With the semester ending, we can be proud of our teaching accomplishments and I am grateful to all who have been part of this most important part of our mission. I am grateful to Dr. Schoborg and the Course Directors for their hard work in helping us plan for the future as well as further improving our already excellent teaching.

Over the last two months since the last Newsletter, we welcomed our newest Faculty members, Drs. Valentin Yakubenko and Diego Rodriguez-Gil. Dr. Qian Xie will join us on January. Together with the other three new Faculty, this is a great start to further growing our research and securing our long-term excellence in teaching. We also welcomed Keith Davenport, our new Fiscal Affairs Manager, and have already benefited greatly from his expertise and kind service-oriented personality. Dr. Sanjay Singh joined Dr. Agrawal’s lab as a Research Assistant Professor, and several new students and technicians also joined the department. We trust that their adjustment will be smooth and that they will increasingly feel at home in Johnson City and among the DBMS team.

At the other end of the spectrum, Dr. Musich retired after a 35 year distinguished career at the Quillen College of Medicine. We wish him well in this new Emeritus phase of his life and are looking forward to seeing his continued contributions to scientific research and benefiting from his expertise.

I believe that 2016 will be even better than 2015 and look forward to working with all of you. Together, we will keep the momentum going.
After 35 Years Dr. Phillip R. Musich Bids Farewell to College of Medicine

Dr. Phillip R. Musich, Professor, retired
October 31, 2015, after 35 years of dedicated service to the College of Medicine.

Phil began his tenure with the James H. Quillen College of Medicine in 1980 when he was employed as an Assistant Professor in the Department of Biochemistry. In 1985 he was promoted to Associate Professor, and in 1991 he received full Professorship. He held the appointed position of Deputy Chair in the Department of Biochemistry (1988-1995), and he was also an Adjunct Professor in the Department of Biological Sciences, College of Arts and Sciences (1996 until retirement). He served as the Course Director for the Molecular Biology Course (1987-2000).

Prior to joining the College of Medicine, he began his postdoctoral training as an National Institutes of Health fellow in the Department of Zoology, MRC Mammalian Genome Unit, University of Edinburgh, Scotland (1973-1975). Thereafter, he held the position of Research Associate with the Department of Cell Biology, Albert Einstein College of Medicine, Bronx, New York (1975-1980).

Phil obtained a doctoral degree from the Department of Biology, University of Chicago, Illinois (1968-1973); held a Summer National Science Foundation Research Program Fellowship in the Chemistry Department, University of Arkansas, Fayetteville, AK (1967 Summer); and obtained a Bachelor of Science degree in Chemistry and Biology from Creighton University, Omaha, Nebraska (1964-1968).

His research interests concentrated around the patterns of differential DNA damage in response to oxidative challenge in mammalian cells, molecular mechanisms of aging in humans, and features of DNA damage and DNA repair in humans. Throughout his research career, he has had many articles published in multiple science journals. His research was supported through the National Institutes of Health, American Heart Association, and internal funding sources. He was a member of numerous dissertation and thesis committees throughout his career, and served as Chair or Co-Chair of several of those committees.

His service to the College for the past 35 years has been commendable. He served on and chaired several committees within the College of Medicine, served as Course Director of Medical Biochemistry, and was friend and mentor to medical and graduate students throughout his teaching and research career.

In this new chapter of Phil’s life, he is looking forward to spending more time with his grandchildren. In addition, he enjoys woodworking, photography, reading and walking/hiking, and, especially, traveling. Our best wishes for a wonderful retirement are extended to Phil.
GRANT FUNDING

Funding Agency: Alector LLC
Principal Investigator: Dr. Hagg
Project Title: Alector LLC
Sponsored Research Agreement
Award Issue Date: July 13, 2015
Project Funding Period: 11/1/15—10/31/16
Total Amount of Award: $22,200
Project Narrative: The Hagg lab will test novel drugs in a spinal cord injury model.

SCIENTIFIC MEETINGS/INVITED PRESENTATIONS

Dr. Tom Ecay, Professor, attended The 7th Annual Meeting of the Tennessee Physiological Society—A Chapter of the American Physiological Society. The meeting held on October 9, 2015, was sponsored by The University of Tennessee-Chattanooga.

