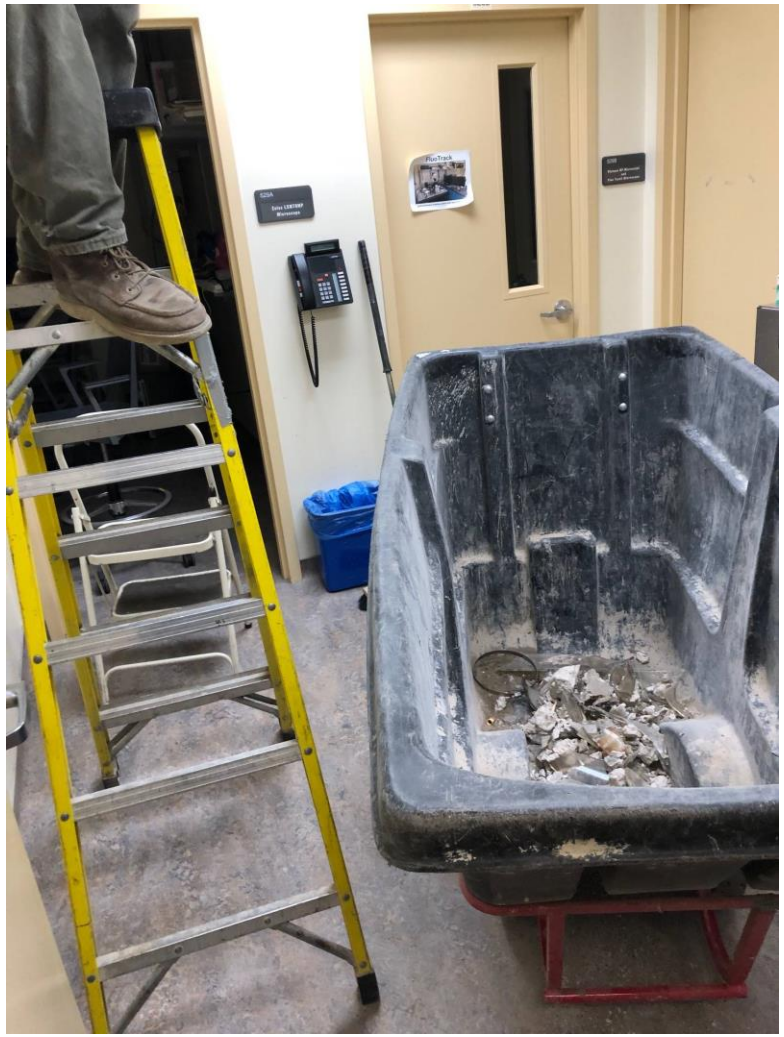
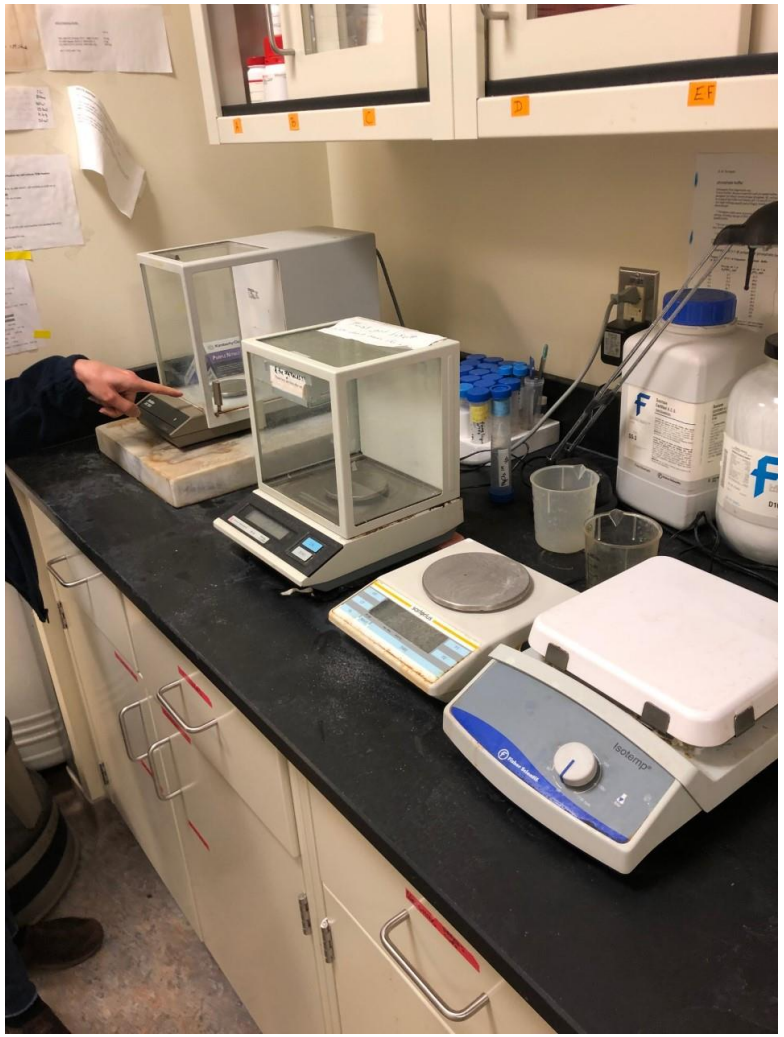
MitoCare moments 2019

MitoCare turns 5 years old on Jan. 6, 2019



Construction above causes flooding of the MitoCare suite. A small benefit is that after the cleanup all the analytic balances, and a high end camera are updated.



MitoCircle 2019

MitoCare Center for Mitochondrial Imaging Research and Diagnostics
Department of Pathology, Anatomy and Cell Biology
Thomas Jefferson University

Location: MitoCare Center, Jefferson Alumni Hall Suite 527, 1020 Locust St.
Day/Time: MONDAY, 11AM

Winter-Spring 2019

Jan. 28 **Luca Pelligrini, Ph.D.**, Professor, Cervo Brain Research Center, Laval University, Quebec, Canada.

Title: **Meet the WrappER, a new type of endoplasmic reticulum: from structure to function in lipoproteins biogenesis**

March 1 **Ildiko Szabo, Ph.D.**, Professor in Biochemistry, Department of Biology, University of Padova, Italy

Title: **Mitochondrial ion channels: from molecular identification to pharmacological targeting**
Note: seminar day is a Friday

April 8 **Lisa Norquay, Ph.D.**, Scientific Director, Cardiovascular and Metabolism Discovery, Janssen Research and Development

Title: **Translating Mitochondrial Biology for Treatment of Metabolic Disease Complications: Challenges and Opportunities**

MitoCare Center for Mitochondrial Imaging Research and Diagnostics
Department of Pathology, Anatomy and Cell Biology
Thomas Jefferson University

Location: MitoCare Center, Jefferson Alumni Hall Suite 527, 1020 Locust St.
Day/Time: TUESDAY, 9:30AM

Fall 2019

Oct. 1 **Doris Germain, Ph.D.**, Professor, Medicine, Hematology and Medical Oncology, Icahn School of Medicine, Mount Sinai
Title: **"Mitohormesis and the UPRmt regulate metastasis"**

Nov. 19 **Christoph Maack, M.D.**, Chair, Department for Translational Science, Comprehensive Heart Failure Center, University Clinic Würzburg, Germany and Senior physician, Medical Clinic I for Internal Medicine, University Clinic Würzburg, Germany
Title: **Mitochondrial redox regulation in heart failure**

Dec. 3 **Ming-Feng Tsai, Ph.D.**, Assistant Professor, School of Medicine, University of Colorado
Title: **Mechanisms of Calcium Activation of the Mitochondrial Calcium Uniporter**

Year opening publications

Cell Calcium
Volume 79, May 2019, Pages 89-97

Redox regulation of ER and mitochondrial Ca^{2+} signaling in cell survival and death

Suresh K. Joseph, David M. Booth, Michael P. Young, György Hajnóczky

Show more

https://doi.org/10.1016/j.ceca.2019.02.006 Get rights and content

Highlights

- Methods for the measurement of IP_3 receptor redox state are described.
- Findings regarding the role of cytosolic and luminal IP_3R thiols are reviewed.
- New findings on redox regulation of mitochondrial Ca^{2+} uptake are discussed.

