

Mit②Care

2024

MitoCircle Seminars: the 2024 edition

Thomas Hurd, PhD - University of Toronto, Toronto, Canada.

Divide and conquer: how deletions in mtDNA are eliminated in the germline Jan 16th

Franck Polleux, PhD - Columbia University.

Extreme compartmentalization of mitochondrial structure and function in neurons Jan 31st

Nelli Mnatsakanyan, PhD - Penn State

Structural and pharmacological characteristics of ATP synthase leak channel: gatekeeper of life and death Feb 9th

George Porter, MD - University of Rochester *co-hosted with Shey-Shing Sheu from CTM*

Empowering heart maturation: cyclophilin D, mitochondria and cardiac development Mar 11th

Dipayan Chaudhuri, MD, PhD - University of Utah

Mitochondrial pathways in liver disease Mar 12th

Chris Obara, PhD - Janelia Farms

Navigating without a map: how single proteins find their way through complex organelle landscapes Apr 2nd

Joseph Baur, PhD - University of Pennsylvania

NAD⁺ metabolism in mitochondria and microbes April 9th

Andrew Thomas, PhD - Rutgers University

New perspectives on calcium signaling in the liver Apr 29th

Tslil Ast, PhD - Weizmann Institute

Ironing out the details of mitochondrial translation Apr 30th

Joanne Garbincius, PhD - Temple University

Noel mechanisms regulating mitochondrial Ca²⁺ exchange in striated muscle in physiology and disease May 21st

Maarten Vanmunster - KU Leuven

Dual role for Bcl-xL in regulating IP3R-mediated cytosolic Ca²⁺ signals June 10th

Julius Rönkkö - University of Helsinki

Charcot-Marie-Tooth disease: IJ-ITPR3 as a new disease causing gene for peripheral neuropathy June 18th

Henry Higgs, PhD - Dartmouth University

Mitochondrial dynamics: integrating the roles of actin and other regulatory factors Oct 29th

Juliet Goldsmith, PhD - Thomas Jefferson University

Autophagic regulation of mitochondria in neurons Nov 26th

Ryan Cupo, PhD - NINDS

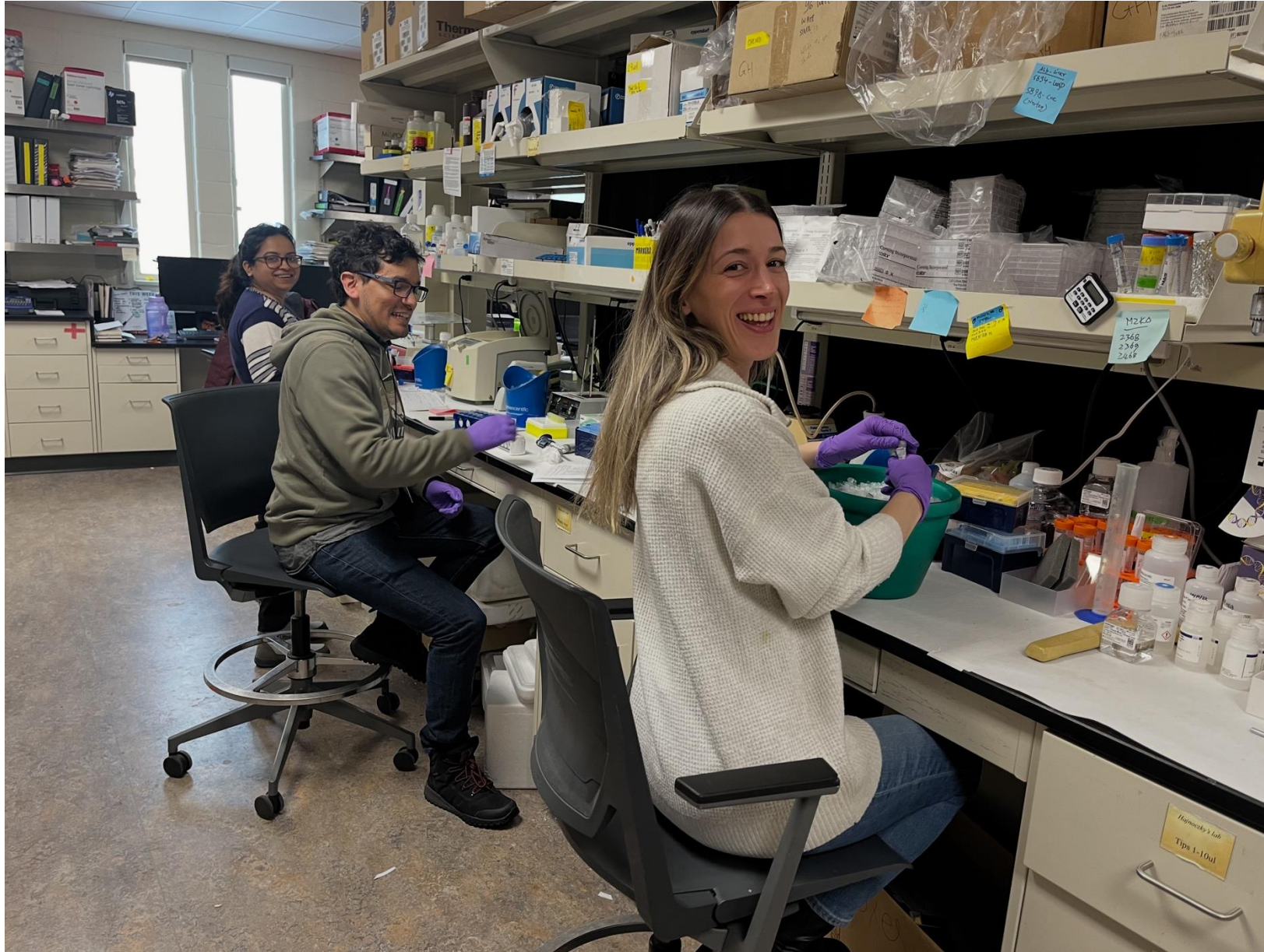
A nuclease barrier in the intermembrane space prevents Drp1-mediated mtDNA escape Dec 3rd

Thanks to Erin for
running MitoCircle
throughout the year!

Mito Circle Journal Club 2024 Summary Thanks to Gyuri Csordas for running MCJC!

Date	Name	Paper
January 8	Steve Hurst	TMEM65-dependent Ca ²⁺ extrusion safeguards mitochondrial homeostasis. Vetralla et al 2023 <i>BioRxiv</i> TMEM65 regulates NCLX-dependent mitochondrial calcium efflux. Garbincius et al 2023 <i>BioRxiv</i>
January 22	Ariele Baggett	Mitochondrial dysfunction in macrophages promotes inflammation and suppresses repair after myocardial infarction. Cai et al. 2023 <i>J Clin Invest</i>
February 5	Marco Tigano	Gasdermin D permeabilization of mitochondrial inner and outer membranes accelerates and enhances pyroptosis. Miao et al. 2023 <i>Immunity</i>
March 4	Biophysics Briefings	
March 18	Victor Hugo Sanchez	Motion of VAPB molecules reveals ER–mitochondria contact site subdomains. Obara et al. 2024 <i>Nature</i>
April 1	Marilen Federico	Activated Drp1 Initiates the Formation of Endoplasmic Reticulum-Mitochondrial Contacts via Shrm4-Mediated Actin Bundling. Duan et al. 2023 <i>Advanced Science</i>
April 15	Chenxiao Yu	Exposure of the inner mitochondrial membrane triggers apoptotic mitophagy. Saunders et al. 2024. <i>Cell Death Diff</i>
May 13	Selin Sečkin	Ischemia-induced cleavage of OPA1 at S1 site aggravates mitochondrial fragmentation and reperfusion injury in neurons. Li et al. 2022 <i>Cell Death & Disease</i>
June 3	Michael Young	TFAM is an autophagy receptor that limits inflammation by binding to cytoplasmic mitochondrial DNA. Liu et al. 2024 <i>Nat Cell Biol</i>
June 17	Gyuri Csordas	ERMA (TMEM94) is a P-type ATPase transporter for Mg ²⁺ uptake in the endoplasmic reticulum. Vishnu et al. 2024 <i>Mol Cell</i>
September 9	Gyuri Hajnoczky	Dissecting the neuroprotective interaction between the BH4 domain of BCL-w and the IP3 receptor. Tang et al. 2024 <i>Cell Chem Biol</i>
September 23	Erin Seifert	Cytosolic calcium regulates hepatic mitochondrial oxidation, intrahepatic lipolysis, and gluconeogenesis via CAMKII activation. LaMoia et al. 2024 <i>Cell Metab.</i>
Otober 30	Dave Booth	A transmitochondrial sodium gradient controls membrane potential in mammalian mitochondria. Hernansanz-Austin et al. 2024 <i>Cell</i>
November 25	Maite Zavala	Regulation of store-operated Ca ²⁺ entry by IP3 receptors independent of their ability to release Ca ²⁺ . Chakraborty et al. 2023. <i>ELife</i>
November 25	Joshua O	Release of mitochondrial dsRNA into the cytosol is a key driver of the inflammatory phenotype of senescent cells. Lopez-Polo et al. 2024. <i>Nat Commun</i>
November 20	Shey-Shing Sheu	Integration of Mitoflash and Time-Series Transcriptomics Facilitates Energy Dynamics Tracking and Substrate Supply Analysis of Floral Thermogenesis in Lotus. Yu et al. 2024 <i>Plant, Cell, Environ</i>

Busy morning at the bench



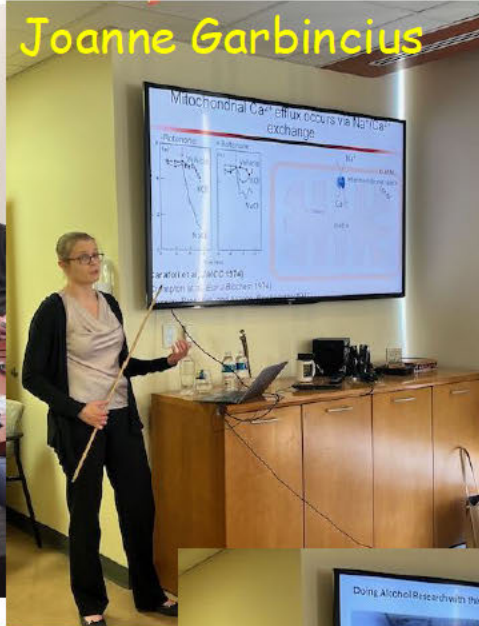
Selin's first committee meeting, with Franck Polleux as external member