Dr. Donald B. Hoover, Professor, was an Invited Guest Lecturer for the Robert E. Stitzel Lecture Series, The West Virginia University, Robert C. Byrd Health Sciences Center on October 15, 2015. The title of Dr. Hoover’s Lecture was “Exploration of Cholinergic Mechanisms: From Brain to Heart to Spleen.”

Dr. Gregory Ordway, Professor, was an invited speaker at the Suicide Research Summit, sponsored by the IASR and AFSP in New York on October 11, 2015. The title of Dr. Ordway’s presentation was “White Matter Oligodendrocyte Pathology in Depression and Suicide.”

Dr. Richard M. Kostrzewa, Professor, and Prof. Lucyna Antkiewicz-Michaluk (Polish Academy of Sciences, Krakow, Poland) co-chaired the symposium “Neurotoxicity and Neuroprotection” at the XIX International Congress of the Polish Pharmacological Society in Swinoujscie, Poland, September 17-20, 2015. The title of Dr. Kostrzewa’s presentation was “Monoaminergic System Interaction in Neurotoxicity.”

Dr. Alok Agrawal, Professor, was invited to present a seminar in the Division of Health Sciences, Integrative Cell Biology Graduate Program, Loyola University, Chicago, on October 5, 2015. The title of Dr. Agrawal’s seminar was “RP in pneumococcal infection.”

Dr. Krishna Singh, Professor, was an Invited Seminar Speaker for the Department of Physiology and Biophysics at the University of Louisville on December 08, 2015. Dr. Singh’s seminar title was “Molecular signals involved in myocyte apoptosis and myocardial remodeling.”

NIH REVIEW STUDY SECTIONS

Dr. Alok Agrawal, Professor, served on the following Study Sections:

The “Atherosclerosis and Inflammation of the Cardiovascular System” study section review committee, NIH, September 28-29, 2015, Potomac, MD.

The “Arthritis, Connective Tissue, and Skin” study section review committee, NIH, October 12-13, 2015, Rockville, MD.

The “Innate Immunity and Inflammation” study section review committee, NIH, October 29-30, 2015, Alexandria, VA.

DR. KRISHNA SINGH SERVED AS DISTINGUISHED FACULTY MARSHAL AT THE ETSU CONVOCATION, HELD ON DECEMBER 12, 2015.


WELCOME NEW FACULTY...

Valentin Yakubenko, PhD, joined the faculty of the Department as Assistant Professor, September 1, 2015. Dr. Yakubenko received his MS in biophysics from the National Kiev University (Ukraine) and a PhD in biochemistry from the National Academy of Sciences of Ukraine. Prior to joining ETSU he grew his career in the Lerner Research Institute at the Cleveland Clinic.

Valentin was born and raised in Kiev, Ukraine (part of the former USSR). After his first year of college, Valentin was recruited to the Soviet Army, where he meaninglessly spent 15 months in the Azerbaijan desert. The compulsory military service further assured him that the biomedical field would be his chosen career path.

He first met his wife Anna in high school. They have a daughter Irina, 22 and son Nicholas, 7. Irina works for IBM after graduating from Case Western Reserve University and Nicholas likes gymnastic, soccer and cats.

Outside of work, Valentin likes to play soccer and tennis. He and his family enjoy hiking, alpine skiing, canoeing, fishing, and mushroom hunting.

Diego Javier Rodriguez-Gil, PhD, joined the faculty of the Department as Assistant Professor, effective October 1, 2015. Prior to joining QCOM he held the position of Associate Research Scientist, Department of Neurosurgery, Yale University School of Medicine, New Haven, CT.

He received his PhD from the School of Exact and Natural Sciences, University of Buenos Aires, Argentina. At Yale University, he developed the foundations of his research, which is focused on understanding how neurons extend processes and find their correct targets in the brain. His areas of expertise include Neurosciences, Sensory systems, Embryology, and Cell and Molecular Biology.

Diego was born and raised in Buenos Aires, Argentina. He is the second of three siblings and he enjoys going back to Buenos Aires to meet with his family, play with his nephew and nieces and catch up with long standing friends. During his graduate studies he met his wife, Claudia, who was also a PhD student, and with whom he got married a few years later. They finished graduate school, accepted postdoctoral positions at the same university and moved to the US.

