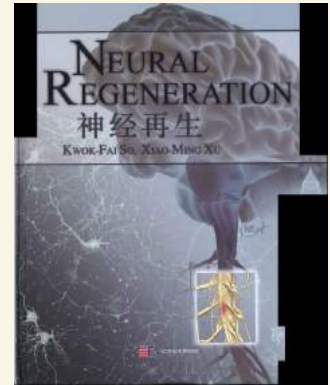
Kostrzewa JP, Kostrzewa RA, **Kostrzewa RM**, Brus R, Nowak P (2016) Perinatal 6-hydroxydopamine to produce a lifelong model of severe Parkinson's Disease. In Geyer M, C Marsden, B Ellenbroek (Eds.) *Curr Top Behav Neurosci* (pp. 1-20) New York: Springer. 2015 Oct 17 [Epub ahead of print] PMID: 26475156.

Archer T, **Kostrzewa RM** (2016) Neuroteratology and animal modeling of brain disorders. In Neurotoxin Modeling of Brain Disorders—Life-long Outcomes in Behavioral Teratology, In Geyer M, C Marsden, B Ellenbroek (Eds.) *Curr Top Behav Neurosci* (pp. 1-40) New York: Springer 2016 Feb 9 [Epub ahead of print] PMID: 26857462.



BOOK CHAPTERS

Citation: Hagg T (2016) Axonal regeneration in the sensory dorsal column pathway. In: *Neural Regeneration*, So KF, Xu XM (Eds.) *Science Press Beijing*. pp 273-287.



Abstract: “This review provides a short historical background to the field of axonal regeneration and discusses the advances made in over 100 studies between 2007 and 2012 in understanding the molecular mechanisms underlying the conditioning lesion and regeneration of primary sensory axons in the dorsal columns of the spinal cord. Treatment strategies to stimulate axon growth and reinnervation of the spinal cord through the dorsal root entry zone and of the dorsal column nuclei in the medulla are highlighted. Major breakthroughs have been made, e.g., reinnervating the nucleus gracilis in the medulla using neurotrophic factor gradients and grafts as relays and identifying chondroitin sulfate proteoglycan receptors. The experimental accessibility of the dorsal column axons has also resulted in new technological advances, including live imaging. Last, future directions are discussed, including some challenges of translation to humans.”



After many years of dedicated service, Drs. Attila and Katalin “Kate” Szebeni (pictured left) have decided it is time to retire.

Prior to Dr. Ordway accepting a position at the Quillen College of Medicine, Kate worked with Dr. Ordway’s laboratory at the University of Mississippi for 8 years. Upon moving to ETSU, Kate along with Attila continued to work in Dr. Ordway’s lab for the past 10 years. They have been invaluable to the research efforts of Dr. Ordway in the fight against depression and suicide.

They plan to return to the city of Brandon, near Jackson, Mississippi, where they have a home and extended

family. Kate plans to spend time gardening, painting, and being involved with the theater and art museum. Attila looks forward to tending to his yard, and especially being involved with special research projects at the University of Mississippi. Both enjoy outdoors, camping, traveling, and extended visits to national parks.

We in the Department of Biomedical Sciences wish the Szebeni’s the best in their retirement. We sincerely hope that they will not forget us—or Tennessee.



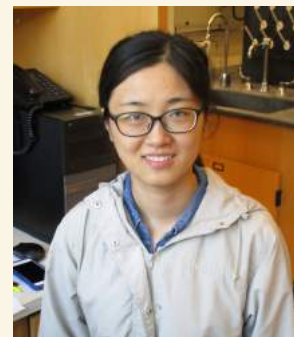
WILLIAM LYMAN JOYNER III
PhD, MSPH, FACA
June 10, 1939—March 14, 2016

Quillen College of Medicine
1989-2016

We bid farewell to a long-standing faculty member, Dr. William “Bill” Joyner. Bill joined the Faculty of James H. Quillen College of Medicine in 1989 as Professor and Chair of the Department of Physiology.

“William (Bill) Joyner, PhD left a significant legacy as Chair of the former Department of Physiology at the Quillen College of Medicine of East Tennessee State University. He was hired and arrived at ETSU as an NIH-funded research scientist charged to impart research success to the Quillen faculty. This he achieved in many ways. However, the Quillen spirit of dedication toward training medical students soon took hold of him. Bill created and fostered a team-based approach to teaching human physiology to medical students. It was a symbiosis that grew during his long tenure as department chair and later as director of the Medical Physiology course. He fostered and directed a collegial effort among the faculty concerning teaching medical physiology. He incorporated case-oriented learning with accumulated knowledge of experimental physiology in his approach to training medical students. Bill was among the first to recognize the importance of early clinical experiences to the education of beginning medical students. The educational mission of Quillen College of Medicine is lessened by his passing.” (Dr. Wondergem and Dr. Ecay).