Some MitoCircle 2024 Speakers and other guests



Nelli Mnatsakanyan



Joanne Garbincius



Julius Rönkkö



Chris Obara



Henry Higgs



Franck Polleux



Andrew P. Thomas

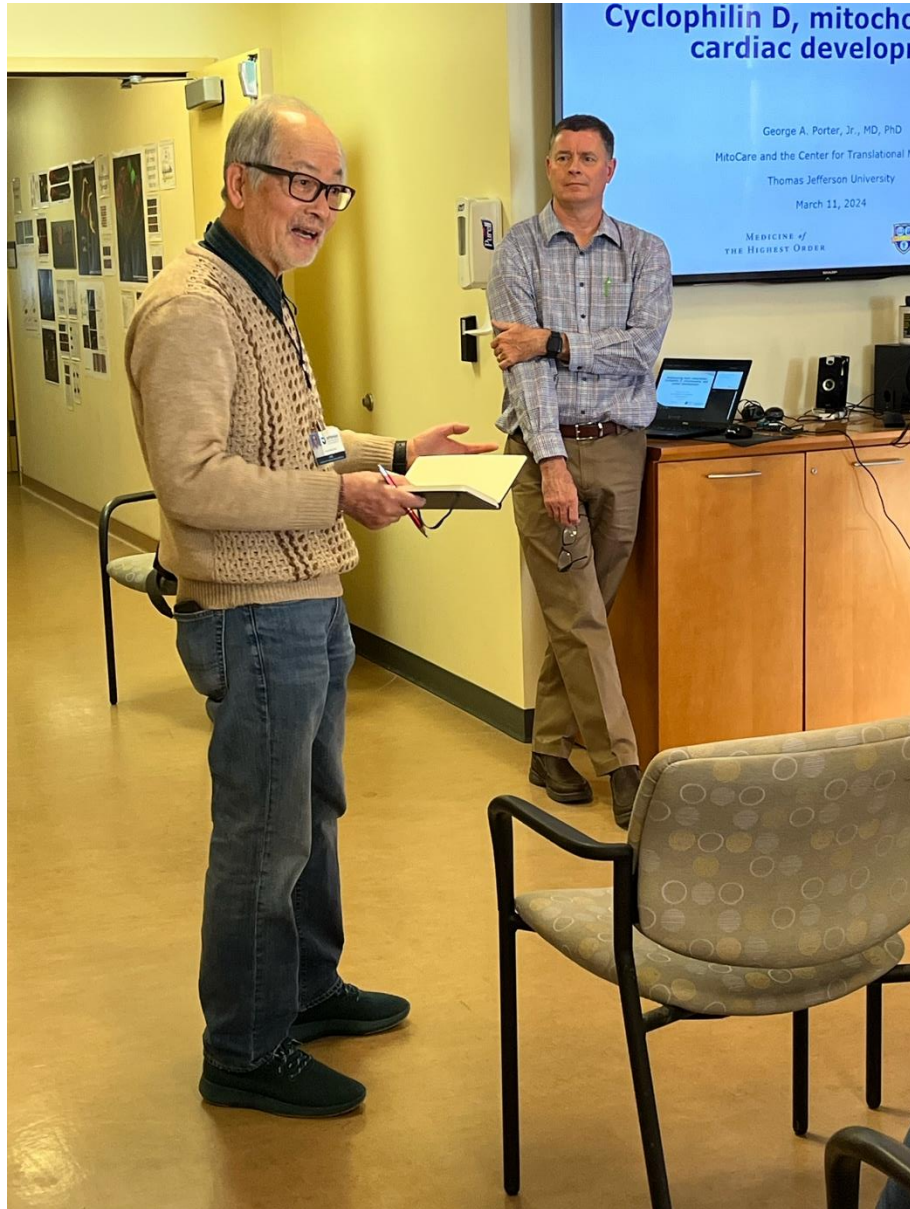


Juliet Goldsmith

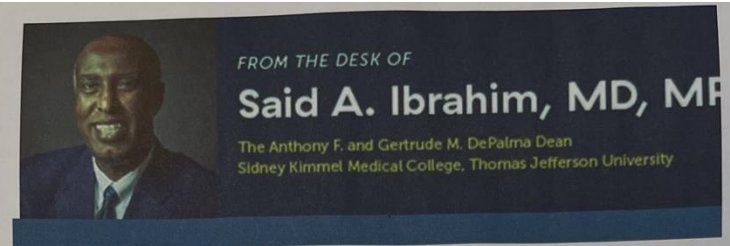


Ryan Cupo

George Porter presents a talk at MitoCircle



Erin is invited to participate in the Dean's Research Executive Council



Dear Colleague,

At the Sidney Kimmel Medical College, one of our strategic initiatives is to advance healthcare research foundation, and industry supported projects. To help inform and guide this process, I am delighted to announce the formation of the Dean's Research Executive Council. This council will have several objectives: 1.) to help SKMC strategize to develop a Center (CTSC) application within the next 1-2 years, 2.) guide the process of establishing and implementing a Pilot Grants program, 3.) to inform SKMC strategy for fundraising to support the research mission of the college.

The council will consist of leaders in basic science, clinical, health outcomes, and population sciences represented by Dr. David Whellan and Dr. Steven McMahon. Council membership will be reevaluated periodically to assure appropriate representation of research stakeholders across the SKMC. The inaugural SKMC Research Executive Council members are:

- Steven McMahon, PhD** (Co-Chair) Senior Associate Dean, Basic Science Research and Chair of the Department of Biology, Sidney Kimmel Medical College, Thomas Jefferson University
- David Whellan, MD, MHS** (Co-Chair) Senior Associate Dean, Clinical Research and the James C. Whelan Center for Translational Research, Sidney Kimmel Medical College, Thomas Jefferson University
- Michael Baram, MD** - Professor of Medicine, Director of In-Hospital Clinical Trials, Division of Pulmonary and Critical Care Medicine, Leonard M. Korman Respiratory Institute, Thomas Jefferson University Hospital & Sidney Kimmel Medical College
- Christine Eischen, PhD** - Professor, Department of Pharmacology, Physiology, & Cancer Biology, Sidney Kimmel Medical College, Thomas Jefferson University

Page 1 of 2

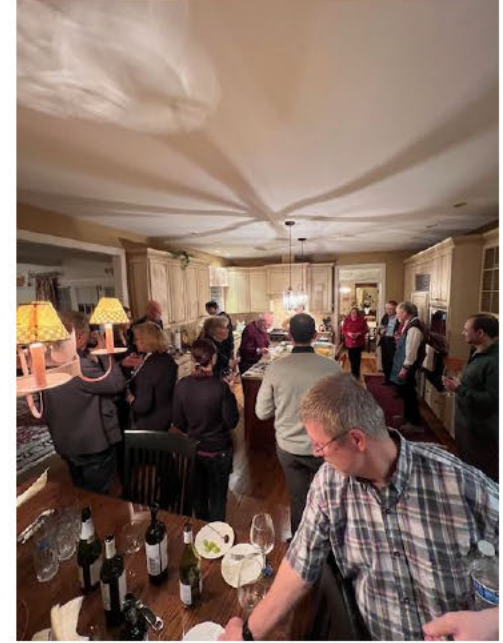
- Terry Hyslop, PhD** - Professor, Division of Biostatistics, Vice Chair, Department of Pharmacology, PI of the Center for Cancer Health Equity, Co-Leader, Cancer Risk and Control, Sidney Kimmel Cancer Center
- Diane Merry, PhD** - Professor, Department of Biochemistry and Molecular Biology, Sidney Kimmel Medical College, Thomas Jefferson University
- Kristin Rising, MD, MSHP** - Director, Jefferson Center for Connected Care, Professor, Department of Medicine, College of Population Health and College of Nursing, Thomas Jefferson University
- Barry Rovner, MD** - Professor, Departments of Neurology, Psychiatry, and Ophthalmology, Jefferson Medical College, Thomas Jefferson University
- Erin Seifert, PhD** - Associate Professor, MitoCare Center, Department of Pathology and Genomic Medicine, Thomas Jefferson University
- Richard Smeyne, PhD** - Director, Jefferson Comprehensive Parkinson's Center, Professor and Chair, Icahn School of Medicine at Mount Sinai, Sidney Kimmel Medical College, Thomas Jefferson University
- Davide Trotti, PhD** - Professor, Department of Neuroscience, Research Director, Weinberg Unit for a Cure in Neurodegeneration, Sidney Kimmel Medical College, Thomas Jefferson University

Please join me in thanking in advance these dedicated leaders for their service and commitment to our college.

Sincerely,

Said A. Ibrahim, MD, MPH, MBA
Anthony F. and Gertrude M. DePalma Dean
Sidney Kimmel Medical College
President, Jefferson University Physicians

Biophysics 2024 in Philly: Shey's dinner for Paolo, Nelli Mnatsakanyan at MitoCircle, BPS-Mito Friends visit MitoCare! (Feb9-13)



Biophysics 2024 in Philly: Shey's dinner for Paolo group photo!



At the same time, Victor presents a poster and wins an award at a Fusion Conference on Contact Sites at Cancun





Luca Scorrano, Heidi McBride, Atan Gross and Janine Santos with Gyuri at Banff



Xingguo, a former postdoctoral fellow and a current professor at Guangzhou, China, gave a talk at and brought his Family to the Keystone Conference



March '24
Back to the saddle
again...

Zuzana rejoins
MitoCare.
(To continue working
with Gyuri Csordas as
research associate, and
ultimately, to enrich
the 2D & 3D EM Team
with her expertise and
unique eyes.)



March '24

Leica EM ICE High-Pressure Freezer expands the 2D & 3D EM instrument park.



And, finally, one is out after 10+ years!

Membrane Contact sites as hubs for Ca^{2+} signaling – Original Research

Supralinear Dependence of the IP_3 Receptor-to-Mitochondria Local Ca^{2+} Transfer on the Endoplasmic Reticulum Ca^{2+} Loading

Contact

Volume 7: 1–17

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DOI: 10.1177/25152564241229273

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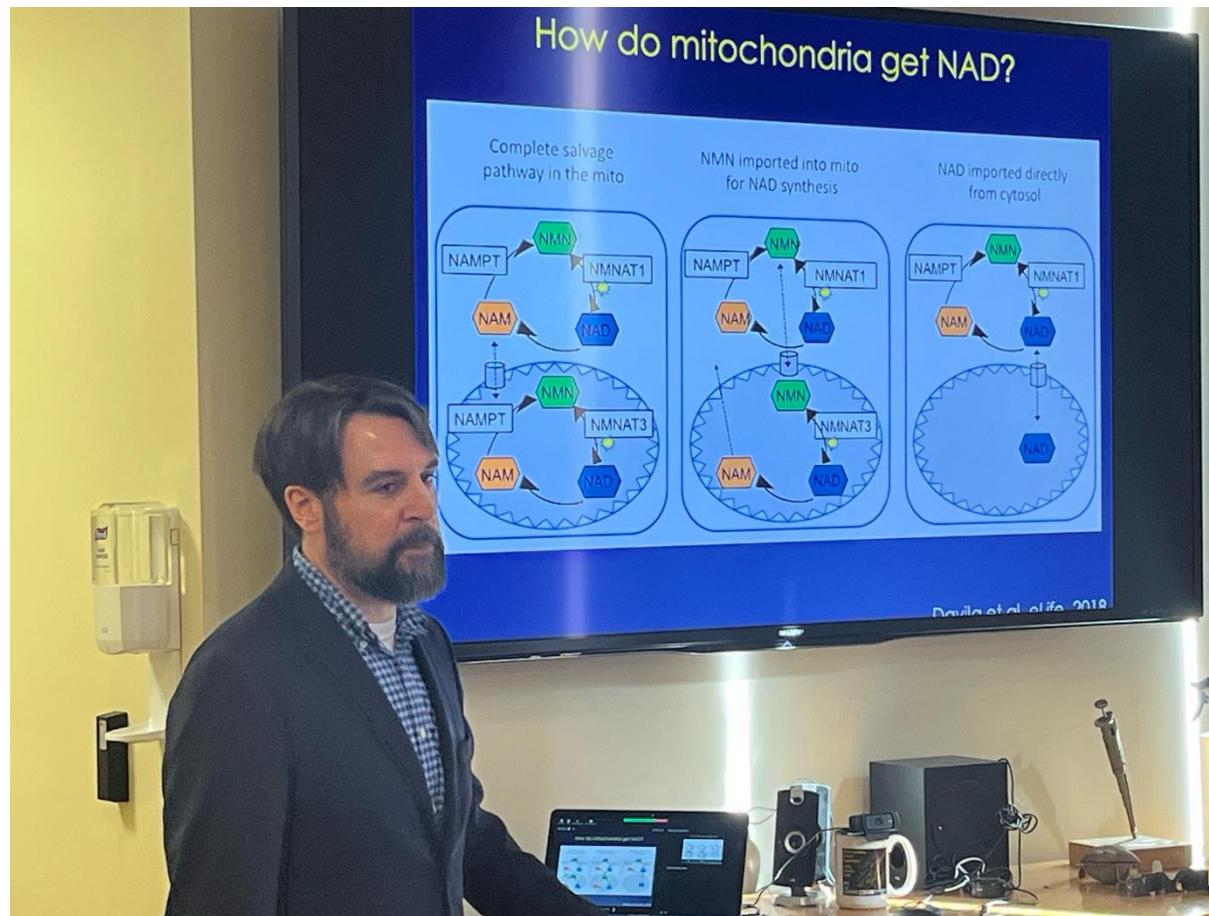


György Csordás¹, David Weaver¹, Péter Várnai²,
and György Hajnóczky¹ 

Abstract

Calcium signal propagation from endoplasmic reticulum (ER) to mitochondria regulates a multitude of mitochondrial and cell functions, including oxidative ATP production and cell fate decisions. Ca^{2+} transfer is optimal at the ER-mitochondrial contacts, where inositol 1,4,5-trisphosphate (IP_3) receptors (IP_3R) can locally expose the mitochondrial Ca^{2+} uniporter (mtCU) to high $[\text{Ca}^{2+}]$ nanodomains. The Ca^{2+} loading state of the ER ($\text{Ca}_{\text{ER}}^{2+}$) can vary broadly in physiological and pathological scenarios, however, the correlation between $\text{Ca}_{\text{ER}}^{2+}$ and the local Ca^{2+} transfer is unclear. Here, we studied IP_3 -induced Ca^{2+} transfer to mitochondria at different $\text{Ca}_{\text{ER}}^{2+}$ in intact and permeabilized RBL-2H3 cells via fluorescence measurements of cytoplasmic $[\text{Ca}^{2+}]$ ($[\text{Ca}^{2+}]_{\text{c}}$) and mitochondrial matrix $[\text{Ca}^{2+}]$ ($[\text{Ca}^{2+}]_{\text{m}}$). Preincubation of intact cells in high versus low extracellular $[\text{Ca}^{2+}]$ caused disproportionately greater increase in $[\text{Ca}^{2+}]_{\text{m}}$ than $[\text{Ca}^{2+}]_{\text{c}}$ responses to IP_3 -mobilizing agonist. Increasing $\text{Ca}_{\text{ER}}^{2+}$ by small Ca^{2+} boluses in suspensions of permeabilized cells supralinearly enhanced the mitochondrial Ca^{2+} uptake from IP_3 -induced Ca^{2+} release. The IP_3 -induced local $[\text{Ca}^{2+}]$ spikes exposing the mitochondrial surface measured using a genetically targeted sensor appeared to linearly correlate with $\text{Ca}_{\text{ER}}^{2+}$, indicating that amplification happened in the mitochondria. Indeed, overexpression of an EF-hand deficient mutant of the mtCU gatekeeper MICU1 reduced the cooperativity of mitochondrial Ca^{2+} uptake. Interestingly, the IP_3 -induced $[\text{Ca}^{2+}]_{\text{m}}$ signal plateaued at high $\text{Ca}_{\text{ER}}^{2+}$, indicating activation of a matrix Ca^{2+} binding/chelating species. Mitochondria thus seem to maintain a “working $[\text{Ca}^{2+}]_{\text{m}}$ range” via a low-affinity and high-capacity buffer species, and the ER loading steeply enhances the IP_3R -linked $[\text{Ca}^{2+}]_{\text{m}}$ signals in this working range.

