

## In This Issue

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### MCRI in the News

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### Upcoming MMS Seminars Stearns Auditorium, Farnsworth 1 12:00 PM

#### October 30, 2018

Lakshmi Pulakat, PhD  
University of Missouri

#### November 6, 2018

Miranda Good, PhD  
University of Virginia

#### November 27, 2018

Samantha Harris, PhD  
University of Arizona

#### December 11, 2018

Jonathan Bogan  
Yale School of Medicine

For a more complete list of speakers, [click here](#).

## MCRI Highlights

### *Honors and Recognition*

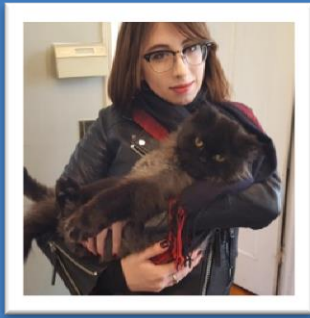
- **Jennifer DuPont, PhD** was elected to the American Physiological Society, Women in Physiology Committee.
- **Jennifer DuPont, PhD** also received the 2018-2019 Charlton Research Award to study “The Role of Smooth Muscle Cell Estrogen Receptor Alpha in Sex Differences in Aging-Associated Vascular Stiffness”.
- **Iris Z. Jaffe, MD, PhD**, was an invited speaker at the Rapid Response to Steroid Hormones: 20th anniversary meeting, hosted by the Royal College of Surgeons in Dublin, Ireland.
- **SK Kim, PhD (Jaffe Lab)** and **Daniel Richards, PhD (Blanton Lab)** received MCRI travel awards. SK will present a poster entitled “Smooth muscle cell mineralocorticoid receptor as an epigenetic regulator of vascular aging” at the Cold Spring Harbor Meeting on Mechanisms of Aging in October and Dan will present his poster entitled “CRD-733, a novel Phosphodiesterase 9 inhibitor, reverses pressure overload-induced cardiac hypertrophy in mice” at the 2018 AHA Scientific Sessions in Chicago in November
- Congratulations to the two MCRI members in the Tufts Medical Center Quarter Century Club! Thank for over 25 years of work and dedication to the MCRI: **Patti Griffiths**, Senior Research Administrator and **Wendy Baur**, Director of the Cell Culture Core.
- Congratulations to the winners of the Poster Competition at the 20<sup>th</sup> Annual MCRI Scientific Retreat:
  - 1<sup>st</sup> Place:** Lija Swain (Kapur Lab)
  - 2<sup>nd</sup> Place:** Daniel Richards (Blanton Lab)
  - 3<sup>rd</sup> Place (tie):** Elizabeth Fletcher (Kuliopulos Lab) and Roger Perreault (Wallingford Lab)



*The winners of the Poster Contest at the 20<sup>th</sup> Annual MCRI Scientific Retreat. Left to Right: Daniel Richards, Lija Swain, Elizabeth Fletcher, Roger Perreault*

(scroll down for a Retreat Recap)

## Employee Spotlight



### Meet Corinne Thomas, PhD Postdoctoral Fellow in the Chin Lab

**Hometown:** Deep River, Connecticut, of Deep River Kettle Chips fame. Although, the chip factory is actually in Old Lyme, but that town already has Lyme disease named after it.

**Favorite restaurant in Boston:** I have yet to decide on a favorite restaurant. I am still on a whirlwind tour of all the places to get takeout in Chinatown, which are convenient, good, and have such a variety I have yet to pick the same place twice.

**What do you like about working at the MCRI:** Since the department and all the people here have such substantial backgrounds in specifically molecular cardiology, I find that the feedback and questions that I get when sharing my own work are uniquely helpful and insightful. I appreciate the enthusiasm of MCRI staff about sharing their experience with people who want to learn, and the environment of cooperation and collaboration that results from this attitude.

