

Mit  Care

2015

# MitoCircle Program (MitoCare JAH 527)

## WINTER-SPRING 2015

Jan 15, 2015

**Clara Franzini-Armstrong, PhD and Manuela LAVORATO, PhD (UPenn)**

Strange mitochondrial behaviour. Friendly or not?

(To complement this talk **Shey-Shing Sheu, PhD** gave a brief presentation on mitochondrial fission in cardiac muscle and **Gyorgy Hajnoczky, MD, PhD** presented a short talk on in vivo studies of mitochondrial fusion in heart.

Feb 19, 2015

**Sandra Maday, PhD (UPenn)**

Spatiotemporal dynamics and regulation of autophagy in neurons

Mar 18, 2015

**Andrew P. Thomas, PhD (Rutgers)**

Calcium signaling and metabolic sensing

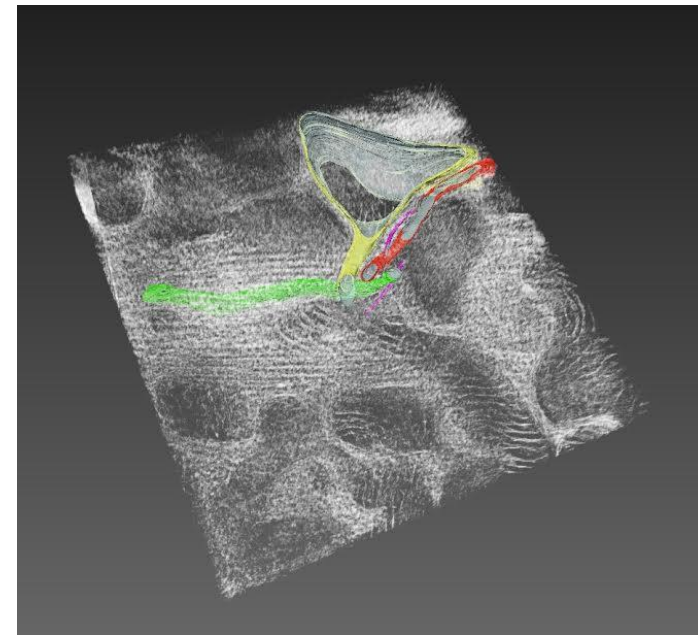
Apr 16, 2015

**Steven Claypool, PhD (Johns Hopkins)**

Cardiolipin remodeling in mammals and yeast: topological differences and dysfunctional similarities



Clara-Franzini Armstrong  
and Manuela Laborato  
visit MitoCare to talk  
about connections among  
mitochondria



# Collaborations with the Mitochondrial Center of CHOP

## ARTICLE

Received 30 Sep 2014 | Accepted 9 Jan 2015 | Published 17 Feb 2015

DOI: 10.1038/ncomms7259

OPEN

# Trans-mitochondrial coordination of cristae at regulated membrane junctions

Martin Picard<sup>1</sup>, Meagan J. McManus<sup>1</sup>, György Csordás<sup>2</sup>, Péter Várnai<sup>3</sup>, Gerald W. Dorn II<sup>4</sup>, Dewight Williams<sup>5</sup>, György Hajnóczy<sup>2</sup> & Douglas C. Wallace<sup>1</sup>

## Mitochondrial functions modulate neuroendocrine, metabolic, inflammatory, and transcriptional responses to acute psychological stress

Martin Picard<sup>a,b,1</sup>, Meagan J. McManus<sup>a,b</sup>, Jason D. Gray<sup>c</sup>, Carla Nasca<sup>c</sup>, Cynthia Moffat<sup>d</sup>, Piotr K. Kopinski<sup>a,b</sup>, Erin L. Seifert<sup>d</sup>, Bruce S. McEwen<sup>c</sup>, and Douglas C. Wallace<sup>a,b,2</sup>

<sup>a</sup>Center for Mitochondrial and Epigenomic Medicine, The Children's Hospital of Philadelphia, Philadelphia, PA 19104; <sup>b</sup>Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA 19104; <sup>c</sup>Laboratory for Neuroendocrinology, The Rockefeller University, New York, NY 10065; and <sup>d</sup>MitoCare Center, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107



# Gyuri Panyi visits and his student Adam Bartok joins as a postdoc MitoCare



# Award to the Mitochondrial Pathogenesis Group

February 8, 2015

Fellow TJU Faculty:

The incredibly strong research in individual laboratories at Jefferson is not currently matched by robust, programmatic federal funding. On behalf of the Provost, Dr. Mark Tykocinski, I am pleased to announce TJU support for seven teams of faculty who are actively pursuing programmatic research grants. These seven "**Theme Teams**" (listed below) were chosen from among 26 who submitted applications for our December deadline.

## THEME TEAMS

**Dr. Lorraine Iacovitti:** *Triggering novel stem cell niches in models of acute injury*

TJU Team members:

Melanie Elliott, PhD

Angelo Lepore, PhD

**Dr. Gyorgy Hajnoczky:** *Mitochondrial pathogenesis*

TJU Team Members:

Gyorgy Csordas, MD

Erin Seifert, PhD

Jan Hoek, PhD

Shey-Shing Sheu, PhD

Ya-Ming Hou, PhD

Ross Summer, MD

Piera Pasinelli, PhD

Davide Trotti, PhD

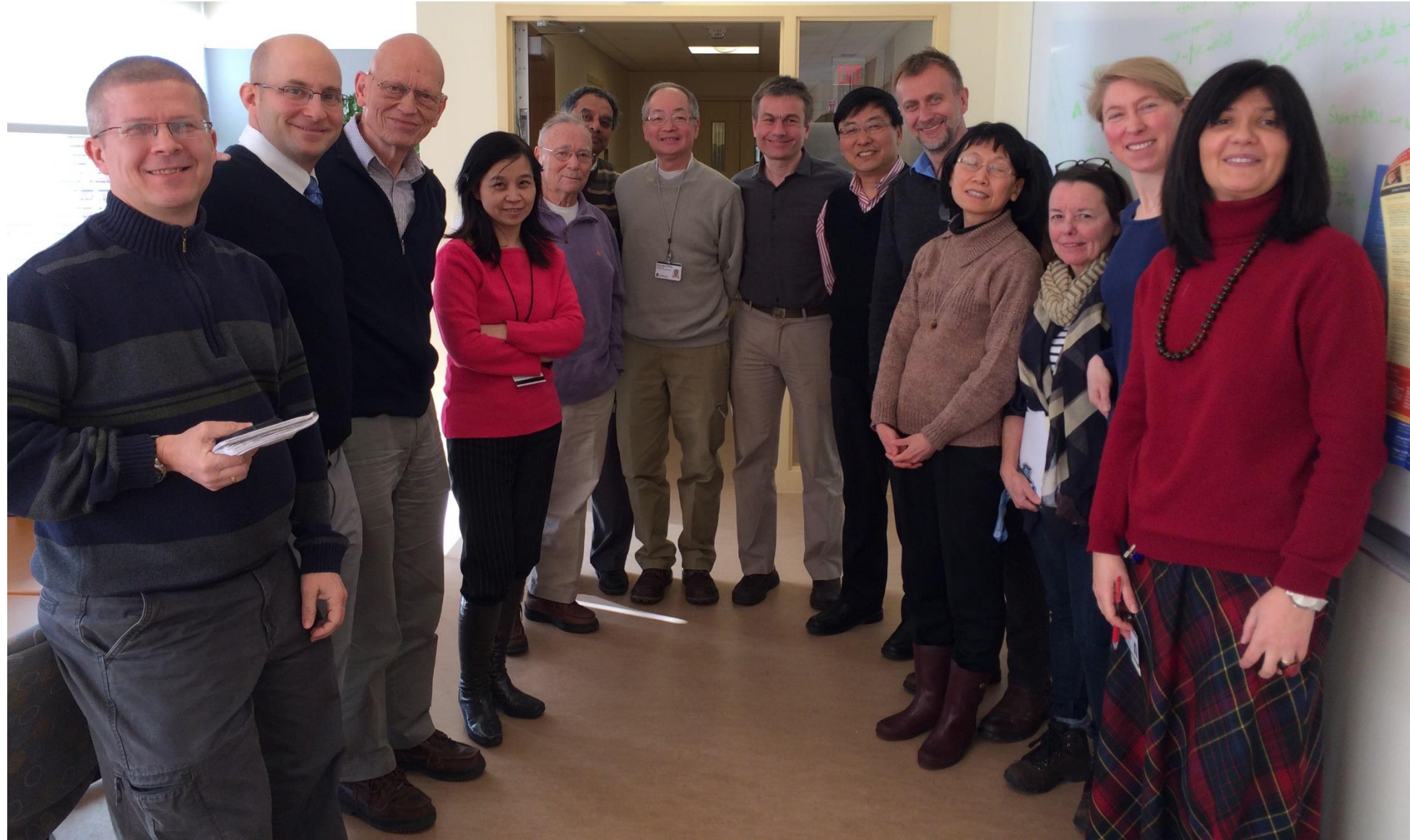
Nancy Philp, PhD

Hui Zhang, PhD

Emanuel Rubin, MD



# The Mitochondrial Pathogenesis Group



# Four pilot projects made possible by the award:

## **Epigenetic methylation of mitochondrial tRNA in ALS**

PIs: Ya-Ming Hou, PhD Department of Biochemistry and Molecular Biology  
Davide Trotti, PhD Department of Neuroscience

## **Role of MICU1 in Midbrain Dopamine (DA) Neurons**

PI: Hui Zhang

## **Polyamines: a starting point for drug discovery for the mitochondrial calcium transporting uniplex**

PI: Suresh K. Joseph, ( other authors ) and Gyorgy Hajnoczky

## **Pathogenesis of Myopathies Caused by Novel Mitochondrial Phosphate Carrier Mutations**

PI: Erin Seifert (submitting PI), György Hajnóczky;