Joe Baur visits MC and gives a MitoCircle talk



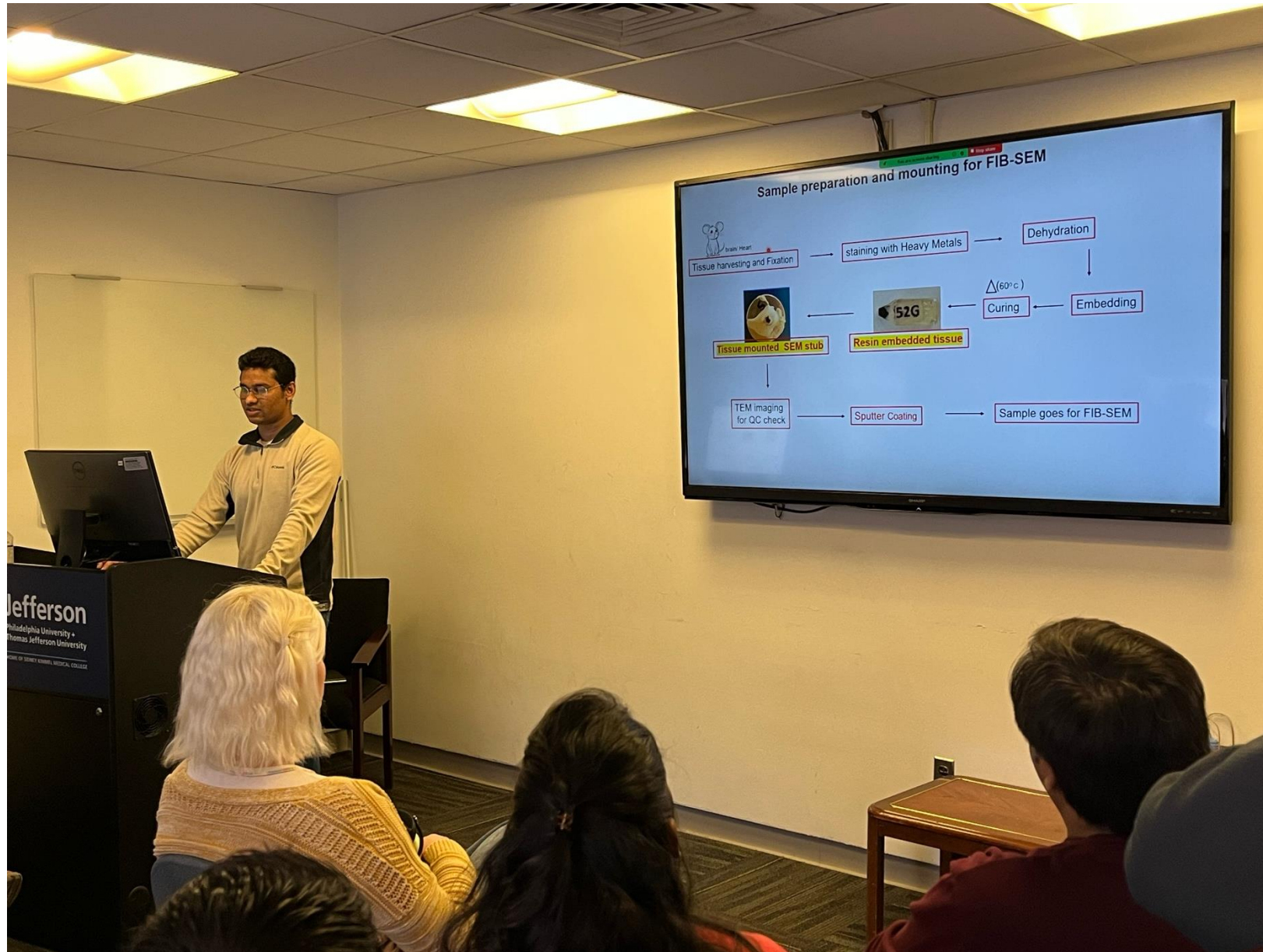
The Birthday Celebration tradition



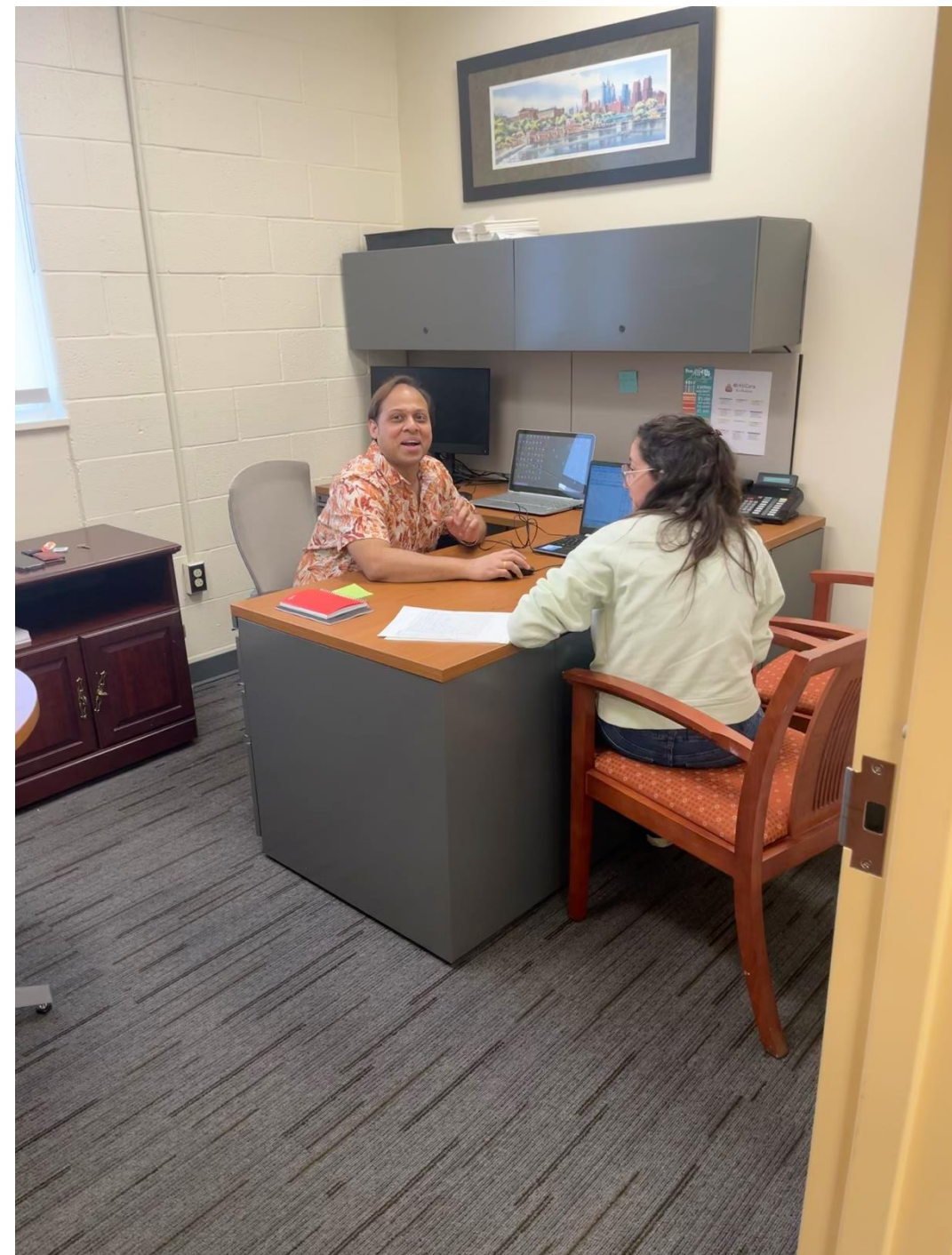
Rajeshwari Krishnamurthy,
postdoc in 1998, who then
established a prominent
antibody producing company
in India, returns to MitoCare



Prashant promotes the 3D ultrastructure facility to broader Jefferson audience



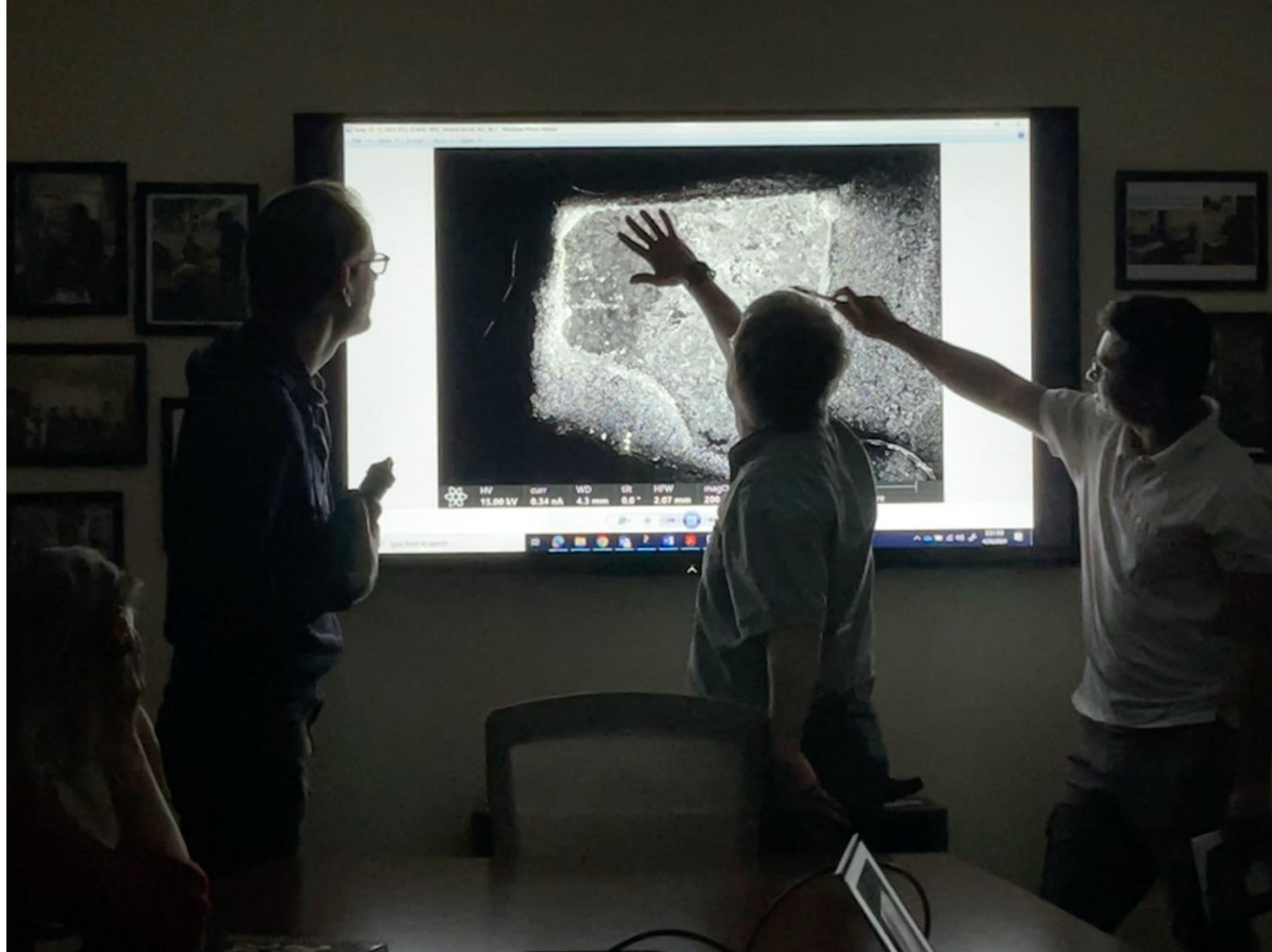
Raj with Maite, his first
postdoctoral fellow



Jan's Retirement from Jefferson: Celebrating Jan on April 29th



Dave, Gyuri C and Prashant are enlightened by 3D ultrastructure data



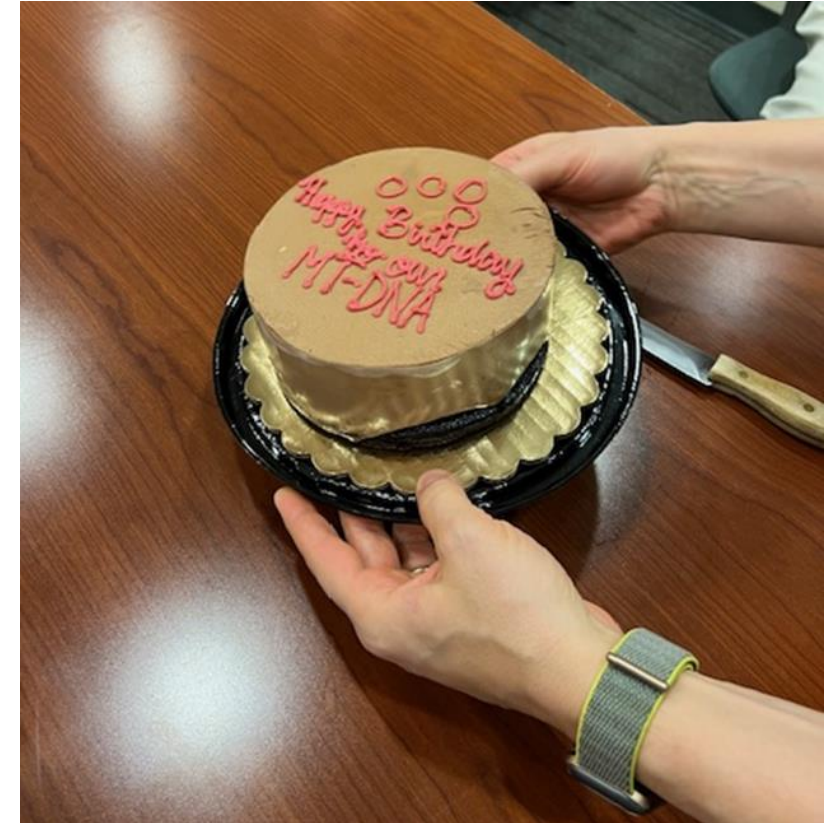
Moments of the final Leducq meeting In Nice



Benjamin presents
on mitochondrial
dynamics,
Tish Murphy
Paolo Bernardi
Janine Santos and
Melanie Paillard
are listening



Birthday celebration and surprise in May for Marco 40!



