

# Billiar Lab News

University of Pittsburgh

Spring & Summer 2014

Volume 22

## *Simmons Lecture and Department of Surgery Research Day*

During the Department's Annual Research Day, we heard 10 outstanding presentations and had an opportunity to view many excellent posters. We are pleased to announce Best Oral Presentation goes to **Brian Boone, MD** (Neutrophil Autophagy Promotes Neutrophil Extracellular Traps (NET) in Pancreatic Adenocarcinoma Contributing to Tumor Growth and Metastases) with runner-up awards to **Katie Sun, MD, PhD** (HMGB1 Protects Hepatocytes from Cell Death by Activating Caspase-1 and Up-Regulating Autophagy after Redox Stress) and **Shahab Shafiey, MD** (Generation of an Artificial Intestine and Validation in a Dog Model). Each will receive cash awards in recognition of

their outstanding presentations.

We also provided awards for Best Poster Presentations. The recipients include Khalid Almahmoud (Impact of Severity on Dynamic Inflammation Networks Following Blunt Trauma), Mostafa Ramadan (B cells play an organ protective role in Trauma + Hemorrhagic Shock), Alexandra Dreyzin (Long-Term Outcomes and Predictors in Pediatric Liver Re-Transplantation), and Hongpeng Jia (Deletion of HMGB1 from the Intestinal Epithelium Exacerbates Experimental Necrotizing Enterocolitis In The Newborn Gut but Protects the Lung from Inflammation). Please join us in congratulating these outstanding young investigators for their excellent presentations.

## *Important Dates*

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### *Simmons Research*

*Tu 8:00am & Th 8:30am*

*F-1275 PUH*

- Jun 24 Ankur Shukla
- Jun 26 Charlotte Egan

### *Billiar Lab Meeting*

*Wed 12:00pm*

*F-1275 PUH*

- Jun 25 Hua Zhong
- DAMP's/Danger Signals*
- Th 10:00am F-1275 PUH*

- June 19
- July 17
- August 21
- September 18

### *Trauma/Sepsis Model*

*Tu 9:30am F-1275 PUH*

- June 17
- July 15
- August 19
- September 16

### *Immunology Seminar Series*

*Scaife Hall, Auditorium 5*

*Thurs 12:00-1:00pm*

*For a full list of events, please go to General and Vascular Surgery Labs website's [Events page](#).*

## New Faces



Please welcome the following people into our labs:

Yong Yang – Visiting Scholar (Fan)

Xubo Wu – Visiting Scholar (Billiar)

Ahmed Al-Khafaji – Med Student (Tsong)

Ghee Rey Lee – Undergrad Student (Tzeng)

Miranda Culley – Med Student (Billiar)

## Good Luck



We'd like to extend our best wishes and good luck in future endeavors to those individuals who have left or are soon leaving the labs.

Kent Zettel

Ben Kautza

Sylvia Martinez Laverde

Daniel Escobar

Ana Maria Botero Qintero

Meihua Bo

Susan Rominski

Christopher Washington

Ankur Shukla

Zhijan Huang

Shengyong Yang

Jiemei Wang

## Lab Updates

### Pcard Restrictions

Due to recent misuse of University issued P-cards, the university has put new restrictions in place and prohibited use of the P-card for the following items:

In order to comply with federal regulations and University purchasing policies, certain items cannot be purchased using a P-Card. Most items shown below should be purchased on a Purchase Order (PO). A Travel and Business Expense Report (T&B) may be appropriate when seeking reimbursement for an item purchased while traveling.

The following P-Card purchases are specifically prohibited (bolded items were added to this list effective October 2013):

- Advertising services
- Alcohol
- Animals
- **Biological materials**
- Cash
- Caterers
- Controlled substances
- Drugs, perscriptions
- Fuel, gasoline
- Gases
- **Gift cards**
- Gifts and contributions

- \*Hotels, car rentals
- **\*\*Foreign good imports**
- Interdepartmental charges
- **Laboratory chemicals**
- Motion picture, video creation
- Personal purchases (any)
- Radioactive materials
- \*\*\*Software
- Testing laboratories
- Travel, entertainment
- Vehicle rentals
- Weapons, ammunition

With these new restrictions in place, you will need to plan your experiments to ensure that you have all required reagents ordered through the Panther Buy system in a timely matter. The P-card can no longer be used for the above mentioned categories.

As the P-card is issued to Deb Williams, personally, and she is fully responsible for its use, she apologizes for any inconvenience that these changes may cause but we must abide by the new policy.

### Summer Weather Attire

Now that the warm weather has finally arrived, please remember to dress appropriately for the lab. Open toe shoes are not

permitted when performing any experiments and are prohibited in the animal facility.