MPI RO1 submitted in 12/2015

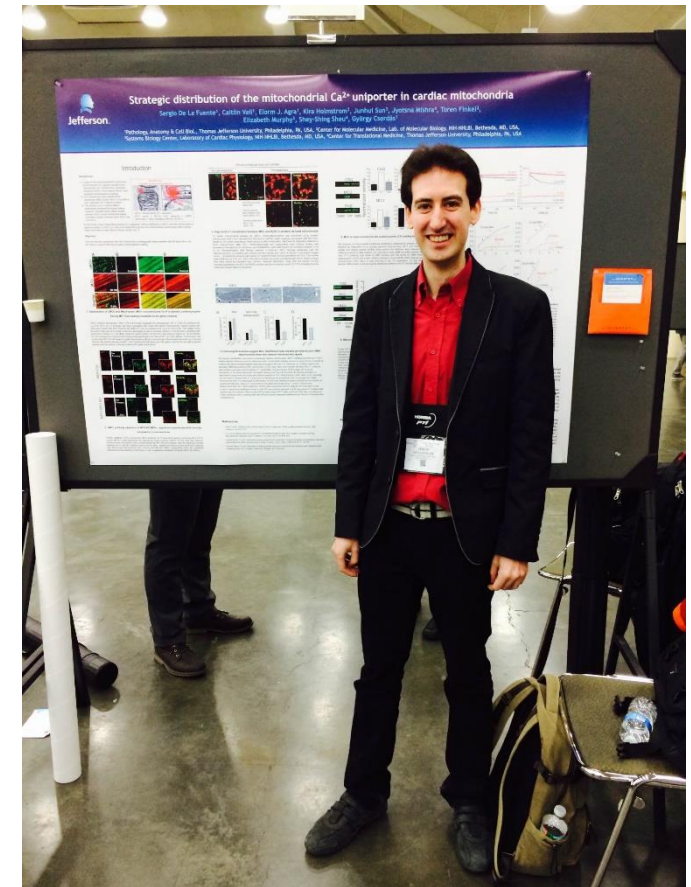


# Biophysics Society Meeting 2015

all had left, but the mitochondriacs were still discussing the posters



Sergio's 1<sup>st</sup> Biophysics





Bioenergetics  
Subgroup  
dinner



The MitoCare  
"house" →

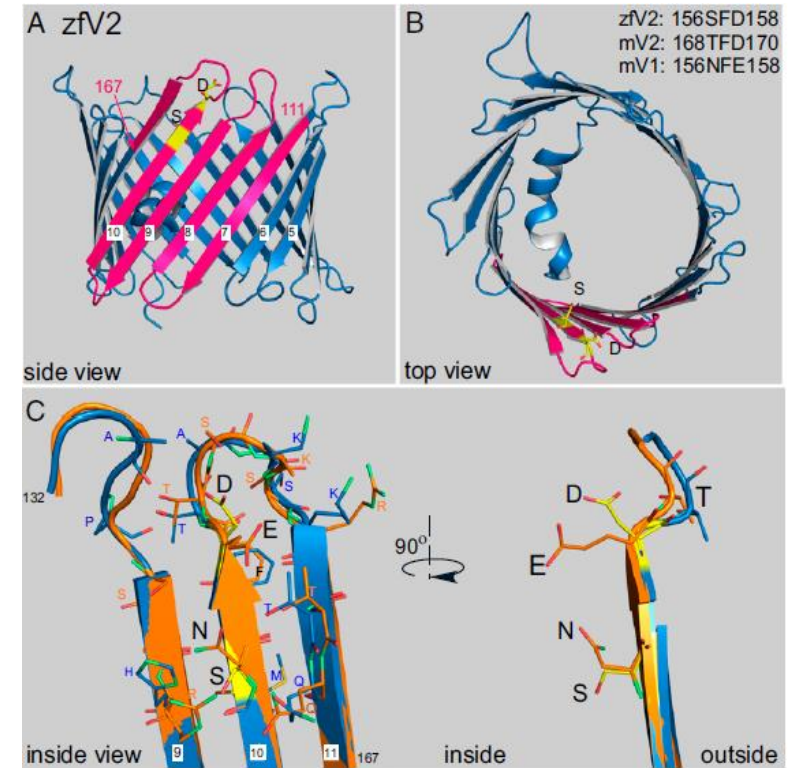




# MitoCare & Friends dinner at the Biophysics



# Five years of dedicated work solves a puzzle of cell death and VDACs



## Motifs of VDAC2 required for mitochondrial Bak import and tBid-induced apoptosis

Shamim Naghdi<sup>a</sup>, Péter Várnai<sup>b</sup>, and György Hajnóczky<sup>a,1</sup>

<sup>a</sup>MitoCare Center for Mitochondrial Imaging Research and Diagnostics, Department of Pathology, Anatomy, and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107; and <sup>b</sup>Department of Physiology, Faculty of Medicine, Semmelweis University, Budapest 1094, Hungary

Edited by Clara Franzini-Armstrong, University of Pennsylvania Medical Center, Philadelphia, PA, and approved August 25, 2015 (received for review May 29, 2015)

Voltage-dependent anion channel (VDAC) proteins are major com-  
munication points for mitochondrial apoptosis. Here, we show that the interaction with Bcl-2 family proteins (either proapoptotic and/or



# No postnatal life without MICU1



**MICU1 regulation of mitochondrial  $\text{Ca}^{2+}$  uptake dictates survival and tissue regeneration**

Anil Noronha Antony<sup>1\*</sup>, Melanie Paillard<sup>1\*</sup>, Cynthia Moffat<sup>1\*</sup>, Egle Juskeviciute<sup>1</sup>, Jason Correnti<sup>1</sup>,  
Brad Bolon<sup>2</sup>, Emanuel Rubin<sup>1</sup>, György Csordás<sup>1</sup>, Erin L. Seifert<sup>1</sup>, Jan B. Hoek<sup>1</sup> and  
György Hajnóczky<sup>1</sup>

Revised ms has been submitted

... but mice lacking MICU1  
in only neurons reaches  
adulthood

Melanie Elliott, a new  
collaborator, assesses the  
behavior of the neuronal  
MICU1 knockout mouse



# Some babysteps towards mitochondrial diseases

Biochemical and Biophysical Research Communications 464 (2015) 369–375



ELSEVIER

Contents lists available at [ScienceDirect](#)

Biochemical and Biophysical Research Communications

journal homepage: [www.elsevier.com/locate/ybbrc](http://www.elsevier.com/locate/ybbrc)

Review

The mitochondrial phosphate carrier: Role in oxidative metabolism, calcium handling and mitochondrial disease

Erin L. Seifert <sup>a,\*</sup>, Erzsébet Ligeti <sup>b</sup>, Johannes A. Mayr <sup>c</sup>, Neal Sondheimer <sup>d</sup>,  
György Hajnóczky <sup>a,\*</sup>

<sup>a</sup> MitoCare Center, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA

<sup>b</sup> Department of Physiology, Semmelweis University, Budapest 1085, Hungary

<sup>c</sup> Department of Paediatrics, Paracelsus Medical University, SALK Salzburg, Salzburg 5020, Austria

<sup>d</sup> Department of Pediatrics, University of Pennsylvania, Philadelphia, PA 19104, USA



Aniko completes her yearlong study of mitochondrial dynamics in cells derived from mitochondrial disease patients





# MitoCare planning to run Broad 2015







# Run and Done







While some were running and celebrating, others were supporting the team at the lab....





# Modeling of mitochondria:

Biochimica et Biophysica Acta (BBA) -  
Bioenergetics

Volume 1847, Issues 6–7, June–July 2015, Pages 656–679



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Computational modeling analysis of mitochondrial superoxide production under varying substrate conditions and upon inhibition of different segments of the electron transport chain

Nikolai I. Markevich<sup>a, b</sup>, , Jan B. Hoek<sup>a</sup>



# A new multi-investigator project

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Notice of Award

Federal Award Date: 05/15/2015



*EXPLORATORY/DEVELOPMENT GRANT*

Department of Health and Human Services  
National Institutes of Health

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

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**Grant Number:** 1R21ES025672-01

