It’s shaping up to be another exciting year for IBP. Our graduate program recruited two more new top ranked Ph.D. graduate students to continue our excellence in building an outstanding graduate program in integrative biology and physiology. We are seeing successes at all phases of our tripartite mission: knowledge, discovery, knowledge dissemination and service to our university and community. This is a great time for our department as we continue to grow and flourish. Next summer many of us will transition our labs to the state-of-the-art Cardiovascular-Cancer Building that will serve as the gateway to the Biomedical Discovery District. I hope you enjoy reading our annual IBP In Focus newsletter and learn about our recent achievements and highlights of the major events to come.

Joe Metzger, Ph.D.
Professor & Head

Dr. Joseph Takahashi, a world leader in the molecular basis of chronobiology, will deliver the keynote address at the next Visscher Symposium scheduled for Wednesday, May 13, 2013 at 4 p.m. in MCB 3-120. Takahashi is Chair of the Department of Neuroscience and an Investigator of the Howard Hughes Medical Institute at UT Southwestern. He currently holds the Loyd B. Sands Distinguished Chair in Neuroscience. Before moving to UT Southwestern, Takahashi was the Walter and Mary Elizabeth Glass Professor in Life Sciences at Northwestern University. During his 26-year tenure at Northwestern, he held appointments as professor in the Department of Neurobiology and Physiology on the Evanston campus and as professor in the Department of Neurology at Northwestern University Medical School. In addition, he was also the director of the Center for Functional Genomics.
Because obesity is the greatest risk factor for Type 2 diabetes, University of Minnesota Integrative Biology and Physiology faculty member Alessandro Bartolomucci, Ph.D. has focused his research on developing an anti-obesity drug. To do so he needed to discover new molecular targets for the drugs. A prime drug candidate is the peptide TLQP-21, which was recently identified in Dr. Bartolomucci’s lab. It has been shown to prevent obesity in mice by increasing fat decomposition and decreasing the size of fat cells. For the next year, his research team will be uncovering how the peptide functions, as well as determining its receptor, its biochemical properties, and chemical structure. That knowledge will form the foundation of a new anti-obesity drug program. The goal is to create medications that, used in combination with lifestyle changes, will limit obesity and thus prevent Type 2 diabetes and associated cardiovascular disease. Dr. Bartolomucci is also the recipient of a TR01 grant through the NIH. Grant title: “Energetics, Disparities, & Lifespan: A unified hypothesis” with Principal Investigator, David Allison, U of Alabama at Birmingham.

Congratulations to Michelle Asp, post-doc in the Metzger Lab, for her recent NIH F32 award titled “Novel calcium buffer for the treatment of diastolic heart failure.” Michelle has been with the Metzger lab since 2010, after receiving her Ph.D. from the Ohio State University in Columbus, Ohio.

The Lifson/Johnson Memorial Award recognized excellence in teaching by undergraduate or graduate students. IBP gave two awards for 2011-2012, one of which went to Dalay Hirsch. Dalay is an IBP graduate student who excelled as a TA in our undergraduate physiology lab course (PHSL 3701).
MEET OUR NEW GRADUATE STUDENTS

SNIDER DESIR

I graduated from Kutztown University in Pennsylvania with a B.S. in biology where my interest for research was developed. While gaining further research experience at Virginia Tech, I decided to seek out a program that placed an emphasis on integrating multiple scientific disciplines in the study of human diseases. IBP at the U of M was that program for me. I am currently rotating in Dr. Joseph Metzger’s lab, where I am working on cardiac enterovirus protease 2A-cleaved dystrophin.

ANTHONY VETTER

I grew up in the Twin Cities and graduated from the University of Minnesota in 2011 with a B.S. in biochemistry and genetics. I am interested in using biochemical and biophysical techniques to study the conformational dynamics of thin filament proteins which regulate contraction of cardiac muscle. The long term goal of my research project is the development of a high-throughput drug screen capable of finding novel small molecule cardiac inotropes.