Outside of work, Diego enjoys quality time with his family and friends. He particularly enjoys exploring new restaurants. Argentina is known for its passion for soccer, hence playing soccer several times a week was an important part of his life. Now he enjoys the sport of his native country as a spectator. He also enjoys reading, drawing, going for a walk, trekking, and biking. When getting ready either for a short walk or a long trip, the first thing he packs is his camera, as he is an enthusiastic amateur photographer.
WELCOME NEW FACULTY (Cont’d)...

Qian Xie, MD/PhD, joined the faculty of the Department as Assistant Professor effective January 4, 2016. Prior to joining the COM she held positions of Research Assistant Professor, Senior Research Scientist, and Research Scientist at Van Andel Research Institute, Grand Rapids, MI. Beforehand, she was an Assistant Investigator at the Experimental Research Center of Fudan University Zhongshan Hospital, Shanghai, China.

Dr. Xie received a Bachelor degree of Medical Science (Equivalent to U.S. M.D.) at Shanghai Medical College of Fudan University (Former Shanghai Medical University). She completed a PhD in Clinical Medicine with a major in Oncology at the same university. Her Postdoctoral Fellowship training was completed at Van Andel Institute in the field of Molecular Oncology.

Her research interest is in the field of Molecular Oncology and Targeted Therapy. According to Dr. Xie, “The success of molecular targeted therapies against cancer depends on the discovery of tumor driver genes and the molecular mechanisms that confer escape pathways.” Her long term goals are to understand the mechanisms of MET pathway activation in glioblastoma, to accelerate strategies to improve therapeutic efficacy targeting MET, and to establish preclinical models for targeted therapy.”

Outside of work, Xie likes sight-seeing. “The most attracting part of any place is always its culture. I like to talk to and hear from diversified people. It is always exciting to learn the beauty of nature.”

WELCOME NEW STAFF...

We welcome KEITH C. DAVENPORT to the Department. Keith accepted the position of Fiscal Affairs Manager effective September 21, 2015, replacing Ms. Robin Montgomery.

Keith is a native and resident of Bristol, Tennessee. He received his undergraduate degree from UT-Knoxville, and his MBA from the University of Georgia, both with a major in Accounting. His professional background is primarily in manufacturing accounting and most recently he was the Cost Accounting Director at legacy King Pharmaceuticals, which was acquired by Pfizer in 2011. He has also worked for GlaxoSmithKline, Eastman Chemical, Kennametal, Tupperware Manufacturing, Hercules Chemical, and NCR. Keith states, “I began my career at Beecham Laboratories in Bristol, saved my money for grad school, and ended up making a full circle back to the same address as King Pharma/Pfizer. Life and career are a journey- make the most of it! I am happy to be learning new ways of working here at ETSU and amazed by the beautiful campus.”

During his leisure time, Keith enjoys working in his yard. His free time will also find him keeping up with the stock market. He owns two rescued animals—a black cat named Shadow, and a dog named Snickers. Snickers is a German Shepherd Golden Retriever mix.
We welcome **Moammir Aziz** to the Department. Moammir joined the laboratory of **Dr. Valentin Yakubenko** on November 1, 2015, as Laboratory Assistant. Dr. Moammir H. Aziz obtained his BS and MS degrees in Biochemistry from Aligarh Muslim University, Aligarh, India in 1995 and 1997 respectively. He completed a Ph.D. in Biochemistry in 2002 from CSIR-Indian Institute of Toxicology Research, Lucknow and Hamdard University, New Delhi, India. His Ph.D. work was devoted to studying the biochemical aspects of chemical toxicity during neuro-developmental period. Since 2002, Dr. Aziz has made significant contributions to Biomedical research by his outstanding work done in several well reputed Universities in USA (University of Wisconsin-Madison, WI, Rush University, Chicago, and Southern Illinois University School of Medicine, Springfield, IL) before joining ETSU, Johnson City, TN. Dr. Aziz lives in Johnson City with his wife, Dr. Saba Aziz, who is an endocrinologist, and two daughters, Inaaya and Samara.