Gene Expr, 19 (2), 97-119 2019 Apr 18

Single-Cell Gene Expression Analysis Identifies Chronic Alcohol-Mediated Shift in Hepatocyte Molecular States After Partial Hepatectomy

Sirisha Achanta [1], Aalap Verma [1], Ankita Srivastava [1], Harshavardhan Nilakantan [1], Jan B Hoek [1], Rajanikanth Vadigepalli [1]

Affiliations

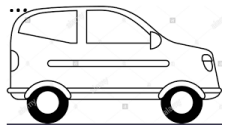
PMID: 30189915 PMCID: PMC6466177 DOI: 10.3727/105221618X15361728786767

Abstract

The analysis of molecular states of individual cells, as defined by their mRNA expression profiles and protein composition, has gained widespread interest in studying biological phenomena ranging from embryonic development to homeostatic tissue function and genesis and evolution of cancers. Although the molecular content of individual cells in a tissue can vary widely, their molecular states tend to be constrained within a transcriptional landscape partly described by the canonical archetypes of a population of cells. In this study, we sought to characterize the effects of an acute (partial hepatectomy) and chronic (alcohol consumption) perturbation on the molecular states of individual hepatocytes during the onset and progression of liver regeneration. We analyzed the expression of 84 genes across 233 individual hepatocytes acquired using laser capture microdissection. Analysis of the single-cell data revealed that hepatocyte molecular states can be considered as distributed across a set of four states irrespective of perturbation, with the proportions of hepatocytes in these states being dependent on the perturbation. In addition to the quiescent, primed, and replicating hepatocytes, we identified a fourth molecular state lying between the primed and replicating subpopulations. Comparison of the proportions of hepatocytes from each experimental condition in these four molecular states suggested that, in addition to aberrant priming, a slower transition from primed to replication state could contribute toward ethanol-mediated suppression of liver regenerative response to partial hepatectomy.

Luca Pellegrini day at MitoCircle

Adorable AirBB that was especially comfortable on Fri night …

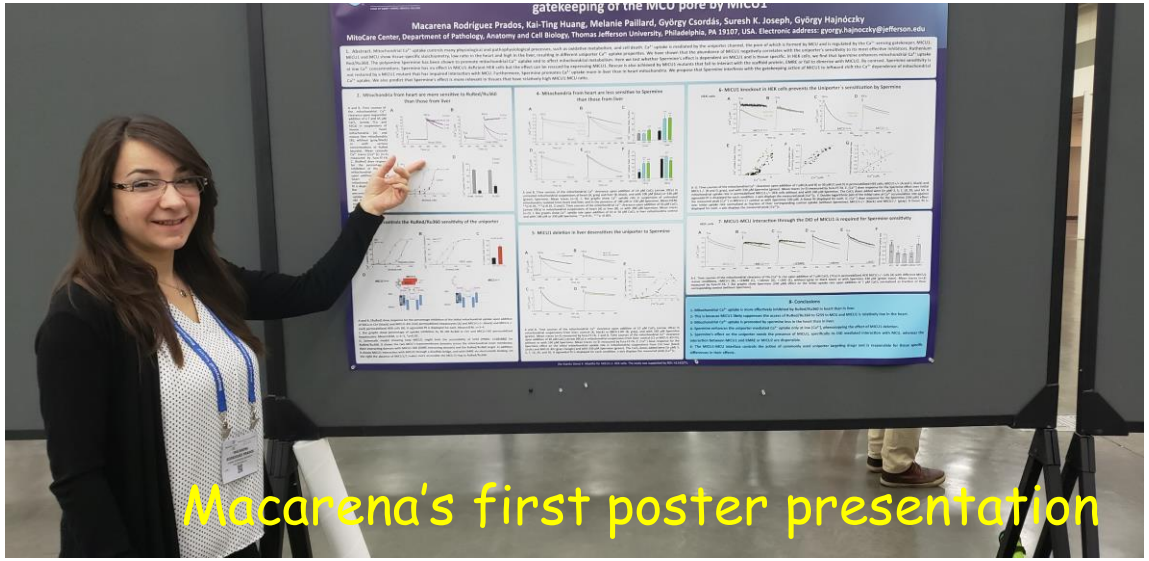


Gyuri C's is the next Chair in Elect for the Subgroup

Subgroup dinner

Biophysics 2019 in Baltimore

Masao arrives together with Prottoy, his student, who soon joins MitoCare as a postdoc



The FIRST Gordon Conference on Mitochondrial Biology

Mitochondria in Health and Disease
Gordon Research Conference

Mitochondrial Dynamics and Signaling

March 17-22, 2019
Ventura Beach Marriott
Ventura, CA

Chairs: Gyorgy Hajnoczky and Carla Koehler
Vice Chairs: Atan Gross and Nika Danial

Contributors

Gordon Research Conferences — Frontiers of Science
Predominantly Undergraduate Institution Fund
Carl Storm Underrepresented Minority Fellowship Program
National Institutes of Health
Agilent — Trusted Answers
BIOLOG MitoPlates
IONIS PHARMACEUTICALS
Avanti Polar Lipids, Inc.
CellPress
HORIBA Scientific
Sutter Instrument
aurora SCIENTIFIC
frontiers
NOVARTIS Institutes for Biomedical Research
Contact
Enspire Bio
BRUKER
Janssen — Johnson & Johnson