Jianqun Kou, Research Scholar, has joined the department effective May 2, 2016. She will be assisting Dr. Quin Xie in her cancer research. Jianqun is originally from Taian City, China.



Crystal Maupin completed and passed the **Certified Administrative Professional (CAP) Exam** on March 11, 2016. **CAP** is an internationally recognized organization with a purpose to provide professional certification to those who work in administrative roles. **Congratulations** to Crystal!



Dr. Rob Wondergem was among those individuals honorably recognized during this year’s Distinguished President’s Trust (DPT) event. The event was held at the Meadowview Conference Resort and Convention Center on Friday, April 22, 2016. The DPT is comprised of individuals, organizations, and businesses whose cumulative giving to ETSU trust fund is in excess of \$10,000. Contributions by DPT greatly benefit many students attending ETSU.



Kimberly Johnson has joined the staff in a temporary technical position. Her skills will be beneficial in the support of Dr. Rob Schoborg in the management of the Pharmacology, Microbiology, Immunology, and Physiology courses. Since 1983, Kimberly helped to run her family-owned electronics repair and service business which her father started in 1952. Recently, Kimberly began to pursue another career and became employed with ETSU. She is a life-long resident of Johnson City/ Washington County. Her husband, Mike, is a telecommunications network technician with IDEACOM which is based out of Knoxville, TN. Her son, Robbie (20) is enrolled at UT Knoxville and is majoring in Sustainability. Her daughter, Rachel(18) is enrolled at Northeast State with a major in Business. In her free time, Kimberly particularly enjoys gardening and travel.



Dr. Moammir Hasan Aziz, has accepted the full-time position of Director of Research for the laboratory of Dr. Valentin Yakubenko. His appointment became effective April 1, 2016. The research focus of Dr. Aziz is to study the structural and functional properties of leukocyte integrins, cell surface signaling receptors, which are involved in cell adhesion and migration during different physiological and pathological conditions. Dr. Aziz is interested in elucidating the molecular and cellular mechanisms involved in integrin-mediated recruitment and accumulation of macrophages during chronic inflammatory diseases such as atherosclerosis, diabetes, obesity and cancer. All these studies involve both in vivo and in vitro strategies. Dr. Aziz uses a variety of approaches to answer these questions including cell and molecular biology assays, histology (immunohistochemistry and immunofluorescence), confocal microscopy and high-throughput assay systems (Fortebio-Octet, flow cytometry). Deciphering the mechanism of integrin-mediated macrophage functions would lead to new, potent and specific therapeutic strategies to limit these devastating diseases.



KUI CUI, first year PHD Graduate student, has joined the laboratory of **Dr. Valentin Yakubenko** effective March 2016.



CHRISTOPHER ARDELL joined the laboratory of **Dr. Valentin Yakubenko** as a temporary Lab Assistant effective December 2015.

Caroline Abercrombie, MD, Assistant Professor, Section of Medical Education, Director-Anatomy Lab of the Quillen College of Medicine, and Adjunct Faculty, Department of Biomedical Sciences, was selected to receive The Jack E. Mobley, MD Memorial Award for Excellence in Innovation for 2016. The award was presented by Dean Means at the Medical School Annual Caduceus Awards Ceremony held in April. Congratulations are extended to Caroline on receiving this well-deserved award.





**DEAN'S DISINGUISHED FACULTY AWARDS 2016
and
CADUCEUS CEREMONY NOMINEES & AWARDS FOR 2016**

CONGRATULATIONS to the following DBMS Faculty on receiving the Dean's Distinguished Faculty Awards for 2016:

Dr. Antonio Rusinol—Teaching

Dr. Yue Zou—Research

Dr. Krishna Singh—Service

The following Faculty/Staff were nominated for the Caduceus Ceremony Awards for 2016.

***Congratulations to those Winners (highlighted in Red!*)**

M1 Outstanding Course of the Year:

Awarded to the basic science course which 1st year students regard as the best educational experience including curriculum, content, and professor interaction with students.

Cell and Tissue Biology

Cellular and Molecular Medicine

Medical Human Gross Anatomy & Embryology*

Physiology

RPCT Rural/Case Oriented Learning

M1 Outstanding Professor of the Year:

Awarded by the 1st year students to basic science faculty demonstrating exemplary professionalism, mentorship, and scholarship.

