
2023

# MitoCircle Seminars: the 2023 edition

Veronica Eisner, PhD - Department of Cellular and Molecular Biology, Pontificia Universidad Católica de Chile
OPA1 disease-causing mutations perturb mitochondrial mtDNA-carrying nucleoid distribution
March 3rd, 9:30AM

Gary Yellen, PhD - Department of Neurobiology, Harvard Medical School
Brain cell metabolism and excitability: a two-way stress
March 7th, 11AM

Gyuri's Birthday Symposium! – 38 talks by Friends and Trainees from Canada, Chile, China, France, Israel, Italy, Switzerland, UK, US (8 states), co-organized with Janine H. Santos, PhD, NIEHS
June 2-3 (1.5 days)

Alessia Ciarrocchi, PhD - Head of Translational Research Laboratory, Emilia-Romagna, Italy
Coding or non-coding? How the two sides of the genome drive transcription adaptation in cancer
May 15th, Noon

Toni Barrientos, PhD - Department of Neurology, University of Miami
The mitochondrial mRNA folding landscape
Nov 7th, 11AM

Roberto Dominguez, PhD - Department of Physiology, University of Pennsylvania
Mechanisms controlling actin filament barbed and pointed end dynamics
Dec 12th, 11AM

# Mito Circle Journal Club 2023 Summary

| Date | Name | Paper |
|---|---|---|
| January 9 | Steve Hurst | **Intercellular Mitochondrial Transfer as a Rescue Mechanism in Response to Protein Import Failure.** Needs et al 2022 *BioRxiv* |
| January 23 | Gyuri Hajnoczky | **EFHD1 ablation inhibits cardiac mitoflash activation and protects cardiomyocytes from ischemia.** Eberhardt et al. 2022 *JMCC* |
| February 27 | Biophysics Briefings | |
| March 13 | Caitlyn Cardetti | **Nuclear genetic control of mtDNA copy number and heteroplasmy in humans. Gupta et al. 2023**. *BioRxiv*. |
| April 3 | Gyuri Csordas | **Structural basis of mitochondrial membrane bending by the I–II–III2–IV2 supercomplex**. Mühleip et al. 2023 *Nature* |
| April 10 | Ariele Baggett | **OMA1-mediated integrated stress response protects against ferroptosis in mitochondrial cardiomyopathy.** Ahola et al. *Cell Metab* |
| April 24 | Erin Seifert | **Lactate metabolism is essential in early-onset mitochondrial myopathy.** Chen et al. 2023. *Sci. Advances* |
| May 8 | Marilen Federico | **Mitochondrial Fission Process 1 controls inner membrane integrity and protects against heart failure.** Donnarumma et al. 2022 *Nat Commun* |
| May 22 | Elena Berezhnaya | **Mitochondria metabolism sets the species-specific tempo of neuronal development**. Iwata et al. 2023 *Science* |
| September 11 | Marco Tigano | **Cooperative sensing of mitochondrial DNA by ZBP1 and cGAS promotes cardiotoxicity**. Lei et al. 2023 *Cell* |
| September 25 | Victor Hugo | **NME3 binds to phosphatidic acid and mediates PLD6-induced mitochondrial tethering.** Su et al. 2023 *J Cell Biol* |
| October 9 | Piyush Mishra | **TRIM21 inhibits irradiation-induced mitochondrial DNA release and impairs antitumour immunity in nasopharyngeal carcinoma tumour models.** Li et al. 2023 *Nat Commun* |
| October 23 | Raghavendra Singh | **Postsynaptic Calcium Extrusion at the Mouse Neuromuscular Junction Alkalinizes the Synaptic Cleft**. Durbin et al. 2023 *J Neurosci.* |
| November 6 | Ben Cartes Saavendra | **The mitochondrial fusion protein OPA1 is dispensable in the liver and its absence induces mitohormesis to protect liver from drug-induced injury.** Lee et al. 2023. *Nat Commun* |
| November 20 | Arijita Gosh | **ESYT1 tethers the ER to mitochondria and is required for mitochondrial lipid and calcium homeostasis.** Janer et al. 2023 *Life Sci Alliance* |
| December 18 | Shey-Shing Sheu | **Exposure to Static Magnetic and Electric Fields Treats Type 2 Diabetes.** Carter et al. 2020. *Cell Metab* |

Mansi & Piyush welcome Anika, their first child on Jan 4th

Aron Andresi, a data scientist joins the crew to work on analysis of 3D ultrastructure by AI

Dave Booth completes his postdoc in the Hajnoczky lab and joins the Joseph lab

# Good Luck Dave!

## Hajnoczky Lab 2011-2022


### Publications from MitoCare:

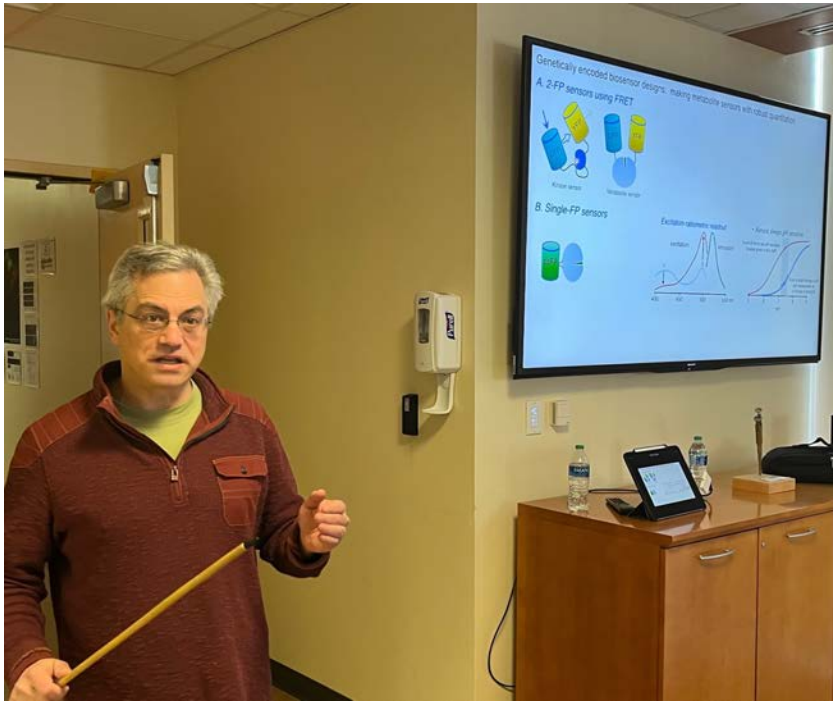
1: Çoku J, Booth DM, et al Reduced ER-mitochondria connectivity promotes neuroblastoma multidrug resistance. EMBO J. 2022
2: Márta K, Booth D, Csordás G, Hajnóczky G. Fluorescent protein transgenic mice for the study of Ca2+ and redox signaling. Free Radic Biol Med. 2022
3: Young MP, Schug ZT, Booth DM, Yule DI, Mikoshiba K, Hajnóczky G, Joseph SK. Metabolic adaptation to the chronic loss of Ca2+ signaling induced by KO of IP3 receptors or the mitochondrial Ca2+ uniporter. J Biol Chem. 2022
4: Booth DM, Várnai P, Joseph SK, Hajnóczky G. Oxidative bursts of single mitochondria mediate retrograde signaling toward the ER. Mol Cell. 2021
5: Joseph SK, Booth DM, et al Redox regulation of ER and mitochondrial Ca2+ signaling in cell survival and death. Cell
Calcium. 2019.
6: Booth DM, Enyedi B, Geiszt M, Várnai P, Hajnóczky G. Redox Nanodomains Are Induced by and Control Calcium Signaling at the ER-Mitochondrial Interface. Mol Cell. 2016
7: Booth DM, Joseph SK, Hajnóczky G. Subcellular ROS imaging methods: Relevance or the study of calcium signaling. Cell Calcium. 2016
8: Hajnóczky G, Booth D, et al Reliance of ER-mitochondrial calcium signaling on mitochondrial EF-hand Ca2+ binding proteins: Miros, MICUs, LETM1 and solute carriers. Curr Opin Cell Biol. 2014

# The 2023 Faculty Photoshoot

From left to right
Sitting;
György **Csordás**
Erin L Seifert
Standing;
Rajarshi Chakrabarti
Jan B Hoek
Suresh K Joseph
David Weaver
György Hajnóczky
Marco Tigano

Shey Shing Sheu
Missed the photoshoot

# Gary Yellen stops by for a presentation and discussion




# Verónica Eisner returns to MitoCare to present a seminar and to celebrate Benjamin Cartes Saavedra's main PhD paper from her lab




PNAS RESEARCH ARTICLE | CELL BIOLOGY

## *OPA1* disease-causing mutants have domain-specific effects on mitochondrial ultrastructure and fusion

Benjamín Cartes-Saavedra[a,b,1], Daniel Lagos[a,1], Josefa Macuada[a], Duxan Arancibia[a,c], Florence Burté[d], Marcela K. Sjöberg-Herrera[a], María Estela Andrés[a], Rita Horvath[e], Patrick Yu-Wai-Man[e,f,g,h,i], György Hajnóczky[b], and Verónica Eisner[a,2]

Edited by Antonio Zorzano, Institut de Recerca Biomedica, Barcelona, Spain; received May 12, 2022; accepted January 23, 2023 by Editorial Board Member Francisco Bezanilla

**Inner mitochondrial membrane fusion and cristae shape depend on optic atrophy protein 1, OPA1. Mutations in *OPA1* lead to autosomal dominant optic atrophy (ADOA), an important cause of inherited blindness. The Guanosin Triphosphatase (GTPase) and GTPase effector domains (GEDs) of OPA1 are essential for mitochondrial fusion; yet, their specific roles remain elusive. Intriguingly, patients carrying *OPA1* GTPase mutations have a higher risk of developing more severe multisystemic symptoms in addition to optic atrophy, suggesting pathogenic contributions for the GTPase and GED domains, respectively. We studied *OPA1* GTPase and GED mutations to understand their domain-specific contribution to protein function by analyzing patient-derived cells and gain-of-function paradigms. Mitochondria from *OPA1* GTPase (c.870+5G>A and c.889C>T) and GED (c.2713C>T and c.2818+5G>A) mutants display distinct aberrant cristae ultrastructure. While all OPA1 mutants inhibited mitochondrial fusion, some GTPase mutants resulted in elongated mitochondria, suggesting fission inhibition. We show that the GED is dispensable for fusion and OPA1 oligomer formation but necessary for GTPase activity. Finally, splicing defect mutants displayed a posttranslational haploinsufficiency-like phenotype but retained domain-specific dysfunctions. Thus, OPA1 domain-specific mutants result in distinct impairments in mitochondrial dynamics, providing insight into OPA1 function and its contribution to ADOA pathogenesis and severity.**

mitochondria | OPA1 | ADOA | dynamics | cristae

### Significance

OPA1 mediates inner mitochondrial membrane dynamic reshaping, and mutations affecting this protein cause autosomal dominant optic atrophy (ADOA), a leading cause of inherited blindness. This study explored *OPA1* GTPase and GTPase effector domain (GED) mutants. The domain-specific *OPA1* mutants exhibited distinctive ultrastructural cristae defects. *OPA1* mutants carrying GED defects retained partial fusion activity and partial GTPase function. In comparison, defects in mitochondrial fusion and fission were observed in GTPase mutants, which are linked to more severe multisystemic forms of ADOA. These contrasting effects on mitochondrial dynamics could account for the diverse mitochondrial morphology phenotypes observed. Thus, our data highlight each domain's contribution to OPA1 dysfunction and might provide clues to the factors driving ADOA pathogenesis and severity.

Mitochondria undergo constant restructuring by fusion, fission, and cristae reshaping. These support bioenergetic function and cellular fate decisions (1–3), helping the cell to adapt to various genetic and environmental conditions (4, 5). The fusion of two contiguous mitochondria involves sequential mixing of the outer membrane (OMM), intermembrane space, inner membrane (IMM), and the matrix components (6, 7). Fusion is required to rescue damaged mitochondria by supporting mitochondria DNA (mtDNA) stability and replication (3, 8), complementation of OMM components (9), and cristae biogenesis (10). Fusion is orchestrated by MFN1/MFN2 (6) and OPA1 proteins (11), assisting OMM and IMM fusion, respectively (6). These proteins are members of the dynamin-related protein family, which displays conserved GTPase and GTPase effector domains (GED) (12).