Congrats to Kai, a former technician in the Hajnoczky lab, for defending her PhD in Rochester with David Yule as her PhD mentor



Confocal microscopes
see everything.

Dr. Tigano's new
Confocal System
MICA is installed.



Hi Piera,

Please use Account# [REDACTED] for all expenses related to your Sheba-Gemelli-Jefferson ALS Project entitled;
The Role of Mitochondrial Nucleic Acids in Cytosolic Inflammatory Responses in ALS.

Thank you,
Lana

Lana Becker
Operations Manager
Vickie & Jack Farber Institute
for Neuroscience
Thomas Jefferson University
233 S. 10th Street, BLSB 308
Philadelphia, PA 19107
(215) 955-4108

**Dr. Tigano is awarded a three years grant
to study Mitochondrial Dysfunction
in Amyotrophic Lateral Sclerosis
(with Dr. Pasinelli and Dr. Trotti from
the Jefferson Weinberg ALS Center)**

Dr. Tigano receives the 2024-2025 PACR Award to study Mitochondrial Dysfunction in Sepsis (with SSS and Dr. Weiss)

Dear Drs. Tigano and Weiss,

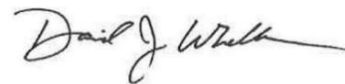
Congratulations! Your application, “Mitochondrial Dysfunction in Early and Late Phases of Pediatric Sepsis”, was selected for the 2024-2025 Jefferson-Nemours Pediatric Award for Clinical Research!

This award provides \$50,000 for the 2023 financial year as outlined in your submitted budget. The award dates are July 1, 2024 through June 30, 2025.

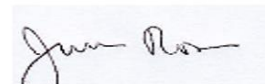
As a condition of your acceptance, you agree to provide six month and yearly progress reports for up to 3 years. You also agree to serve as a reviewer for future rounds of funding for this and other internal awards when it is reasonable and feasible for you to do so.

Please provide a statement of your acceptance of this award to Tyler Kmiec (Tyler.Kmiec@jefferson.edu) in order to begin processing and activating your award.

We are enthusiastic about this study and your work on this important topic. Please accept our congratulations on behalf of Thomas Jefferson University and Nemours Children's Health System.



David Whellan, MD
James C. Wilson Professor of Medicine
Deputy Provost for Research
Thomas Jefferson University
Executive Director, Jefferson Clinical Research
Institute



Judith Ross, MD
Associate Chair and Director, Nemours/AIDHC
Clinical Research
Professor, Department of Pediatrics
Thomas Jefferson University

Marco's group publishes a review

JOURNAL ARTICLE

Molecular and cellular consequences of mitochondrial DNA double-stranded breaks

Get access >

Chenxiao Yu, Samieh Asadian, Marco Tigano ✉

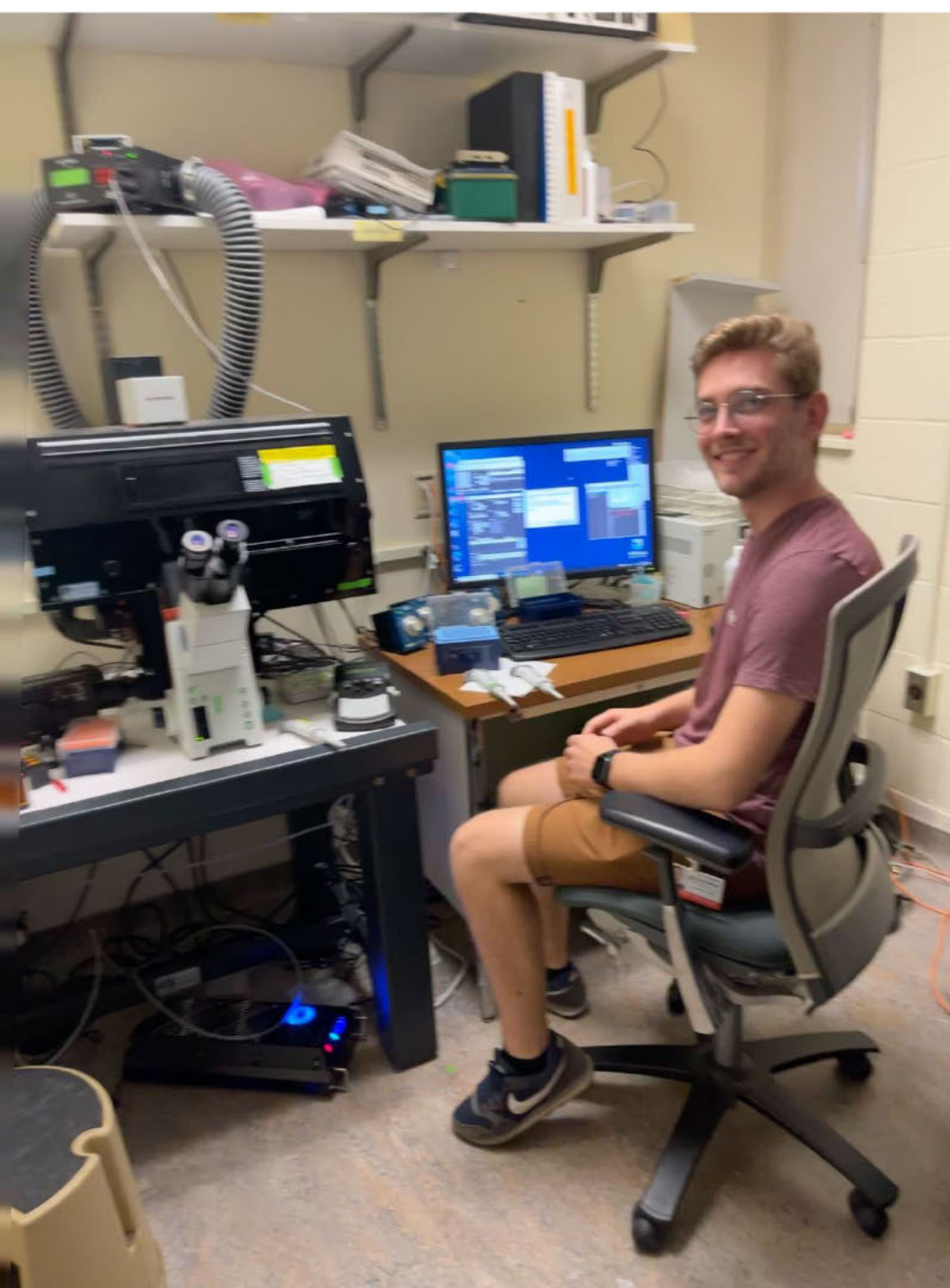
Human Molecular Genetics, Volume 33, Issue R1, 1 June 2024, Pages R12–R18,
<https://doi.org/10.1093/hmg/ddae048>

Published: 23 May 2024 **Article history** ▼

“ Cite 🔑 Permissions ➦ Share ▼

Abstract

Mitochondria are subcellular organelles essential for life. Beyond their role in producing energy, mitochondria govern various physiological mechanisms, encompassing energy generation, metabolic processes, apoptotic events, and immune responses. Mitochondria also contain genetic material that is susceptible to various forms of damage. Mitochondrial double-stranded breaks (DSB) are toxic lesions that the nucleus repairs promptly. Nevertheless, the significance of DSB repair in mammalian mitochondria is controversial. This review presents an updated view of the available research on the consequences of mitochondrial DNA DSB from the molecular to the cellular level. We discuss



Marteen
Vanmunster
from Geert
Bultynck's lab,
KU Leuven
learns Ca^{2+}
imaging
in MitoCare
and meet the
Phillies



Great teamwork in a new research paper

PNAS

RESEARCH ARTICLE

PHYSIOLOGY



MICU1 and MICU2 control mitochondrial calcium signaling in the mammalian heart

Prottoy Hasan^{a,1}, Elena Berezhnaya^{a,1} , Macarena Rodríguez-Prados^{a,1}, David Weaver^a, Carmen Bekeova^a, Benjamin Cartes-Saavedra^a , Erin Birch^b, Andreas M. Beyer^b, Janine H. Santos^c , Erin L. Seifert^a , John W. Elrod^d , and György Hajnóczky^{a,2}

Affiliations are included on p. 11.

Edited by Jeffery D. Molkentin, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; received February 5, 2024; accepted July 8, 2024 by Editorial Board Member Andrew R. Marks

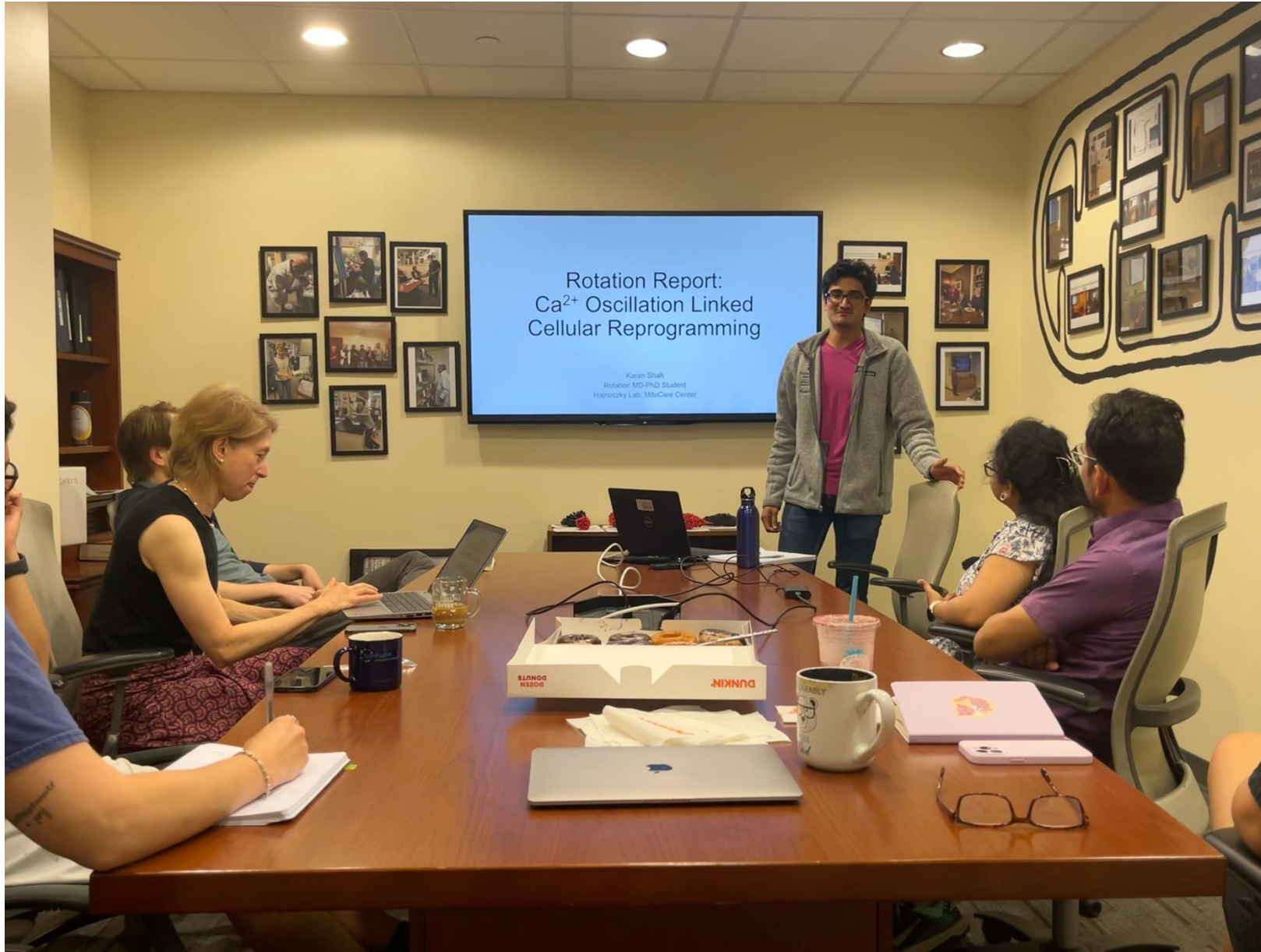
Activating Ca^{2+} -sensitive enzymes of oxidative metabolism while preventing calcium overload that leads to mitochondrial and cellular injury requires dynamic control of mitochondrial Ca^{2+} uptake. This is ensured by the mitochondrial calcium uptake (MICU)1/2 proteins that gate the pore of the mitochondrial calcium uniporter (mtCU). MICU1 is relatively sparse in the heart, and recent studies claimed the mammalian heart lacks MICU1 gating of mtCU. However, genetic models have not been tested. We find that MICU1 is present in a complex with MCU in nonfailing human hearts. Furthermore, using murine genetic models and pharmacology, we show that MICU1 and MICU2 control cardiac mitochondrial Ca^{2+} influx, and that MICU1 deletion alters cardiomyocyte mitochondrial calcium signaling and energy metabolism. MICU1 loss causes substantial compensatory changes in the mtCU composition and abundance, increased turnover of essential MCU regulator (EMRE) early on and, later, of MCU, that limit mitochondrial Ca^{2+} uptake and allow cell survival. Thus, both the primary consequences of MICU1 loss and the ensuing robust compensation highlight MICU1's relevance in the beating heart.