Dr. Thomas Ecay

Dr. Thomas Kwasigroch

Dr. Paul Monaco

Dr. Mitchell Robinson

Dr. Antonio Rusinol*

Dr. Krishna Singh

M2 Outstanding Course of the Year:

Awarded to the basic science course which 2nd year students regard as the best educational experience including curriculum, content, and professor interaction with students.

Immunology

Medical Microbiology*

Pharmacology

M2 Outstanding Professor of the Year:

Awarded by the 1st year students to basic science faculty demonstrating exemplary professionalism, mentorship, and scholarship.

Dr. Michelle Duffourc

Dr. Kenneth Ferslew

Dr. Jennifer Hall

Dr. Russ Hayman

Dr. Donald Hoover

Dr. Rob Schoborg*

M1/M2 Outstanding College of

Medicine Staff Award: *Awarded to those individuals who go beyond their usual duties to assist students in the pursuit of their medical education.*

Rob Becker

Ronnie Hill*

Jerry Keplinger

Tonya Ward



Dr. Antonio Rusinol
Dean's Distinguished Faculty Award-Teaching and M1 Outstanding Professor of the Year



Dr. Yue Zou
Dean's Distinguished Faculty Award-Research



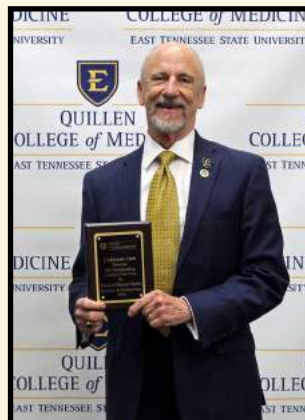
Dr. Krishna Singh
Dean's Distinguished Faculty Award-Service



Dr. Rob Schoborg
M2 Outstanding Professor of the Year



Ronnie Hill
M1/M2 Outstanding College of Medicine Staff



Dr. Tom Kwasigroch
M1 Outstanding Course of the year Medical Human Gross Anatomy & Embryology



Dr. Russ Hayman
M2 Outstanding Course of the Year Microbiology



**Dissertation Defense
of
Benjamin A. Hilton**

**Candidate for the Degree of
Doctor of Philosophy In Biomedical Science**

Tuesday, March 22, 2016

2:00 p.m.

VA Building-178 , Small auditorium, B-003

Dissertation Abstract

**Investigation of Novel Functions for DNA
Damage Response and Repair Proteins in
Escherichia coli and Humans**

Endogenous and exogenous agents that can damage DNA are a constant threat to genome stability in all living cells. In response, cells have evolved an array of mechanisms to repair DNA damage or to eliminate the cells damaged beyond repair. One of these mechanisms is nucleotide excision repair (NER) which is the major repair pathway responsible for removing a wide variety of bulky DNA lesions such as UV-induced pyrimidine dimers and chemically-adducted nucleotides. Deficiency, or mutation, in one or several of the NER repair proteins is responsible for many diseases, including cancer. Prokaryotic NER involves only three proteins to recognize and incise a damaged site, while eukaryotic NER requires more than 25 proteins to efficiently recognize and incise a damaged site. XPC-RAD23B (XPC) is the damage recognition factor in eukaryotic global genome NER. The association rate of XPC to damaged DNA has been extensively studied; however, our data suggests that the dissociation of the XPC-DNA complex is the rate-limiting step in

NER. The factor that verifies DNA-damage downstream of XPC is XPA. XPA also has been implicated in binding of ds-ssDNA junctions and has been found to bind at or near double-strand break sites in the premature aging syndrome Hutchinson-Gilford progeria (HGPS). This role for XPA is outside of its known function in NER and suggests that XPA may bind at collapsed replication forks in HGPS that are unprotected due to a lack of binding by replication proteins. One such replication protein is Replication factor C1 (RFC1), which is part of the pre-replication complex and is proteolytically cleaved in HGPS cells resulting in a naked DNA junction, which then can be bound by XPA. Another replication protein, PCNA, also is lacking due to sequestration by interaction with progerin; the absence of PCNA leads to the collapse of replication forks in HGPS and, progerin is a hallmark protein of HGPS and is formed due to a mutation in the lamin A gene. Along with XPC and XPA, *ataxia telangiectasia* and Rad3-related (ATR) is activated in response to DNA damage and initiates the cell cycle checkpoint pathway to rescue cells from genomic instability. We found that ATR functions outside of its known role in the checkpoint signaling cascade. Our data demonstrate that ATR also can rescue cells from apoptosis by inhibiting cytochrome c release at the mitochondria through direct interaction with the outer mitochondrial membrane and the proapoptotic protein tBid. The role of ATR in apoptosis is regulated by Pin1, a proline isomerase that has important functions in cell homeostasis, which can change the structure of ATR at the backbone level. All of the results presented here suggest novel roles for DNA repair proteins in the maintenance of genome stability.