**FAIN:** R21ES025672

**Principal Investigator(s):**

GYORGY CSORDAS, MD

Gyorgy Hajnoczky (contact), MD

+Erin Seifert

**Project Title:** Study of the mitochondrial-cellular response to environmental stress by fluorescence imaging

# ... and another one:



*RESEARCH*

Department of Health and Human Services  
National Institutes of Health

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

Notice of Award

**Federal Award Date:** 07/03/2015

**Grant Number:** 2R01AA018873-06A1

**FAIN:** R01AA018873

**Principal Investigator(s):**

JOANNES B HOEK (contact), PHD

Rajanikanth Vadigepalli, PHD

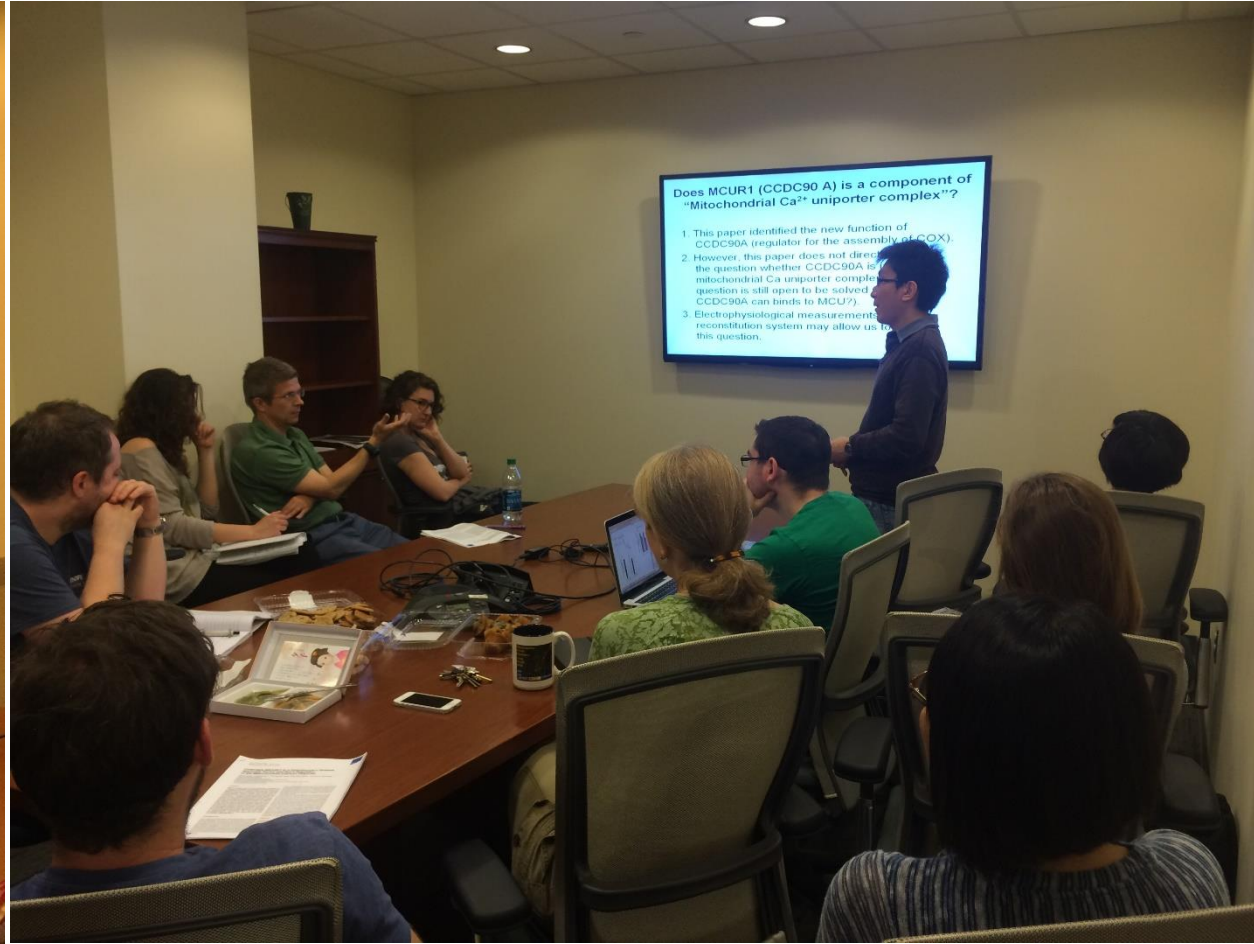
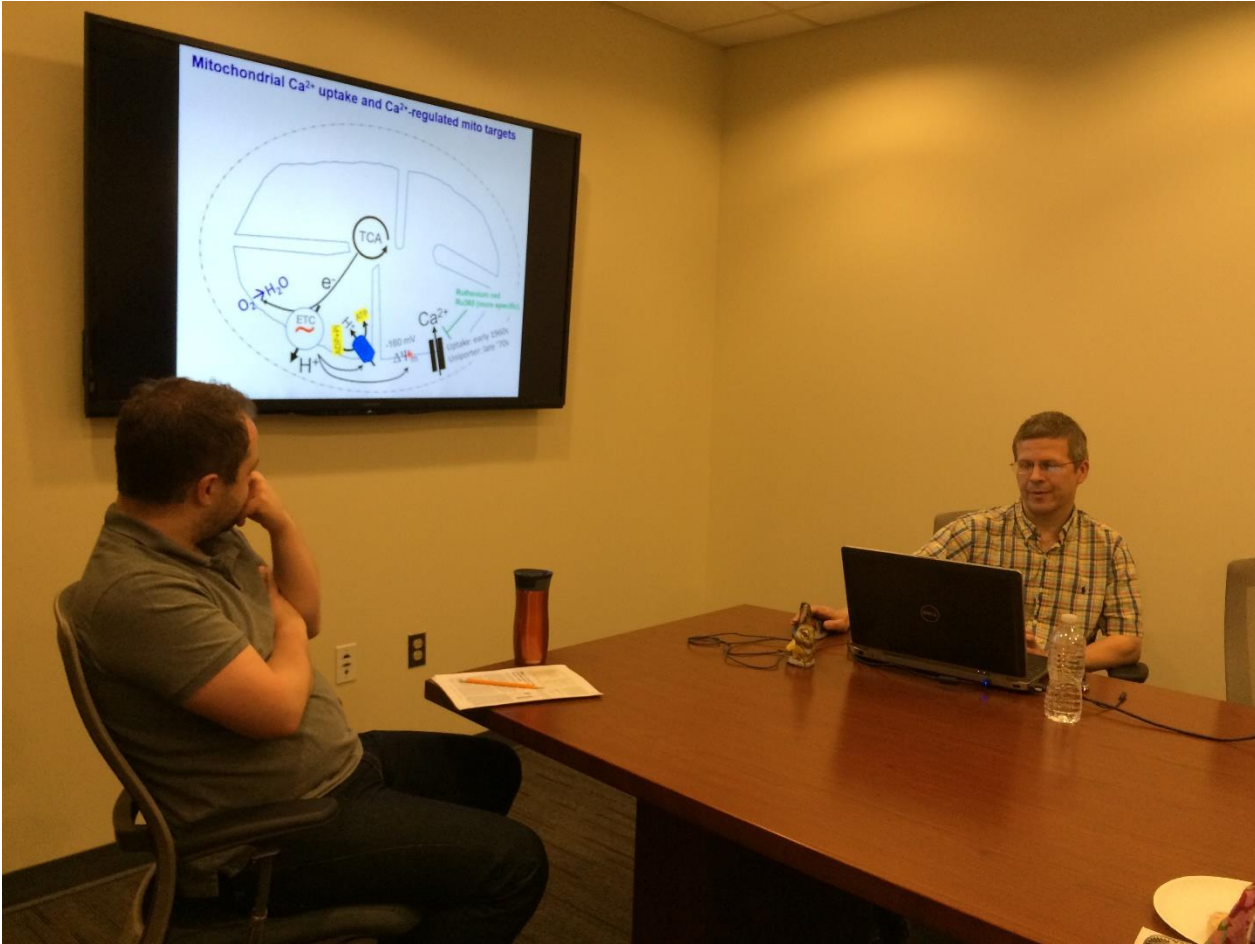
**Project Title:** Ethanol Effects on the Transcriptional Regulatory Network in Liver Regeneration