calcium | MICU1 | MICU2 | mitochondrial calcium uniporter gating | cardiomyocyte

Significance

Calcium enters mitochondria via the calcium uniporter to regulate energy production and survival. The uniporter activity is controlled by calcium via binding the EF-hands of the regulatory MICU subunits. There is controversy in the presence and relevance of this mechanism in the heart. We developed both chronic and acute cardiomyocyte-specific genetic models for MICU1/MICU2 and provide

Karan Shah, MD, PhD student, presents his summer research



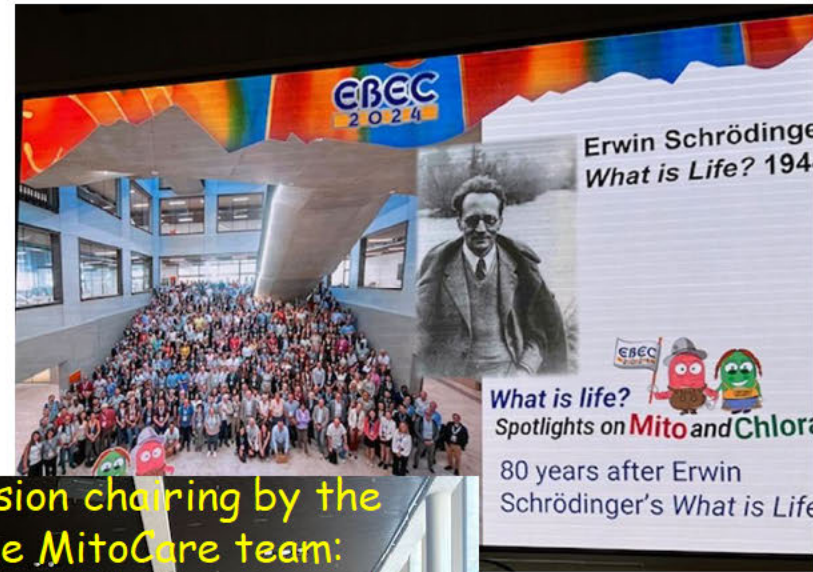
EBEC 2024



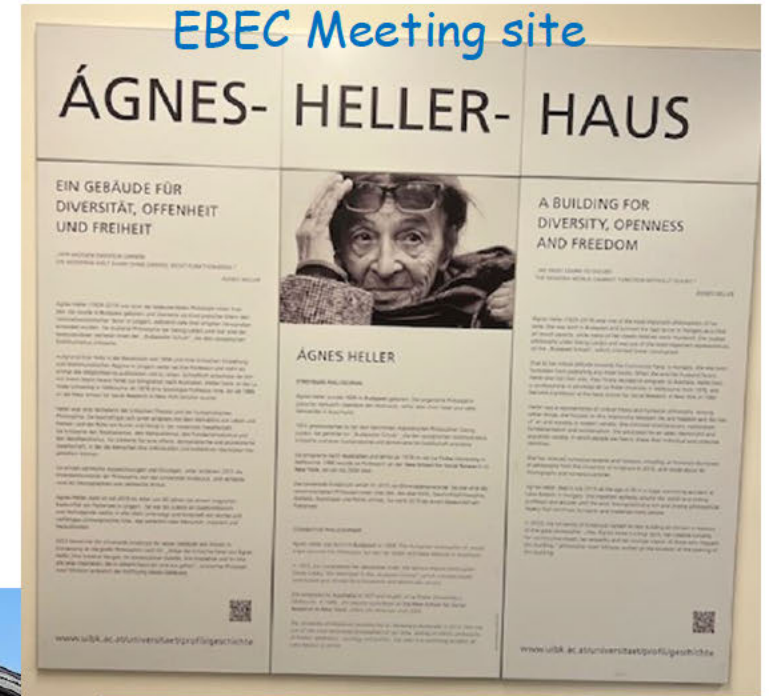
Session chairing by the
the MitoCare team:
We kept things on track



Was great to see
Barbara Cannon again



Shey and Gyuri on a
mountain in Austria



Innsbruck:
Home of Oroboros

With David Nicholls

and Loren Walensky
Luca Scorrano
Orian Shirihi
Ambre Bertholet
and Karin Busch

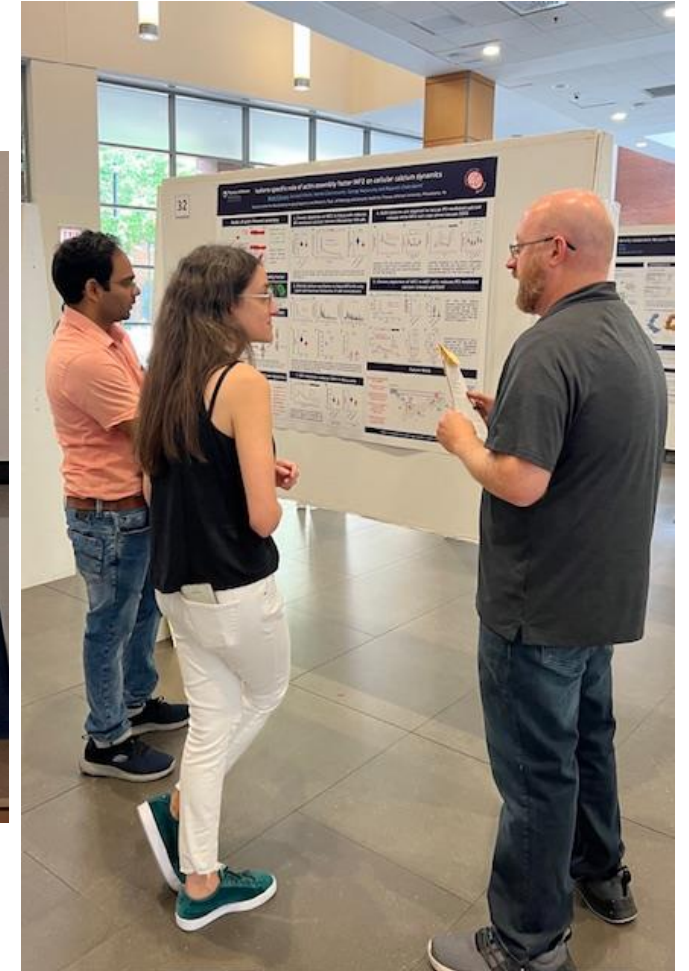


Jefferson's Annual Post-Doc Research Day

Arijita and Benjamin, 2023 award winners, 2024 organizers



Victor wins award and
likely becomes a 2025
organizer



September '24

Postdoctoral Symposium Awardees

Circled:

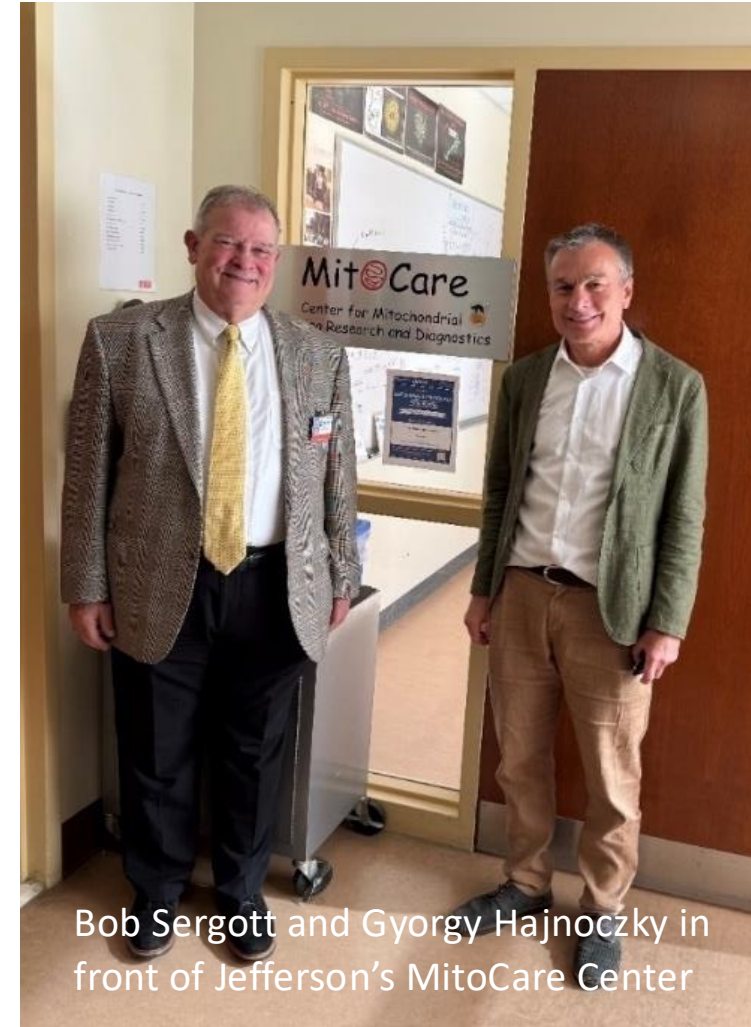
Victor (Hajnoczky
lab)

Marilen (Sheu lab)



Meg & Dick Hayne make a 2nd donation to fund Bob Sergott's EyeBrain Institute and its Collaboration with MitoCare