***Ben has accepted a Clinical
Cytogenetics Fellowship at ARUP
Laboratories University of Utah, Salt
Lake City, UT. "ARUP Laboratories is a
national clinical and anatomic pathology
reference laboratory and a worldwide
leader in innovative laboratory research
and development."***



Dissertation Defense
of
Jessica A. Slade

**Candidate for the Degree of
Doctor of Philosophy In Biomedical Science**

**Thursday, March 24, 2016
10:00 a.m.
Carl A. Jones Hall , Room B-06**

Dissertation Abstract

***In Vitro* and *In Vivo* Characterization of
Chlamydia and HSV Co-infection**

The obligate intracellular bacterium, *Chlamydia trachomatis*, and Herpes Simplex Virus Type-2 (HSV-2) are the leading sexually transmitted pathogens in the world. These infections are usually asymptomatic and clinically mild, but complications can be severe. Reports of dual detection of *Chlamydia* and HSV within the genital tracts of humans led our laboratory to develop an *in vitro* *Chlamydia*/HSV co-infection model. Little is known regarding the specific pathogenesis of *Chlamydia* and HSV co-infections, but HSV-super-infection of *Chlamydia*-infected cells caused the chlamydiae to deviate from their normal developmental cycle into a non-replicative state termed persistence, or the chlamydial stress response. Interactions between HSV envelope protein, gD with host cell junction protein, nectin-1, were enough to stimulate the departure from normal chlamydial development. Additional data also suggested that there might be differences between single

infection and co-infection outcomes *in vivo*. Thus, two diverging hypotheses were investigated here: i) that host nectin-1 is required for normal chlamydial development; and ii) that pathogen shedding and/or disease progression in *Chlamydia* and HSV-2 co-infected animals will differ from that observed in singly-infected animals. Chlamydial infection of nectin-1 knockdown cell lines revealed no inhibition of chlamydial entry, but significant reductions in inclusion size and production of infectious chlamydiae. Additionally, nectin-1 knockout mice shed fewer *Chlamydia* compared to wild type mice. In other studies, we developed a novel *in vivo* *Chlamydia* and HSV-2 intravaginal super-infection model in BALB/c mice. Infection with *Chlamydia muridarum*, followed up to 9 days later by HSV-2 super-infection, both reduced HSV shedding and protected mice from HSV-induced fatal neurologic disease compared to HSV singly-infected animals. Protection is lost when: i) infected animals are no longer shedding *C. muridarum*; ii) when mice are inoculated with UV-inactivated *C. muridarum*; or iii) when viable chlamydiae are eliminated from the genital tract using antibiotics prior to HSV-2 super-infection. Altogether, we have determined that host nectin-1 is required for chlamydial development both *in vitro* and *in vivo*, and that chlamydial pre-infection protects mice from subsequent HSV infection. We predict that these observations may lead to novel approaches to prevent human infection by these two common sexually transmitted pathogens.

Jessica has accepted a Postdoctoral Fellowship with the laboratory of Dr. Anthony Maurelli, Department of Environmental & Global Health, College of Public Health and Health Professions, at the University of Florida, Gainesville, FL.

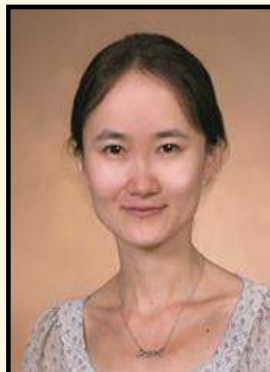
INTERNAL SEMINAR SPEAKERS



January 15, 2016

Patrick Bradshaw, PhD
Assistant Professor

**Natural therapies for
improving mitochondrial
function in
neurodegenerative disease**



January 29, 2016

Hui Wang
Graduate Student
Biomedical Graduate Program

**ATR plays a role in suppressing the
ionomycin induced necrotic
response**



February 12, 2016

Matt Palmatier, PhD
Assistant Professor
Department of Psychology

**Drugs of abuse as
amplifiers of brain
incentive circuits**



March 11, 2016

David L. Williams, PhD
Professor of Surgery

**Training innate
immunity: A new solution
to an old problem!**



February 26, 2016

Greg Hanley, DVM, PhD
DACLAM
Director, DLAR, University
Veterinarian
The Animal Care and Use
Program at ETSU

**What do they do and
why should I care**



April 8, 2016

Diego Rodriguez-Gil, PhD
Assistant Professor

**A cilia-associated protein
alters axon extension in
Meckel Gruber Syndrome**

INTERNAL SEMINAR SPEAKERS



April 22, 2016

Eric Sellers, PhD
Associate Professor
Department of Psychology
**Brain-Computer Interface
Technology: Clinical and
Practical Issues**