### *Updates to Animal Housing Rooms Due to Construction*

Due to the ongoing BST facility renovations, the current housing rooms of

some of our PIs have changed. The current list of locations by PI is:

Mike Bauer - 921, 940

Alex Chen - 909

Jie Fan - 908

David Geller - 921, 1501B

Bruce Pitt - 907, 1501B

Matt Rosengart - 935

Ulka Sachdev - 908, 1501B

Melanie Scott - 907, 908, 911

Allan Tsung - 935, 907, 921, 940, 1501B

Edith Tzeng - 911, 940

Yoram Vodovotz - 921

Qingde Wang - 908, 1501B

Brian Zuckerbraun - 921, 1501B

## *Staff Highlight*



### *John Brumfield*

I studied for my undergraduate degree at the University of Pittsburgh and attended the Graduate School of Biology at Edinboro University. I then attended the Lake Erie College of Osteopathic medicine. I have been working in the lab for 8 years for both Dr. Billiar and Dr. Zuckerbraun. My current projects include the therapeutic effects of CO in multiple trauma induced mice as well as the effects of trauma on old versus young mice.

Outside the lab, I am an avid player in the fitness arena. After competing in bodybuilding for several years, I still continue to be an active personal trainer to many inside and out of the gym. Three years ago I started a company: Private Money Solutions LLC, along with my business partner, I own over 20 rental units in and around the Pittsburgh area. The main goal of this company is to provide investments for private money lenders that are secured with real estate. I currently own several houses that are on the market and others that are currently being rehabbed and it is most likely I own in one of your neighborhoods. Our goal is to take the ugliest house on the block and make it the one that everyone wants to live in.

## *Messages from IACUC and DLAR*

*Extended Release*

*Buprenorphine is Available for Mice*

A FDA Indexed injectable suspension of extended release buprenorphine for use in mice is

now commercially available from Henry Schein and marketed under the trade name *Animalgesics® for Mice*. A single injection provides clinically effective

analgesia for moderate to severe pain in mice for up to 3 days. The IACUC has approved the use of this product for mouse analgesia. However, the

product, like any analgesic, cannot be used for study related procedures unless it is listed on an IACUC approved protocol. Existing

protocols require an IACUC approved modification prior to using *Animalgesics® for Mice*. This drug is not approved for any other

species but mice.

*Animalgesics® for Mice* is supplied in a 3.0 ml multi-dose vial. Once opened, the vial should be stored refrigerated (36-46 °F) and discarded after 28 days. *Animalgesics® for Mice* is not intended to be administered by any other than the subcutaneous route. The product cannot be diluted and must be administered as formulated. Dilution of the product alters the formulation and the efficacy of the product. A dosage chart is provided below.

## Faculty Highlight



### Ruben Zamora

My main research projects are:

1) Combined experimental and computational studies to provide novel insights into Pediatric Acute Liver Failure (PALF). In close collaboration with Dr. Yoram Vodovotz (Dept. of Surgery), I am involved in experimental design and data analysis and responsible for directing the overall research effort, for reporting on the research results, for manuscript preparation, and for scientific presentations. I also coordinate the collaboration with Dr. Robert Squires and other investigators of the PALFSQ at Children's Hospital of Pittsburgh.

2) Study of the expression and localization of BNIP3 in mouse and human hepatocytes, and the contribution of BNIP3 to hepatic cell death by apoptosis and/or necrosis *in vitro* and *in vivo*.

3) Analysis of the inflammatory response of various patient cohorts, including trauma and spinal cord injury, using multiplexing cytokine analysis (Luminex technology) coupled with data-driven modeling (Collaboration with Drs. Timothy Billiar and Yoram Vodovotz).

4) Collaboration with Dr. Shirley Luckhart (University of California-Davis), Yoram Vodovotz (Dept. of Surgery), Bard Ermentrout (University of Pittsburgh, Department of Mathematics), and Greg Constantine (University of Pittsburgh, Department of Mathematics) to examine the cross-regulation of NO and TGF-beta1 between the immune systems of *Anopheles stephensi* mosquitoes and their mammalian hosts, and to create computational simulations of cross-species immune modulation in the setting of malaria.

Body Weight (g)	<i>Animalgesics</i> (mL)
15	0.0375
20	0.05
25	0.0625
30	0.075
35	0.0875
40	0.1
45	0.1125
50	0.125

*Animalgesics® for Mice* has a slightly yellow to white opaque appearance. The refrigerated product should be warmed to room temperature prior to administration. Mice may exhibit an "obtunded" (lethargic, mentally dull)

response to stimuli for up to 6 hours after administration. An oily sheen may be observed on the skin for up to 5 days post-administration due to leakage at the injection site. This does not cause any clinical complications to the animal.

Additional information can be found on the [Animalgesic Labs website](#). Note that all formulations of Buprenorphine are Class III Controlled Substances, and must be ordered, secured, and dispensed in accordance with the [University's Controlled Substance Guidelines](#). In order to procure or use *Animalgesics® for Mice* an investigator must hold a current DEA Registration.

### *Renovations to EBST Vivarium Underway!* To All BST Investigators:

The 9<sup>th</sup> floor BST will undergo another series of renovations to increase animal housing capacity. Two sets of 3 housing rooms each will be converted to a total of 4 high



capacity housing rooms. These renovations will be a repeat of the November/December renovations to rooms 930 and 933.

Part 1 of the project began the first week in June with rooms 912, 914, and 915. Part 2 (rooms 921, 923, and 925) will begin once part 1 is

completed. All work is expected to be completed by mid to late September.