*OPA1* is a nuclear gene that encodes eight different isoforms (gene ID: 4876). Splice sites 1 and 2 are relevant for protein processing and lead to long and short forms of OPA1 (13, 14). Originally linked to IMM fusion (15), OPA1 plays additional roles in cristae maintenance (16) and mitochondrial fission (17). OPA1 facilitates IMM fusion by means of a GTP-coupled reaction and interaction with cardiolipin (18, 19). To support cristae biogenesis and cristae junction maintenance, OPA1 interacts with the mitochondrial contact site and cristae organizing system (MICOS) complex (20, 21). The different domains of the OPA1 protein are involved in distinct functions. For example, the coiled-coil domain 1 is important for protein–protein interaction, and the GTPase domain is relevant for fusion activity (22); while the GED region, predicted as coiled-coil domain 2, is required to assist the GTPase activity (23). Although all 8 OPA1 isoforms carry both GTPase and GED domains (24) and have redundant roles on mitochondrial ultrastructure, only the long forms of OPA1 rescue mitochondrial fusion in *Opa1* null cells (25). We recently showed that the OPA1 GED region determines endoplasmic reticulum-to-mitochondria $Ca^{2+}$ transference (26). An open question remaining in the field is whether the GTPase and GED regions have specific contributions to the roles of OPA1 in IMM fusion, cristae maintenance, or fission.

The complete absence of OPA1 is incompatible with life, as demonstrated by the embryonic lethality of *Opa1* knock-out mice (27). Heterozygous *OPA1* mutations lead to autosomal dominant optic atrophy (ADOA, Mendelian Inheritance in Man (MIM)

The authors declare no competing interest.

This article is a PNAS Direct Submission. A.Z. is a guest editor invited by the Editorial Board.



[1]B.C.-S. and D.L. contributed equally to this work.

[2]To whom correspondence may be addressed. Email: veisner@bio.puc.cl.

This article contains supporting information online at https://www.pnas.org/lookup/suppl/doi:10.1073/pnas.2207471120/-/DCSupplemental.

Published March 16, 2023.

Verónica's sons:
Juan-Diego
Alonso
who was born
while Verónica
was a postdoc
at MitoCare

# Marta welcomes Emma on March 25th!

Budapest, Hungary

# The first brain mitochondrion with completely resolved internal membrane structure

# Happy Raj Lab Start

# Raj's Incredible start with grants

BROWN BROTHERS HARRIMAN

February 8, 2023

Thomas Jefferson University
833 Chestnut Street
Philadelphia, PA 19107-4414

Attention: Jeanmarie Johnston, Assistant to the Director

***RE: Margaret Q. Landenberger Research Foundation***
***Principal Investigator: Rajarshi Chakrabarti, Ph.D.***

Dear Ms. Johnston:

Please be advised that Brown Brothers Harriman Trust Company of Delaware, N.A., as Trustee of the Margaret Q. Landenberger Research Foundation, has approved your grant request in the amount of $200,000.00 over two (2) consecutive years, to study Roles of peri-mitochondrial actin assembly in models of mitochondrial dysfunction, as submitted by Rajarshi Chakrabarti, Ph.D.. You will receive the first year's grant payment shortly. The second year of this grant will be **contingent** on the receipt by **December 1, 2023** of a progress report, to be reviewed by the Foundation's Scientific Advisory Board, and approved by the Trustee.

Upon receipt of the grant payment, kindly acknowledge your receipt of the grant and your agreement to furnish a progress report by executing and returning the acknowledgement copy of this letter to me at susan.whartnaby@bbh.com, or at the address below.

Congratulations, and we look forward to learning more about your work in this area!

Respectfully,

Susan J. Whartnaby

Susan J. Whartnaby
Assistant Vice President

Enclosures
cc: Rajarshi Chakrabarti, Ph.D. (rajarshi.chakrabarti@jefferson.edu)
Melissa Elgendy (Melissa.Elgendy@jefferson.edu)
Justin McCusker (Justin.McCusker@jefferson.edu)

**Department of Health and Human Services**
National Institutes of Health
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

**Notice of Award**
FAIN# R35GM150811
**Federal Award Date**
08/21/2023

**Recipient Information**

**1. Recipient Name**
THOMAS JEFFERSON UNIVERSITY
1020 WALNUT ST
PHILADELPHIA, PA 19107

**2. Congressional District of Recipient**
02

**3. Payment System Identifier (ID)**
1231352651A1

**4. Employer Identification Number (EIN)**
231352651

**5. Data Universal Numbering System (DUNS)**
053284659

**6. Recipient's Unique Entity Identifier**
R8JEVL4ULGB7

**7. Project Director or Principal Investigator**
Rajarshi Chakrabarti, PHD

ryc092@jefferson.edu
215-503-1594

**8. Authorized Official**
Mrs Jeanmarie Johnston

**Federal Agency Information**

**9. Awarding Agency Contact Information**
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Program Officer
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**Federal Award Information**

**11. Award Number**
1R35GM150811-01

**12. Unique Federal Award Identification Number (FAIN)**
R35GM150811

**13. Statutory Authority**
42 USC 241 42 CFR 52

**14. Federal Award Project Title**
Elucidating the roles for discrete actin filaments in maintenance of organelle and cellular homeostasis

**15. Assistance Listing Number**
93.859

**16. Assistance Listing Program Title**
Biomedical Research and Research Training

**17. Award Action Type**
New Competing

**18. Is the Award R&D?**
Yes

**Summary Federal Award Financial Information**

| | |
|---|---|
| **19. Budget Period Start Date** 08/21/2023 – **End Date** 07/31/2024 | |
| **20. Total Amount of Federal Funds Obligated by this Action** | $390,000 |
| 20 a. Direct Cost Amount | $250,000 |
| 20 b. Indirect Cost Amount | $140,000 |
| **21.** Authorized Carryover | |
| **22.** Offset | |
| **23.** Total Amount of Federal Funds Obligated this budget period | $390,000 |
| **24. Total Approved Cost Sharing or Matching, where applicable** | $0 |
| **25. Total Federal and Non-Federal Approved this Budget Period** | $390,000 |
| **26. Project Period Start Date** 08/21/2023 – **End Date** 07/31/2028 | |
| **27.** Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period | $390,000 |

**28. Authorized Treatment of Program Income**
Additional Costs

**29. Grants Management Officer - Signature**
Brett Hodgkins

**30. Remarks**
Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise

# Also, NIH grant success for the Hajnoczky lab

**SUMMARY STATEMENT**

**PROGRAM CONTACT:**
**Jill Morris**
**301-496-5745**
**morrisja2@mail.nih.gov**

**( Privileged Communication )**

***Release Date:*** **11/29/2022**
***Revised Date:***

***Application Number:*** **1 R01 NS132056-01**

**Principal Investigator**

**HAJNOCZKY, GYORGY**

**Applicant Organization: THOMAS JEFFERSON UNIVERSITY**

***Review Group:*** **NOMD**
**Neural Oxidative Metabolism and Death Study Section**

***Meeting Date:*** **11/03/2022**
***Council:*** **JAN 2023**
***Requested Start:*** **04/01/2023**

***RFA/PA:*** **PA20-185**
***PCC:*** **MORRIJNG**

***Project Title:*** **Mitochondrial Calcium and Neuronal Health**

***SRG Action:*** **Impact Score:20 Percentile:1**
***Next Steps:*** **Visit https://grants.nih.gov/grants/next_steps.htm**
**Human Subjects:** **10-No human subjects involved**
**Animal Subjects:** **30-Vertebrate animals involved - no SRG concerns noted**

**SUMMARY STATEMENT**

**PROGRAM CONTACT:**
**CHIEN-CHUNG Chao**
**301 594 3474**
**chris.chao@nih.gov**

**( Privileged Communication )**

***Release Date:*** **02/02/2023**
***Revised Date:***

***Application Number:*** **1 R01 GM151536-01**

**Principal Investigator**

**HAJNOCZKY, GYORGY**

**Applicant Organization: THOMAS JEFFERSON UNIVERSITY**

***Review Group:*** **CSRS**
**Cellular Signaling and Regulatory Systems Study Section**

***Meeting Date:*** **01/26/2023**
***Council:*** **MAY 2023**
***Requested Start:*** **07/01/2023**

***RFA/PA:*** **PA20-185**
***PCC:*** **P164CC**

***Project Title:*** **Mitochondrial Calcium Uniporter in Signaling and Dynamics**

***SRG Action:*** **Impact Score:24 Percentile:6**
***Next Steps:*** **Visit https://grants.nih.gov/grants/next_steps.htm**
**Human Subjects:** **10-No human subjects involved**
**Animal Subjects:** **30-Vertebrate animals involved - no SRG concerns noted**

Heroic effort and great success by the Csordas & Sheu labs

Circulation Research

FULL ACCESS | RESEARCH ARTICLE

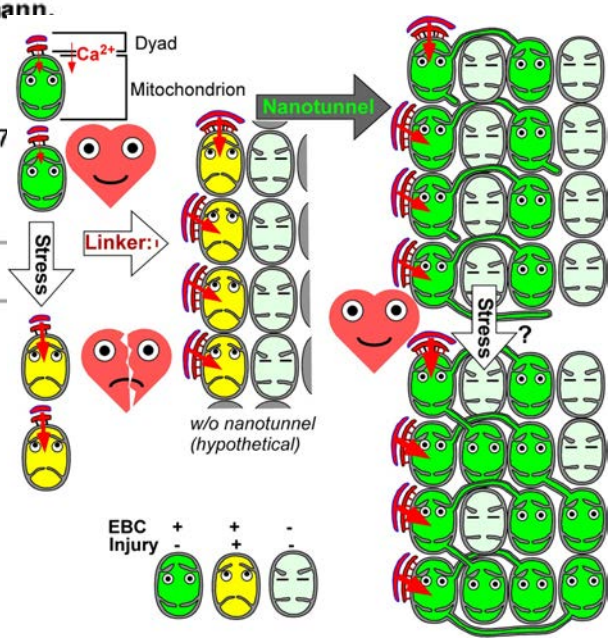
Details Related References Figures

# Enhanced Mitochondria-SR Tethering Triggers Adaptive Cardiac Muscle Remodeling

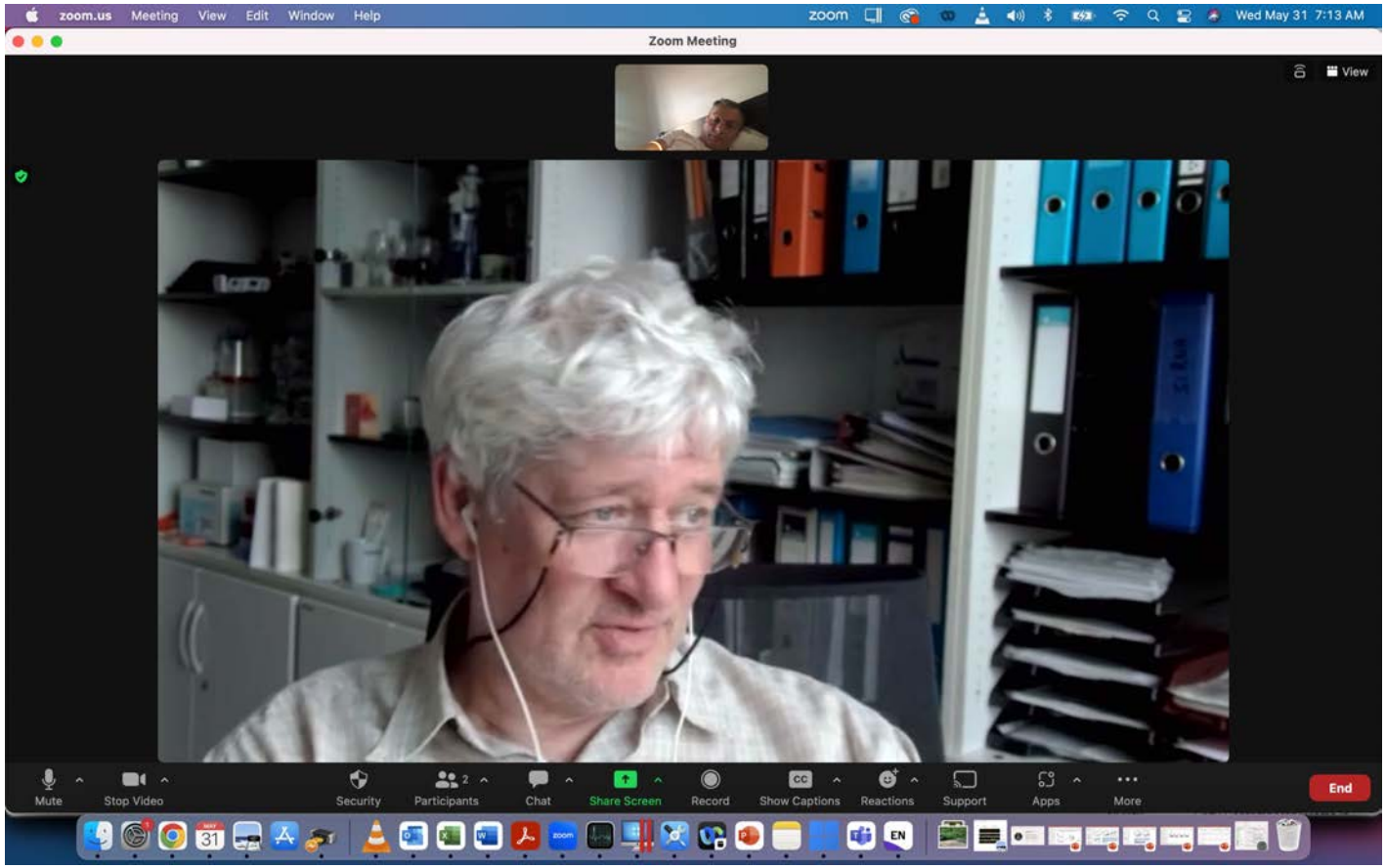
Zuzana Nichtová, Celia Fernandez-Sanz, Sergio De La Fuente, Yuexing Yuan, Stephen Hurst, Sebastian Lanvermann, Hui-Ying Tsai, David Weaver, Ariele Baggett, Christopher Thompson, Cedric Bouchet-Marquis, Péter Várnai, Erin L. Seifert, Gerald W. Dorn II, Shey-Shing Sheu and György Csordás