Leica Microsystems
CHROMA
Stealth BIOTHERAPEUTICS

Mitochondria in Health and Disease

Gordon Research Conference

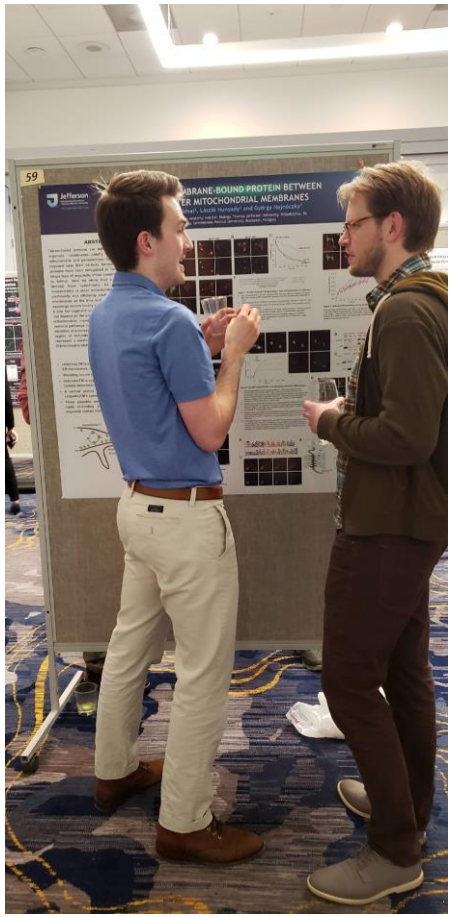
March 17-22, 2019

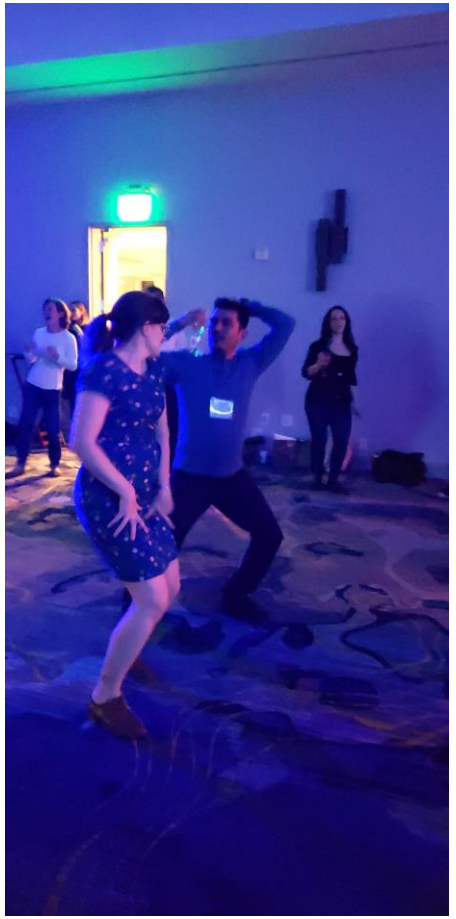
Ventura Beach Marriott, Ventura, CA

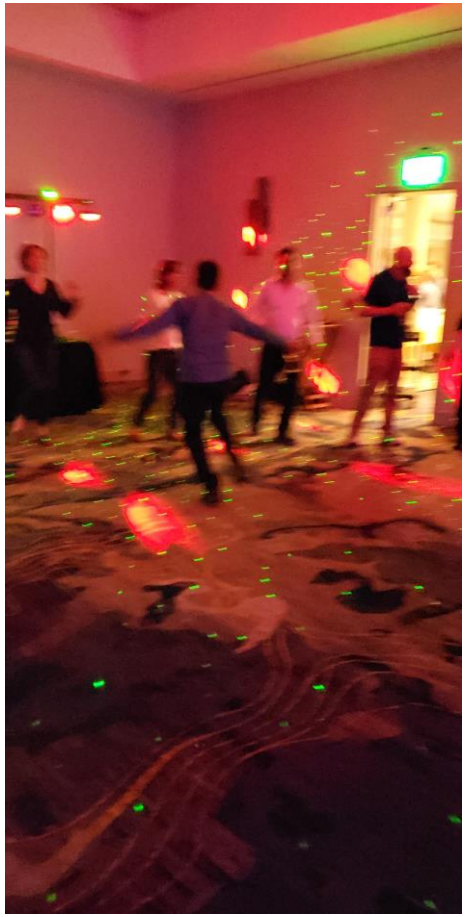
Chairs: Gyorgy Hajnoczky and Carla Koehler

Vice Chairs: Atan Gross and Nika Danial

Presentation, Reunion and Dynamics at the Conference







Zumba hour, more Reunion, and Poster Awards

Our parents

Mrs. E. Hajnoczky and Mr. E. Shirihai

Science Education Foundation

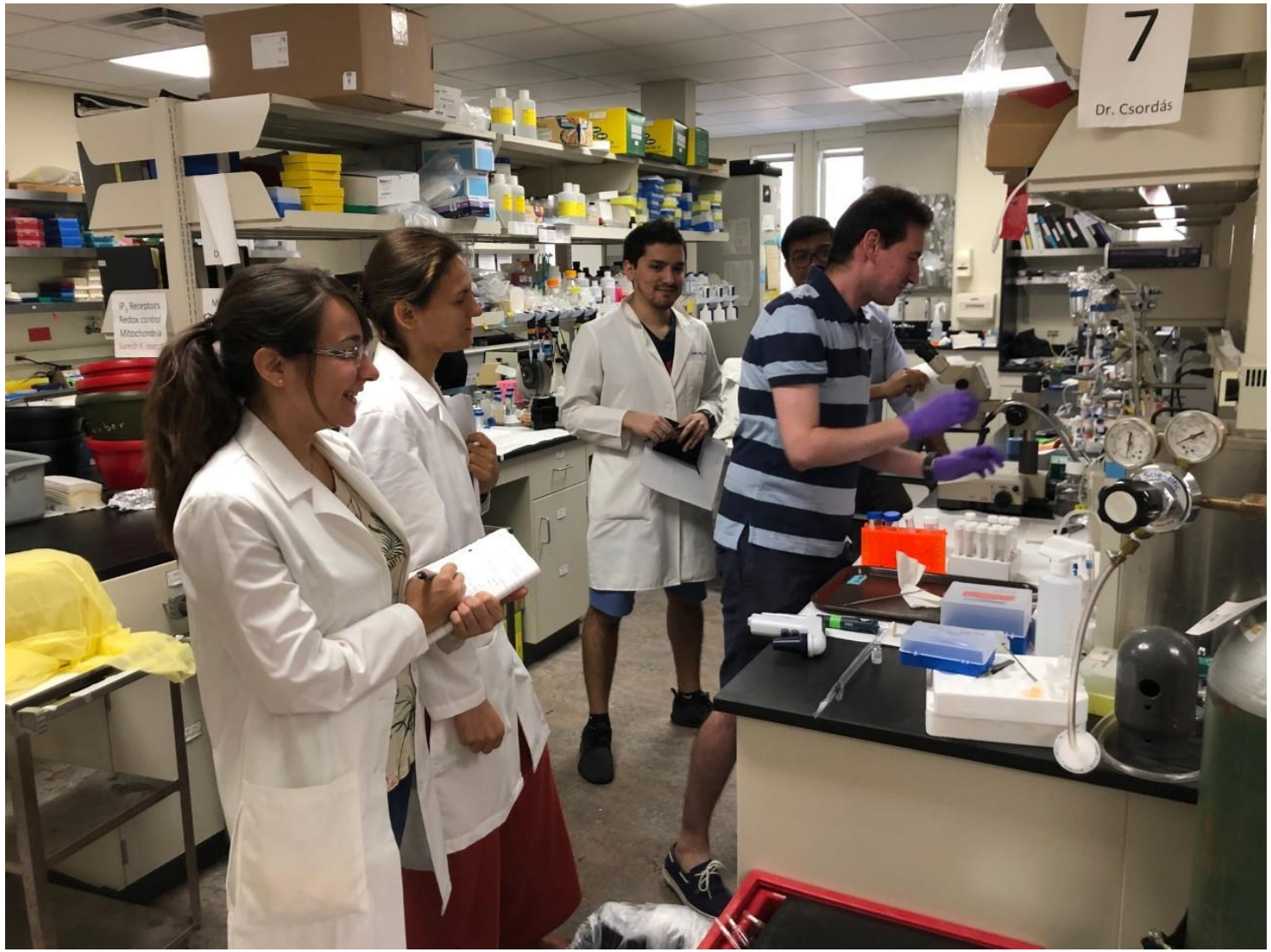
Kai, who joined U Rochester as a graduate student, returns for a visit

And Amy, who has just competed her PhD at UC Davis and starts her postdoc in Denmark stops by with some of her homemade cookies

Prottoy, Arijita, Sergio and Kata join as postdocs MitoCare

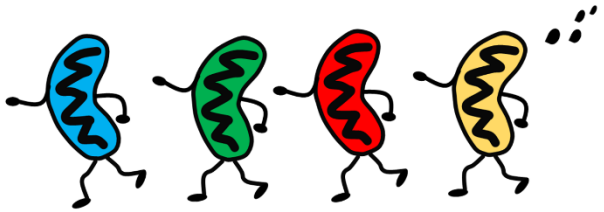
Broad Street 10 miler 2019

Learning the isolation of cardiomyocytes from Sergio



Benjamin is back for another summer of studying cardiac mitochondrial dynamics

MitoCircle Summer Marathon



MitoCare Suite JAH 527
June 27th, 2019, 8:45AM start

A Mini-Symposium on Mitochondrial Dynamics and Signaling in Disease

8:45AM Introduction by György Hajnóczky, Director of MitoCare

9:00 – 9:55AM Veronica Eisner (Pontificia Universidad Catolica de Chile): Mitochondrial reshaping and disease.

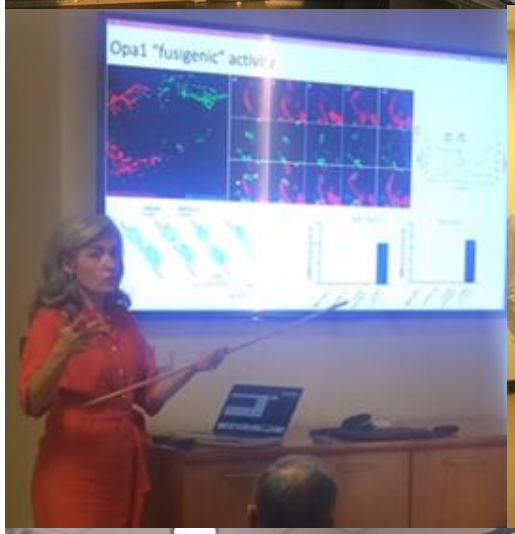
9:55 – 10:30AM Marco Tigano (NYU): Nuclear Sensing of Mitochondrial DNA Damage Drives Immune Surveillance.