As always, noise and vibrations will be kept to a minimum, and should be comparable to the November/December work. No significant issues with animal health and

breeding are anticipated.

During the renovations, space in mouse housing rooms will be limited. The Space Committee will attempt to satisfy requests for additional

housing space, but may not be able to approve some requests until the completion of the project in September. We appreciate efforts to minimize colony size during this project so that everyone's needs can be accommodated.

Investigators in rooms 912, 914, and 915 will be

contacted individually to coordinate the temporary relocation of their animals. Please contact Matt Mihalik, BST Supervisor, with any concerns that you may have regarding this project.

Thank you in advance, for your patience and support.

*Possible Pinworm Contamination of Taconic Rodents*

The DLAR was recently notified by Taconic of a self-identified contamination of rodent pinworms (*Syphacia spp.*) within

their IBU 506 barrier facility that produces and supplies Tac:WKY rats and C57BL/6NTac, DBA/2NTac, and FVB/NTac mice. The contamination was identified by Taconic during routine health monitoring of their colonies, confirmed by further comprehensive testing, and potentially impacts orders sourced from the IBU 506 facility between March 15 and May 30, 2014.

The University is one of many institutions that received mice and rats from the Taconic IBU 506 facility

during this time period. The DLAR is reviewing animal receipt records to determine what animal facilities may have potentially been placed at risk and evaluating mechanisms to determine whether or not any DLAR facilities were subsequently contaminated. Additional information will be distributed as it becomes available. Please contact your facility assigned DLAR veterinarian if you have any specific concerns.

## Colony Status: As of May 30, 2014

### Established Colonies: Knockouts, Transgenics, and Double Knockouts

ATF3 KO	Nalp 3 KO	TLR4 KO/TL9 <sup>CpG1/CpG1</sup>
Caspase1KO	Myd88 KO	TLR4 KO/RAGE KO
Caspase11 KO (small quantities)	Myd88 WT	TLR4 KO/TLR2 KO
iNos KO	RAGE KO	TLR9 <sup>CpG1/CpG1</sup>
Jα281-/-	TLR2 KO	Trif <sup>LPS-2</sup> (Jax #005037)

### Established Colonies: Cell Specific Knockouts and Controls

Adipose TLR4KO	Lyz cre Myd88 KO	TLR4 flox
DC TLR4 KO	Lyz Cre TLR4 KO	TLR4 KO (global)
HC HMGB1 KO	Myd88 flox	Pf4cre HMGB1 KO
HC Myd88 KO	ROSA <sup>mT/mG</sup>	Pf4cre TLR4 KO
HC TLR4 KO	ROSA Pf4cre HMGB1 KO	VEC cre TLR4 (small quantities)
Het TLR4KO/TLR4flox	Reporter (small quantities)	
HMGB1 flox	TACE flox (small quantities)	

### Colonies in Development

Cathespin L KO (N=6 gen)	iHMGB1 KO (waiting on pups)	Rorc GFP (BP on order from Jax)
DC Myd88 KO	Lyz cre HMGB1 KO	TACE flox Backcross
HC TACE KO (waiting on pups)	TLR4 KO/Caspase 11 KO	

### Strains Available from Collaborators

CAV KO (Michael Bauer)	TSP-1 KO (A. Chen)	GDF-15 KO (Yoram Vodovotz)
IFNabR KO (M. Bauer)	TSP-2 KO (A. Chen)	NFκB luc (David Hackam)
IRF-2 KO (David Geller)	CD36 KO (A. Chen)	iHMGB1 KO (Qingde Wang)
eNos GCHtg (A. Chen)	hph-1 (A. Chen)	

### Cryopreserved Strains \*at Jacksons Labs unless otherwise noted

eNos tg	EGR1 KO	TLR-4 KO (Taconic, Hackam)
CD36 KO	IFNabR KO	HMGB1 +/-
TLR2 KO	TLR-9 (eggs, in house)	
AIM2 KO	TLR-4 flox (Hackam)	

### Stud Colonies

HMGB1 flox x Albumin Cre	Myd88 flox x Albumin Cre	TLR4 KO x CD11c
HMGB1 flox x ER cre	Myd88 flox x CD11c	TLR4 KO x Fab cre
HMGB1 flox x Lyz cre	Myd88 flox x Lyz cre	TLR4 KO x Lyz Cre
HMGB1 flox x Pf4 cre	TACE flox x Albumin cre	TLR4 KO x Pf4 cre
HMGB1 flox x ROSA <sup>mT/mG</sup>	TLR4 KO x Albumin Cre	TLR4 KO x VEC cre

If you have any questions regarding the contents of this newsletter, contact Deb Williams  
([williamsd8@upmc.edu](mailto:williamsd8@upmc.edu))

If you know of anything exciting or newsworthy going on in the lab that you want to share with others email  
Alicia Frank ([franka@upmc.edu](mailto:franka@upmc.edu)) with the information

For more information, please visit the General and Vascular Surgery Labs website  
(<http://www.gensurgerylabs.pitt.edu/>)