Originally published 14 Apr 2023 | https://doi.org/10.1161/CIRCRESAHA.122.321833 | Circulation Research. 2023;132:e171–e187

Zuzana joins the celebration



# Peter Varnai agrees to construct some new MICU mutants and chimeras



Marco is the only Broad Street 10 miler Trooper in 2023

MitoCare

presents:

# MitoCircle Seminar Series

## "Coding or non Coding? How the two sides of the genome drive transcription adaptation in cancer"

**SPEAKER**

**Alessia Ciarrocchi, Ph.D.**

IRCCS in Advanced Technologies and Care Models in Oncology
Head of the Translational Research Laboratory

**MAY 15 TH | AT 12PM**

MitoCare

*Jefferson Alumni Hall Room 527*

*1020 Locust Street, Philadelphia*

www.mitocare.org

Making the Invisible Visible
MitoCare

# Both Marco and Raj gave talks at the PGM Departmental Retreat

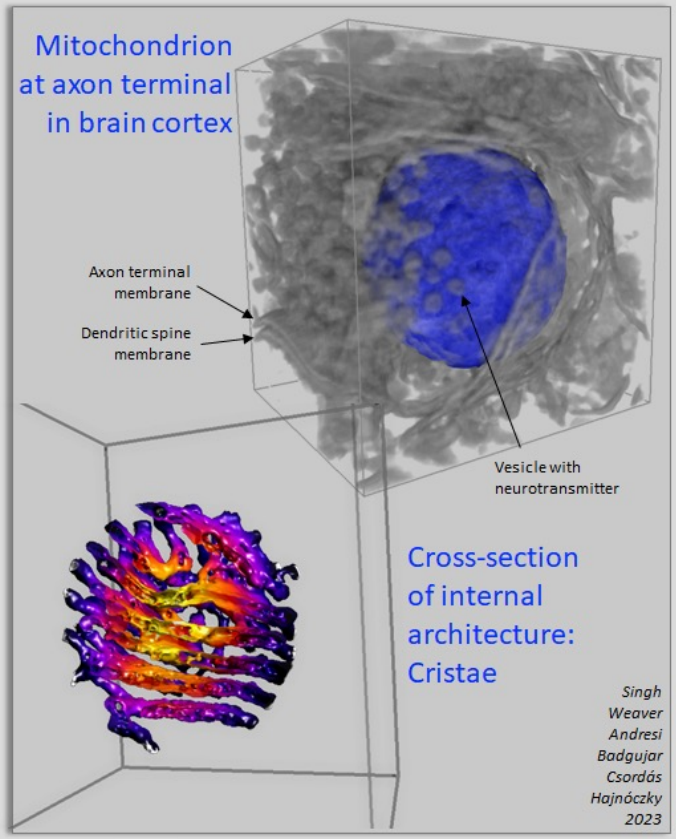
Elena (53cm  and 3595 gr) came to meet Pam and Benjamin on May 20th.

# Lets celebrate 7 birthdays at once

# Reconstructing and traveling inside brain mitochondria


Aron on a Virtual Reality Tour in a Mitochondrion

# $Ca^{2+}$, ER, Mitochondria, Friends and more: A Tribute to Gyuri Hajnóczky's Contributions to Science




MitoCare Est 2013

## $Ca^{2+}$, ER, Mitochondria, Friends and More: A Tribute to Gyuri Hajnóczky's Contributions to Science

**FRIDAY June 2nd 2023**

Eakins Lounge

**12:55 - 1:05 PM – Speakers check their talks**
**1:05 - 1:30 - Opening**

1:05 – 1:15 Organizers: Erin L Seifert (Thomas Jefferson University, TJU, USA) & Janine H Santos (NIEHS/NIH, USA)

1:15 – 1:20 PM Mark Tykocinski PhD, President of Thomas Jefferson University

1:20 – 1:30 PM Introduction: Andrew Thomas (Rutgers University, USA)

**Session 1: Mitochondria in the Brain and Beyond**

Chairs: Gyuri Hajnóczky (TJU, USA) and Thomas Schwarz (Harvard University, USA)

1:30 – 1:50 PM - Heidi McBride (McGill University) *Mitochondrial control of immune signaling and death*

1:50 – 2:05 PM - Bob Sergott (TJU) *Fluorescent lifetime imaging ophthalmoscopy (FLIO): detecting short-lived chromophore abnormalities in multiple sclerosis, Parkinson's and Alzheimer's and rare genetic diseases*

2:05 – 2:20 PM - Elena Berezhnaya (TJU) *MICU2 loss is associated with altered mitochondrial calcium signaling in the nervous system during development*

2:20 – 2:35 PM - Raghavendra Singh (TJU) *Synaptic dysfunction and neurodegeneration are associated with dysregulation of mitochondrial calcium homeostasis in MICU1KO mouse*

2:35 – 2:55 PM - Thomas Schwarz (Harvard University) *Mitos moving mRNA for mitophagy and mito-maintenance*

**2:55 – 3:20 PM Break - Speakers check their talks**

**Session 2: Mitochondria and Disease**

Chairs: Veronica Eisner (Pontificia Universidad Catolica de Chile, Chile) and Orian Shirihai (University of California Los Angeles, USA)

3:20 – 3:40 PM - Atan Gross (Weizmann Institute) *My career with BID, MTCH2, and α-Synuclein*

3:40 – 4:00 PM - Martin Picard (Columbia University) *The mitochondrial information processing system*

4:00 – 4:15 PM - Maria Castromonte (TJU) *Uveal melanoma*

4:15 – 4:35 PM - Michael Hogarty (Children's Hospital of Philadelphia) *The contribution of ERMCs to neuroblastoma therapy resistance*

4:35 – 4:55 PM - Doug Wallace (Children's Hospital of Philadelphia) *The mitochondrial physiology of COVID-19*

**4:55-5:15 PM Break - Speakers check their talks**

**Session 3: Structure and Dynamics of Mitochondria in Health and Disease**

Chairs: Janine Santos (NIEHS/NIH, USA) and Luca Scorrano (University of Padua, Italy)

5:15 – 5:35 PM - Veronica Eisner (Pontificia Universidad Catolica de Chile) *Mitochondria cristae adaptations in the aged heart*

5:35 – 5:50 PM - Dave Weaver (TJU) *Evaluating mitochondrial ultrastructure with deep learning*

5:50 – 6:10 PM - Xingguo Liu (Guangzhou Institutes of Biomedicine and Health) *Mitochondrial remodeling in pluripotent stem cell fate determination*

6:10 – 6:25 PM - Benjamin Cartes Saavedra (TJU) *Deciphering the role of MICU1 in mitochondrial dynamics*

6:25 – 6:45 PM - Orian Shirihai (University of California Los Angeles) *The great Hajnóczky*

**7:00 PM - Dinner - Eakins Lounge**

## SATURDAY June 3rd 2023

Eakins Lounge

**8:45 – 8:55 am Speakers check their talks**

**Session 4: Mitochondria in Calcium Signaling**

Chairs: Andrew Thomas (Rutgers University, USA) and Kai Ting Huang (University of Rochester, USA)

9:00 – 9:20 AM - David Yule (University of Rochester) *In vivo measurement of cytosolic and mitochondrial [Ca2+] in the exocrine pancreas*

9:20 – 9:40 AM - Yubin Zhou (Texas A&M University) *Engineering of novel genetically-encoded calcium indicators with high sensitivity*

9:40 – 9:55 AM - Mate Katona (University of Pittsburgh) *CYB5R5, a novel regulator of SOCE?*

9:55 – 10:15 AM - Mohamed Trebak (University of Pittsburgh) *Regulation of metabolism by CRAC channels in disease*

**10:15 - 10:30 AM Break - Speakers check their talks**

**Session 5: ER-Mitochondria Contacts**

Chairs: Nicolas Demaurex (University of Geneva, Switzerland) and György Csordás (TJU, USA)

10:30 – 10:50 AM - Tamás Balla (NICHD/NIH) *Control of mitochondrial fission-fusion dynamics by membrane lipids*

10:50 – 11:05 AM - Arijita Ghosh (TJU) *Effect of high-fat diet on ERMC in liver with a focus on IP3R*

11:05 – 11:25 AM - Rajarshi Chakrabarti (TJU) *Insights into actin mediated ER-Mitochondria crosstalk*

11:25 – 11:40 AM - David Booth (TJU) *Interorganelle redox signaling: Imaging dynamic redox nanodomains*

11:40 – 12:00 PM - Luca Scorrano (University of Padova) *Splice variants of mitofusin 2 shape the endoplasmic reticulum and tether it to mitochondria*

**12:00 - 1:30 PM Lunch Break (Eakins Lounge) - visit to MitoCare**

**1:15 – 1:30 - Speakers check their talks**

**Session 6: Mitochondrial Cell Death, Repair and Health Outcomes**

Chairs: Heidi McBride (McGill University, Canada) and Atan Gross (Weizmann Institute, Israel)

1:30 – 1:50 PM - György Szabadkai (University College London) *Myc and mitochondria: is it all plain sailing*

1:50 – 2:05 PM - Piyush Mishra (TJU) *Heterogeneity of VDAC2-Bak mediated apoptosis can be exploited for effective and selective treatment against primary and metastatic liver cancer*

2:05 – 2:25 PM - Zachary Schug (Wistar Institute) *Acetate metabolism in cancer*

2:25 – 2:45 PM - Paolo Bernardi (University of Padova). *Assessing the mechanism of channel formation by mitochondrial ATP synthase*

**2:45-3:15 PM Break - Speakers check their talks**

**Session 7: Mitochondria in tissue homeostasis - I**

Chairs: Paolo Bernardi (University of Padova, Italy) and Gyuri Szabadkai (University College London, UK)

3:15 – 3:35 PM - John Elrod (Temple University) *Discovery of an essential regulator of mitochondrial calcium efflux*

3:35 – 3:50 PM - Prottoy Hasan (TJU) *Role of MICU1 and MICU2 in the control of cardiac mitochondrial Calcium Uniporter*

3:50 – 4:10 PM - Gyuri Csordás (TJU) *Cardiac mitochondrial adaptations to local encounters: inter-organelle and interpersonal links*

4:10 – 4:30 PM - Melanie Paillard (University of Lyon) *Regulation of mitochondrial $Ca^{2+}$ uptake: a therapeutic target in cardiometabolic diseases*

4:30 – 4:50 PM - Wally Koch (Temple University) *The GRK2 Interactome in cardiac myocytes: insights into stress-dependent signaling*

**4:50 - 5:10 PM Coffee Break - Speakers check their talks**

**Session 8: Mitochondria in tissue homeostasis -II**

Chairs: Larry Gaspers (Rutgers University, USA) and Erin Seifert (TJU, USA)

5:10 – 5:30 PM - Nika Danial (Harvard University) *Metabolic crosstalk and cellular adaptation to stress*

5:30 – 5:50 PM - Jyoti Jaiswal (George Washington University) *Opposing effects of acute and chronic mitochondrial ROS regulate muscle repair and disease*

5:50 – 6:10 PM - Rita Horvath (Cambridge University) *Secondary mitochondrial dysfunction in neuromuscular diseases*