## Mito Circle Journal Club Presentations 2015

April 6	Gyuri Csordas	Sancak et al. 2013. EMRE is an essential component of the mitochondrial calcium uniporter complex. <i>Science</i> . PMID: 24231807
April 20	Jin Ouchi	Paupe et al. 2015. CCDC90A (MCUR1) Is a Cytochrome c Oxidase Assembly Factor and Not a Regulator of the Mitochondrial Calcium Uniporter. <i>Cell Metab</i> . PMID: 25565209 (Chocolate Bunny Award for saving the day)
May 4	Sergio De La Fuente	Filadi et al. 2015. Mitofusin 2 ablation increases endoplasmic reticulum–mitochondria coupling. <i>PNAS</i> . PMID: 25870285
May 18	Dave Booth	Prosser et al. 2011. X-ROS signaling: rapid mechano-chemo transduction in heart. <i>Science</i> . PMID: 21903813
June 1	Adam Bartok	D’Orsi et al. 2015. Bax regulates neuronal Ca <sup>2+</sup> homeostasis. <i>J Neurosci</i> . PMID: 25632145
June 15	Gyuri Hajnoczky	Hung et al. 2014. Proteomic mapping of the human mitochondrial intermembrane space in live cells via ratiometric APEX tagging. <i>Mol Cell</i> . PMID: 25002142
Sept. 7	Steve Hurst	Giorgio et al. 2013. Dimers of mitochondrial ATP synthase form the permeability transition pore. PMID: 23530243. versus Alavian et al. 2014. An uncoupling channel within the c-subunit ring of the F1FO ATP synthase is the mitochondrial permeability transition pore. <i>PNAS</i> . PMID: 24979777
Oct. 5	Valentina Debattisti	Kanfer et al. 2015. Mitotic redistribution of the mitochondrial network by Miro and Cenp-F. <i>Nat Commun</i> . PMID: 26259702
Oct. 26	Jan Hoek	Gandhi et al. 2015. Liver-specific deletion of augmenter of liver regeneration accelerates development of steatohepatitis and hepatocellular carcinoma in mice. <i>Gastroenterology</i> . PMID: 25448926
Nov. 2	Melanie Paillard	Waldeck-Weiermair et al. 2015. Rearrangement of MICU1 multimers for activation of MCU is solely controlled by cytosolic Ca <sup>2+</sup> . <i>Sci Rep</i> . PMID: 26489515
Nov. 23	Bong Sook Jhun	Pietrangelo et al. 2015. Age-dependent uncoupling of mitochondria from Ca <sup>2+</sup> release units in skeletal muscle. <i>Oncotarget</i> . PMID: 26485763
Nov. 30	Erin Seifert	Wei et al. 2015. Dual Effect of Phosphate Transport on Mitochondrial Ca <sup>2+</sup> Dynamics. <i>J Biol Chem</i> . PMID: 25963147
Dec. 7	Ludovic Gomez	Chung et al. 2015. Cyclosporine before PCI in Patients with Acute Myocardial Infarction. <i>N Engl J Med</i> . PMID: 26321103
Dec. 21	Shamim Naghdi	Montero et al. 2015. Drug-induced death signaling strategy rapidly predicts cancer response to chemotherapy. <i>Cell</i> . PMID: 25723171



# The first of the MitoCircle Journal Clubs



# MitoCircle Program (MitoCare JAH 527)

## SUMMER 2015

May 12, 2015

**Andrew Wojtovich, PhD (University of Rochester)**

Optogenetic Control of Mitochondrial ROS

May 21, 2015

**Pal Pacher (NIH)**

Interplay of mitochondrial dysfunction with oxidative/nitrative stress, poly(ADP)ribose polymerase (PARP), and inflammation during tissue injury

June 18, 2015

**Natalie Porat-Shliom, PhD (NIH)**

Mitochondrial Dynamics & Metabolism In Vivo: From Organ Physiology to Cell Biology