**What are you currently working on in the MCRI?** My project focuses on producing a recombinant therapeutic protein optimized for drug delivery in the treatment of Barth Syndrome, a genetic disease caused by the lack of functional tafazzin. Currently, I am studying the specificity, activity, and uptake behavior of tafazzin upon the addition of sequence "tags" called cell penetrating peptides that should signal the deficient heart cells to

## Grants

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- **Mike Chin, MD, PhD** was awarded an AHA Innovative Project Award entitled "Pathological Pathway Activation at Single Cell Resolution and biomarker detection in Human Hypertrophic Cardiomyopathy"
- **Gordon Huggins, MD**, was awarded an R21 subcontract from Tufts University. He is a co-Investigator on a grant entitled "Diagnosis of Heart Failure Status using Epidermal Metabolomics."
- **Jennifer DuPont, PhD** was awarded a Charlton Research Grant entitled "The Role of Smooth Muscle Cell Estrogen Receptor Alpha in Sex Differences in Aging-Associated Vascular Stiffness"

## New Staff

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Welcome to the following new staff members in the MCRI:

- **Briggett Carvajal**, a Scholar in the Sackler School of Graduate Biomedical Sciences' **Post-Baccalaureate Research Program (PREP)**, recently joined the Jaffe lab. Briggett is located on Tupper 12.
- **Lin Meng, MD, PhD**, recently joined the **Chen** lab as a Visiting Research Scientist. She is located on Tupper 13.

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## MCRI Announcements

### Save the Date

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- The MCRI is participating in the Cambridge Monster Dash 5K run on Sunday, October 28<sup>th</sup>.

#### To sign up:

1. Go to: <http://events.racewire.com/monster-dash/>
2. Click "Register Today"
3. Under "Team Registration Style" click "Join a team"
4. Select "MCRI Molecular Movers"
5. Fill out all the info it prompts you for and voila! You are now a member of the MCRI Molecular Movers

\*For questions, contact Chrissie at [cconnors@tuftsmedicalcenter.org](mailto:cconnors@tuftsmedicalcenter.org)

### MCRI in the News

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- **Jennifer DuPont, PhD** was mentioned for her work she presented at The Cardiovascular, Renal and Metabolic Diseases: Sex-Specific Implications for Physiology conference

[Read the article here](#)

absorb the protein.

**What do you like to do when you are not in the lab?** I enjoy gaming and watching movies, particularly ones involving science fiction and horror. I spend a great deal of time working on craft projects such as origami, electronics, sculpting, and painting, the results of which are often given as gifts, worn to comic conventions, or unceremoniously sat upon by my roommate's cats.

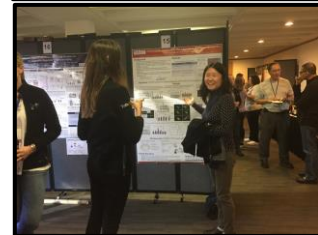
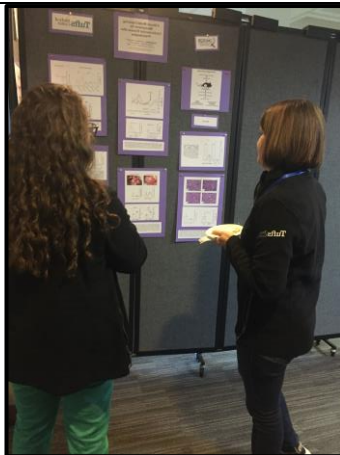
**Favorite place you've visited and why:** While I was visiting family in Australia, we took several trips to a wildlife park in Adelaide. I went to the park with the intention of holding a koala, who was cute but aloof; instead, I found that wallabies are cuter, less smelly, and much friendlier, and have since decided that they are the superior marsupial. Outside the park, I encountered geckos on the walls, kangaroos on the roads, snakes in the trees, and giant spiders where you would least expect.

## MCRI 20<sup>th</sup> Annual Scientific Retreat Recap

- The MCRI held its 20<sup>th</sup> annual scientific retreat in Woods Hole, MA in late September. Here is a recap by the numbers:
  - ✓ 20 years of Cardiovascular Research and Scientific Retreats
  - ✓ Over 50 participants in attendance
  - ✓ Over 30 posters presented
  - ✓ 4 distinguished guest speakers
  - ✓ 1 special guest speaker, the Founding Executive Director of the MCRI, Mike Mendelsohn, MD.