We welcome **Aruna Visavadiya** to the Department. Aruna joined the laboratory of **Dr. Theo Hagg**, November 1, 2015, as Research Assistant 2. Aruna was employed in the Department of Molecular and Biomedical Pharmacology, at the University of Kentucky. She obtained a M.Phil (Animal Science) degree from Saurashtra University, India. She also holds a MSc Degree (Zoology) from North Gujarat University, Patan, Gujarat, India, and BSc (Zoology) from the Saurashtra University, Rajkot, Gujarat, India. Aruna’s husband, Dr. Nishant Visavadiya, had previously joined Dr. Hagg’s laboratory as a Research Associate, in March of 2015.

We welcome **Muhammad Ummear Raza** to the Department. Mr. Raza joined the laboratory of **Dr. Meng-Yang Zhu** on September 11, 2015, as Laboratory Assistant. He received his M.Phil. degree (Human Genetics, 2012-2014) and M.Sc. (Zoology, 2010-2012) from Quaid-I-Azam University Islamabad. Mr. Raza is a native of Punjab, Pakistan and has previously participated in projects involving clinical and genetic epidemiological study of skeletal limb anomalies in local populations.

We welcome **Dr. Kangjun Li** to the Department. Dr. Li came from Sua Yat-sen University, China. He is working in **Dr. Meng-Yang Zhu**’s laboratory as a Visiting Scholar. Dr. Li got his MD degree in 2009 and currently is a PhD candidate in the Zhongshan Ophthalmic Center. In China his main project is related to intraocular transplantation in the animal model of the visual nerve injury using the combination of stem cell induced differentiation and nano tissue engineering technology. He will take part in the research project of DNA damage *in vitro* and *in vivo* oxidative stress models.
We welcome Chris Ardell to the Department. Chris joined the laboratory of Dr. Valentin Yakubenko on November 23, 2015, as Temporary Lab Assistant.

CONGRATULATIONS are extended to Hannah Malone who has been appointed to a full time position as Research Assistant 2, effective November 1, 2015. Hannah works in the laboratory of Dr. Theo Hagg.

Makenzie Fulmer, Graduate Student in the laboratory of Dr. Doug Thewke, presented a poster at the 7th European Workshop on Cannabinoid Research and IACM 8th Conference on Cannabinoids in Medicine. September 17-19th in Sestri Levante, Italy.

MODULATION OF LATE STAGE ATHEROSCLEROSIS BY THE TYPE-2 CANNABINOID RECEPTOR

Makenzie L. Fulmer1, Emilee Englehaupt1, Chris Garst2, Stacy Brown2, and Douglas Thewke1
1Department of Biomedical Sciences, Quillen College of Medicine and 2Pharmaceutical Sciences, Gatton College of Pharmacy, ETSU, Johnson City, Tennessee 37614, U.S.

Introduction: Atherosclerosis is a chronic inflammatory disease of the vascular system that is characterized by the build up of plaques, composed of lipids and other cellular debris, within arterial walls. Instability of advanced plaques can lead to rupture, manifesting serious health consequences such as myocardial infarction or stroke. As atherosclerosis advances, plaques can calcify; a factor which increases their vulnerability to rupture. The mechanism of plaque calcification is unclear but is thought to be a cell-mediated process similar to bone remodeling. The type-2 cannabinoid receptor (CB2) modulates processes in immune cells involved in atherogenesis as well as in osteogenic precursor cells involved in bone remodeling. Prior studies showed that CB2 alters the composition of early stage plaques in Ldlr−/− mice, a murine model of atherosclerosis; however, the function of CB2 in more advanced plaques has not yet been elucidated. We hypothesized that CB2 modulates the composition of advanced plaques and tested this by evaluating the effects of systemic CB2 gene deletion on advanced plaque formation and calcification in Ldlr−/− mice.