TIMOTHY MATSUURA

I was born and raised in Minnesota. After graduating in 2005 with a BA in Biology from Dartmouth College, I returned to Minnesota and worked in health care and pre-clinical research. I transitioned from a medical device company into the laboratory of Dr. Yannopoulos, a University of Minnesota physician and investigator. His research focuses on identifying novel methods to improve outcomes following cardiac arrest. Last year I joined the IBP program and greatly enjoyed returning to the classroom for a more rigorous understanding of a broad array of physiology topics. I remain very interested in resuscitation research, but I am also excited to experience new research pursuits and techniques. I am currently learning about dystrophin and its role in muscle organization while rotating in Dr. Townsend’s laboratory.

FROM THE DGS

John Osborn, Ph.D.
Professor, Director of Graduate Studies

The Graduate Program in Integrative Biology and Physiology (IBP) is in its fourth year and expanding. We now have eleven graduate students. Second year students Dan Rossi (Mortari lab), Nathan Zaidman (O’Grady lab) and Tim Matsuura (Townsend lab rotation) have successfully completed their first year in the program.

We are excited to welcome two new outstanding students into the program this fall: Snider Desir and Anthony Vetter. Snider and Anthony were introduced to the IBP graduate faculty at the annual Fall Welcome held at the Campus Club on September 6th. See profiles (to the right) for more information about Snider and Anthony.

Third year students Evelyne Houang (Metzger lab), Cheryl Cero (Bartolomucci lab) and Dalay Hirsch (Bernlohr lab) will be taking their preliminary exams in the near future. Forum Kamdar, Physical Scientist Ph.D. candidate, passed her POE August 27th. Congratulations, Forum! Preceding her in this achievement are IBP graduate students Jason Foss (Osborn lab) and Dusty Moore (Tranquillo lab).
**VISSCHER YOUNG INVESTIGATOR AWARD WINNERS**

**Kristin Hellberg, Ph.D. Candidate**

“Fatty Acids Induce Cysteinyl Leukotriene Synthesis in Macrophages”

**Antoinio Filareto, Post-Doc Associate**

“An ex vivo Gene Therapy Approach to Treat Muscular Dystrophy Using iPS Cells”


**ABSTRACT**

Obesity-induced insulin resistance is associated with chronic low-grade inflammation linked to macrophage infiltration of adipose tissue. Macrophages produce a variety of eicosanoids linked to the propagation of the inflammatory state and as such, we evaluated the role of fatty acids in eicosanoid synthesis using a variety of macrophage cell lines as well as in high fat fed C57Bl/6J mice that develop obesity-linked insulin resistance. Treatment of either RAW264.7 or primary macrophages with saturated, mono-unsaturated or polyunsaturated free fatty acids induced a sustained increase in intracellular calcium arising largely from influx from the extracellular medium. In RAW264.7 cells and primary peritoneal macrophages, fatty acid treatment led to secretion of leukotriene C₄ (LTC₄) whereas in THP-1 monocytes, palmitate treatment led to synthesis of LTC₄ and its metabolism to leukotriene D₄ (LTD₄). Adipocyte Fatty acid binding protein (AFABP) knockout mice are protected against high fat diet-induced insulin resistance and inflammation. FABPs are capable of stabilizing the leukotriene precursor, leukotriene A₄ (LTA₄). Interestingly, treatment of primary peritoneal macrophages with saturated, mono-unsaturated or polyunsaturated free fatty acids induced a sustained increase in nucleotide binding of both basal and fatty acid-stimulated LTC₄ secretion. In high fat fed C57Bl/6J mice, LTC₄ levels increased in the visceral depot but decreased in the subcutaneous depot relative to lean, chow fed control mice. These results indicate that fatty acids can stimulate macrophage production of pro-inflammatory leukotrienes that may contribute to the insulin-resistant state.