May 6, 2016

Matt Keasey, PhD
Research Associate
**Vitronectin uniquely
activates LIF and IL-6
expression through
integrin-FAK signaling**



May 20, 2016

Makenzie L. Fulmer
Graduate Student
**Systemic Type-2 Cannabinoid
Receptor Deletion Alters
Atherosclerotic Lesion
Composition in Ldlr-null Mice**

EXTERNAL SEMINAR SPEAKERS



April 18, 2016

Arturo Casadevall, MD, PhD
Chair, W. Harry Feinstone
Department of Molecular
Microbiology & Immunology
Johns Hopkins Bloomberg School
of Public Health
Baltimore, MD
**Thoughts on the origin of
microbial virulence**



June 1, 2016

Carlos A. Bolanos-Guzman, PhD
Professor
Department of Psychology
Florida State University
Tallahassee, FL
**Neurobiological Sequelae of
Witnessing
Stressful Events Early in Life**



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| | 2016 Appalachian Student Research Forum | |
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We express our appreciation to the Department of Biomedical Sciences Faculty that gave their time and efforts to serve as Judges for the Appalachian Student Research Forum. (ASRF). Also, many thanks to the students that participated in the oral and poster presentations for the ASRF and Boland Research Symposium. A Special CONGRATULATIONS is extended to the WINNERS.

Judges

ORAL PRESENTATIONS:

- Dr. Alok Agrawal
- Dr. Michael Kruppa
- Dr. Robert Schoborg
- Dr. Valentin Yakubenko

POSTER PRESENTATIONS:

- | | |
|-------------------------|------------------------|
| Dr. Alok Agrawal | Dr. Antonio Rusinol |
| Dr. Eric Beaumont | Dr. Rlobert Schoborg |
| Dr. Patrick Bradshaw | Dr. Sanjay Singh |
| Dr. Russ Brown | Dr. Douglas Thewke |
| Dr. Don Hoover | Dr. Qian Xie |
| Dr. Michael Kruppa | Dr. Valentin Yakubenko |
| Dr. Diego Rodriguez-Gil | |

Winners*

ORAL PRESENTATIONS:

Master Students—First Place
 Aubrey Sciara
 Faculty Sponsor: Dr. Greg Ordway

Doctoral Students—First Place
 Hui Wang
 Faculty Sponsor: Dr. Yue Zou

Medical Student-First Place:
 John Kirby
 Faculty Sponsor: Dr. Michael Kruppa



POSTER PRESENTATIONS:

Undergraduate—First Place
 Emma Pendola
 Faculty Sponsor: Dr. Greg Ordway

Undergraduate—Second Place
 Adam Denton/Charlotte Kaestner
 Faculty Sponsor: Dr. Russ Brown

Master Students—First Place
 Tuqa Alkhateeb
 Faculty Sponsor: Dr. Don Hoover

Doctoral Students—First Place:
 Stephanie Scofield
 Faculty Sponsor: Dr. Krishna Singh

Medical Student-First Place:
 Lizzie Monroe
 Faculty Sponsor: Dr. Don Hoover



***See details on Pages 17-20**



2016 Appalachian Student Research Forum

ORAL PRESENTATIONS—

Master's & Doctoral Candidates: Biomedical & Health Sciences

- ◆ THE NOVEL ROLE OF ATR IN SUPPRESSING THE IONOMYCIN-INDUCED NECROTIC CELL DEATH RESPONSE. Hui Wang, Benjamin A. Hilton, **Phillip Musich** and **Yue Zou**. **WON FIRST PLACE!**
- ◆ SYSTEMIC TYPE-2 CANNABINOID RECEPTOR DELETION ALTERS ATHEROSCLEROTIC LESION CALCIFICATION IN LDLR-NULL MICE. Makenzie L. Fulmer, Emilee Engelhaupt, and **Dr. Douglas Thewke**.
- ◆ ENGINEERED C-REACTIVE PROTEIN WITH IMPROVED PROTECTIVE ACTION AGAINST PNEUMOCOCCAL INFECTION. Donald N. Ngwa, Toh B. Gang, **Sanjay K. Singh** and **Alok Agrawal**.
- ◆ EVOLUTION OF HOST-DEFENSE FUNCTION OF C-REACTIVE PROTEIN FROM HORSESHOE CRAB TO HUMANS. Asmita Pathak, **Sanjay K. Singh**, Avinash Thirumalai, Peter B. Armstrong and **Alok Agrawal**.
- ◆ VAGUS NERVE STIMULATION IMPROVES NEURONAL ACTION POTENTIAL SYNCHRONY WITH CARDIAC AND RESPIRATORY CYCLE IN HEART FAILURE ANIMAL MODEL. Nathan Cantrell, Dr. Regenia Phillips Campbell, Stephanie Scofield, **Dr. Krishna Singh**, and **Dr. Eric Beaumont**.