July 23, 2015

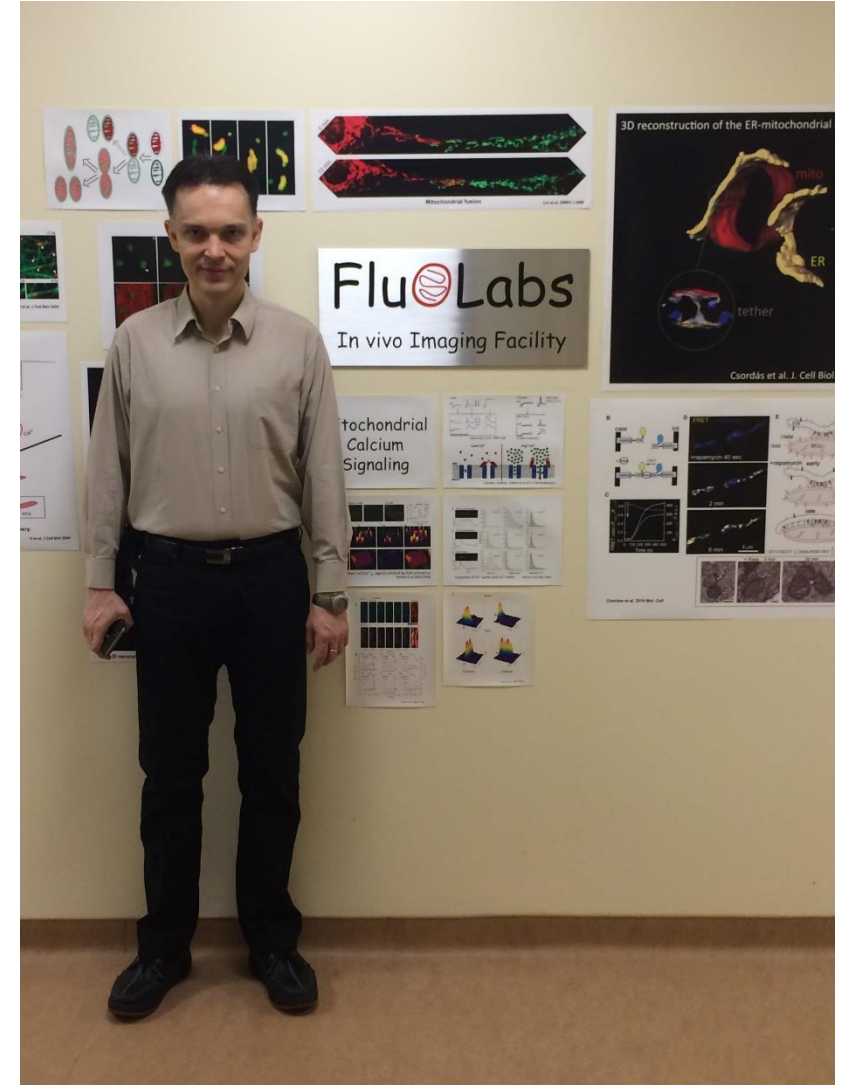
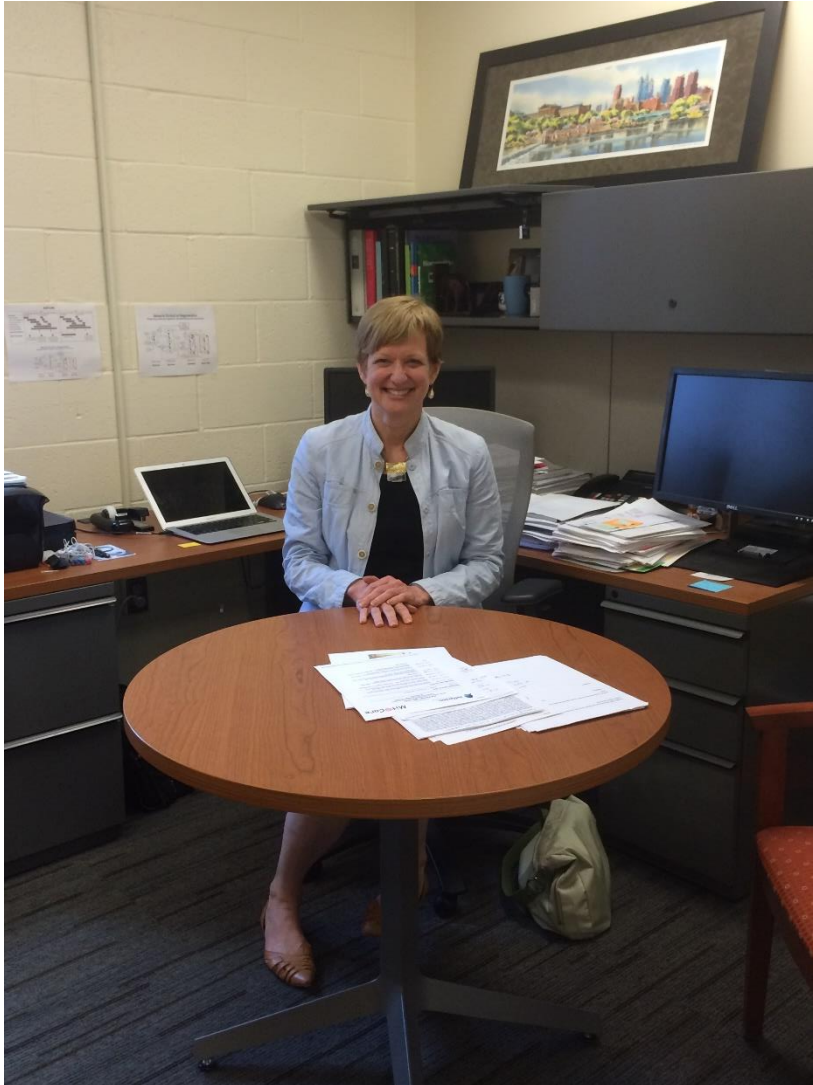
**Jennifer Rieusset, PhD (INSERM, Lyon, France)**

Role of endoplasmic reticulum-mitochondria interactions in the control of hepatic metabolism and insulin action