6:10 – 6:30 PM - Shey-Shing Sheu (TJU) *Magnetoreception of cardiac mitochondria: from quantum biology to oxidative phosphorylation*

6:30 – 6:50 PM - Andrew Thomas (Rutgers University) *(Dis)integration of calcium signaling in non-alcoholic fatty liver disease*

**6:50 – 7:10 PM Final Thoughts and Closing Remarks**

Jan Hoek (TJU) and Orian Shirihai (UCLA)
Janine Santos (NIEHS/NIH) and Erin Seifert (TJU)

## Thank you to our Sponsors

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Cardiovascular Research Center, Lewis Katz School of Medicine

TEMPLE UNIVERSITY

VECTOR BIOLABS
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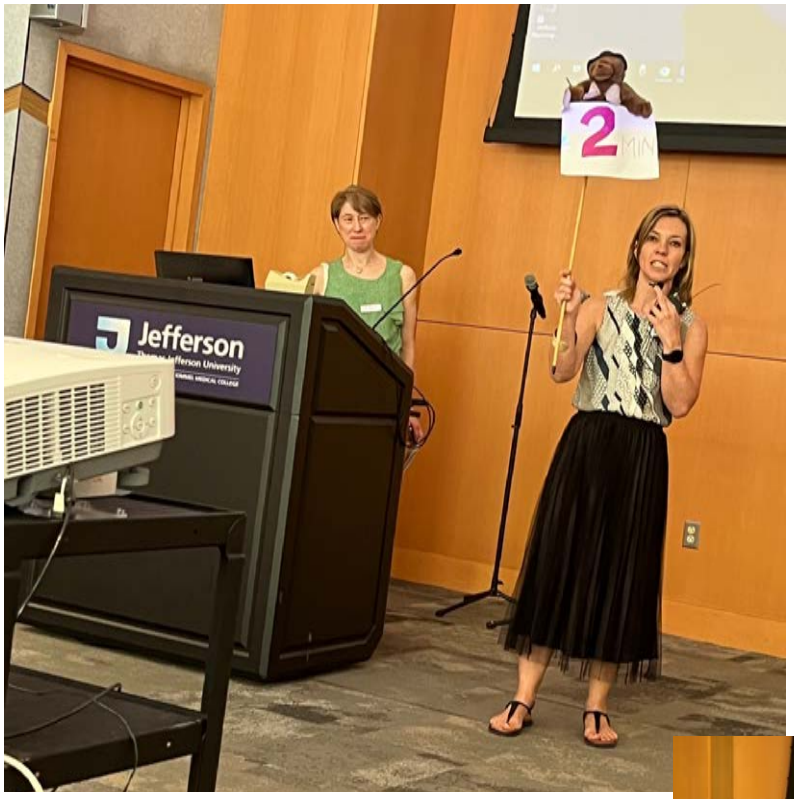
Leica BIOSYSTEMS

ingenious targeting laboratory

Thanks to Jenny Ngo for the t-shirt design!

# The Opening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2 MIN


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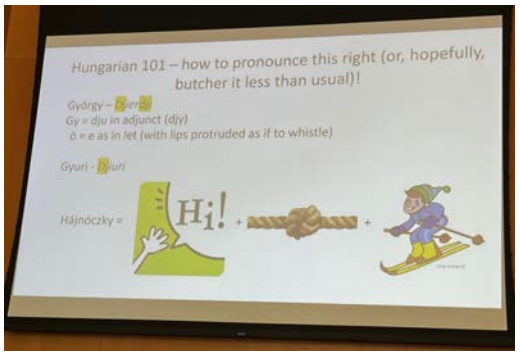
Thomas Jefferson University
HOME OF SIDNEY KIMMEL MEDICAL COLLEGE


Ca2+, ER, Mitochondria, Friends and More:
A Tribute to Gyuri Hajnóczky's Contributions to Science
Jefferson


Hungarian 101 – how to pronounce this right (or, hopefully, butcher it less than usual)!
György – Djerdj
Gy = dju in adjunct (djv)
ő = e as in let (with lips protruded as if to whistle)
Gyuri - Djuri
Hajnóczky =
Hi!

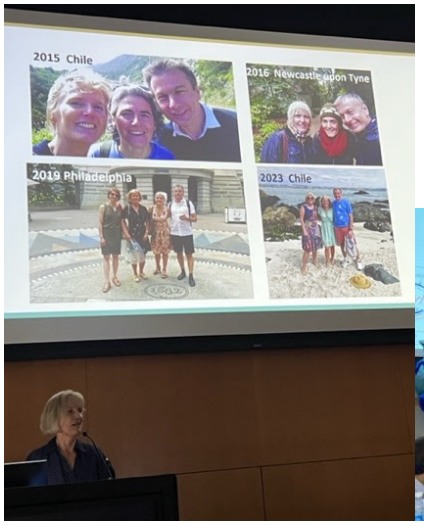

Jefferson




Some of the speakers (apology for not showing all)









Puskin utca (street) - where all started
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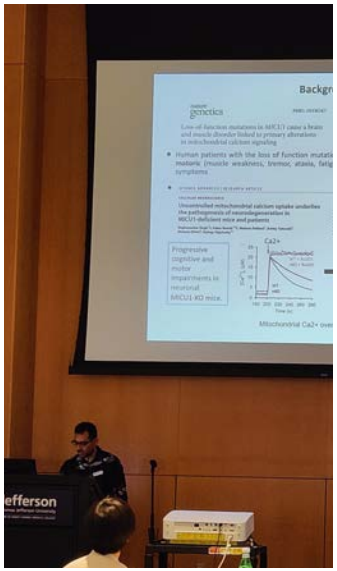
MICU2 loss is associated v
calcium signaling in the
develo
Elena Be
Hajnoczky Sympos
Jefferson
Thomas Jefferson University


nature genetics
Progressive cognitive and motor impairments in neuronal MICU1-KO mice.
Jefferson


Structure needs semantic understanding
Recognizing and extracting high-level features from the visual data
Coloring
Segmentation
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Thomas Jefferson University


Deciphering the role of
MICU1 on mitochondrial
fusion dynamics
Benjamin Carles-Saavedra, PhD.
bbd11@jefferson.edu
Postdoctoral Research Fellow
György Hajnóczky's lab
06-02-2023
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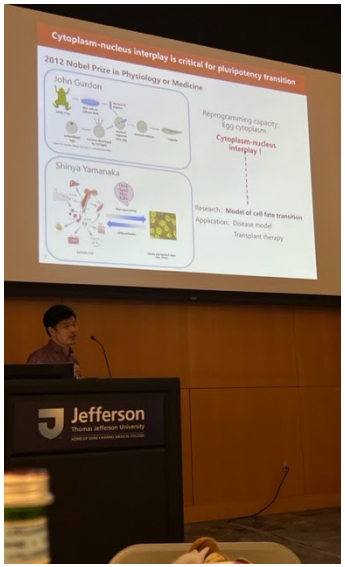
Thomas Jefferson University


Cytoplasm-nucleus interplay is critical for pluripotency transition
2012 Nobel Prize in Physiology or Medicine
John Gurdon
Reprogramming capacity:
Egg cytoplasm
Cytoplasm-nucleus interplay !
Shinya Yamanaka
Research: Model of cell fate transition
Application: Disease model
Transplant therapy
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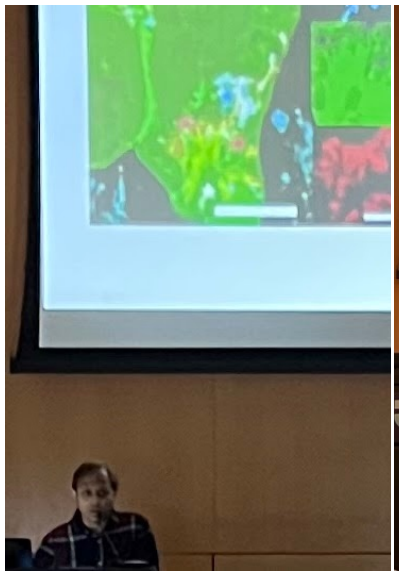


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Effect of high-fat diet (HFD) on
ERMC in liver with a focus on IP3R
ARIJITA GHOSH
MitoCare Center, Department of Pathology, Anatomy and Cell Biology,
Thomas Jefferson University, Philadelphia, USA
Jefferson
Thomas Jefferson University


In summary: Thanks to science we build friendships, a community, and a home.
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JOYEUX ANNIVERSAIRE GYURI
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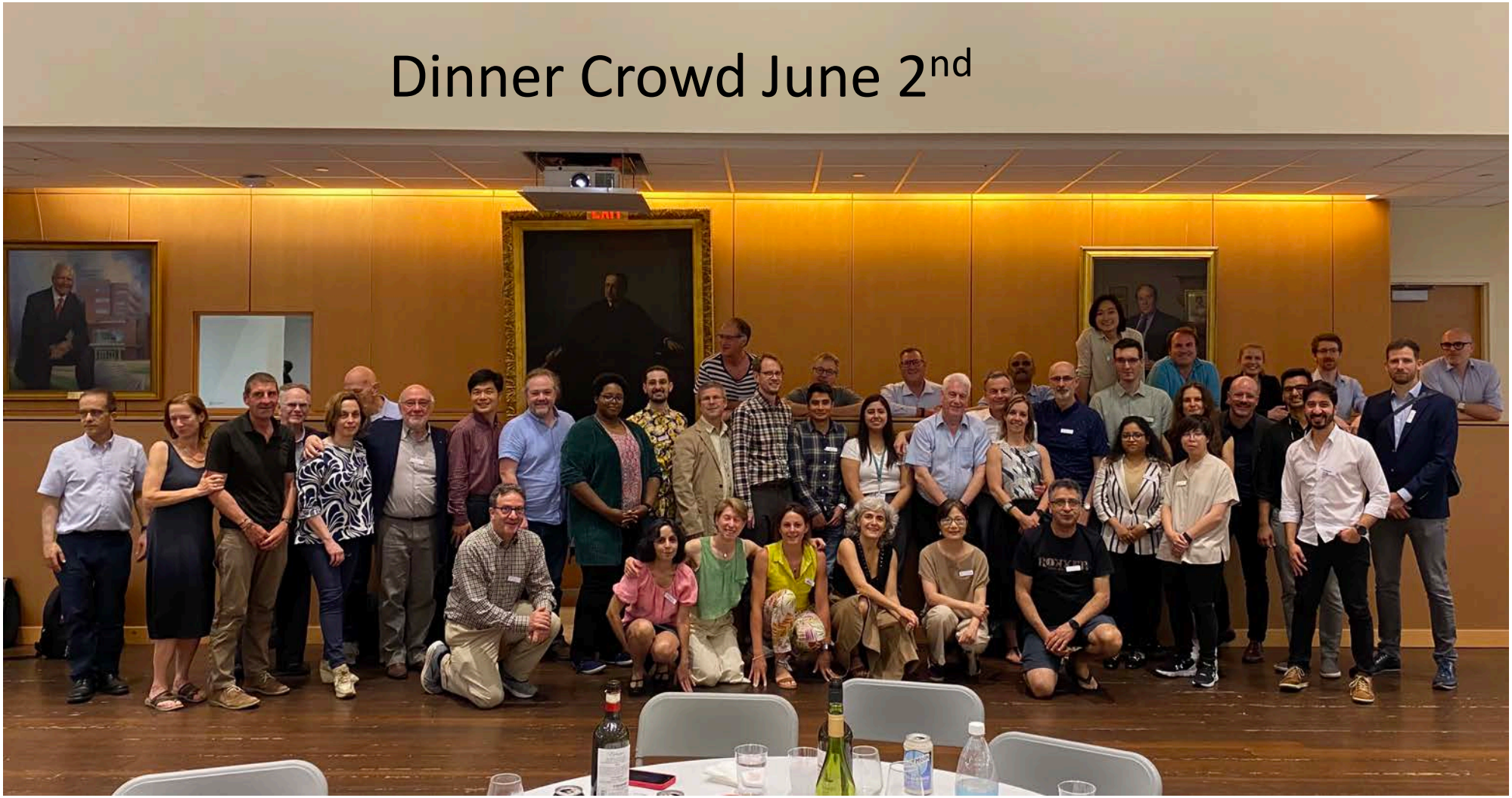
Thomas Jefferson University


Melanoma
Maria Teresa Marcia Castromonte Albina
Hajnóczky Symposium
June 2-4th 2023
Philadelphia, PA
Jefferson
Thomas Jefferson University