Methods and Results: Groups (n≥8) of 8-week old CB2+/+Ldlr−/− (WT) and CB2−/- Ldlr−/−(CB2−/-) mice were fed a high fat diet (HFD) for up to 24 weeks to induce advanced atherosclerosis. Hyperlipidemia induced by the HFD did not differ between WT and CB2−/- mice, as determined using standard blood plasma analysis methods. LC-MS/MS analysis of aortic endocannabinoid levels showed increased anandamide (AEA) and 2-archidonylglycerol (2-AG) after 12 weeks of HFD for both groups compared to chow fed controls. After 24 weeks, aortic 2-AG levels were significantly elevated while the AEA levels decreased significantly in both groups. En face analysis revealed the extent of atherosclerosis in the aortic arch and thoracic aorta did not differ between WT and CB2−/- mice, but was ~1.9-fold greater in the abdominal aortas of CB2−/- mice (17.0±1.3% vs 9.0±1.3%, p=0.002). Morphometric analysis of von kossa stained serial cross sections showed calcium deposition in advanced aortic root plaque to be ~2.3 fold greater in CB2−/- mice compared to WT mice (12.9±1.1% vs 5.6±1.2%, p=0.002). Conclusion: These results are consistent with our hypothesis that CB2 modulates plaque calcification in advanced atherosclerotic lesions. Information from this and future investigations could translate into CB2-targeted therapies for atherosclerosis.
Emma Pendola, Undergraduate Student, was awarded the Student-Faculty Collaborative Grant by ETSU Honors College, in the amount of $1,188. Emma will be working in conjunction with Dr. Michelle Chandley and Dr. Gregory Ordway to determine microglia pathology in postmortem tissue of subjects with autism. The project completion date is May 2016.

Elizabeth Kwenda, Undergraduate Student, was awarded the Student-Faculty Collaborative Grant by ETSU Honors College, in the amount of $1,182. Elizabeth is working with the laboratory of Dr. Gregory Ordway to help determine white matter protein and lipid abnormalities in depression. The project completion date is May 2016.

2nd YEAR GRADUATE STUDENTS - 2015-2016

Jun Dai  
Laboratory: Dr. Bradshaw

Henry Gong  
Laboratory: Dr. Zou

Richard Sante  
Laboratory: Dr. Hagg

Patsy Thrasher  
Laboratory: Dr. Singh

Li Ying  
Laboratory: Dr. Wright
Graduate Student Seminar

ATR Plays a Direct Antiapoptotic Role at Mitochondria Which Is Regulated by Prolyl Isomerase Pin1

By

Benjamin Hilton

Wednesday, December 16, 2015
3:00 p.m.
VA Bldg. 178, Small Auditorium

Abstract: ATR, a PI3K-like protein kinase, plays a key role in regulating DNA damage responses (DDR). Its nuclear checkpoint kinase function is well documented but little is known about its function outside the nucleus. Here we report that ATR has a potent anti-apoptotic activity at mitochondria in response to UV damage, and this activity is independent of its hallmark checkpoint/kinase activity and nuclear partner ATRIP. Our data reveal that ATR contains a BH3-like domain, characteristic of Bcl2 family proteins, which, after UV activation, allows ATR-tBid interaction at mitochondria, blocking pro-apoptotic Bax/Bak mitochondrial accumulation, cytochrome c release and apoptosis. Pin1, a peptidyl-prolyl isomerase, isomerizes ATR at the phospho-Ser428-Pro429 motif, converting cytoplasmic ATR from the cis-isomer to the trans-isomer in unstressed cells. The isomerization-induced conformational change silences the mitochondria-specific function of ATR. However, UV inactivates Pin1 via Ser71 phosphorylation by DAPK1 kinase, stabilizing cytoplasmic ATR in the cis-isoform which is able to bind to tBid to function as a pro-survival protein, and the BH3-like domain of ATR is essential for this binding. In contrast, interestingly, nuclear ATR remains in the trans-isoform disregarding UV irradiation. This cytoplasmic response of ATR may provide a molecular mechanism for the observed physiological roles of ATR and its disease relevance such as the potential anti-apoptotic role of ATR in suppressing carcinogenesis and its inhibition in sensitizing anticancer agents for killing of cancer cells.

Dr. Yue Zou and his research team gain recognition for their research article published in Molecular Cell, October 2015, Volume 6, Issue 1, Pages 35-46. Citation: Hilton BA, Li Z, Musich PR, Wang H, Cartwright BM, Serrano M, Zhou XZ, Lu KP, Zou Y (2015) ATR Plays a Direct Antiapoptotic Role at Mitochondria, which is Regulated by Prolyl Isomerase Pin1.