* denotes co-first authors

Antonio Filareto, Sarah Parker, Radbod Darabi, Luciene Borges, Iacovino Michelina, Tory Schaaf, Timothy Mayerhofer, Jeffrey S. Chamberlain, James M. Ervasti, R. Scott McIvor, Michael Kyba and Rita C.R. Perlingeiro

**ABSTRACT**

Duchenne muscular dystrophy (DMD) is a progressive and fatal neuromuscular disease caused by genetic and biochemical defects of the dystrophin-glycoprotein complex (DGC). These alterations lead to cell membrane damage and apoptosis of muscle cells, resulting in chronic tissue degeneration and impaired muscle contractility. To date, there is no cure for DMD. Approaches to date involving cell transplantation and gene therapy have given suboptimal results. An alternative strategy that holds promise is the direct reprogramming of adult fibroblasts to a pluripotent state, generating patient- and disease-specific stem cells, and correcting these in vitro prior to transplantation. Here we show the regenerative potential of myogenic progenitors derived from corrected dystrophic iPS cells generated from fibroblasts of mice lacking both dystrophin and utrophin (dKO). We corrected the phenotype of these dystrophic iPS cells using a Sleeping Beauty transposon carrying the micro-utrophin (µUTRN) gene, differentiated these cells into skeletal muscle progenitors, and assessed whether their transplantation back into dystrophic mice would ameliorate the muscle wasting phenotype. Transplanted muscles displayed large numbers of µ-UTRN⁺ myofibers, with biochemically restored DGC, and demonstrated significantly improved contractile strength. Notably, we show that donor cells also seed the satellite cell compartment and respond to injury. Our results represent an important advance toward the treatment of muscular dystrophies using genetically corrected autologous iPS cells.

―first of all, pay attention to your scientific creativity and productivity. But also remember that you live in a society… in which the ethic of truthfulness, which is at the heart of the scientific method, may be infused into societal decisions.‖

~Maurice Visscher
EDUCATION UPDATE FROM STEVE KATZ

The education mission of the department of Integrative Biology and Physiology (IBP) is accomplished in part by both Anatomy and Physiology classes aimed at undergraduate, graduate, and professional students. We continue to see high demand for our classes and have responded by adding both new class sections and new classes. For the year ending in June, 2012, the sum of all of our Physiology and Anatomy classes yielded total tuition revenue of approximately $5,000,000, with more than 3,000 students enrolled in almost 50 IBP classes.

Two assistant professors are now new course directors: Alessandro Bartolomucci is the new course director for our new Stress Physiology class, and DeWayne Townsend is the course director for our graduate student Critical Readings in Physiology course.

Finally, congratulations to Mark Cook who once again received the MMF Distinguished Teaching Award during the MMF Award Ceremony in April.

UNDERGRADUATE PHYSIOLOGY NEWS

The IBP undergraduate physiology major serves approximately 200 junior and senior undergraduate physiology majors per year. Our newest project is the planned formation of a B.S. degree in Physiology to accompany our pre-existing BA degree.

IBP graduated forty-eight students this spring, including nine who graduated with distinction (>3.75 GPA) and three who graduated Summa Cum Laude. Patrick McGarrah (see photo below) received an award from Dr. Metzger for a perfect 4.0 GPA.

The IBP Undergraduate Physiology Society (pictured below) is beginning its fourth year with a new leadership team. UPS students actively engage in departmental activities during the year and have plans for several health and wellness related philanthropy outreach events for the upcoming school year.

LISA ANDERSON RECEIVES NATIONAL TEACHING AWARD

IBP Assistant Professor, Dr. Lisa Carney Anderson, received the prestigious 2012 Didactic Instructor of the Year Award from the American Association of Nurse Anesthetists (AANA) in a ceremony in San Francisco in August. The award recognized Lisa’s excellence in teaching in the UMN nursing program since 1997.

MAKE A GIFT TO IBP

The generosity of individuals who recognize the importance of our department’s work is indispensable to our success. Donate online at www.mmf.umn.edu/give and select MMF fund #6819.

Congratulations to Patrick McGarrah, who graduated in May 2012 with a perfect GPA of 4.0.
CARDIO PALOOZA FEATURES RESEARCH

Tara Rasmussen (center), a post-doc in cardiology, receives the Investigator Award from Drs. Dan Garry (left) and Joe Metzger (right) at the 4th Annual Cardio Palooza research event held in the McNamara Alumni Center August 1, 2012.