POSTER PRESENTATIONS— UNDERGRADUATES

Society, Behavior, Learning, Humanities, and Engineering (Group A):

- ◆ ADOLESCENT METHYLPHENIDATE EXPOSURE ALTERS THE BEHAVIORAL RESPONSE TO NICOTINE AND SENSITIZES ACCUMBAL BDNF. Caitlynn C. DePreter, Seth L. Kirby, Lauren A. Beuttel, Dr. Matthew I. Palmatier, **Dr. Russell W. Brown**.
- ◆ THE EFFECTS OF ANTIPSYCHOTIC TREATMENT UPON NICOTINE ASSOCIATIVE REWARD IN A NEONATAL QUINPIROLE MODEL OF SCHIZOPHRENIA. Adam Denton/Charlotte Kaestner, Seth Kirby, Kate Burgess and **Dr. Russell Brown**. **WON SECOND PLACE!**
- ◆ A DOUBLE HIT STRESS RODENT MODEL OF MAJOR DEPRESSIVE DISORDER. Liza J. Hernandez, Katherine C. Burgess, James Wherry, **Attila Szebeni**, **Gregory Ordway**, and **Russell W. Brown**.

Society, Behavior, Learning, Humanities, and Engineering (Group B):

Master's Candidates: Natural Sciences:

- ◆ CHARACTERIZATION OF ANTI-INFLAMMATORY MICROGLIA IN ANTERIOR CINGULATE CORTEX WHITE MATTER IN AUTISM SPECTRUM DISORDER. Aubrey N. Sciara, Emma E. Pendola, **Dr. Jessica D. Crawford**, Dr. Michelle J. Chandley (Co-Advisor), and **Dr. Gregory A. Ordway** (Advisor). **WON FIRST PLACE!**

Medical Students/Pharmacy Students:

- ◆ POLYMICROBIAL INTERACTIONS: REDISCOVERY AND CHARACTERIZATION OF AN INHIBITOR OF NEISSERIA GONORRHOEAE. John Kirby and **Dr. Michael Kruppa**. **WON FIRST PLACE!**
- ◆ MODERNIZING EDUCATIONAL RESOURCES FOR AN ADVANCED ANATOMY LAB EXPERIENCE. Savannah Mattie, Amber Brooks, **Rob Becker**, **Dr. Caroline Abercrombie**, **Dr. Thomas Kwasigroch**.



2016 Appalachian Student Research Forum

Natural Sciences (Group A):

- ◆ IMPACT OF REDUCED CALCIUM DURING DEVELOPMENT IN SNAKES. Kaitlyn Mathis, Dr. Rebecca Pyles, Dr. James Stewart, and **Dr. Tom Ecay**.

Biomedical & Health Sciences (Group A):

- ◆ PIN1 IN THE DNA DAMAGE RESPONSE IN RELATION TO RPA MODIFICATION. Rowdy Jones and **Dr. Yue Zou**.

Biomedical & Health Sciences (Group B):

- ◆ EFFECTS OF SPINAL CORD STIMULATION ON HEART FAILURE INDUCED HIPPOCAMPAL DAMAGE. Mahon Mahmodian, Elizabeth Kwenda, Timothy DiPeri, **Attila Szebeni**, **Katalin Szebeni**, Jeffrey L. Ardell, and **Gregory A. Ordway**.
- ◆ PRO-INFLAMMATORY MICROGLIA PATHOLOGY IN THE ANTERIOR CINGULATE CORTEX IN ASD. Emma E. Pendola, Aubrey N. Sciara, **Jessica D. Crawford**, **Gregory A. Ordway**, and Michelle J. Chandley. **WON FIRST PLACE!**

POSTER PRESENTATIONS— GRADUATE STUDENTS MASTER'S CANDIDATES

Society, Behavior and Learning (Group B):

- ◆ NUCLEUS ACCUMBENS BDNF OVEREXPRESSION ALTERS THE BEHAVIORAL RESPONSE TO NICOTINE. Seth L. Kirby, Katherine C. Burgess, Lauren A. Beuttel, Sara Dean, Curtis A. Bradley, Matthew I. Palmatier, **Meng-Yang Zhu**, and **Russell W. Brown**.