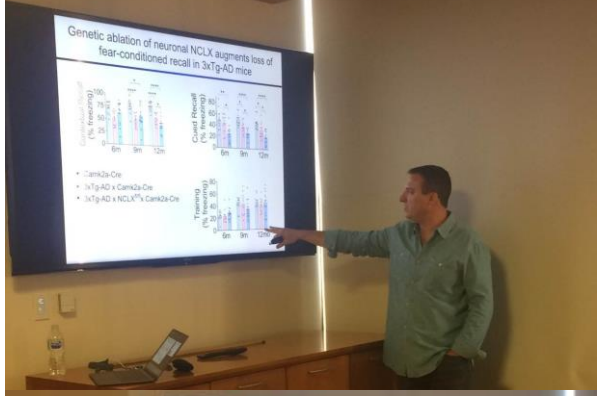
10:30 – 11:00AM Coffee

11:00 – 11:35AM John Elrod (Temple University): Role of the mitochondrial calcium uniporter in Alzheimer's Disease.

11:35AM – 12:30PM Rita Horvath (Cambridge University): What is causing tissue specific phenotypes in mitochondrial disease?

12:30PM Lunch

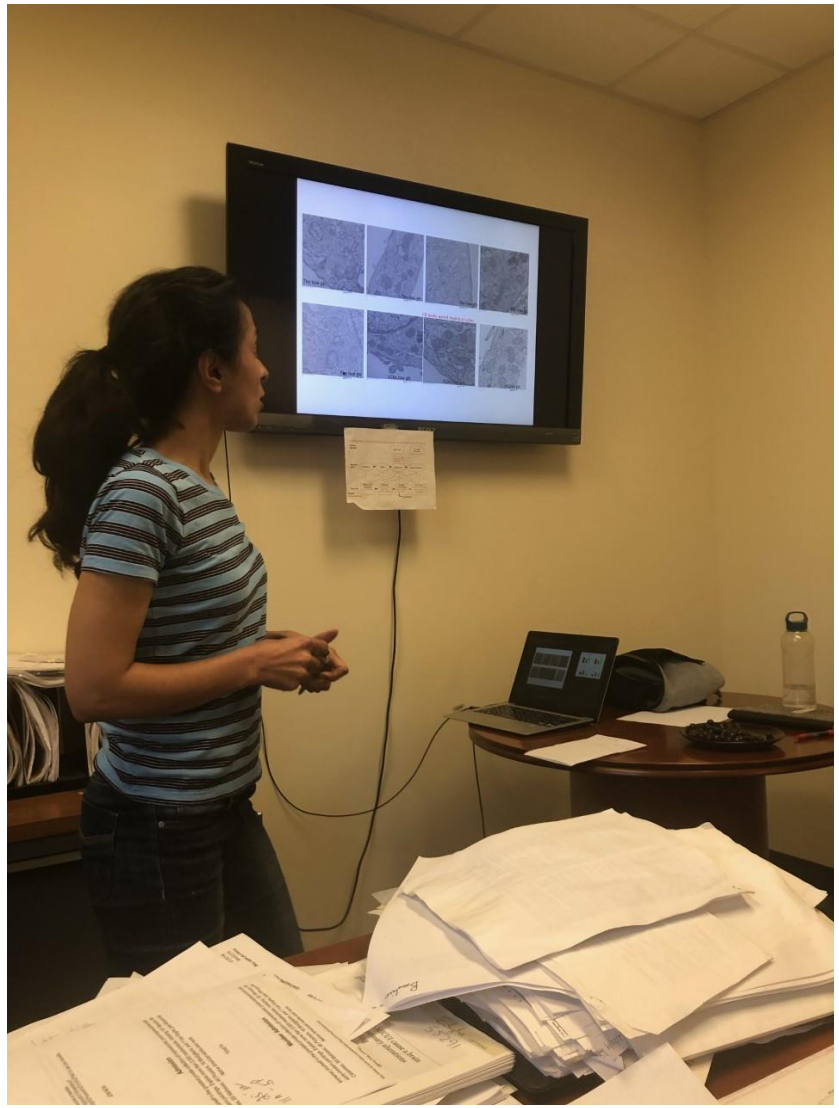




Postdoctoral Symposium 2019, Zuzana shines

Labmeetings start to go by topics:

-Uniporter,
-Contacts,
-VDACs and Liver Cancer,
-Mitochondrial Dynamics

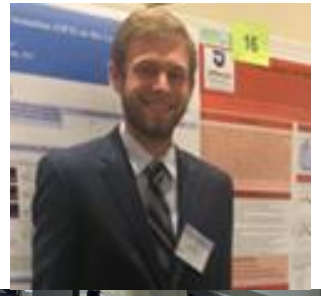


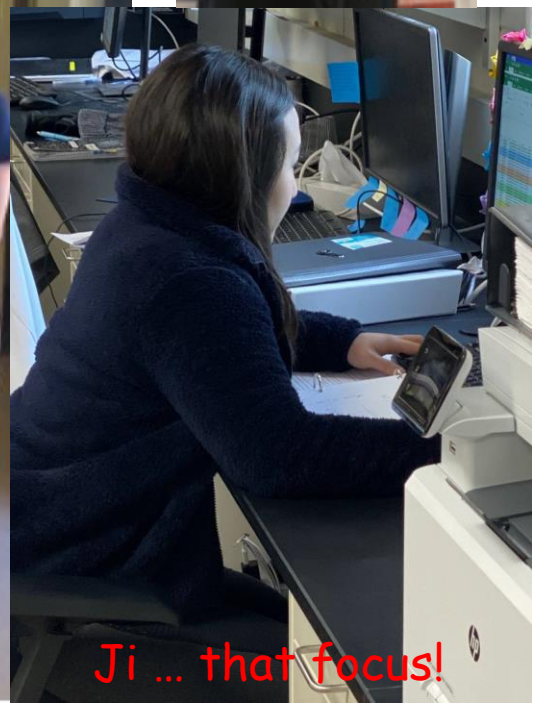
Shamim's summary on VDAC and Mitochondrial Ultrastructure at one of the first VDAC meetings

Exposing the new fellows to the local sport culture at a Phillies game

Seifert lab welcomes Heli, Briyanna, Ji and Ellen …. And says goodbye (sniff!) to Aish and Kyle


Summer 2019 (plus a cake … of course!)




Ji … that focus!


Aish: Now a Grad student in Sweden!

A story with long history finally gets published.
It builds on a stimulating collaboration with David Yule

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-11646-3 OPEN

IP_3 receptor isoforms differently regulate ER-mitochondrial contacts and local calcium transfer

Adam Bartok[1,2], David Weaver[1], Tünde Golenár[1], Zuzana Nichtova[1], Máté Katona[1], Száva Bánsághi[1], Kamil J. Alzayady[3], V. Kaye Thomas[3], Hideaki Ando[4,5], Katsuhiko Mikoshiba[4,6], Suresh K. Joseph[1], David I. Yule[3], György Csordás[1] & György Hajnóczky[1]

Contact sites of endoplasmic reticulum (ER) and mitochondria locally convey calcium signals between the IP_3 receptors (IP3R) and the mitochondrial calcium uniporter, and are central to cell survival. It remains unclear whether IP3Rs also have a structural role in contact formation and whether the different IP3R isoforms have redundant functions. Using an IP3R-deficient cell model rescued with each of the three IP3R isoforms and an array of super-resolution and ultrastructural approaches we demonstrate that IP3Rs are required for maintaining ER-mitochondrial contacts. This role is independent of calcium fluxes. We also show that, while each isoform can support contacts, type 2 IP3R is the most effective in delivering calcium to the mitochondria. Thus, these studies reveal a non-canonical, structural role for the IP3Rs and direct attention towards the type 2 IP3R that was previously neglected in the context of ER-mitochondrial calcium signaling.