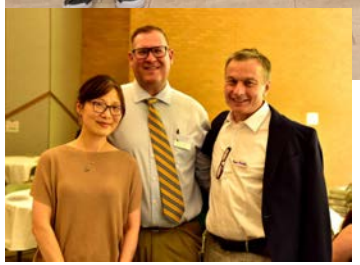
# Dinner Crowd June 2nd




Trivia

# The Closing

Thanks to
Erin and
Janine
for the
wonderful
organization




Hajnoczky Lab
Past members
(left)
And Current

# Dinner on June 3rd at Armada






# Garden Party on June 4th

## Garden Menu and Schedule *June 4, 2023*

Appetizers (starting 12 - 12:30pm)

- Hungarian Téliszalámi Sandwich (optional toppings: eggs, mini pickles, mayonnaise, horseradish mayonnaise)
- Foie Gras w Onion Jam and Red Pepper Jam
- Körözött (Hungarian Cottage Cheese Spread)
- Fresh Vegetables
- Olives
- Baguette *Erin Seifert*/Italian Bread/Crackers (GF Options Available)

Main (starting 1 - 1:30pm)

- Light Vegetarian Dish with Hungarian Touch *Julia Hajnoczky*
- Hungarian Spinach Stew *Éva Kőhegyi*
- Halászlé (Hungarian Fish soup), Erős Pista, Bread
- Paprikás Csirke with Nokedli (Hungarian Dumpling) *Éva Kőhegyi* and Hungarian Cucumber Salad *Gyuri Csordás*
- Beef Brisket and Chicken on the Grill *Norbert Csordás*

Dessert (starting 2:30 - 3:30pm)

- Somloi Galuska (Hungarian Trifle) *Áron Andrasi*
- Gesztenye Torta (Chestnut Cake) *Éva Kőhegyi*
- Berry cake *Janine Santos*
- Hungarian cookies & Marzipan
- Watermelon

Drinks

- Cava
- Collection of Hungarian wines from Lake Balaton, Villany & Szekszárd Regions
- Beer
- Soda + water + lemonade/juice

Virtual Reality Tour Inside an Axonal Mitochondrion (12 - 4pm)

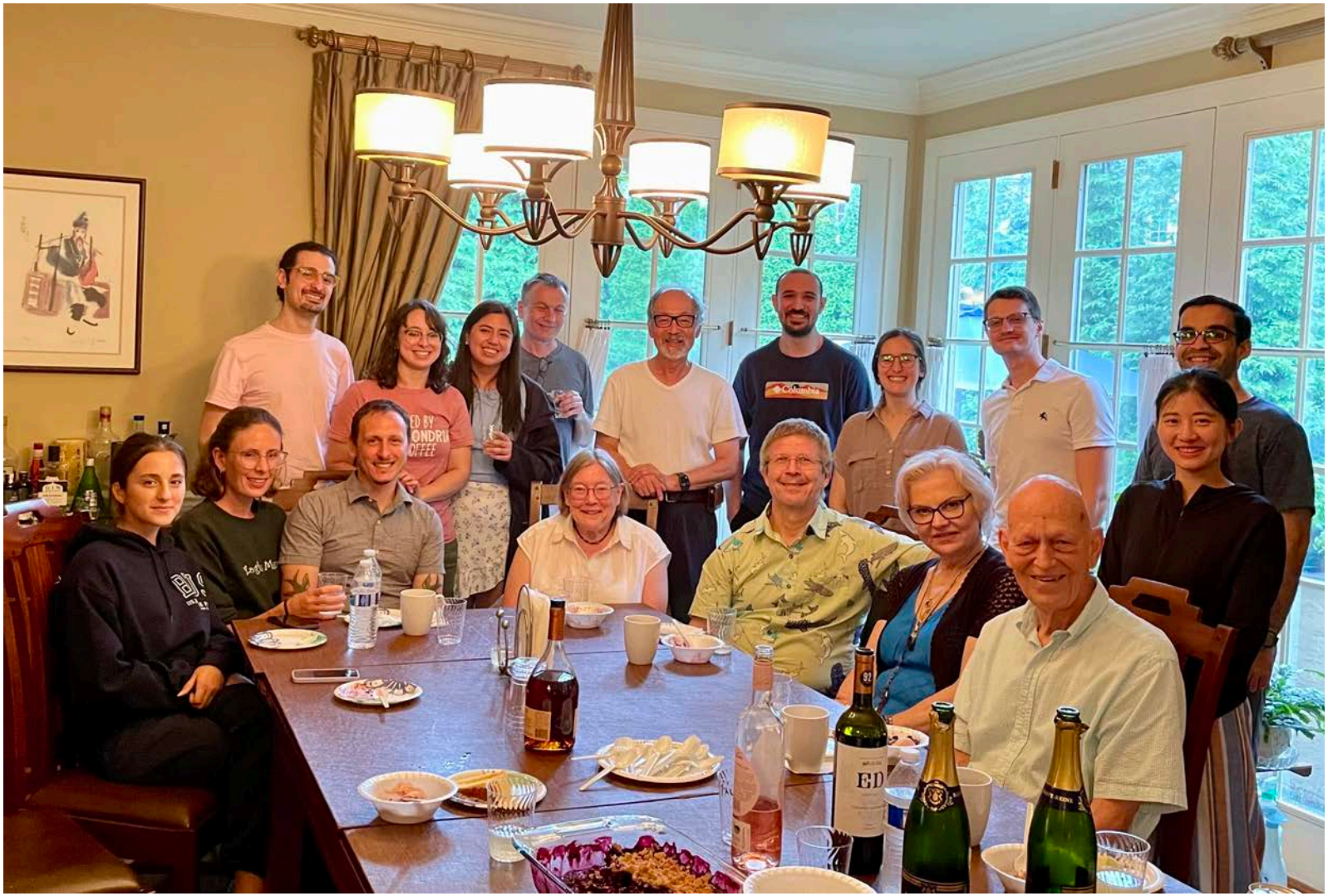
(10 - 15 min per person, please schedule with Áron Andrasi, Aron.Andrasi@jefferson.edu)

Setup: Janine Santos, Tamás Balla, Gyuri Szabadkai


Xingguo travelled back from China with his Daughter,
who was born while he did his postdoc in the Hajnoczky lab


# Ryan Cupo's happy announcement: Liam Cupo 06/13/23

# Party in Shey's House

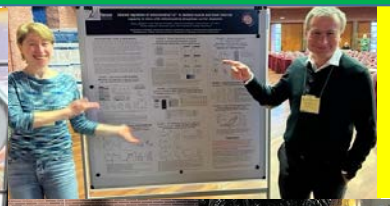


# Seifert Lab @ MitoCare 2023!

Brittney Blackburne, Amanda Collins, Shannon Lynch, and Matt Dina and Tiffany Veliz

Matt Dina's poster: therapeutics in Fxn kd mice

Tiffany Veliz's summer project wrap-up, with the lab



Presenting Cesar Vasquez's PiC-$Ca^{2+}$ study at the Mito Gordon, in Lucca

At UCLA: More feedback on Cesar PiC-$Ca^{2+}$ study

Welcome to Amanda, already fully into MCJC (the first post pandemic in vivo session)

Acyl-CoA colleagues, CoA meeting, Madison

In Suzhou

New grants:
DoD Discovery Award
NIH R01 GM136116
NIH R01 DK138011

| AWARD/CONTRACT | 1. THIS CONTRACT IS A RATED ORDER UNDER DPAS (15 CFR 700) | RATING | PAGE OF PAGES 1 \| 6 |
|---|---|---|---|
| 2. CONTRACT (Proc. Inst. Ident.) NO. HT94252310798 | 3. EFFECTIVE DATE 01 Sep 2023 | 4. REQUISITION/PURCHASE REQUEST/PROJECT NO. 0011872805 | |
| 5. ISSUED BY CODE HT9425 ARMY MED RES ACQ ACTIVITY 808 SCHREIDER ST FORT DETRICK MD 21702 | 6. ADMINISTERED BY (If other than Item 5) See Item 5 | CODE | |

**U.S. ARMY MEDICAL RESEARCH ACQUISITION ACTIVITY**
**AWARD SPECIFIC RESEARCH TERMS AND CONDITIONS**

**DIVISION I – AWARD COVER PAGES**

**DoD Discovery Award**

**A. Award Information**

1. **Department of Defense Awarding Office:** USAMRAA
2. **Award number/Project title:** HT9425-23-1-0798
3. **Type of Award:** Grant
4. **Type of Award Action:** New
5. **i. Brief description of project or program:** Inhibiting Mitochondrial Permeability Transition Pore Opening to Treat Mitochondrial Myopathy
   **ii. Funding Overview**

**From:** Laughlin, Maren (NIH/NIDDK) [E] <laughlinm@extra.niddk.nih.gov>
**Sent:** Friday, November 3, 2023 3:07 PM
**To:** Erin Seifert <Erin.Seifert@jefferson.edu>
**Subject:** NIH Business--1R01DK138011-01

**R01 from NIH NIDDK**

Dear Erin,

First, congratulations! We have permission to make an award on your grant application 1R01DK138011-01. At this point in time, we do not yet have our appropriation for FY24 and are on a continuing resolution until Nov 17, 2023. Your grant has a December 1 start date, and so please be aware that while we hope to make an award by that time, we do not have complete control over our business or schedule until we have a signed congressional appropriations bill.

I do expect that there will be a substantial cut in your budget, which will be over 25% of that requested. The proposed budget is $397,818 for each of 4 years. Given that, you may want to reduce your specific aims to be more in keeping with the actual award. Whereas in the past that was often done during the first year, it has become our policy to do that negotiation prior to award.

Please let me know if you have any questions for me. I will be in contact if I have additional questions for you as we work up your award.

Take care,
Maren

**Department of Health and Human Services**
National Institutes of Health
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

**Notice of Award**
FAIN# R01GM146116
**Federal Award Date**
08/31/2023

**R01 from NIH NIGMS**

**Recipient Information**

**1. Recipient Name**
THOMAS JEFFERSON UNIVERSITY
1020 WALNUT ST
PHILADELPHIA, PA 19107

**2. Congressional District of Recipient**
02

**3. Payment System Identifier (ID)**
1231352651A1

**4. Employer Identification Number (EIN)**
231352651

**5. Data Universal Numbering System (DUNS)**
053284659

**6. Recipient's Unique Entity Identifier**
R8JEVL4ULGB7

**7. Project Director or Principal Investigator**
Erin Seifert, PHD
Assistant Professor
els012@jefferson.edu
215-503-5030

**8. Authorized Official**
Burwell, Margaret
resadmin@jefferson.edu
215-503-6976

**Federal Agency Information**

**9. Awarding Agency Contact Information**
Kaui MacDonald Porche
Grants Management Specialist
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
kaui.macdonaldporche@nih.gov
(301) 594-1858

**10. Program Official Contact Information**
CHARLES KWAKU Ansong

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
charles.ansong@nih.gov
301-402-7421

**Federal Award Information**

**11. Award Number**
1R01GM146116-01A1

**12. Unique Federal Award Identification Number (FAIN)**
R01GM146116

**13. Statutory Authority**
42 USC 241 42 CFR 52

**14. Federal Award Project Title**
Relevance of mitochondrial calcium uniporter for mitochondrial myopathy

**15. Assistance Listing Number**
93.859

**16. Assistance Listing Program Title**
Biomedical Research and Research Training

**17. Award Action Type**
New Competing

**18. Is the Award R&D?**
Yes

**Summary Federal Award Financial Information**

| | |
|---|---|
| **19. Budget Period Start Date** 09/01/2023 – **End Date** 08/31/2024 | |
| **20. Total Amount of Federal Funds Obligated by this Action** | $411,840 |
| 20 a. Direct Cost Amount | $264,000 |
| 20 b. Indirect Cost Amount | $147,840 |
| **21.** Authorized Carryover | |
| **22.** Offset | |
| **23.** Total Amount of Federal Funds Obligated this budget period | $411,840 |
| **24. Total Approved Cost Sharing or Matching, where applicable** | $0 |
| **25. Total Federal and Non-Federal Approved this Budget Period** | $411,840 |
| **26. Project Period Start Date** 09/01/2023 – **End Date** 08/31/2027 | |
| **27.** Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period | $411,840 |

**28. Authorized Treatment of Program Income**
Additional Costs

**29. Grants Management Officer - Signature**
Kelly Aubrecht

**30. Remarks**
Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

# Melanie & Ludivine reminiscing about MitoCare in France

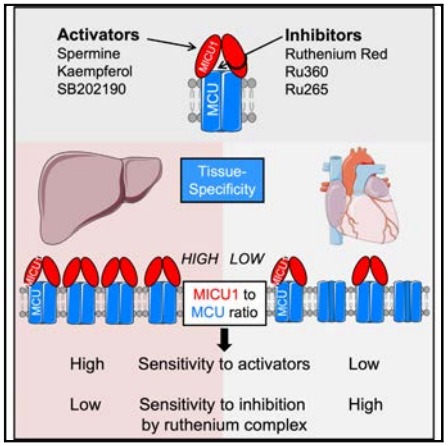
# New research papers highlighting Macarena's & Elena's work

Article

Cell Chemical Biology

## MICU1 controls the sensitivity of the mitochondrial $Ca^{2+}$ uniporter to activators and inhibitors

### Graphical abstract




### Authors

Macarena Rodríguez-Prados, Kai-Ting Huang, Katalin Márta, Melanie Paillard, György Csordás, Suresh K. Joseph, György Hajnóczky

### Correspondence

gyorgy.hajnoczky@jefferson.edu

### In brief

Rodríguez-Prados et al. report that the mitochondrial calcium uniporter's gating by MICU1 is the target of uniporter agonists and is a barrier for inhibitors like RuRed/Ru360/Ru265, which likely underlie heterogeneity in pharmacological targeting among tissues with different stoichiometry between MICU1 and the pore-forming protein, MCU.