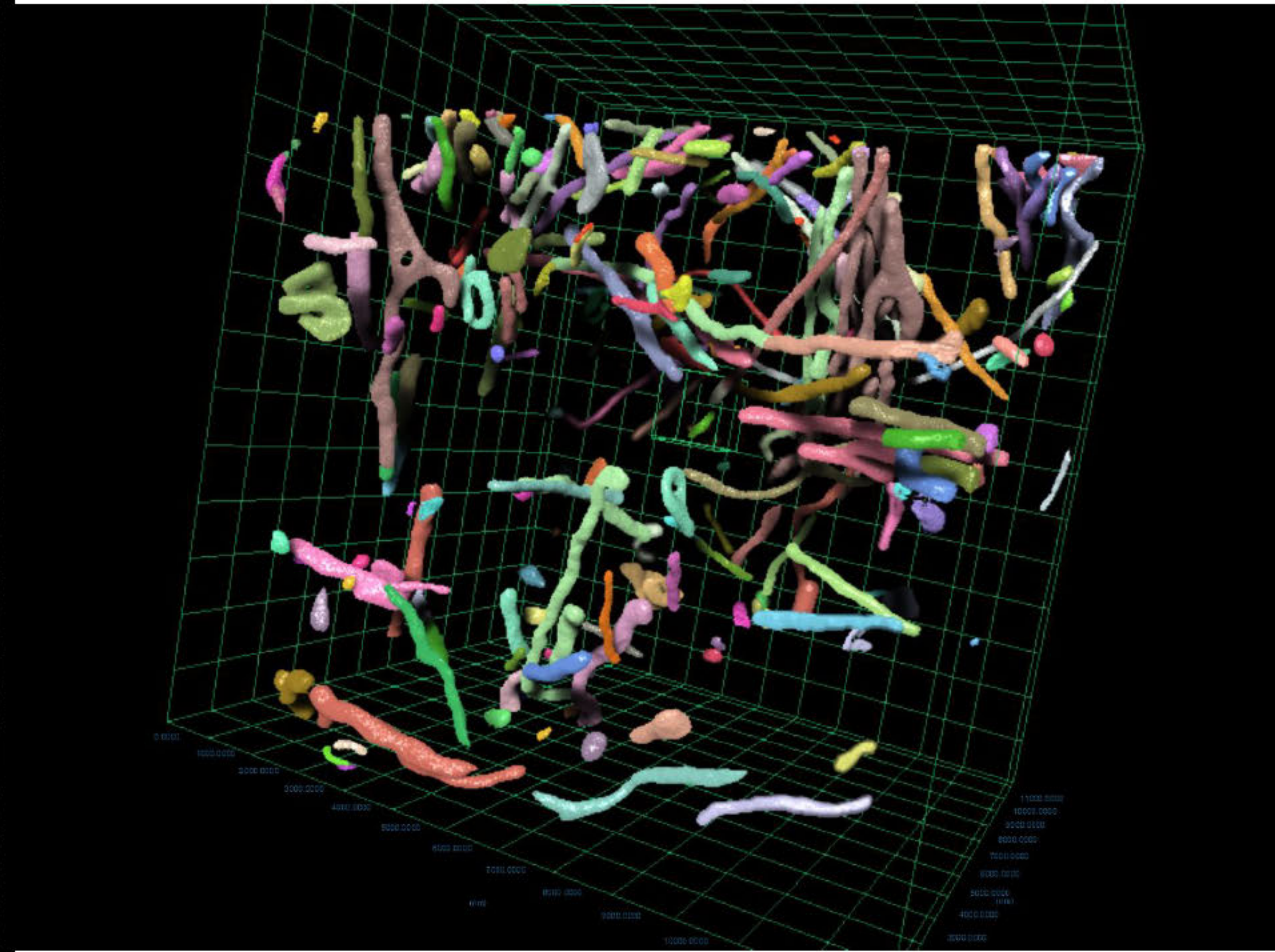
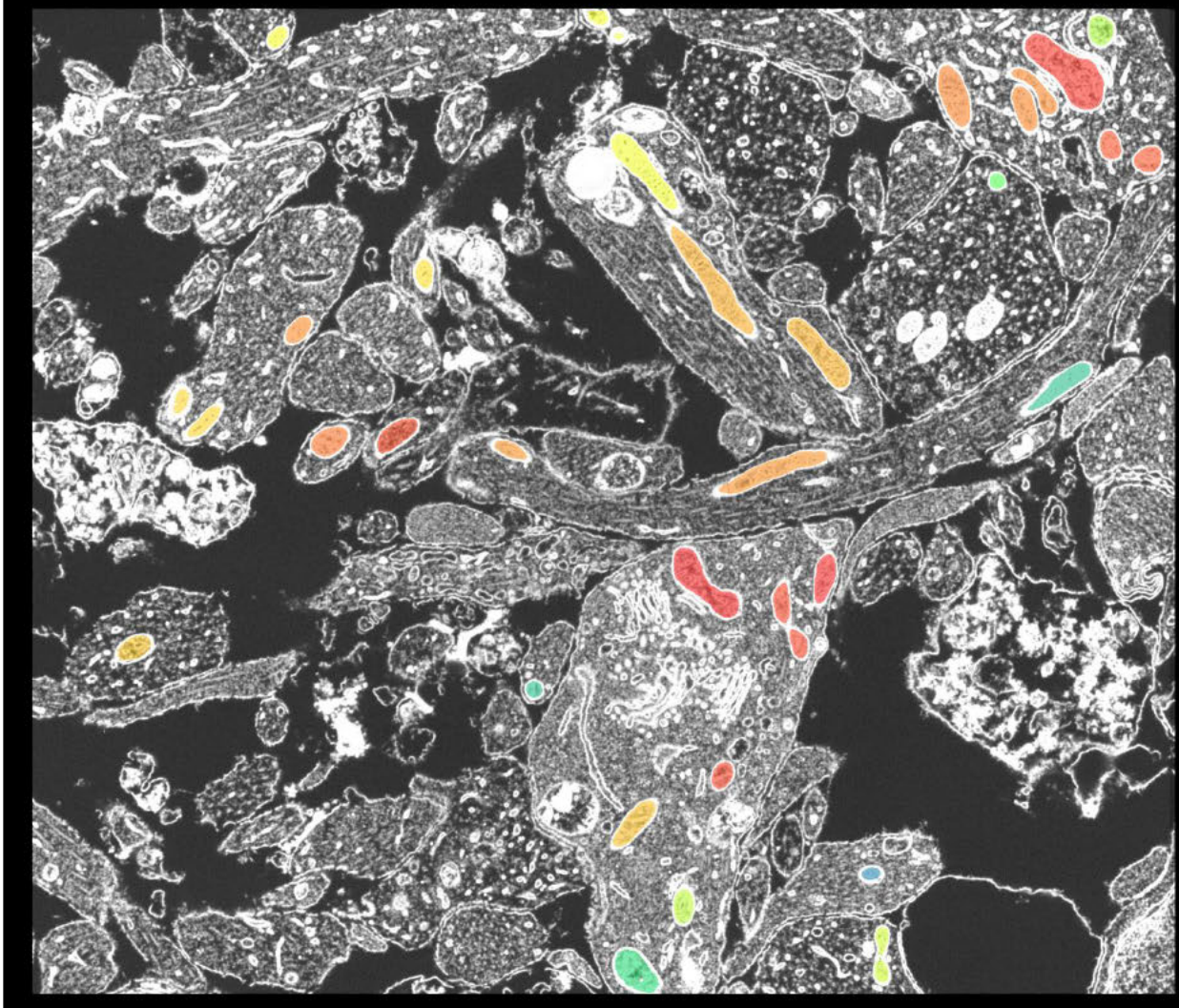
EyeBrain & MitoCare Crew in the FIB-SEM facility



Bob Sergott and Gyorgy Hajnoczky in
front of Jefferson's MitoCare Center

All mitochondria identified by AI in a brain organoid

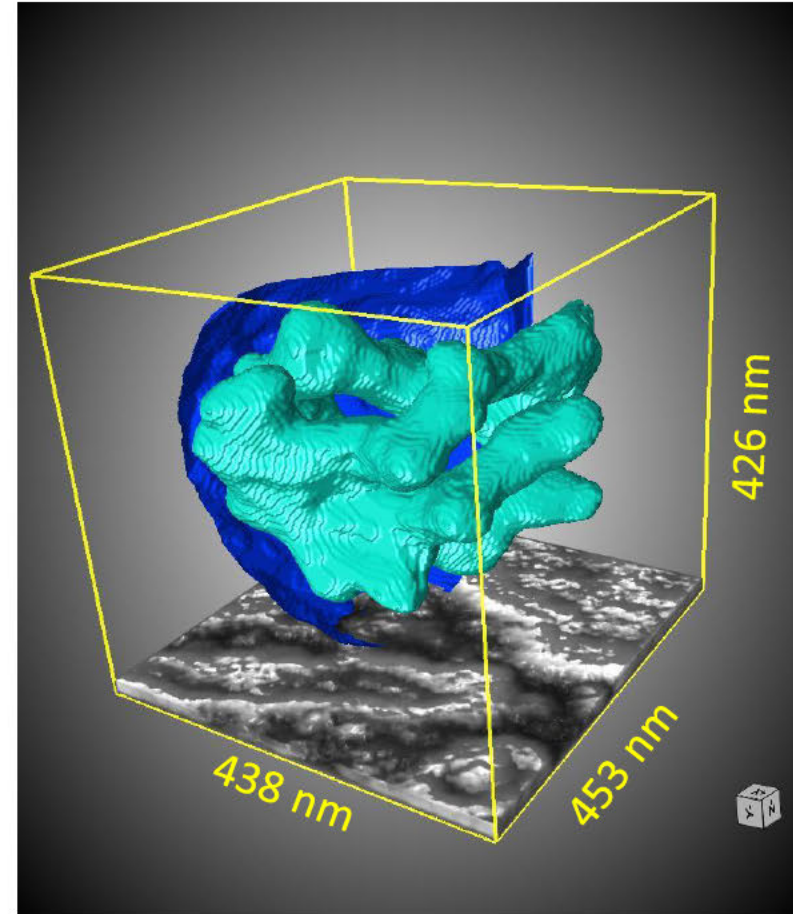
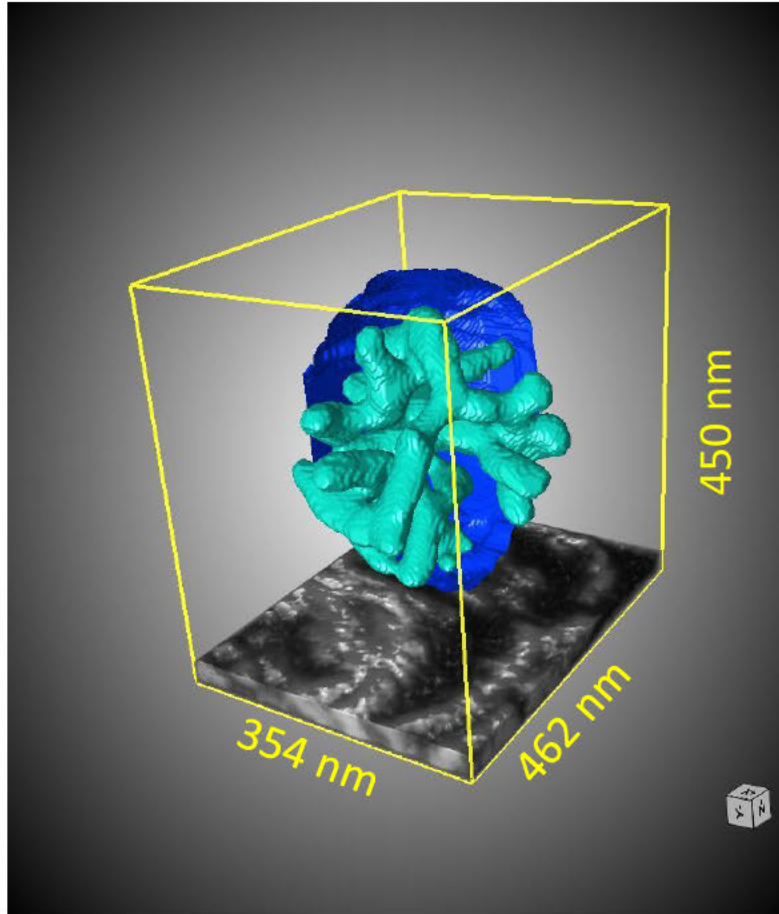
2D image of the tissue (grayscale), mitochondria (colors)



Collaboration with Rita Horvath (Cambridge University)

Interior of a brain organoid mitochondrion

(blue: outer membrane shell (only shown in back); cyan: internal membrane forming cristae, the sites of energy production)



Paolo Bernardi's retirement conference



FRONTIERS IN MITOCHONDRIAL RESEARCH

A TRIBUTE TO THE LEGACY OF PAOLO BERNARDI ON THE OCCASION OF HIS RETIREMENT

26-28 September 2024

THURSDAY, 26th

14:00-14:30 - Registration
14:30-16:30 - Session 1
16:30-17:00 - Break
17:00-19:20 - Session 2

SATURDAY, 28th

9:40-11:00 - Session 8
11:00-11:20 - Break
11:20-13:00 - Session 9/10
13:00-14:00 - Lunch
14:00-14:40 - Session 11