Biomedical, Health, and Health Sciences:

- ◆ EFFECTS OF SEPSIS ON RENAL STRUCTURE AND SYMPATHETIC INNERVATION IN MICE. **Tuqa Alkhateeb**, Dr. Tammy Ozment², Dr. George Youngberg, Dr. David Williams², and **Dr. Donald Hoover**. **WON FIRST PLACE!**

POSTER PRESENTATIONS— GRADUATE STUDENTS DOCTORAL CANDIDATES

Biomedical Health & Natural Sciences (Group A):

- ◆ BEHAVIORAL EPIGENETIC EVIDENCE OF INCREASES IN DOPAMINE D2 RECEPTOR SENSITIVITY AFTER NEONATAL QUINPIROLE TREATMENT IN RATS. W. Drew Gill, James D. Wherry, and **Russell W. Brown**.
- ◆ HEPATIC CELL METABOLISM REGULATION BY C1q TUMOR NECROSIS FACTOR-RELATED PROTEIN-3. Ying Li, **Dr. Gary Wright** and Dr. Jonathan Peterson.

Biomedical Health & Natural Sciences (Group B):

- ◆ EXTRACELLULAR UBIQUITIN DECREASES ADVERSE EFFECTS OF MYOCARDIAL ISCHEMIA/REPERFUSION INJURY IN MICE. **Stephanie L.C. Scofield**, Kristina A. Lim, Dr. Christopher R. Daniels, **Dr. Suman Dalal**, **Dr. Mahipal Singh**, and **Dr. Krishna Singh**. **WON FIRST PLACE!**
- ◆ ATAXIA-TELANGIECTASIA MUTATED KINASE INDUCES AUTOPHAGY IN MICE FOLLOWING MYOCARDIAL INFARCTION. **Patsy R. Thrasher**, **Stephanie L.C. Scofield**, **Dr. Suman Dalal**, **Dr. Mahipal Singh**, **Dr. Krishna Singh**.



2016 Appalachian Student Research Forum

- ◆ TWO ISOMERIC FLAVONOIDS HAVE A SYNERGISTIC EFFECT IN COLON CANCER WHEN USED IN COMBINATION WITH 5-FLUOROURACIL CELLS DUE TO INCREASED DNA DAMAGE. Crystal Whitted, Michael Cartwright, Zachary Walls, **Yue Zou**, Ruben Torrenegra, and Victoria Palau. **WON FIRST PLACE!**

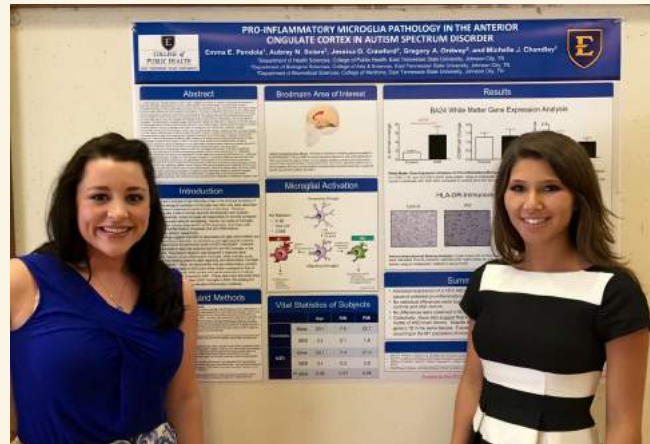
POSTER PRESENTATIONS— MEDICAL STUDENT

Medical Students (Group A):

- ◆ DEVELOPMENT OF MULTIPOLAR CELL SHAPE IN MOUSE CORNEAL ENDOTHELIUM. Jacob W. Fleenor, Kathleen A. King, **Dr. Theresa A. Harrison** and **Dr. Dennis M. Defoe**.

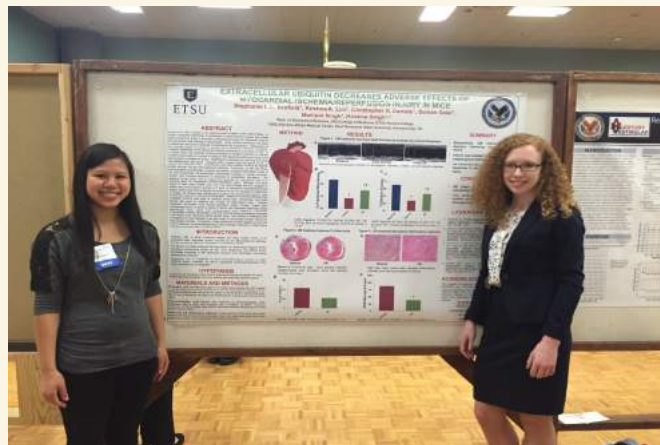
Medical Students (Group B):