*The annual Retreat photo outside the Lillie Building at the Marine Biological Laboratories*



*Trainees and Research Staff in the MCRI presenting at the poster session*



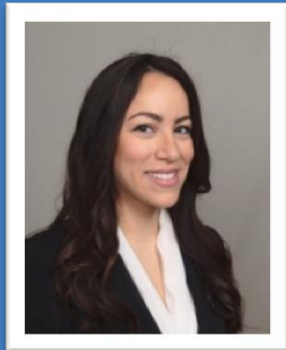
*Members of the Kapur Lab with the Founding Director of the MCRI, Mike Mendelsohn, MD*



*Amy Larson of the Chin lab presenting her lightning talk*

## Research Spotlight

Michele Esposito, MD, Cardiac Fellow in the Kapur lab discusses her recent paper



“Left Ventricular Unloading Before Reperfusion Promotes Functional Recovery After Acute Myocardial Infarction”

[Read the paper here](#)

### What is the topic of your study and why is it important:

This study investigates the effects of implanting study animals with a mechanical heart pump during a heart attack prior to opening their blocked coronary artery (known as "primary unloading"), in order to reduce heart attack size. These results could have a highly relevant clinical impact, given that larger heart attack sizes can lead to heart failure in our patients. Reducing heart attack size has been a relevant topic of investigation in the field of cardiology for several decades. Unfortunately, the only therapy that has been proven to work has been timely opening of a blocked coronary artery in the cardiac catheterization lab, which is the current "standard of care."

**What did you discover:** In this study, we discovered that 1) implanting animals with a mechanical heart pump, prior to opening their coronary artery ("primary unloading"), reduced the size of their heart attack compared to animals that did not receive a heart pump and only had their coronary artery opened (the "standard of care"); 2) we also investigated the biologic mechanisms related to this phenomenon and showed that a specific pathway that controls programmed cell death is closely involved in the pathophysiology; and 3) we saw that at a genetic level, there is a significant shift in gene expression in

## Quarterly Publications

1: Esposito ML, Morine KJ, Annamalai SK, O'Kelly R, Aghili N, Pedicini R, Breton C, Mullin A, Hamadeh A, Kiernan MS, DeNofrio D, **Kapur NK**. Increased Plasma-Free Hemoglobin Levels Identify Hemolysis in Patients With Cardiogenic Shock and a Trans valvular Micro-Axial Flow Pump. *Artif Organs*. 2018 Sep 14. doi:

10.1111/aor.13319. [Epub ahead of print] PubMed PMID: 30216467.

[Pub Med Abstract](#)

2: Saha M, Reddy HM, Salih M, Estrella E, Jones MD, Mitsuhashi S, Cho KA, Suzuki-Hatano S, Rizzo SA, Hamad MH, Mukhtar MM, Hamed AA, Elseed MA, Lek M, Valkanas E, MacArthur DG, Kunkel LM, Pacak CA, **Draper I**, Kang PB. The impact of PYROXD1 deficiency on cellular respiration and correlations with genetic analyses of limb-girdle muscular dystrophy in Saudi Arabia and Sudan. *Physiol Genomics*. 2018 Aug 31. doi: 10.1152/physiolgenomics.00036.2018. [Epub ahead of print] PubMed PMID: 30169133.

[Pub Med Abstract](#)

3: **Wallingford MC**, Benson C, Chavkin NW, **Chin MT**, Frasch MG. Placental Vascular Calcification and Cardiovascular Health: It Is Time to Determine How Much of Maternal and Offspring Health Is Written in Stone. *Front Physiol*. 2018 Aug 7;9:1044. doi: 10.3389/fphys.2018.01044. eCollection 2018. PubMed PMID: 30131710; PubMed Central PMCID: PMC6090024.

[Pub Med Abstract](#)

4: Uriel N, Sayer G, Annamalai S, **Kapur NK**, Burkhoff D. Mechanical Unloading in Heart Failure. *J Am Coll Cardiol*. 2018 Jul 31;72(5):569-580. doi: 10.1016/j.jacc.2018.05.038. Epub 2018 Jul 2. Review. PubMed PMID: 30056830.