FRIDAY, 27th

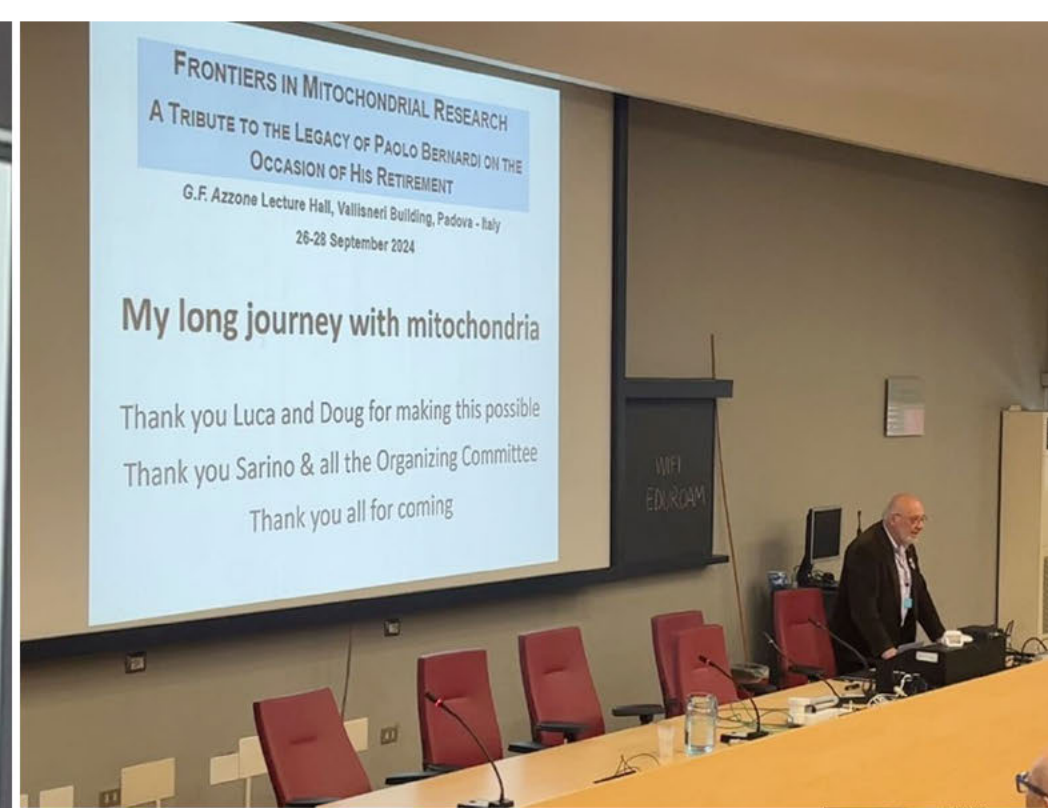
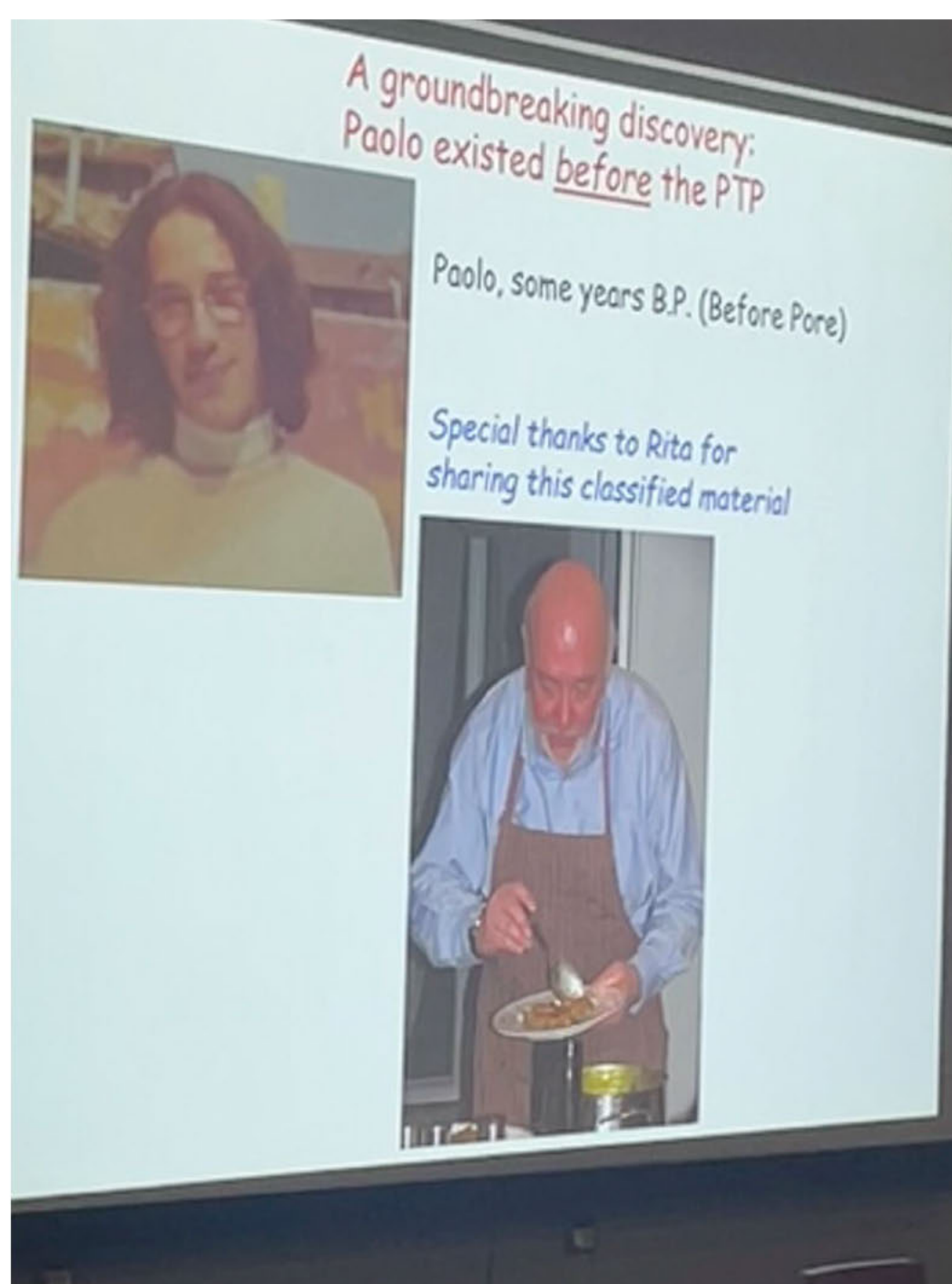
9:00-10:40 - Session 3
10:40-11:00 - Break
11:00-12:40 - Session 4
12:40-13:40 - Lunch
13:40-15:40 - Session 5
15:40-16:00 - Break
16:00-19:00 - Sessions 6/7
20:30-Dinner, «Caffè Pedrocchi»

**LOCATION: G.F. Azzone Lecture Hall,
Vallisneri Building**

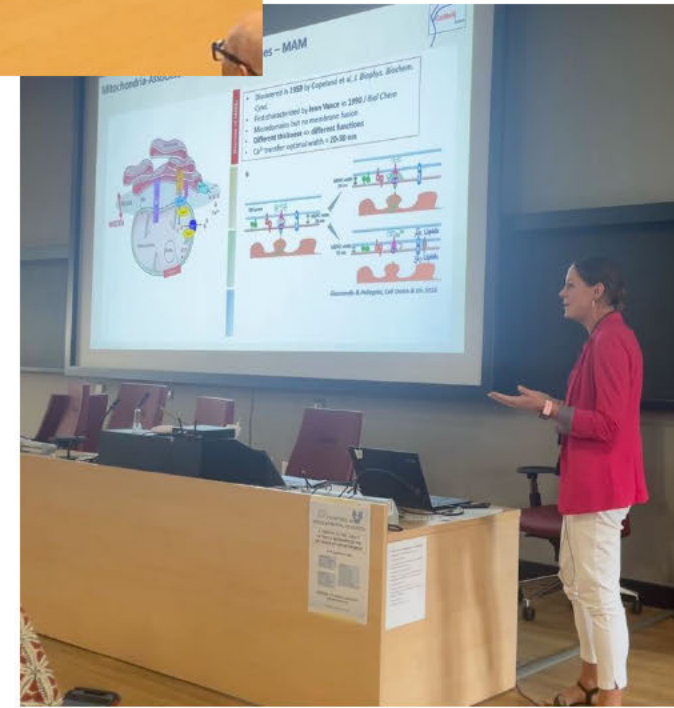
Attendance upon registration



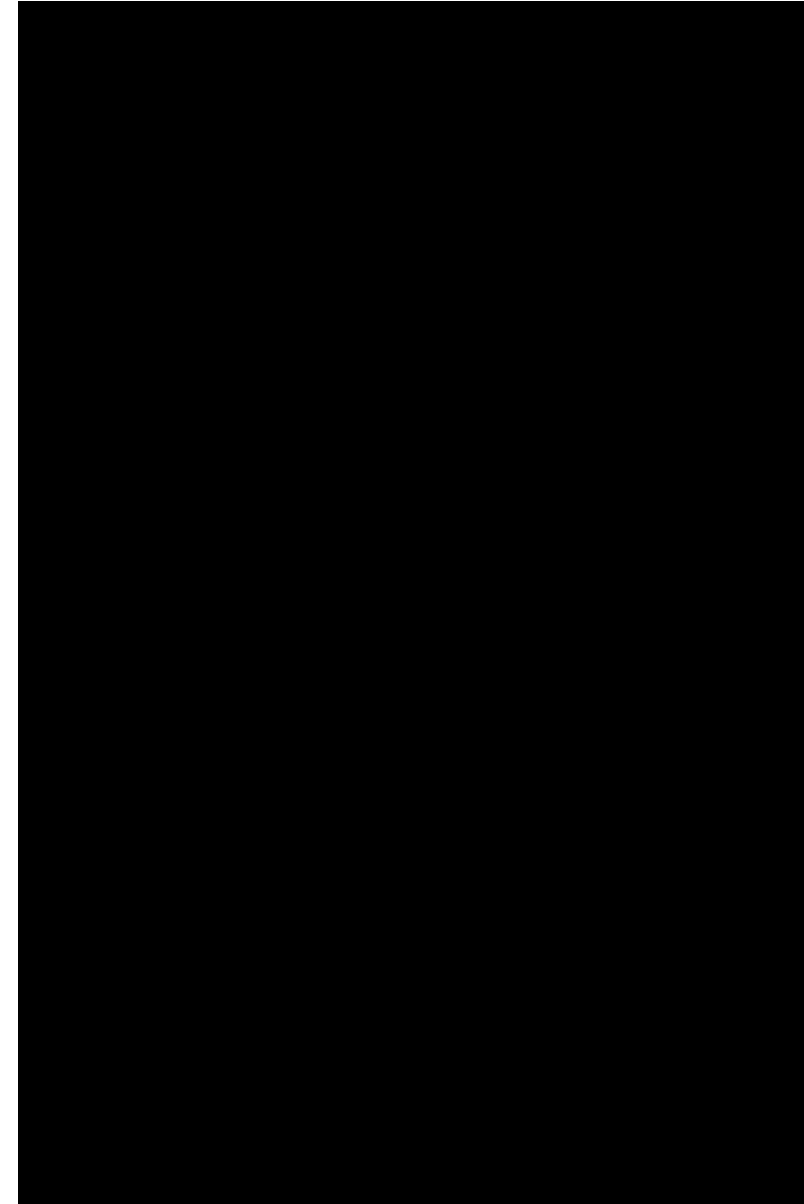
Paolo's introduction



Melanie, a former MC postdoc and current INSERM investigator, gives a talk



Paolo with his former trainees



October '24 TriMad Meeting at U Rochester.



Shey inaugurates Siegfried Heikimi (from McGill) as the First Shey-Shing Sheu Lecturer in Mitochondrial Biology



Pablo Peixoto's vision of 'Super Shey'

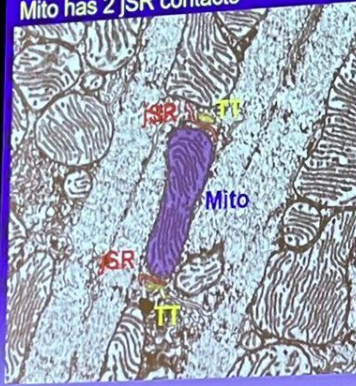
October '24
TriMad Meeting at
U Rochester.

Gyuri Csordas
gives a talk on the
adaptation of
cardiac
mitochondrial
cristae to the
local environment.
Highlights the
need for FIB-SEM

Can we really trust the TEM data in terms of cristae behavior in the context of the Mito-jSR contact versus the rest of the mitochondrion?