### Highlights

- MICU1 is required for mtCU activators and is a barrier for inhibitors like RuRed
- The activators likely bind to MICU1 and prevent its gatekeeping activity
- Agonist-induced acute loss of the MICU1-dependent gatekeeping causes $Mn^{2+}$ toxicity
- Varying MICU1:MCU ratios yield tissue-specific outcomes for agonists and antagonists

Rodríguez-Prados et al., 2023, Cell Chemical Biology *30*, 1–12
June 15, 2023 
https://doi.org/10.1016/j.chembiol.2023.05.002

CellPress



PNAS RESEARCH ARTICLE | PHYSIOLOGY

## MICU1 occludes the mitochondrial calcium uniporter in divalent-free conditions

Macarena Rodríguez-Prados[a,1], Elena Berezhnaya[a,1], Maria Teresa Castromonte[a], Sergio L. Menezes-Filho[a], Melanie Paillard[a], and György Hajnóczky[a,2]

Edited by Richard Lewis, Stanford University, Stanford, CA; received November 6, 2022; accepted March 30, 2023

**Mitochondrial $Ca^{2+}$ uptake is mediated by the mitochondrial uniporter complex (mtCU) that includes a tetramer of the pore-forming subunit, MCU, a scaffold protein, EMRE, and the EF-hand regulatory subunit, MICU1 either homodimerized or heterodimerized with MICU2/3. MICU1 has been proposed to regulate $Ca^{2+}$ uptake via the mtCU by physically occluding the pore and preventing $Ca^{2+}$ flux at resting cytoplasmic [$Ca^{2+}$] (free calcium concentration) and to increase $Ca^{2+}$ flux at high [$Ca^{2+}$] due to cooperative activation of MICUs EF-hands. However, mtCU and MICU1 functioning when its EF-hands are unoccupied by $Ca^{2+}$ is poorly studied due to technical limitations. To overcome this barrier, we have studied the mtCU in divalent-free conditions by assessing the Ru265-sensitive $Na^+$ influx using fluorescence-based measurement of mitochondrial matrix [$Na^+$] (free sodium concentration) rise and the ensuing depolarization and swelling. We show an increase in all these measures of $Na^+$ uptake in MICU1KO cells as compared to wild-type (WT) and rescued MICU1KO HEK cells. However, mitochondria in WT cells and MICU1 stable-rescued cells still allowed some Ru265-sensitive $Na^+$ influx that was prevented by MICU1 in excess upon acute overexpression. Thus, MICU1 restricts the cation flux across the mtCU in the absence of $Ca^{2+}$, but even in cells with high endogenous MICU1 expression such as HEK, some mtCU seem to lack MICU1-dependent gating. We also show rearrangement of the mtCU and altered number of functional channels in MICU1KO and different rescues, and loss of MICU1 during mitoplast preparation, that together might have obscured the pore-blocking function of MICU1 in divalent-free conditions in previous studies.**

mitochondrial calcium uniporter | MICU1 | $Na^+$ | EMRE | mitoplast

$Ca^{2+}$ entry into mitochondria regulates cellular bioenergetics and survival and shapes intracellular $Ca^{2+}$ signals (1–3). Mitochondrial $Ca^{2+}$ uptake is mediated by the mitochondrial uniporter complex (mtCU) that includes a tetramer of the pore-forming subunit, mitochondrial calcium uniporter (MCU) (4, 5), and scaffold protein, essential MCU regulator (EMRE) (6), with the regulatory subunit, mitochondrial calcium uptake 1 (MICU1) (7) either homodimerized or heterodimerized with MICU2 (8) or MICU3 (9–16). MICUs have a pair of EF-hands that allows them to regulate $Ca^{2+}$ uptake via mtCU in a $Ca^{2+}$-dependent fashion (7). MICU1 and MICU2 EF-hand mutants were reported to completely abolish mitochondrial $Ca^{2+}$ uptake (17). MICU1 absence leads to the loss of $Ca^{2+}$ dependence of mitochondrial $Ca^{2+}$ uptake that was first observed as an increased $Ca^{2+}$ uptake via mtCU at low [$Ca^{2+}$] (free calcium concentration) and decreased $Ca^{2+}$ uptake at high [$Ca^{2+}$] in MICU1KO cells (17–20). This led to a conclusion that the MICU1 function is to set the threshold for $Ca^{2+}$ uptake via mtCU at low [$Ca^{2+}$] (20, 21), while enhancing it at high [$Ca^{2+}$] (20). MICU1 coimmunoprecipitation with MCU (5, 19) and mutational analysis suggested that MICU1 prevents $Ca^{2+}$ uptake via mtCU at low [$Ca^{2+}$] by electrostatically interacting with MCU and physically blocking the pore (22, 23). This was later confirmed in two human and beetle mtCU structures with human MICU1 in the presence and absence of $Ca^{2+}$ (24–26). A fourth structure showed only one state for mtCU with MICUs (27), which is similar to the structure obtained at high [$Ca^{2+}$] in the other studies.

MICU1 functioning in the mtCU at high [$Ca^{2+}$] is difficult to isolate from possible involvements of EMRE (28, 29), whereas its operation at resting low nanomolar physiological cytoplasmic [$Ca^{2+}$] remains poorly studied due to technical limitations. The threshold (or set point) for mitochondrial $Ca^{2+}$ uptake was well known before from studies on isolated mitochondria (30, 31) and is currently attributed to the occlusion of the mtCU pore by MICU1 when its EF-hands are unoccupied by $Ca^{2+}$ (21). However, little is known about ion permeation via mtCU under these conditions. A well-known approach to estimate $Ca^{2+}$ channel properties at low [$Ca^{2+}$] is to study permeation of monovalent ions in divalent-free conditions (32, 33). In the past, this allowed clarification of the gating mechanism and ion permeation through the pore for several $Ca^{2+}$ channels that were found to readily conduct $Na^+$ in the absence of divalent ions (32, 33).

### Significance

Calcium enters mitochondria via calcium uniporter and regulates cellular energy production and survival. The uniporter activity is tightly regulated by calcium that changes the channel functioning mainly by binding EF-hands of the regulatory MICU subunits. However, there is a controversy on how exactly this is implemented. Particularly, little is known on MICU1 and channel functioning in low-calcium conditions. We have demonstrated that MICU1 prevents ion permeation through the uniporter in divalent-free conditions, but MICU1-free channels seem to occur even in cells with high MICU1 abundance. Our finding is important for better understanding of the uniporter functioning in cells at resting calcium concentrations and for development of channel modulators as their action is often MICU1 dependent.

Author affiliations: [a]MitoCare Center, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107

Author contributions: M.R.-P., E.B., and G.H. designed research; M.R.-P., E.B., M.T.C., M.P., and G.H. performed research; S.L.M.-F. contributed new reagents/analytic tools; M.R.-P., E.B., M.T.C., and M.P. analyzed data; and M.R.-P., E.B., and G.H. wrote the paper.

The authors declare no competing interest.

This article is a PNAS Direct Submission.



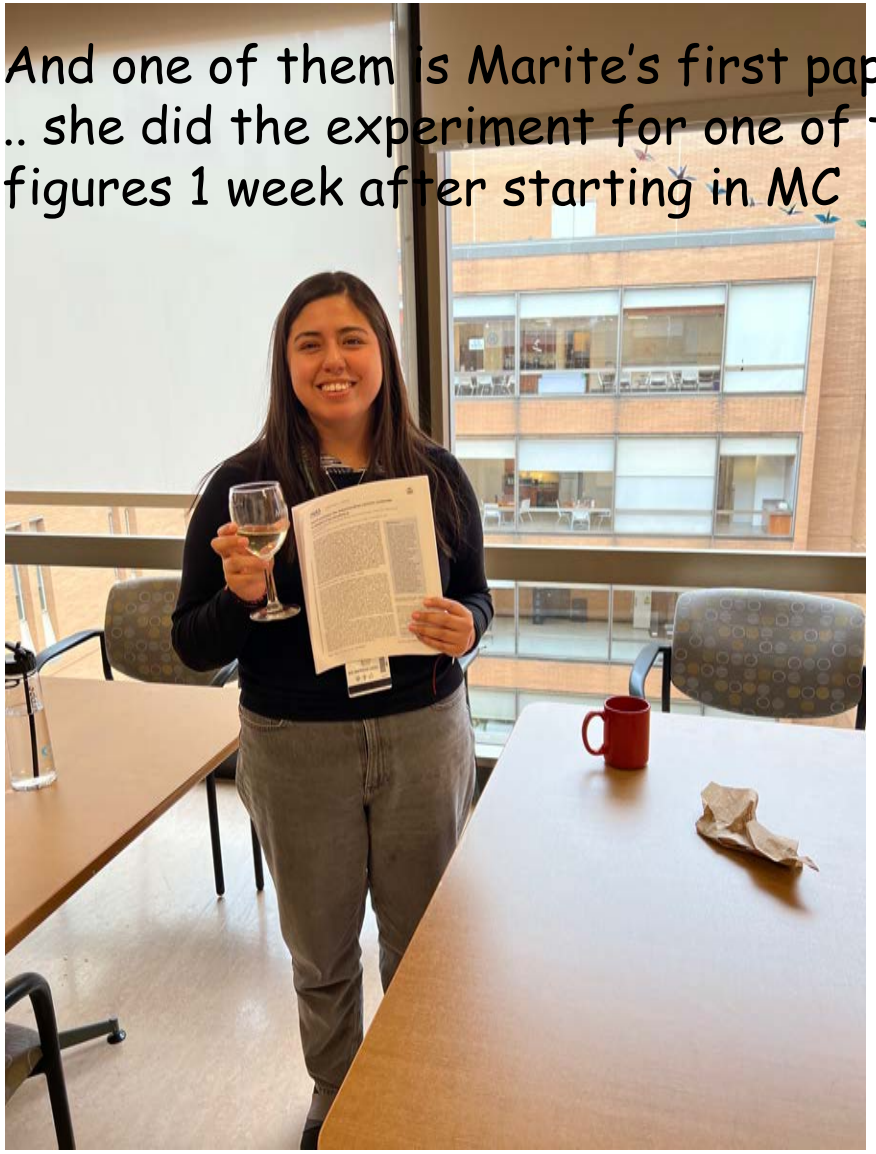
[1]M.R.-P. and E.B. contributed equally to this work.

[2]To whom correspondence may be addressed. Email: Gyorgy.hajnoczky@jefferson.edu.

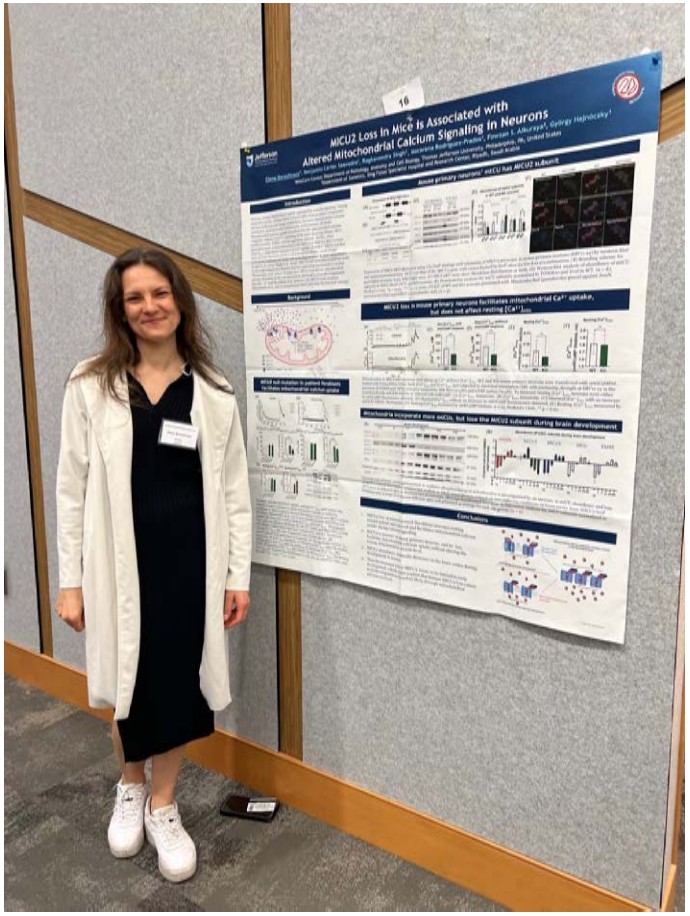
This article contains supporting information online at https://www.pnas.org/lookup/suppl/doi:10.1073/pnas.2218999120/-/DCSupplemental.