The article was reviewed and published in Nature Reviews Molecular Cell Biology, Volume 1, November 2015, and entitled, DNA Damage Response, ATR prevents premature apoptosis, authored by Kirsty Minton. The full publication can be found on Molecular Cell website. It was also featured in Planit ETSU.


Once again, the Department of Biomedical Sciences obtained a satisfactory OSHA laboratory review for 2015 with minor deficiencies. We must continue to strive to keep our labs safe. Health & Safety will be organizing an additional training session for all lab personnel sometime in the upcoming new year. Reminder, online training must be completed by all laboratory personnel and renewals completed on an annual basis.
We are delighted that Dr. Bill Joyner is recovering nicely from his recent operation. Our get well wishes go out to him and his family as he continues to recuperate at home.

Matthew Keasey, Richard Sante, and Turan Tufan participated in the ETSU Intramural Soccer Competition this year. The team was called “Dream Team” and was organized by Richard Sante. On December 6, 2015, the “Dream Team” won the Final game 3-0 and won all of our preceding games and so had a perfect record. The following players are shown in photo in no specific order: Matthew Keasey, Turan Tufan, Richard Sante, Hadi Lasso, Joey Ike, Don Jabal, Sime Freddy, Murad Alwusaybie, Ahmed Alabssi. The following played but were not in the photo: Sodiq Dayo, Itode Fubara, Simon Chiba.

Congratulations to the DREAM TEAM for a job well done!

Tonya Ward, Crystal Maupin, and Cindy Canter enjoyed the Tacky Sweatshirt Contest on December 4, 2015.

Department of Biomedical Sciences
Holiday Gathering
DECEMBER 18, 2015
6:00—9:00 pm
In the Pavilion at the Blackthorn Club at the Ridges

We are delighted that Dr. Bill Joyner is recovering nicely from his recent operation. Our get well wishes go out to him and his family as he continues to recuperate at home.
INTERNAL SPEAKERS

September 4, 2015
Theodoor Hagg, MD, PhD
Professor and Chair
Department of Biomedical Sciences

Title: Microvascular damage regulates outcomes after nervous system injury

September 11, 2015
Robert V. Schoborg, PhD
Professor
Department of Biomedical Sciences

Title: Ascertaining the role of acetylcholine producing cells in chlamydial genital tract infection

September 25, 2015
Antonio Rusinol, PhD
Professor
Department of Biomedical Sciences

Title: Prelamin A in cell cycle control

October 23, 2015
Regenia Phillips Campbell, PhD
Research Associate
Department of Biomedical Sciences

Title: Effect of vagal nerve stimulation on gut flora in guinea pigs with heart failure

November 6, 2015
Victoria Palau, PhD
Associate Professor
Bill Gatton College of Pharmacy

Title: Differential anti-neoplastic activity of flavones derived from andean plants with ethnobotanical importance

November 13, 2015
Valentin Yakubenko, PhD
Assistant Professor
Department of Biomedical Sciences

New potential mechanism for neutrophil-mediated macrophage recruitment during inflammation
INTERNAL SPEAKERS (Cont’d)

November 20, 2015
Michelle Chandley, PhD
Assistant Professor, Department of Health Sciences
Cell pathology in autism spectrum disorder

December 4, 2015
Cuihong Jia, PhD
Research Assistant Professor, Department of Biomedical Sciences
Integrin signaling regulates CNTF, LIF and neurogenesis in vivo

December 11, 2015
Michelle Duffourc, PhD
Associate Professor, Department of Biomedical Sciences
Introduction to RNA-seq: Key considerations for project design

EXTERNAL SPEAKERS

September 14, 2015
John Quindry, PhD, FACSM
Associate Professor, School of Kinesiology, Auburn University
Title: Exercise and cardioprotection against ischemia/reperfusion injury

October 12, 2015
Bruce D. Carter, PhD
Professor, Department of Biochemistry
Associate Director, Vanderbilt Brain Institute
Director of Graduate Studies for Neuroscience
Vanderbilt University School of Medicine
Title: Killing and eating neurons: Mechanisms of retrograde apoptotic signaling and phagocytic clearance of the cell corpses