[Pub Med Abstract](#)

5: Esposito ML, Zhang Y, Qiao X, Reyelt L, Paruchuri V, Schnitzler GR, Morine KJ, Annamalai SK, Bogins C, Natov PS, Pedicini R, Breton C, Mullin A, Mackey EE, Patel A, Rowin E, **Jaffe IZ**, Karas RH, **Kapur NK**. Left Ventricular Unloading Before Reperfusion Promotes Functional Recovery After Acute Myocardial Infarction. *J Am Coll Cardiol*. 2018 Jul 31;72(5):501-514. doi: 10.1016/j.jacc.2018.05.034. PubMed PMID: 30049311.

[Pub Med Abstract](#)

6: Moss ME, DuPont JJ, Iyer SL, McGraw AP, **Jaffe IZ**. No Significant Role for Smooth Muscle Cell Mineralocorticoid Receptors in Atherosclerosis in the Apolipoprotein-E Knockout Mouse Model. *Front Cardiovasc Med*. 2018 Jul 9;5:81. doi: 10.3389/fcvm.2018.00081. eCollection 2018. PubMed PMID: 30038907; PubMed Central PMCID: PMC6046374.

[Pub Med Abstract](#)



animals that underwent "primary unloading," such that their genetic profiles more closely resembled that of animals who had no heart attack at all when compared to the animals in the control group who received the "standard of care."

#### **Was there an unexpected finding:**

A novel finding of this study was the long-term effects that we saw. After the animals underwent the acute study, the mechanical heart pumps were removed, and the animals were monitored for 1 month after their heart attack. What we saw was that animals who received the pump had better recovery of their heart function and less scar in their hearts. This is the first time that long-term effects of "primary unloading" have been studied in an animal model.

#### **What impact will this have on the field or on medical care:**

We believe that this study, and similar studies that have been done prior, collectively will advance the field by promoting the use of mechanical heart pumps in the setting of a heart attack to promote native heart recovery. After heart attacks, some patients will go on to develop heart failure requiring placement of a permanent mechanical pump or even a heart transplant. With the integration of "primary unloading" into clinical care, we hope that some patients will be able to preserve enough of their heart muscle so that they can recover and potentially avoid the need for invasive therapies in the future.

**What is your next step?:** The next step is a clinical trial. Currently, the "Door-to-Unload" safety and feasibility trial has finished enrolling, which is a multi-center, randomized human clinical trial that examines the effects of "primary unloading" in patients having a heart attack. We will release the results of this trial later this year, and hope to use that data to inform our next steps.

### **Contact Us**

Have questions or updates for the next newsletter? Contact Chrissie Connors-  
cconnors@tuftsmedicalcenter.org

7: Gopal S, Lu Q, Man JJ, Baur W, Rao SP, Litichevskiy L, Papanastasiou M, Creech AL, DeRuff KC, Mullahoo J, Officer A, Egri SB, Davison D, Jaffe JD, **Jaffe IZ**. A phosphoproteomic signature in endothelial cells predicts vascular toxicity of tyrosine kinase inhibitors used in CML. *Blood Adv*. 2018 Jul 24;2(14):1680-1684. doi: 10.1182/bloodadvances.2018020396. PubMed PMID: 30021779; PubMed Central PMCID: PMC6058230.

#### **Pub Med Abstract**

8: Ueda K, Takimoto E, Lu Q, Liu P, Fukuma N, Adachi Y, Suzuki R, Chou S, Baur W, Aronovitz MJ, Greenberg AS, Komuro I, **Karas RH**. Membrane-Initiated Estrogen Receptor Signaling Mediates Metabolic Homeostasis via Central Activation of Protein Phosphatase 2A. *Diabetes*. 2018 Aug;67(8):1524-1537. doi: 10.2337/db17-1342. Epub 2018 May 15. PubMed PMID: 29764860; PubMed Central PMCID: PMC6054435.

#### **Pub Med Abstract**

9: Esposito ML, Jablonski J, Kras A, Krasney S, **Kapur NK**. Maximum level of mobility with axillary deployment of the Impella 5.0 is associated with improved survival. *Int J Artif Organs*. 2018 Apr;41(4):236-239. doi: 10.1177/0391398817752575. Epub 2018 Feb 20. PubMed PMID: 29637832.

#### **Pub Med Abstract**