Congratulations to our Cardio Palooza (a.k.a. CV Retreat) research award winners: Monica Knaack, summer scholar; Tara Rasmussen, post-doc; Forum Kamdar, clinical fellow; and Cheryl Cero, graduate student.

To see additional award winners and event photos, visit http://physiology.med.umn.edu

EDUCATION UPDATES

SHORT COURSES TO BE OFFERED IN JANUARY 2013

This coming January 2013, IBP will again offer two short courses: Advanced Cardiac Physiology and Anatomy and Anatomy and Physiology of the Pelvis and Urinary System. The courses are attractive to the biomedical-industrial community, as well as to graduate and undergraduate physiology majors. Our goal is to increase enrollment by 50% in both courses in January.

For course content and photos from past courses, visit http://physiology.med.umn.edu/shortcourses

Register Online for January 2013
Advanced Cardiac Anatomy Pelvic Short Courses at http://physiology.med.umn.edu/shortcourses
IN MEMORIAM

ESTEEMED COLLEAGUE AND FRIEND, PROFESSOR ZOFIA ZUKOWSKA, M.D., Ph.D., PASSED AWAY AT HER HOME ON APRIL 25, 2012. WORDS CANNOT BEGIN TO EXPRESS OUR SORROW AT HER PASSING. I KNOW THAT I SPEAK ON BEHALF OF THE ENTIRE UMN COMMUNITY IN EXTENDING OUR DEEPEST SYMPATHY AND CONDOLENCES TO HER FAMILY.

ZOFIA obtained both her M.D. and Ph.D. from the Medical Academy in Warsaw, Poland, and came to the US in 1980 to train as a Fellow and Associate with Dr. Irv Kopin in the Laboratory of Clinical Science, NIHM. In 1985 she took a faculty position in the Department of Physiology & Biophysics at Georgetown University, where she was promoted to full professor in 1995, and went on to become department chair in 2006. Zofia also founded the Stress Physiology Center at Georgetown in 2006 where she served as its director until 2010.

Zofia’s work centered on neuropeptide Y function in obesity and cardiovascular disease and her studies were well known and highly regarded in context of the unique insights made in stress physiology. Her work was published in the most rigorous peer-reviewed journals and her dynamic laboratory was funded by numerous NIH and foundation grants, including the prestigious NIH MERIT award. She received many notable awards for her work including the prestigious Copernicus Award for Excellence in Neuropeptide Research. Zofia was a highly valued member of the American Physiological Society. As chair of the physiology department at Georgetown she was a strong and effective advocate for the physiological-centric pursuit of new knowledge in biomedical research.

We were thrilled to recruit Zofia to our new Integrative Biology and Physiology department in 2010. She came to the University of Minnesota with her vision to direct a world-class center in “Stress Physiology.” Her passion and drive put her well on the way toward placing this initiative on the map as a leader in this highly competitive and vibrant area of research.

Zofia’s warm smile and generous spirit, together with her legacy of scholarship and discovery, touched all who met her. She will be deeply missed by all of us.

May she rest in peace,

Joe Metzger, Ph.D.
Professor and Chair, Department of Integrative Biology and Physiology
Above top: UPS members at Visscher reception
Above, bottom: Dr. Kahn receives t-shirt from Dr. Metzger

Above, top: String trio at the Visscher reception
Above, bottom: Anthony Filareto receives the Young Investigator Award from John Osborn

State Fair 2012

DeWayne Townsend explains cardiac physiology to State Fair fans

Staff of Goldy’s Locker Room prepares for EKG readings at the State Fair with Lisa Anderson and grad student Tony Vetter

IBP faculty at the Grad Student Welcome at Coffman Union

IBP Grad Student Welcome Party

IBP graduate students continue to build a strong program

For more fun photos from the 2012 events, visit http://physiology.med.umn.edu, Recent Events in right column.