# Guest speakers:

Laura Nagy takes over Jan's office Pali Pacher's homecoming



# MitoCare Birthdays





# Jefferson Postdoctoral Research Symposium



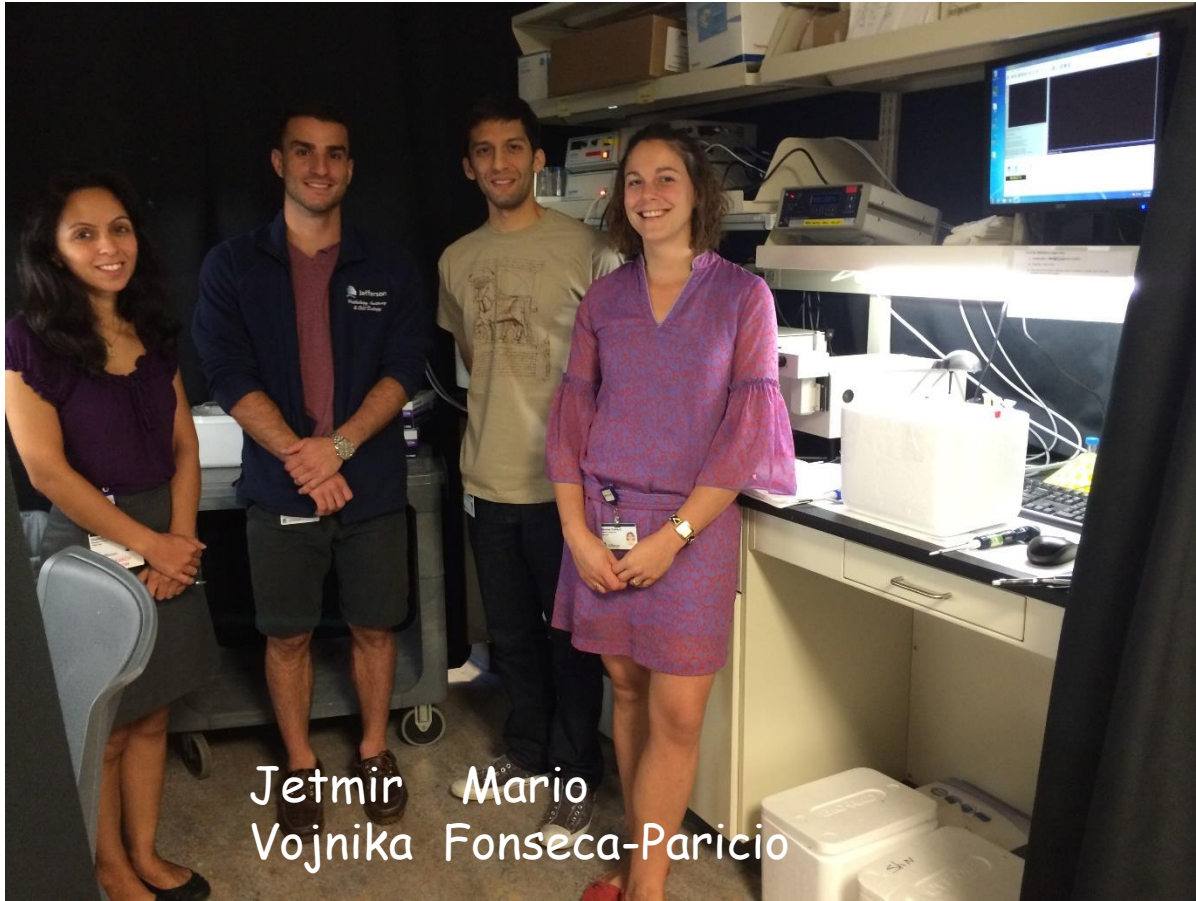


# Mit Care

## Summer Student Diploma 2015



Devon Michele Dibello

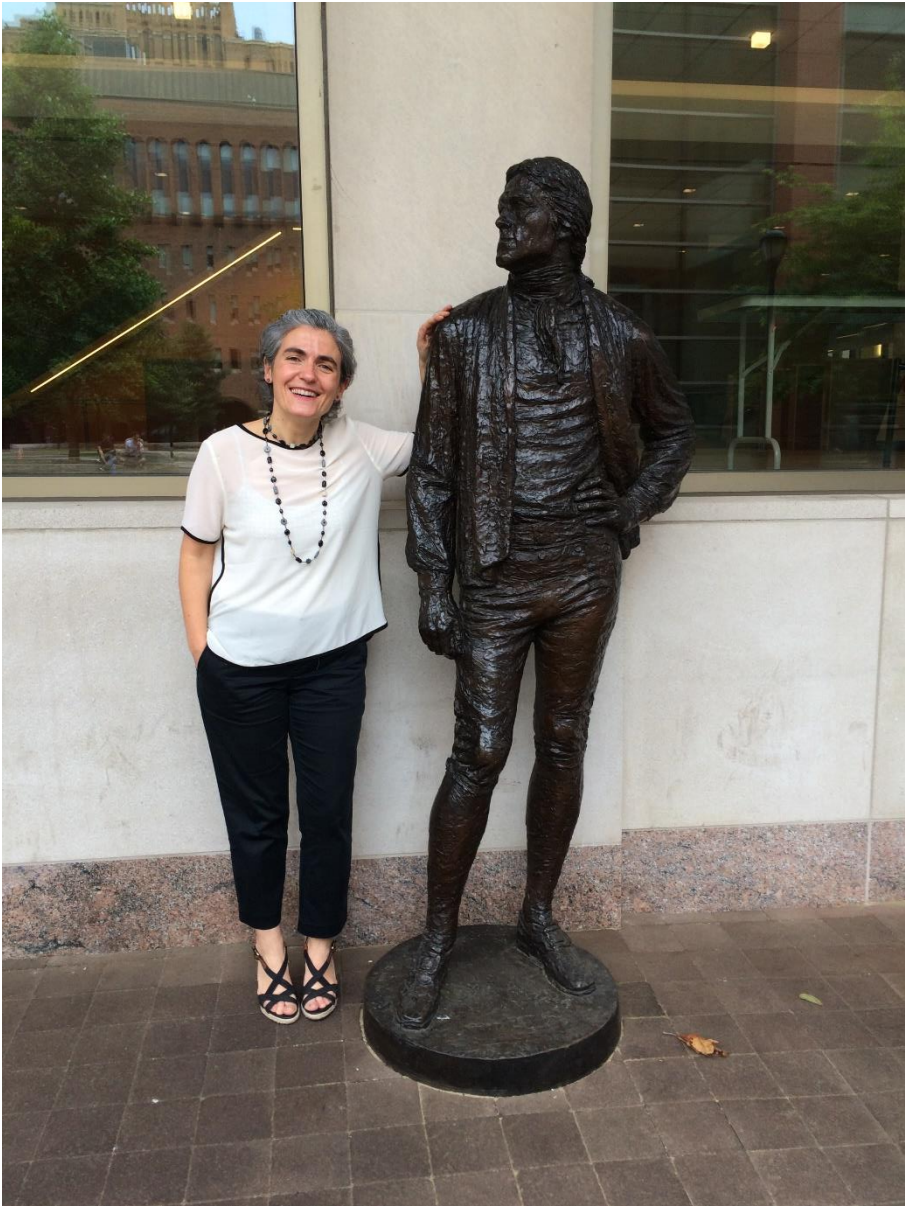


Jetmir Vojnika Mario Fonseca-Paricio



Ryan Cupo





Verónica meets  
Jefferson  
and drives a  
pisco sour project



Julia continues the  
Mitochondrial Disease  
Database project



# MitoCircle Program (MitoCare JAH 527)

## FALL 2015, WINTER-SPRING 2016

Oct 22, 2015

**John Elrod, PhD (Temple)**

Mitochondrial calcium regulation in the heart

Nov 19, 2015

**Will Prinz, PhD (NIH)**

Taking the leap: Lipid exchange at contact sites

Jan 21, 2016

**Shey-Shing Sheu, Ph.D. (Thomas Jefferson University)**

Feb 25, 2016

**Feliciano Protasi, Ph.D. (University G. d'Annunzio, Chieti, Italy)**

Mar 27, 2016

**Rong Tian MD, PhD (University of Washington)**

Apr 21, 2016

**John Pastorino, PhD (Rowan University)**

May 26, 2016

**Dario Altieri, MD (The Wistar Institute)**

Mitochondria and metastasis

June 23, 2016

**Gyorgy Csordas, MD and Erin Seifert, PhD (Thomas Jefferson University)**



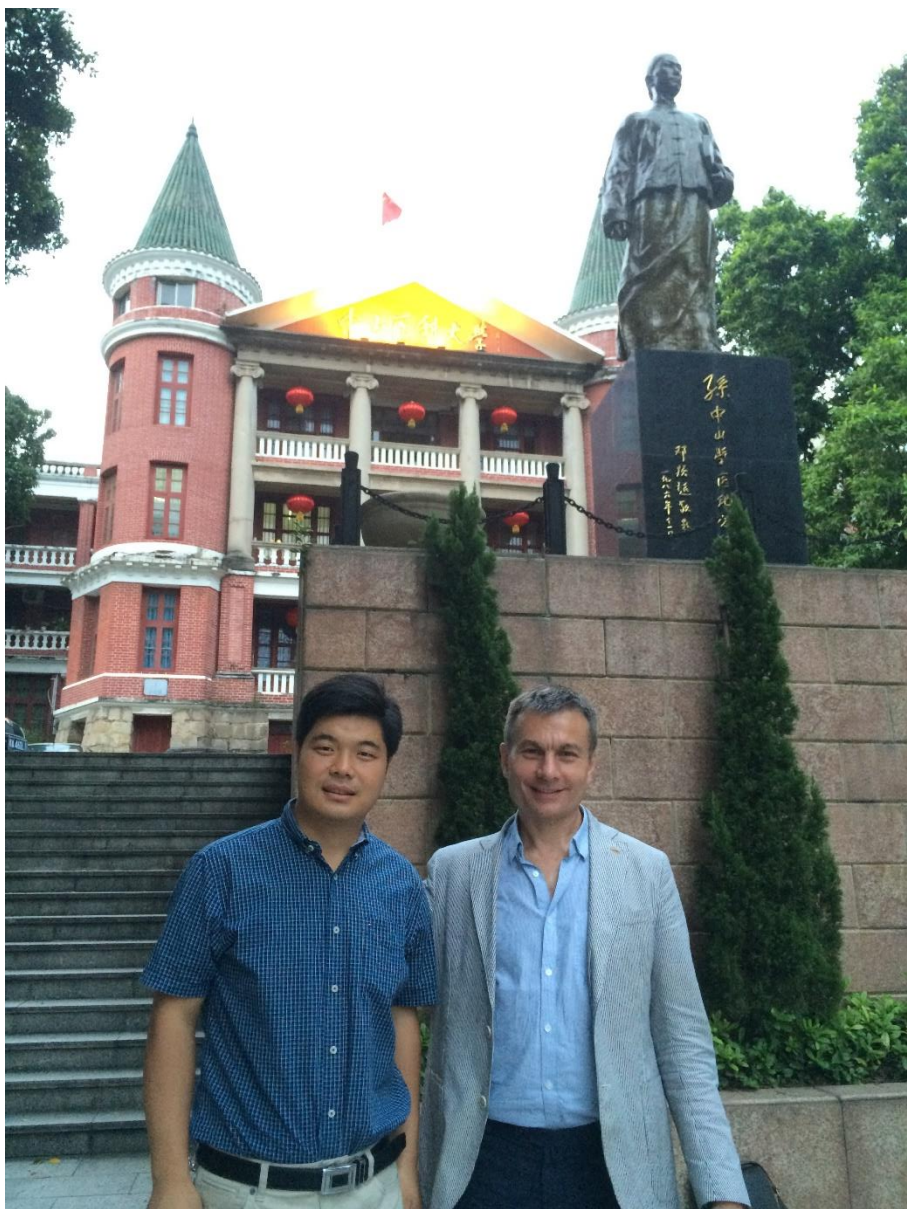