Pamela's paper is published!

© 2019. Published by The Company of Biologists Ltd | Journal of Cell Science (2019) 132, jcs229906. doi:10.1242/jcs.229906

RESEARCH ARTICLE

Perturbed mitochondria–ER contacts in live neurons that model the amyloid pathology of Alzheimer's disease

Pamela V. Martino Adami[1,2], Zuzana Nichtová[3], David B. Weaver[3], Adam Bartok[3], Thomas Wisniewski[4], Drew R. Jones[5], Sonia Do Carmo[6], Eduardo M. Castaño[1], A. Claudio Cuello[6], György Hajnóczky[3] and Laura Morelli[1,*]

ABSTRACT

The use of fixed fibroblasts from familial and sporadic Alzheimer's disease patients has previously indicated an upregulation of mitochondria–ER contacts (MERCs) as a hallmark of Alzheimer's disease. Despite its potential significance, the relevance of these results is limited because they were not extended to live neurons. Here we performed a dynamic *in vivo* analysis of MERCs in hippocampal neurons from McGill-R-Thy1-APP transgenic rats, a model of Alzheimer's disease-like amyloid pathology. Live FRET imaging of neurons from transgenic rats revealed perturbed 'lipid-MERCs' (gap width <10 nm), while 'Ca^{2+}-MERCs' (10–20 nm gap width) were unchanged. *In situ* TEM showed no significant differences in the lipid-MERCs:total MERCs or lipid-MERCs:mitochondria ratios; however, the average length of lipid-MERCs was significantly decreased in neurons from transgenic rats as compared to controls. In accordance with FRET results, untargeted lipidomics showed significant decreases in levels of 12 lipids and bioenergetic analysis revealed respiratory dysfunction of mitochondria from transgenic rats. Thus, our results reveal changes in MERC structures coupled with impaired mitochondrial functions in Alzheimer's disease-related neurons.

(Leuner et al., 2007; Mancuso et al., 2007; Mosconi et al., 2009; Kapogiannis and Mattson, 2011). It has been shown that amyloid β precursor protein (APP) and Aβ colocalize with mitochondria (Devi and Ohno, 2012; Hansson Petersen et al., 2008), that Aβ inhibits respiratory chain function (reviewed in Swerdlow, 2012) and that mitochondrial function also changes APP processing increasing or decreasing the production of amyloidogenic derivatives (Gabuzda et al., 1994; Gasparini et al., 1997; Leuner et al., 2012; Pereira et al., 1998). Apart from their essential role in bioenergetics, mitochondria are also involved in a great variety of other cellular processes, such as Ca^{2+} homeostasis and lipid biosynthesis. These functions require a dynamic spatial organization that allows signaling from and to other organelles. In particular, mitochondria are associated with the endoplasmic reticulum (ER) – i.e. the mitochondria–ER contacts (MERCs) – form between the outer mitochondrial membrane (OMM) and specialized regions of the ER, in which membrane and luminal components can intermix and exchange (Shore and Tata, 1977; Vance, 1990). These membranes can run in juxtaposition for hundreds of nanometers with a gap width of 5–30 nm between them when mitochondria are associated with smooth ER. The number of contacts, the interface length and the gap width are parameters

Andrew Thomas stops by to say hello

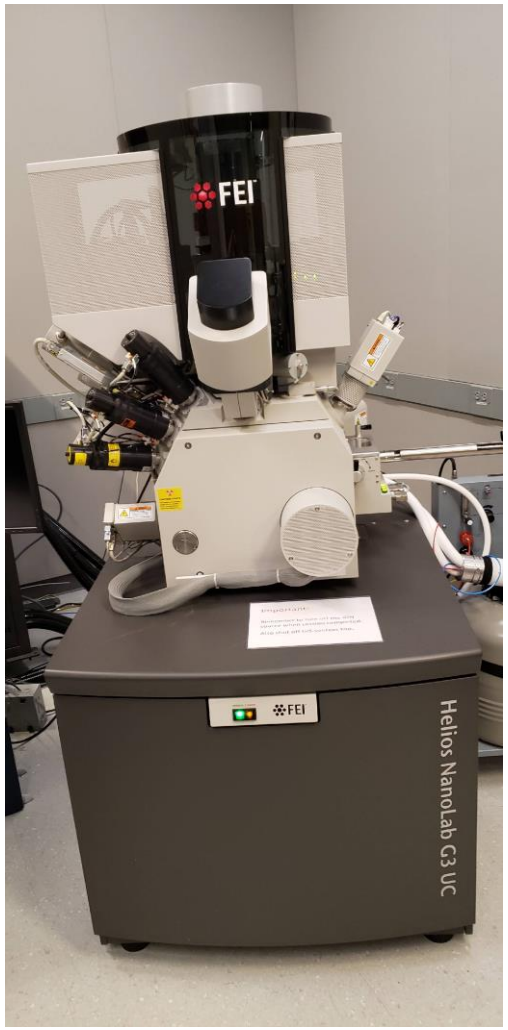
Shamim's Last Tango
at the PTI.....
it was not really the last one

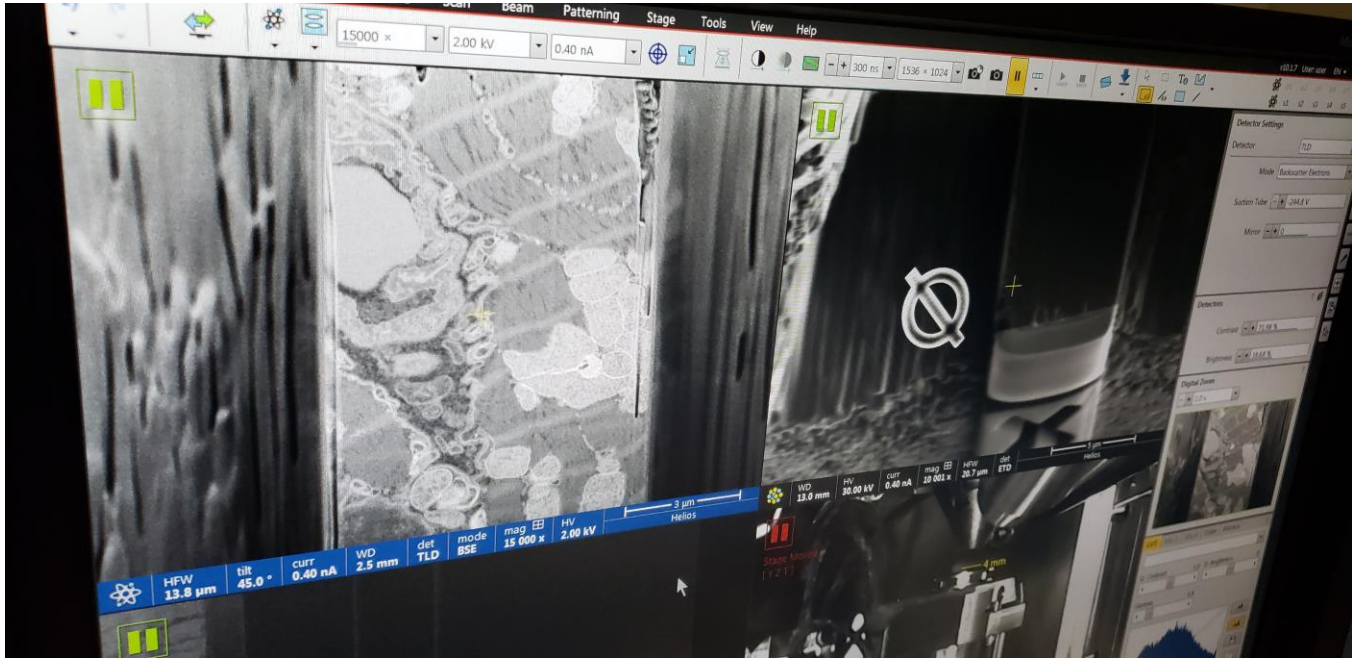
Just before we start to miss Shamim

Conference on Microscopy and Microanalysis

Gyuri Cs diligently evaluates new 3D ultrastructure strategies and falls for FIB-SEM technology