- ◆ ZYMOBAN-INDUCED SIRS RESULTS IN SEVERE HYPOTHERMIA AND MILD DEPRESSION OF CARDIAC DROMOTROPIC FUNCTION IN MICE. Lizzie L. Monroe, Michael G. Armstrong, David L. Williams, and **Donald B. Hoover**. **WON FIRST PLACE!**
- ◆ THE EFFECTS OF VAGAL NERVE STIMULATION ON TRIMETHYLAMINE-N-OXIDE LEVELS IN A RAT HEART FAILURE MODEL. Parth Sheth, **Dr. Regenia Campbell**, Dr. Stacy Brown, **Dr. Michelle Duffourc**, **Dr. Rob Schoborg**, and **Dr. Eric Beaumont**.



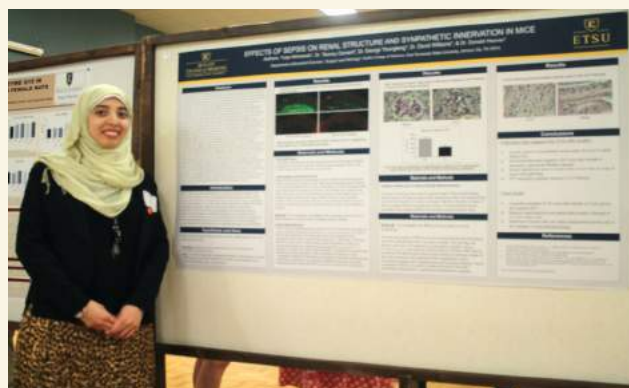
Aubrey Sciarra (Left)
Master Student
First Place (Oral)

Emma Pendola (Right)
Undergrad Student
First Place (Poster)



Kim Lim (Left)
Undergrad Student
Second Author

Stephanie Scofield (Right)
Doctoral Student
First Place (Poster)



TUQA ALKHATEEB
Master Student
First Place (Poster)

2016 ETSU Boland Undergraduate Research Symposium

STUDENT PARTICIPANTS:

- ◆ Matthew Hinkle (Senior-Biological Sciences) Sympathetic overdrive observed in heart failure. **ADVISOR: Dr. Eric Beaumont.**
- ◆ Rowdy Jones (Senior-Biological Sciences) Pin1 interaction in the hyperphosphorylation of RPA. **ADVISOR: Dr. Yue Zou.**
- ◆ Daniel Rabulinski (Senior-Health Sciences) Modulation of osteogenic gene expression in cultured murine vascular smooth muscle cells by the cannabinoid receptor Type 2. **ADVISOR: Dr. Douglas Thewke.**
- ◆ Chase Mussard, (Senior-Chemistry) In vitro investigation of the effect of exogenous ubiquitin on processes associated with atherosclerosis. **ADVISOR: Dr. Douglas Thewke.**
- ◆ Caitlynn De Preter (Junior-Psychology) Adolescent Methylphenidate Exposure Alters the Behavioral Response to Nicotine. **ADIVSOR: Dr. Russell Brown.**
- ◆ Adam Denton (Senior-Psychology) The effects of antipsychotic treatment upon associative learning in a neonatal quinpirole model of schizophrenia. **ADIVSOR: Dr. Russell Brown.**
- ◆ Gage Armstrong (Senior-Biological Sciences) Effect of sterile peritonitis on the expression of substance p in primary sensory neurons and nerves. **ADVISOR: Dr. Donald Hoover.**
- ◆ Virginia Ingram (Audiology and Speech-Language Pathology) 3D Printed Food & Dysphagia: Food of the Future has a Purpose. **ADVISOR: Dr. Gregory Ordway.**
- ◆ Kristina Lim (Sophomore-Biological Sciences) Role of Exogenous Ubiquitin (Ex-UB) in Myocardial Ischemia/ Reperfusion Injury (IRI). **ADVISOR: Dr. Krishna Singh.**
- ◆ Megan Butler (Senior-Biological Sciences) Influence of Estrogen and Progesterone on Chlamydial Infections. **ADVISOR: Dr. Jennifer Hall.**
- ◆ Dustin Gilmer (Junior-Physiology) Focal adhesion kinase mediates adult olfactory stem cell proliferation through regulating ciliary neurotrophic factor. **ADVISOR: Dr. Cuihong Jia**
- ◆ Kaitlyn Mathis (Senior-Biological Sciences) Impact of Reduced Calcium during development in Snakes. **ADVISOR: Dr. Rebecca Pyles and Dr. Tom Ecay.**