# New postdoctoral fellows start at MitoCare:

Bill Slovinsky: alcohol and mitochondria

Rafaela Bagur: ER-mitochondrial signaling

Thamara Hewavitharana: assembly of the uniporter

..... and Sergio de la Fuente is awarded by  
an AHA postdoctoral fellowship



# Xingguo in Guangzhou, China and his follow up on the mitochondrial donuts

## Biophysical *Journal*

Volume 109, Issue 5, 1 September 2015, Pages 892–899

Article

### Modeling of Mitochondrial Donut Formation

Qi Long<sup>1</sup>, Danyun Zhao<sup>1</sup>, Weimin Fan<sup>1</sup>, Liang Yang<sup>1</sup>, Yanshuang Zhou<sup>1</sup>, Juntao Qi<sup>1</sup>, Xin Wang<sup>1</sup>,  
Xingguo Liu<sup>1</sup>



# Verónica's lab, team, family and visitors in Santiago, Chile



# The Zeiss LSM880 confocal microscope with Airyscan arrives to MitoCare



**New confocal technology enables fast and sensitive superresolution microscopy.**





# News about former members of the group:

Chris Buzas  
visits as a Surgeon

Raji's husband and co-director  
of their biotech company

Masao becomes a second time dad



Happy  
Holidays!  
from

MitCare

Join us for an  
afternoon of  
hearty  
and  
energetic  
holiday  
cheer!

100 nm

Rat heart mitochondria by super-resolution microscopy.

Monday, December 21, 2015

MitoCare JAH 527

3 PM





Est. 2014