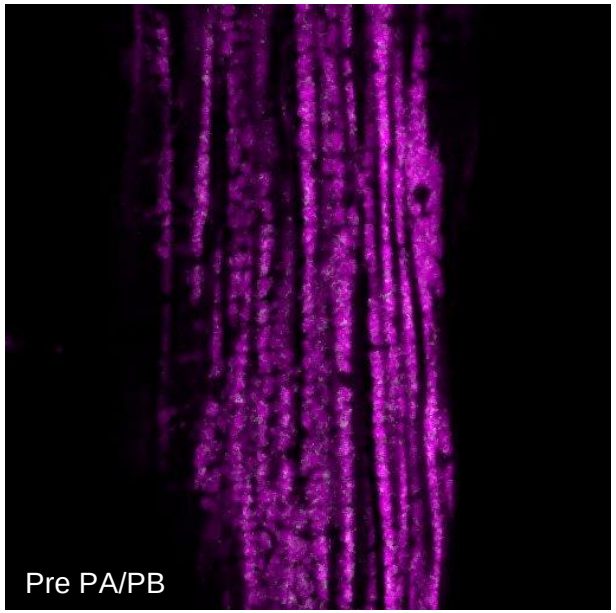
Some impressive data obtained with the FIB-SEM we wish to obtain

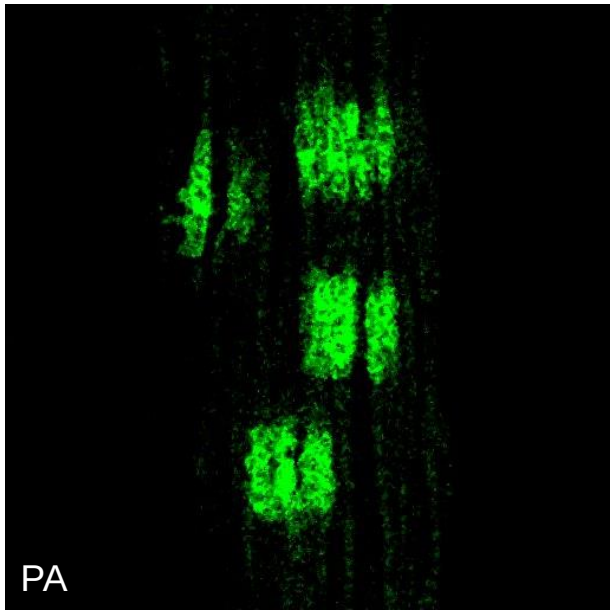


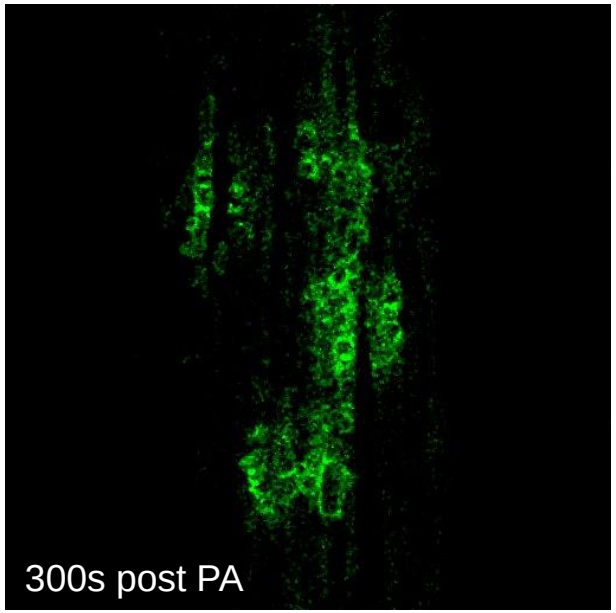


Mate's MitoCare "Bachelor Party"

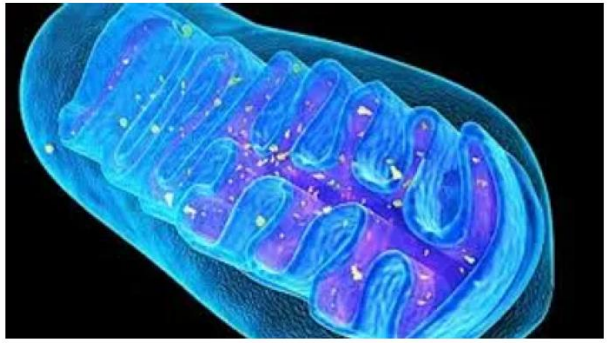
Benjamin's summer efforts provide important insights into the dynamics of mitochondrial outer membrane in the heart







Thanks to Prottoy and the Elrod crew for forming a great support team

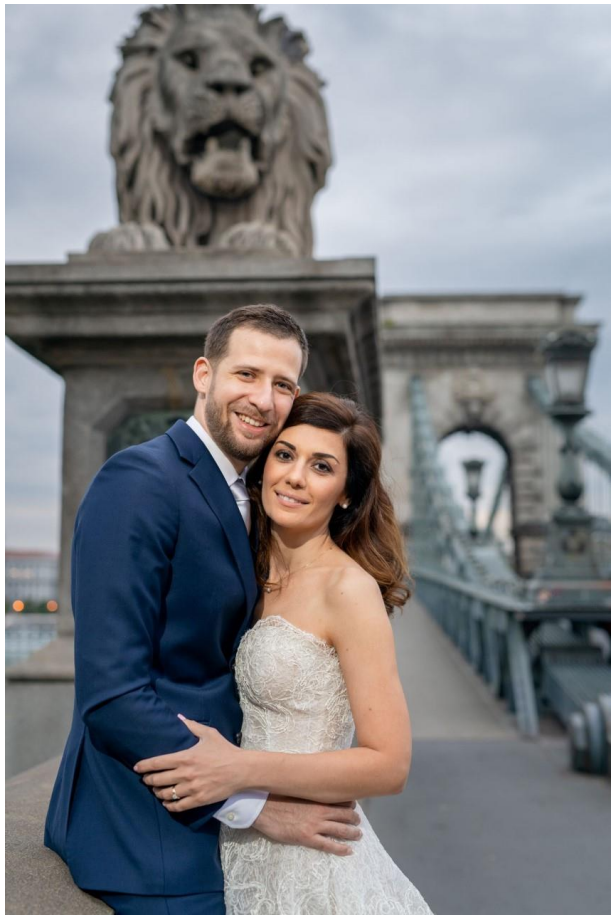


MitoCare becomes part of the Leducq MitoCardia network. This gives a last opportunity to collaborate with Mike Forte, a great mitochondriac and collaborator of MitoCare who retires from the Vollum Institute in the end of 2019

MitoCardia is a Network of 7 world renowned fundamental and clinical research teams working within a trans-atlantic partnership to identify new approaches for treating a global health problem.

Supported by the Fondation Leducq, these teams are working together to better understand dysregulation in the energy producing centre (mitochondria) of the cell itself. Opening of the mitochondrial permeability transition pore (PTP), a large conductance channel in the inner mitochondrial membrane, can initiate cell death. Sustained opening of the PTP triggers cell death; perpetuating cardiovascular disease and increasing the possibility of heart failure. We are identifying ways to correct this dysregulation, identify ways to close the pores and reverse the progression of cardiovascular disease.