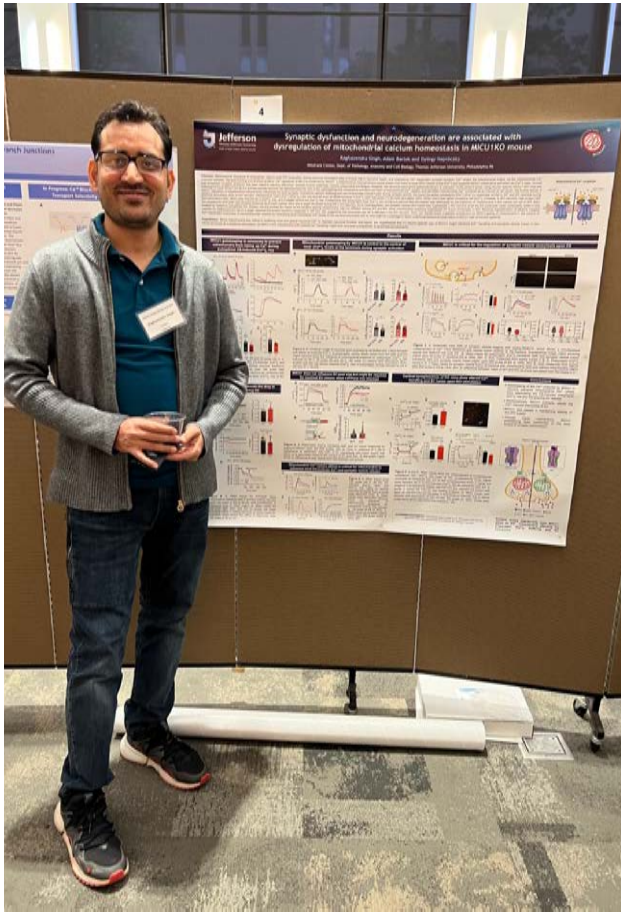
Published May 1, 2023.

And one of them is Marite's first paper .. she did the experiment for one of the figures 1 week after starting in MC



# MitoCare posters at the Neuroscience symposium honoring Irv Levitan



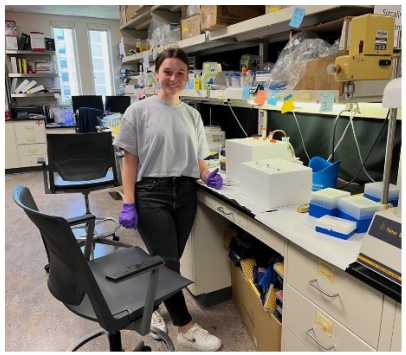



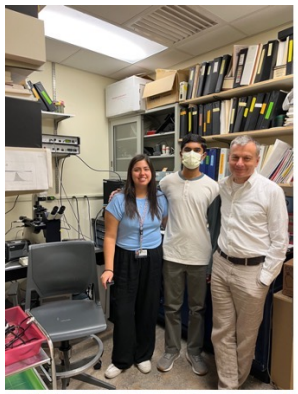
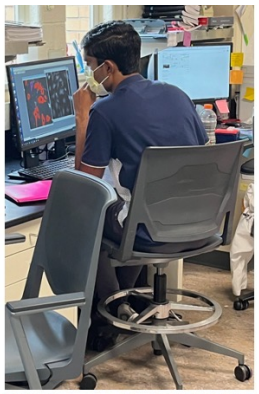

Elena's farewell

....

She hasn't stopped working on her papers from MitoCare

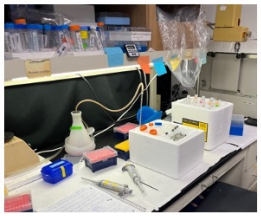
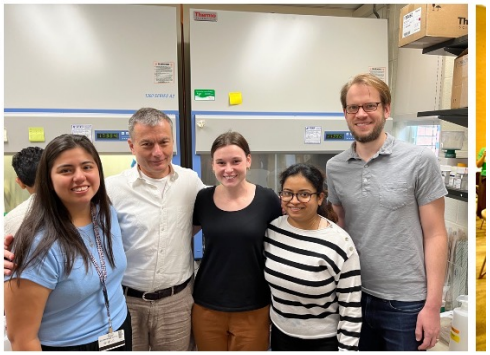
# Grace & Ashrith's productive research studentship

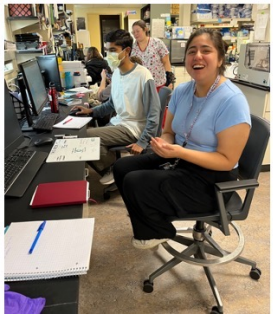


MitoCare

2023 Summer



# Raghavendra is awarded by a 3-yr long Developmental Grant by MDA

Muscular Dystrophy Association
mda.org

August 1, 2023

Raghavendra Singh, Ph.D
Thomas Jefferson University
Pathology and Genomic Medicine
Office of Research Administration
833 Chestnut Street Suite 900
Philadelphia, PA 19107

Dear Dr. Singh,

On behalf of the Muscular Dystrophy Association Board of Directors, staff, and millions of people touched by neuromuscular disease, we are pleased to inform you that your project, titled **"Pathomechanism of motor neuron degeneration and myopathy in MICU1 deficiency (MDA 1068731)**," has been approved for funding.

Your research progress is very important to MDA, to those we serve, and to the donors who keep the research pipeline flowing. Therefore, as reiterated in the attached policy manual, it is crucial that MDA receive all manuscripts resulting from this research project immediately upon their acceptance for publication so that we can communicate the results to our community. MDA adheres strictly to all journal embargos. Please send your publications and news of other research advances, accolades, or items of interest to your MDA Scientific Portfolio Director, Evrim Atas, at eatas@mdausa.org.

Congratulations and thank you for turning to MDA to support your work and for joining in our mission to save lives. We look forward to working with you and celebrating your successes, and we hope to have the opportunity to further support your research in the future.

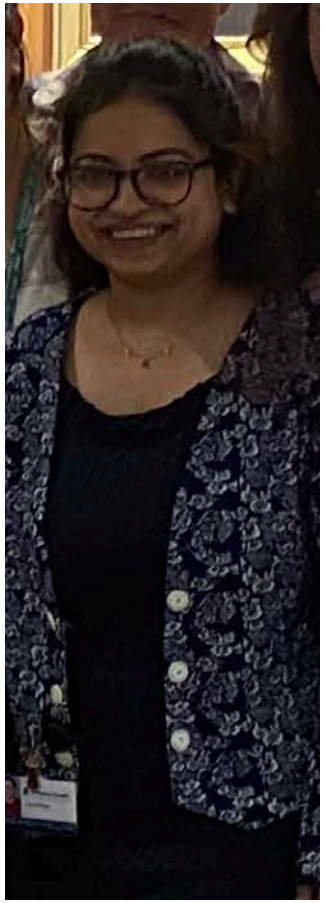
Please call on me or my colleagues if we can be of assistance to you as a research partner!

Sincerely,

Bryan Criswell
Manager, Special Grants

CC: Brad Henry, Chairman of the Board of Directors, MDA
Sharon Hesterlee, Ph.D., EVP, Chief Research Officer, MDA

# A new NIH-RO3 grant largely because of Arijita's great efforts



**Department of Health and Human Services**
National Institutes of Health
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

**Notice of Award**
FAIN# R03TR004644
**Federal Award Date**
08/23/2023

**Recipient Information**

**1. Recipient Name**
THOMAS JEFFERSON UNIVERSITY
1020 WALNUT ST
PHILADELPHIA, PA 19107

**2. Congressional District of Recipient**
02

**3. Payment System Identifier (ID)**
1231352651A1

**4. Employer Identification Number (EIN)**
231352651

**5. Data Universal Numbering System (DUNS)**
053284659

**6. Recipient's Unique Entity Identifier**
R8JEVL4ULGB7

**7. Project Director or Principal Investigator**
Gyorgy Hajnoczky, MD
Professor
gxh110@jefferson.edu
610/389-2168

**8. Authorized Official**
Mrs Jeanmarie Johnston

**Federal Agency Information**

**9. Awarding Agency Contact Information**
JULIANA PINA De Santis

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

**10. Program Official Contact Information**
KARLIE ROXANNE Sharma

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
karlie.sharma@nih.gov
301-451-4965

**Federal Award Information**

**11. Award Number**
1R03TR004644-01

**12. Unique Federal Award Identification Number (FAIN)**
R03TR004644

**13. Statutory Authority**
42 USC 241 42 CFR 52

**14. Federal Award Project Title**
Developing tools for calcium imaging in ITPR2-linked liver pathogenesis

**15. Assistance Listing Number**
93.350

**16. Assistance Listing Program Title**
National Center for Advancing Translational Sciences

**17. Award Action Type**
New Competing

**18. Is the Award R&D?**
Yes

**Summary Federal Award Financial Information**

| | |
|---|---|
| **19. Budget Period Start Date** 09/01/2023 – **End Date** 08/31/2024 | |
| **20. Total Amount of Federal Funds Obligated by this Action** | $156,000 |
| 20 a. Direct Cost Amount | $100,000 |
| 20 b. Indirect Cost Amount | $56,000 |
| **21.** Authorized Carryover | |
| **22.** Offset | |
| **23.** Total Amount of Federal Funds Obligated this budget period | $156,000 |
| **24. Total Approved Cost Sharing or Matching, where applicable** | $0 |
| **25. Total Federal and Non-Federal Approved this Budget Period** | $156,000 |
| **26. Project Period Start Date** 09/01/2023 – **End Date** 08/31/2024 | |
| **27.** Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period | $156,000 |

**28. Authorized Treatment of Program Income**
Additional Costs

**29. Grants Management Officer - Signature**
Erin A Davis

**30. Remarks**

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.


Emanuele Vitale
says goodbye after
completing his 6 months
PhD student research
in Marco's lab

# Michael defends his PhD and receives a priceless gift

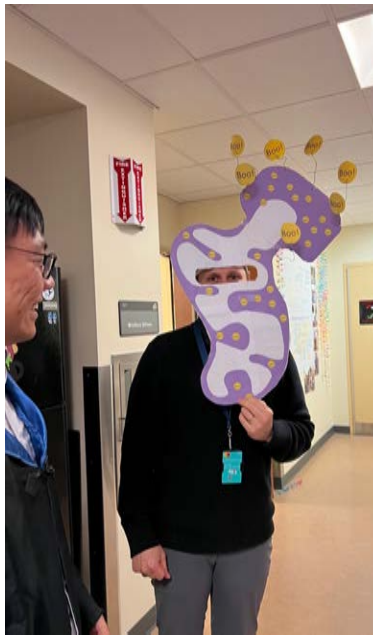

# Sangria Party

# Benjamin wins the best oral presentation award at the Jefferson Postdoctoral Research Symposium

# Selin joins MitoCare for PhD thesis work In Neuroscience

# Labmeeting presentations

# Halloween: Who has the most spooky costume of 23?





# First time Pumpkin Carvers

# The Real MitoCare Kids


MitoCare

presents:

# MitoCircle Seminar Series

## "The mitochondrial mRNA folding landscape."

**SPEAKER**

**Antoni Barrientos, Ph.D.**

University of Miami, Department of Neurology

**NOVEMBER 07 TH** | **11 AM**

MitoCare

*Jefferson Alumni Hall Room 527*

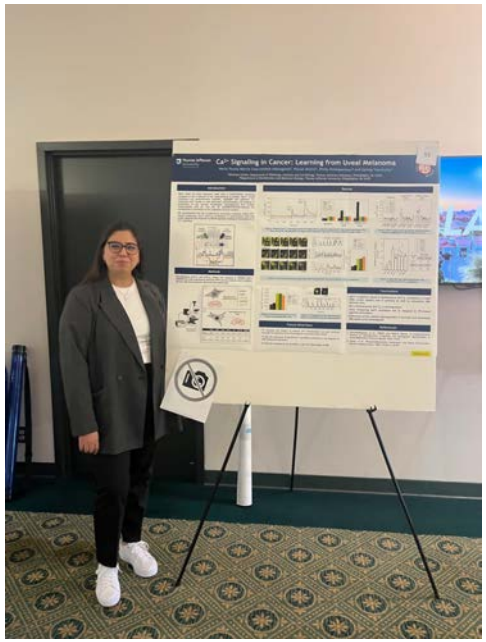
*1020 Locust Street, Philadelphia*

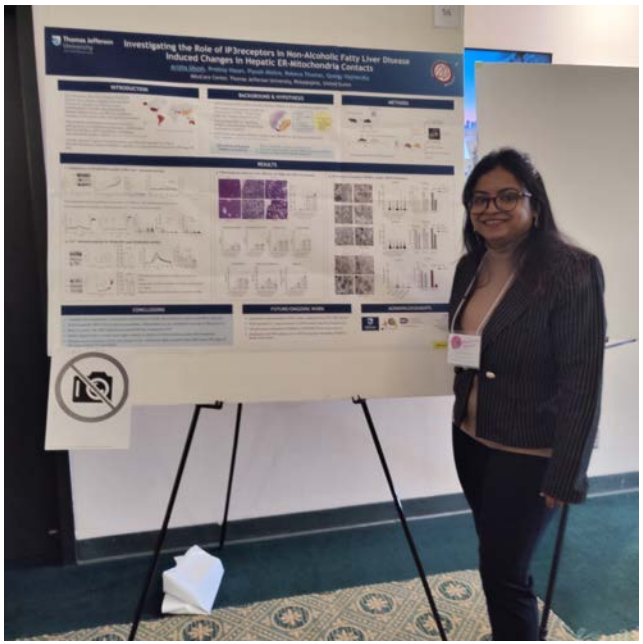
www.mitocare.org

Host: Erin L. Seifert & Marco Tigano

# 2023 UCLA Conference, where Erin, Gyuri C, Marco and Raj gave talks

# UCLA Conference posters presented by Marite & Arijita




# Marco gets a grant for an automated imaging system

MitoCare

presents:

# MitoCircle Seminar Series

## "Mechanisms Controlling Actin Filament Barbed and Pointed end Dynamics"

**SPEAKER**


**Roberto Dominguez, Ph.D.**

Department of Physiology
University of Pennsylvania


**DEC 12 | AT 11 AM**

MitoCare

*Jefferson Alumni Hall Room 527*

*1020 Locust Street, Philadelphia*

www.mitocare.org

Host: Erin L. Seifert

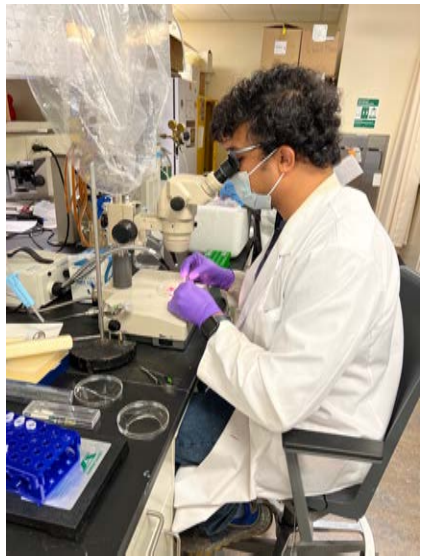
# Year end photos of the MitoCare Crew:

Erin and her lab: Amanda, Shannon & Brittney

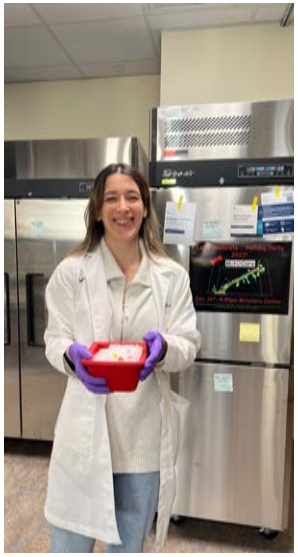



Hajnoczky lab:
Raghavendra, Piyush, Prottoy
Arijita, Benjamin, Victor, Selin



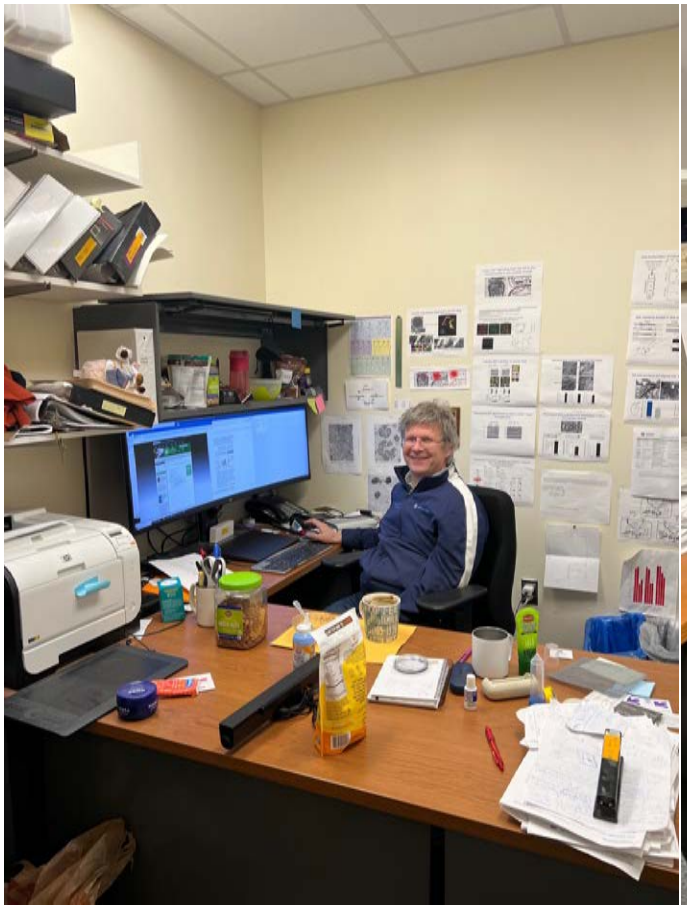


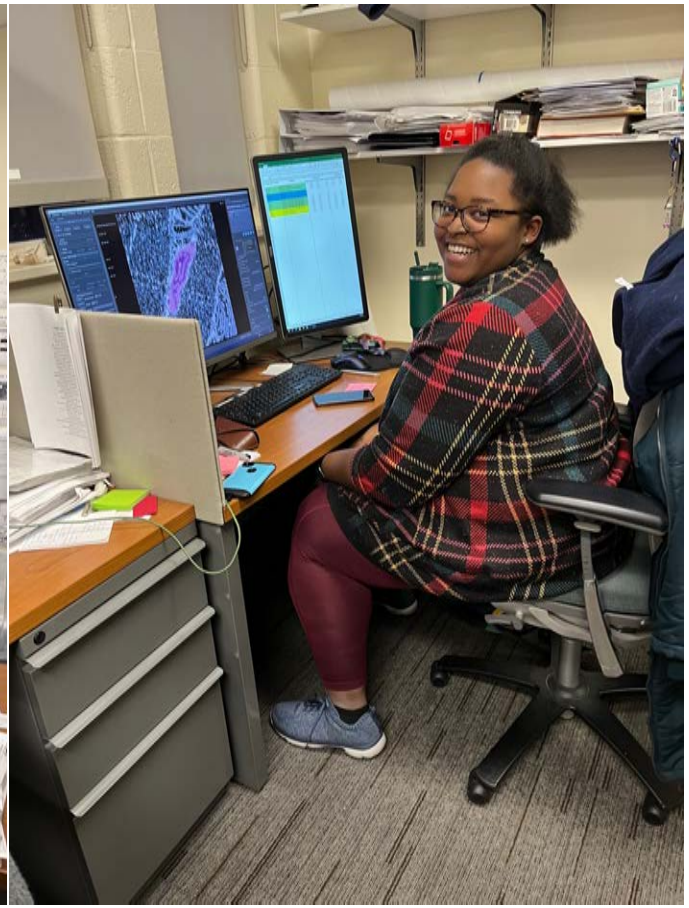




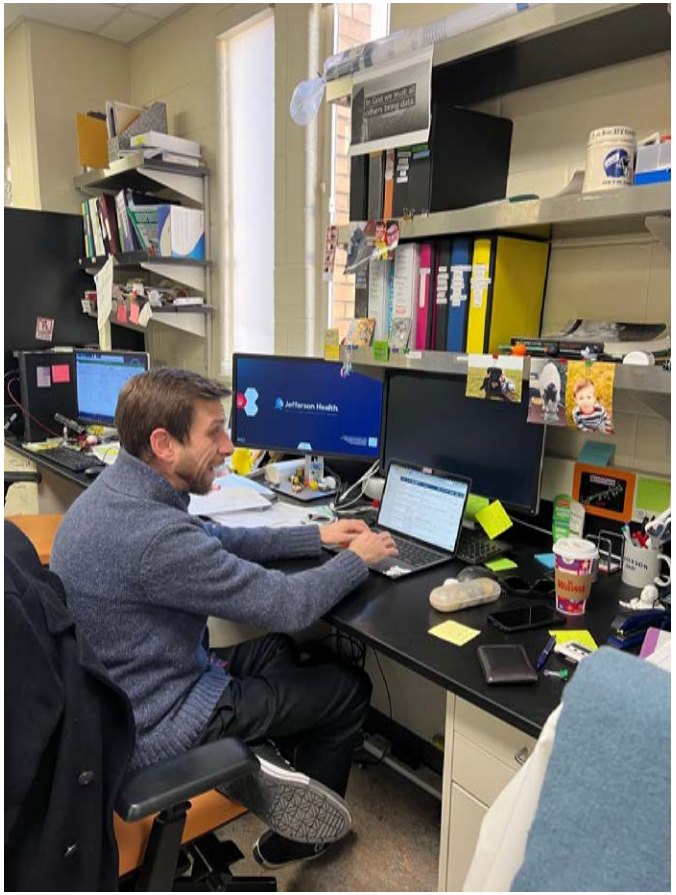

# Dave & Aron

# Gyuri Csordas and his lab: Ariele and Steve





Jan, Maarten, Joe, Gayle and Joe's team: Michael & Dave



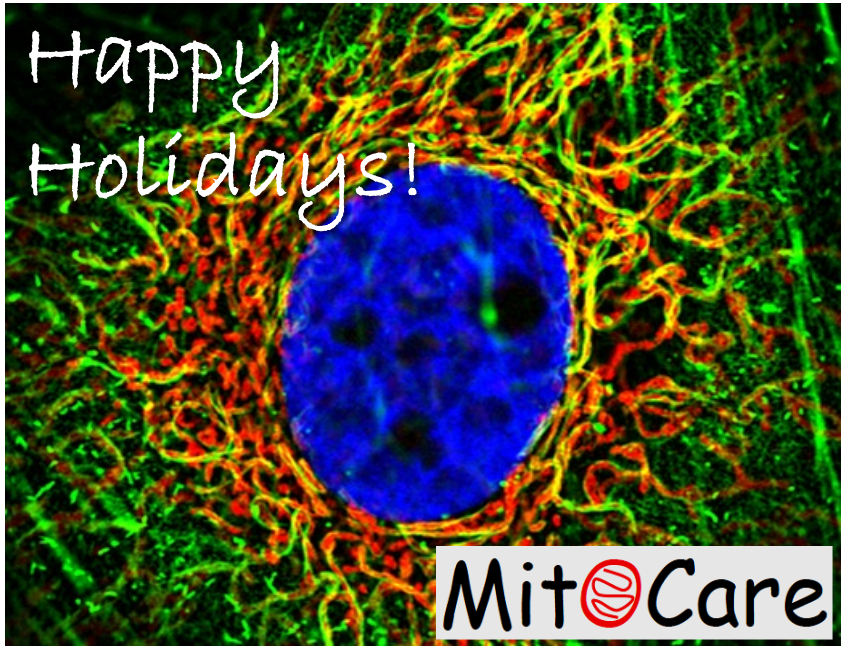


Holiday party
2023


EXIT


Trivia
Champions
EXIT

Urmi & Prottoy welcomed their baby boy on December 22nd




We Thank You for your
wonderful support
throughout the year!

Wishing you a Happy Holidays
and Healthy, Prosperous and
Energized 2024!