Mate's wedding in Budapest



The MitoCare contingent at Mate's wedding

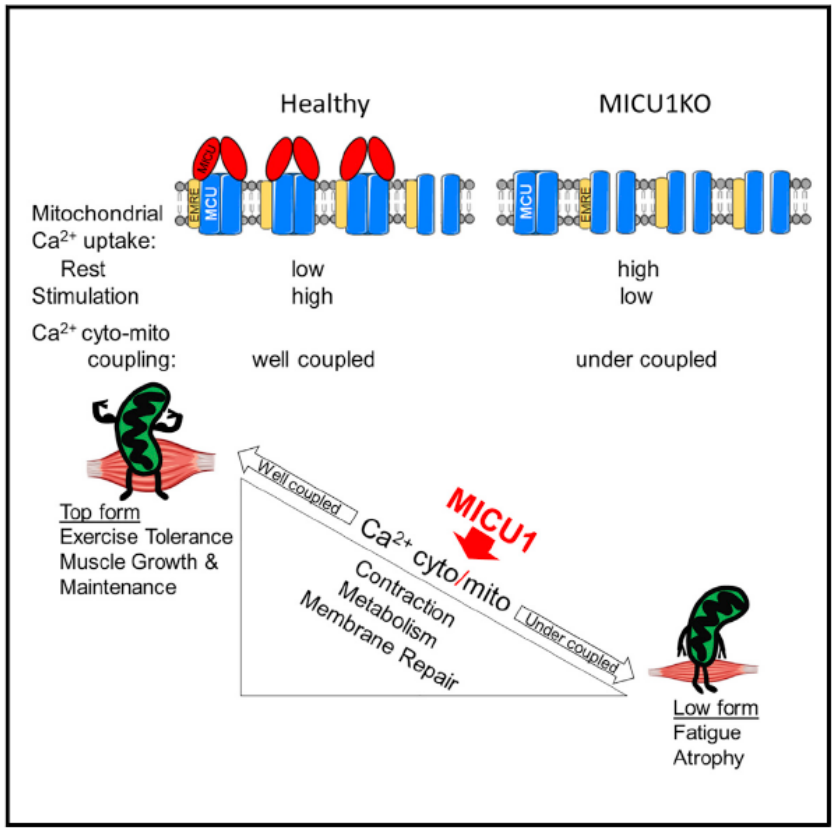
Doris Germain visits MitoCircle

Shamim and Dave's wedding

Cell Reports

Dysregulation of Mitochondrial Ca^{2+} Uptake and Sarcolemma Repair Underlie Muscle Weakness and Wasting in Patients and Mice Lacking MICU1

Graphical Abstract



Authors

Valentina Debattisti, Adam Horn, Raghavendra Singh, ..., Rita Horvath, Jyoti K. Jaiswal, György Hajnóczky

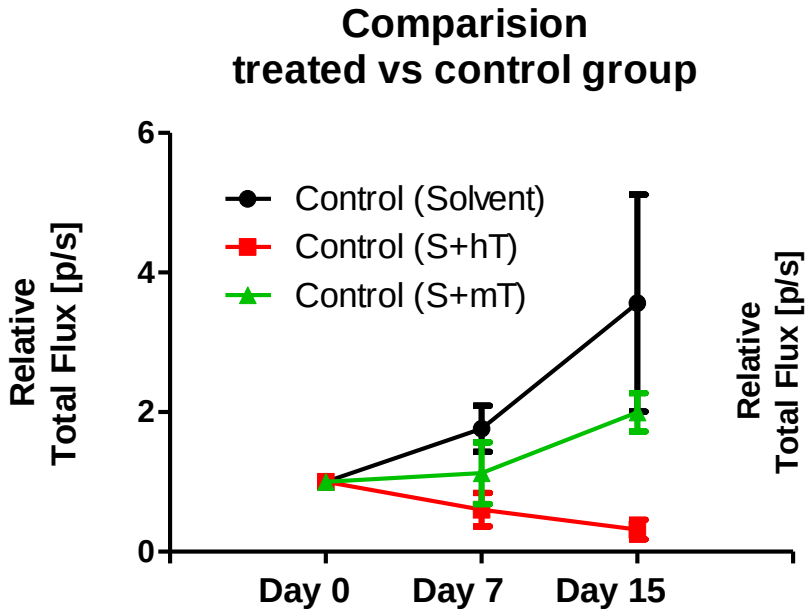
Correspondence

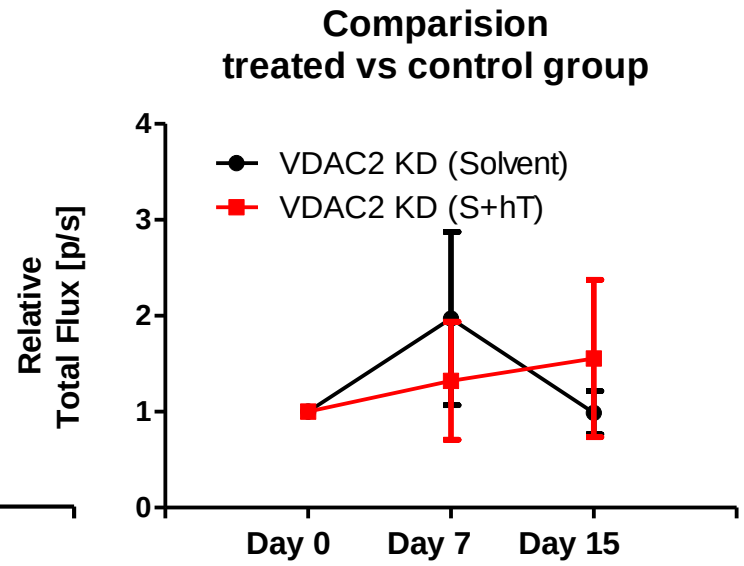
jkjaiswal@cnmc.org (J.K.J.), gyorgy.hajnoczky@jefferson.edu (G.H.)

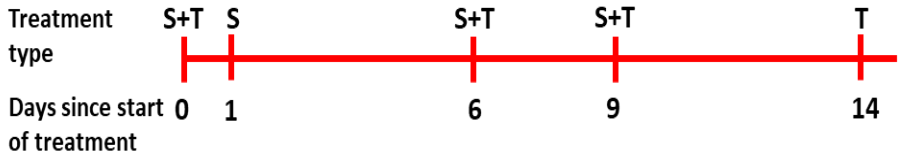
In Brief

Debattisti et al. report that skeletal muscle-specific loss of mitochondrial Ca^{2+} uptake 1 (MICU1) in mouse impairs mitochondrial calcium signaling, energy metabolism, and membrane repair, leading to muscle weakness, fatigue, myofiber damage, and high CK levels, recapitulating the muscle symptoms of MICU1 loss in patients.

After years of efforts VDAC2 and Liver cancer are studied in vivo…… and the results are promising







The VDAC and Liver Cancer Labmeetings regularly benefit from consultations with Hien Dang and her Crew

Seifert lab Presentations … and Carmen's 1st publication in the lab!

JBC ARTICLE

Multiple mitochondrial thioesterases have distinct tissue and substrate specificity and CoA regulation, suggesting unique functional roles

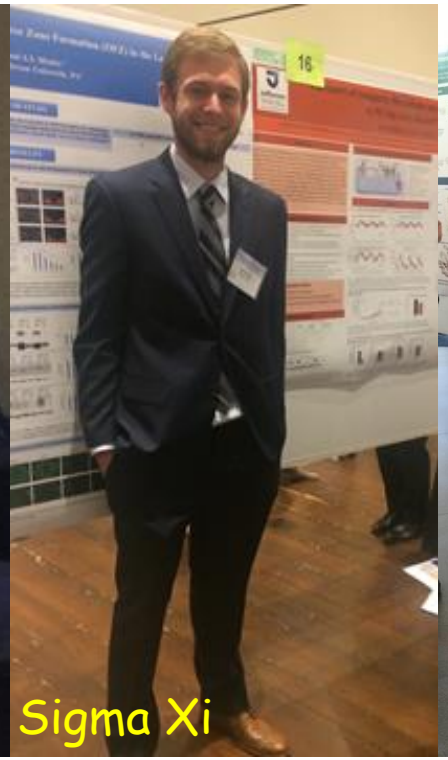
Received for publication, September 3, 2019, and in revised form, October 16, 2019 Published, Papers in Press, November 1, 2019, DOI 10.1074/jbc.RA119.010901

Carmen Bekeova[‡], Lauren Anderson-Pullinger[‡], Kevin Boye[‡], Felix Boos[§], Yana Sharpadskaya[‡], Johannes M. Herrmann[§], and Erin L. Seifert[‡1]

From the [‡]MitoCare Center, Department of Pathology, Anatomy, and Cell Biology, Thomas Jefferson University, Philadelphia, Pennsylvania 19107 and the [§]Division of Cellular Biology, Department of Biology, University of Kaiserslautern, 67663 Kaiserslautern, Germany

Edited by Jeffrey E. Pessin

Gyuri's Gordon



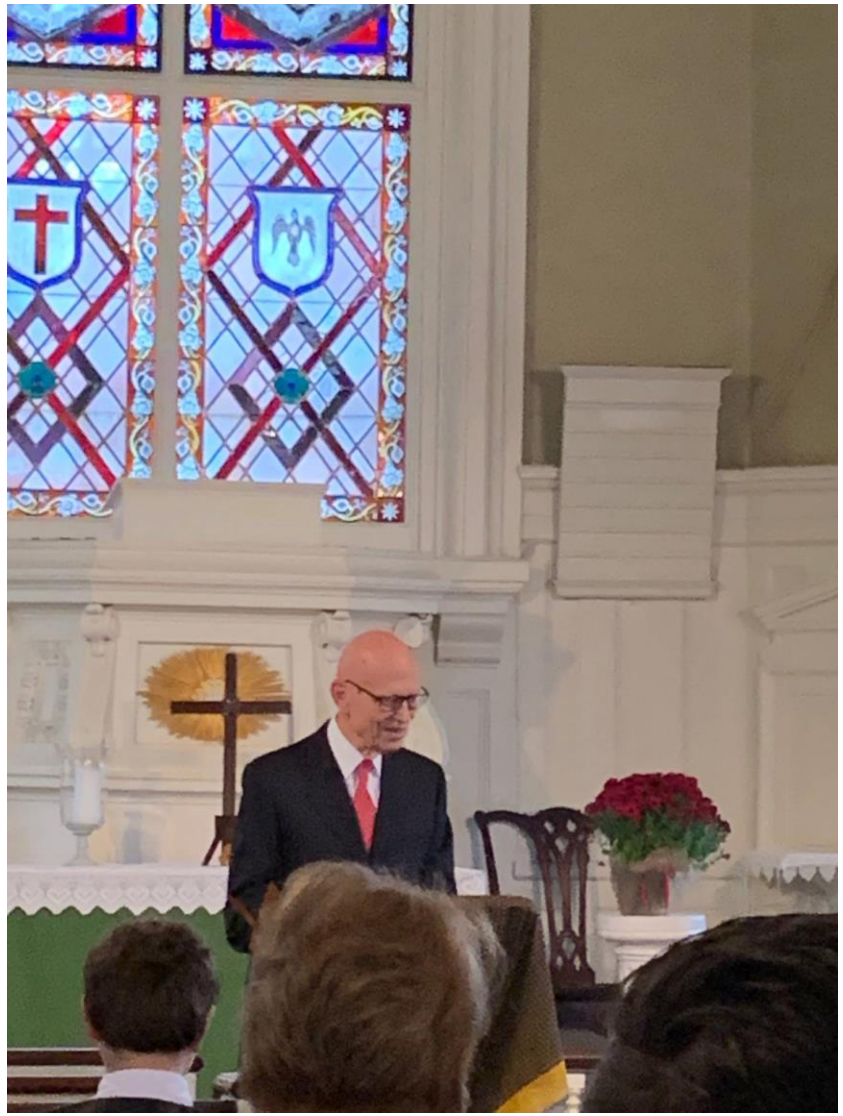
Sigma Xi

TJU Post Doc Day

The wedding of Noro and John October 26, 2019

Historic Old Swedes' Church

Guests of the Wedding Ceremony



Steve's successful PhD defense

coupled with a symposium celebrating his life in science

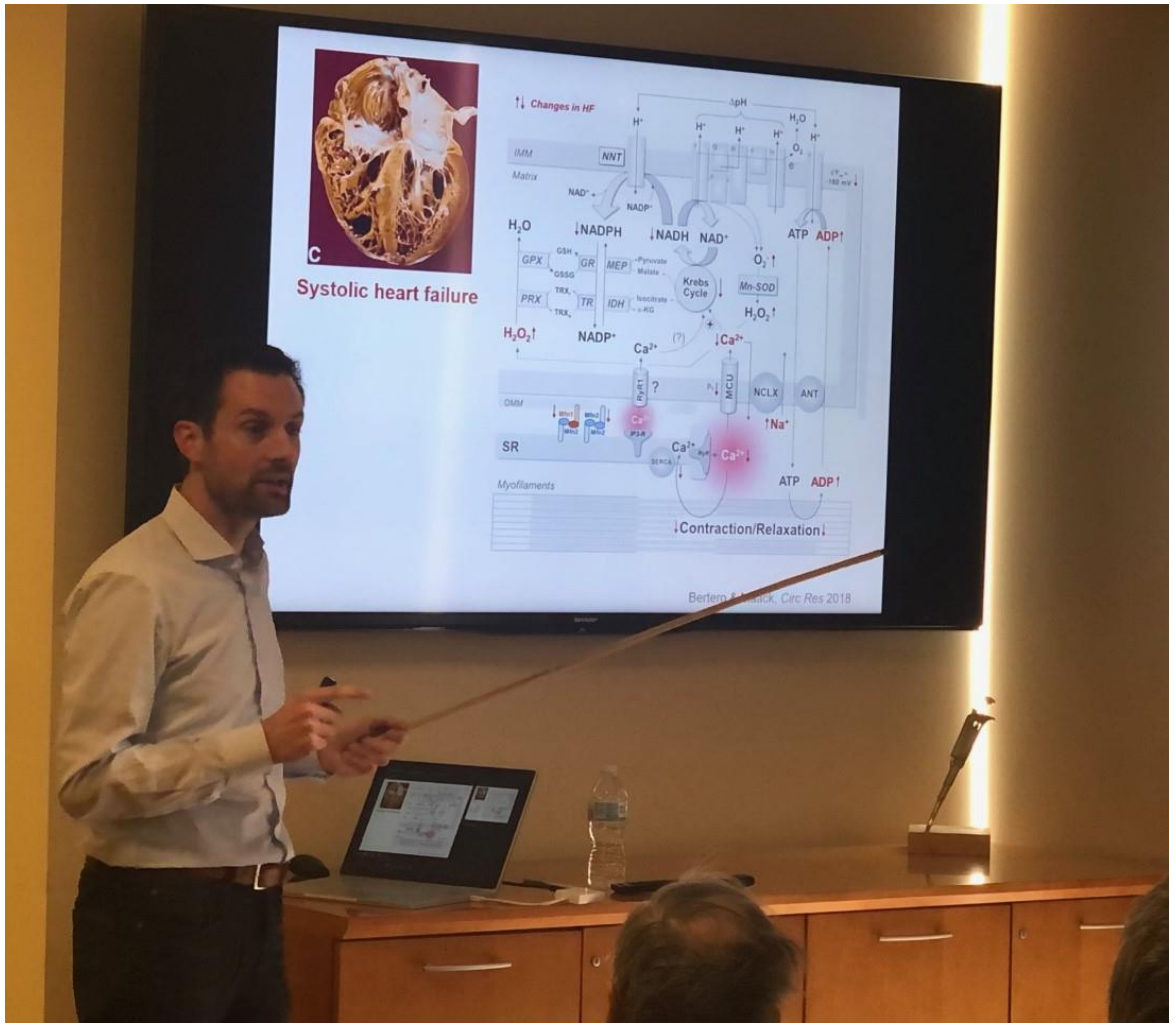
Mitoween


EXIT


Autophagy
Lipid
droplet
tethered to
the mito
Mito
Apoptosis
(Fire = ATP)
tBid

The 2019 Cold Spring Harbor Mitochondria conference gives an opportunity to visit Xingguo in Guangzhou

Cristoph Maack at MitoCircle



Bye Bye decade 10s, Hello to the waves of the 20s!!!