TEM-like views (tomographic slices) from an "auto slice-and-view" image stack (ThermoFisher Sci. Helios 5 FIB-SEM)

Mito has 2 jSR contacts



Same Mito has 1 jSR contact



~300 nm (!) Z axis progression

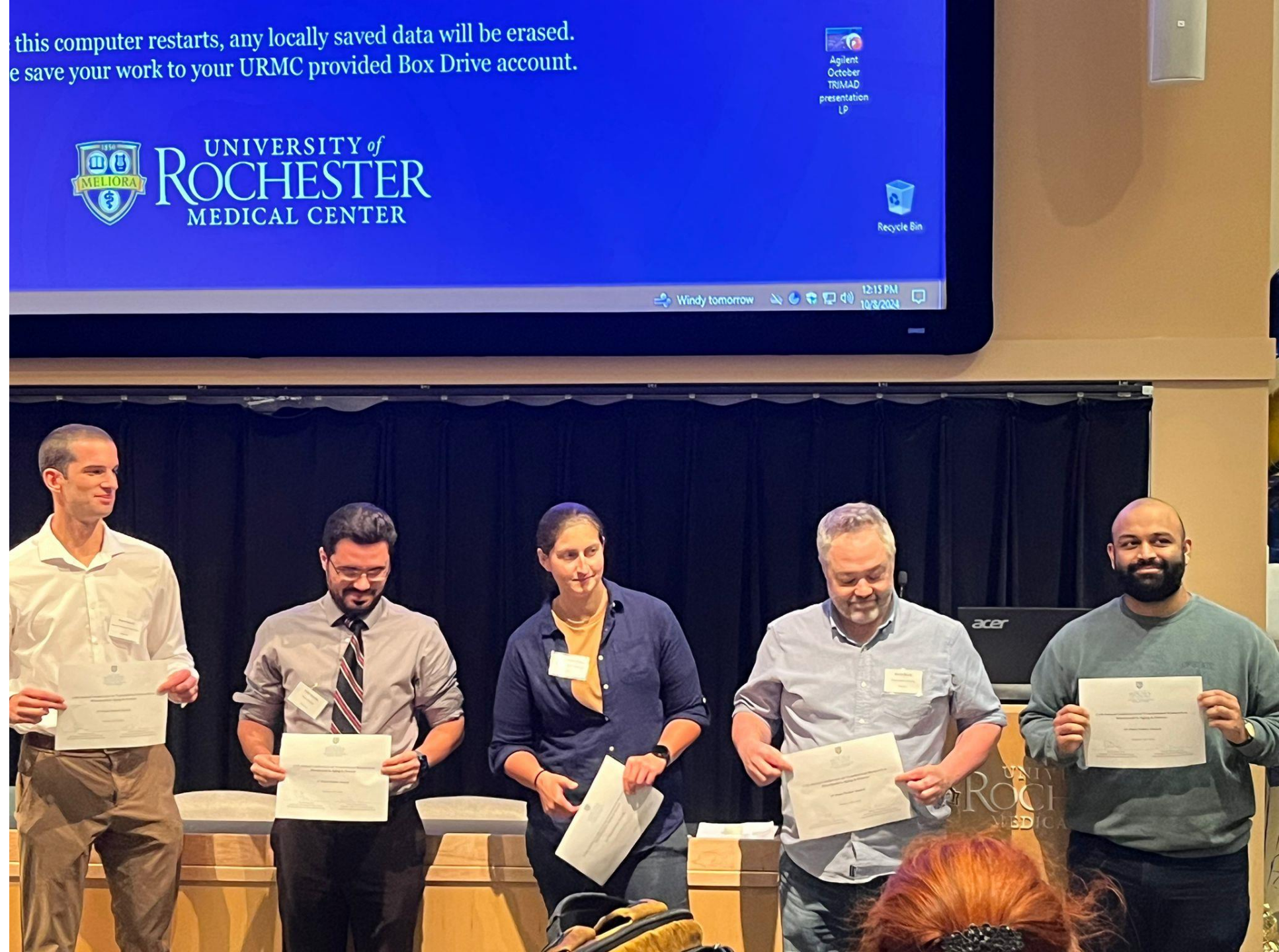
Same Mito has no jSR contact



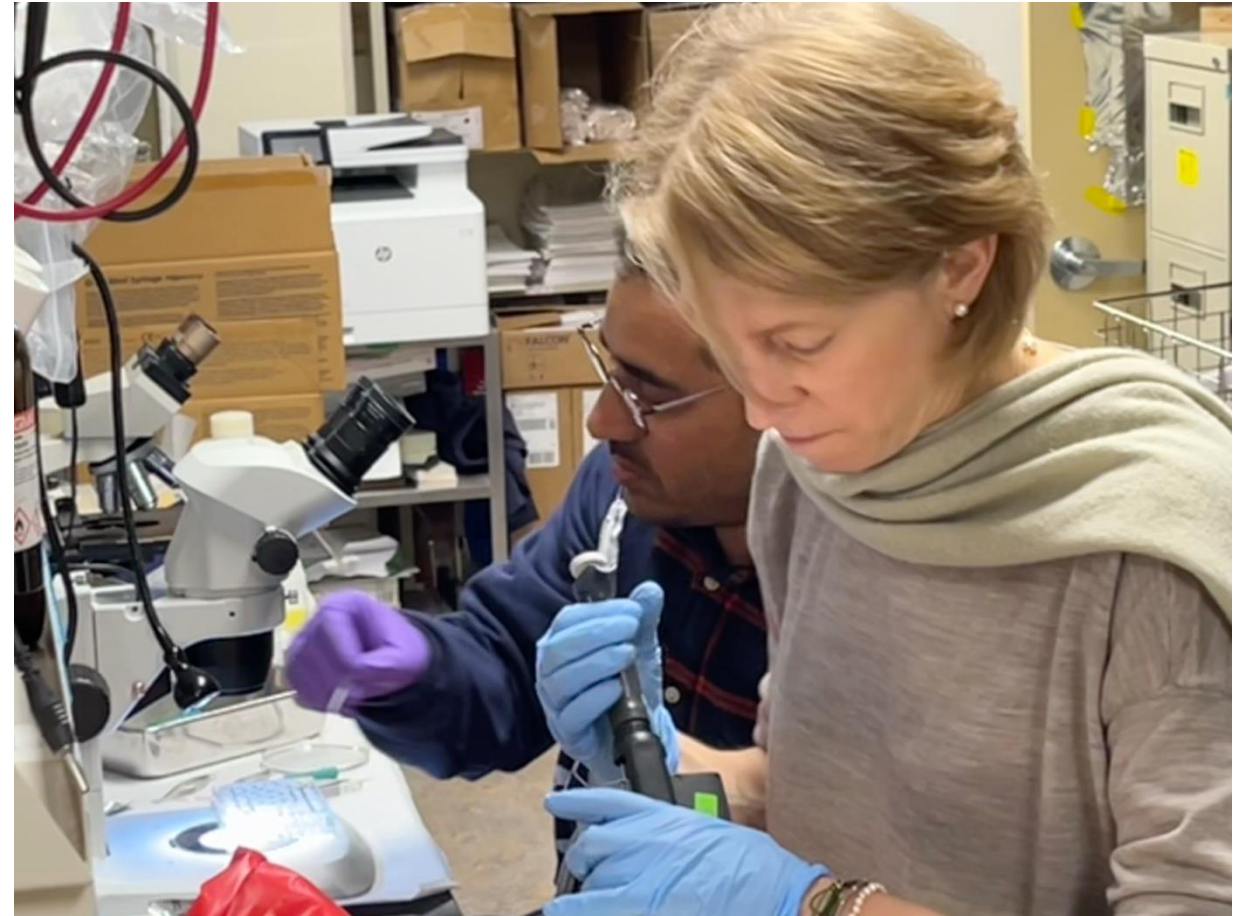
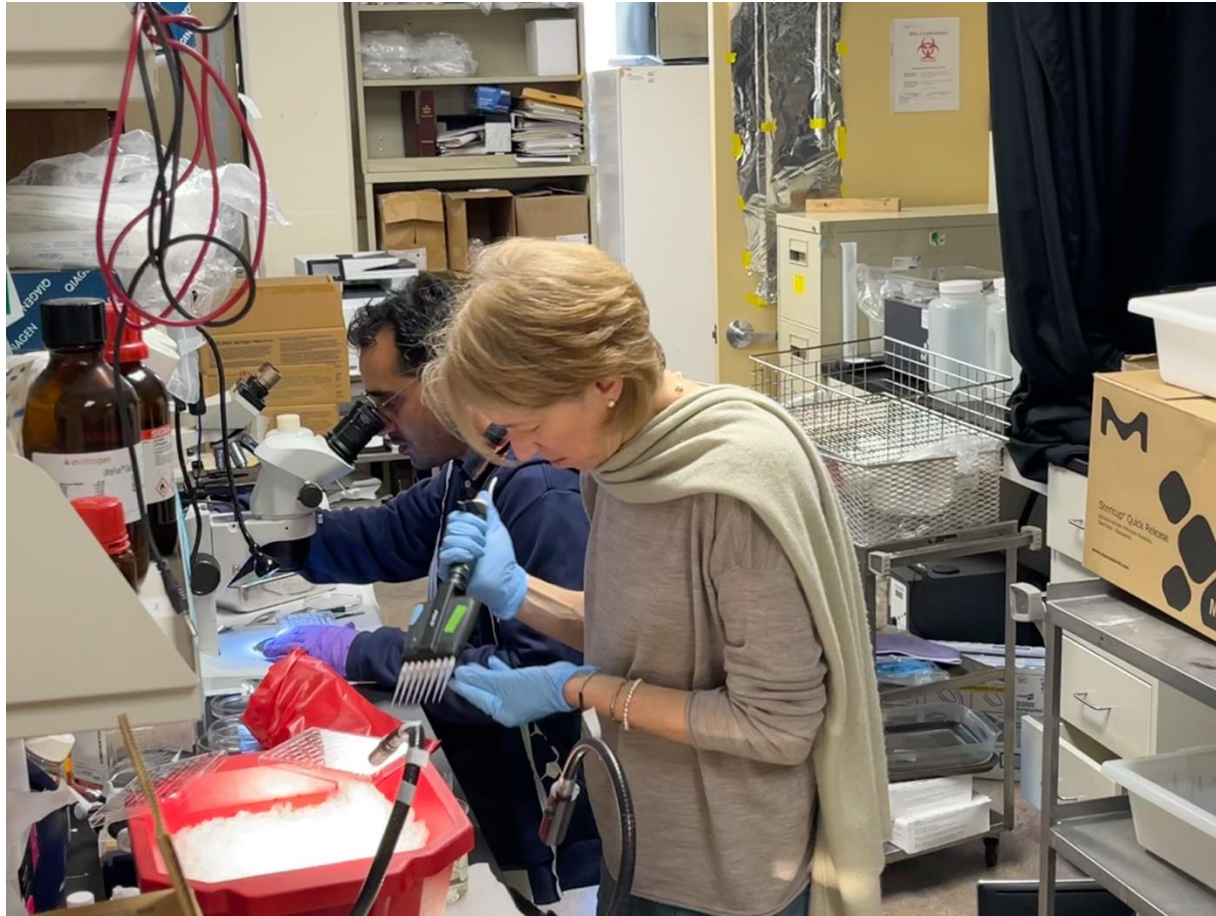
~300 nm (!) Z axis progression

October '24
TriMad Meeting at
U Rochester.

Dave Booth was
recognized with a
poster award.



Retina isolation and punching a la Raghavendra and Erin



Julius Ronkko's PhD Defense in Helsinki



Julius' PhD sword

With Anu Suomalainen at a Helsinki Nature walk



Paolo Bernardi delivers the 1s Seminar of the new Dept'al Seminar Series, organized by Marco, Nov 18, 2024



Raghavendra presents to Paolo and MitoCare



We said Bye to

student !

Everyone has been hard at work, with exciting and novel results emerging!

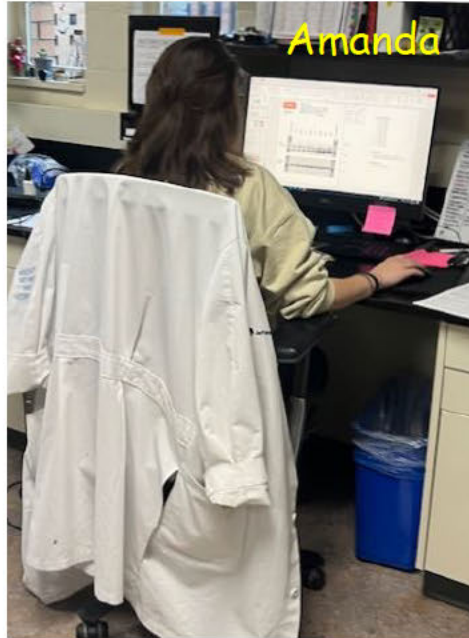
Mehak



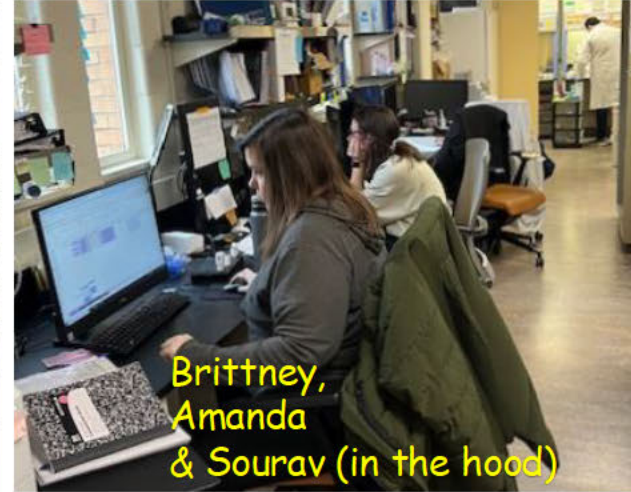
Brittney & Sourav



Amanda



Brittney, Amanda & Sourav (in the hood)



Brittney has definitely be-friended the PTI (and Oroboros)



PLUS:

Great collaborations at MitoCare: with the Hajnóczky lab on MICUs in the heart, and with Tigano lab on "thought experiments" on mt-tRNA processing.

Hasan et al PNAS 2024 PMID 39163336

Yu, Tigano and Seifert EMBO Mol Med PMID 39567836

Great collaborations outside of MitoCare too.

Kantner et al Anal Biochem 2024 PMID 38016493

daCosta et al Mol Metab 2024 PMID 39617267

Maharjan et al Nat Comm 2024 PMID 3942479



Erin publishes a News and Views with Marco and Chenxiao

News & Views | 20 November 2024 | 

PDE12 mediated pruning of the poly-A tail of mitochondrial DNA-encoded tRNAs is essential for survival

 See also: L VAN HAUTE ET AL

Chenxiao Yu , Marco Tigano  , and Erin L Seifert   | [AUTHOR INFORMATION](#)

EMBO Mol Med (2024) | <https://doi.org/10.1038/s44321-024-00171-6>

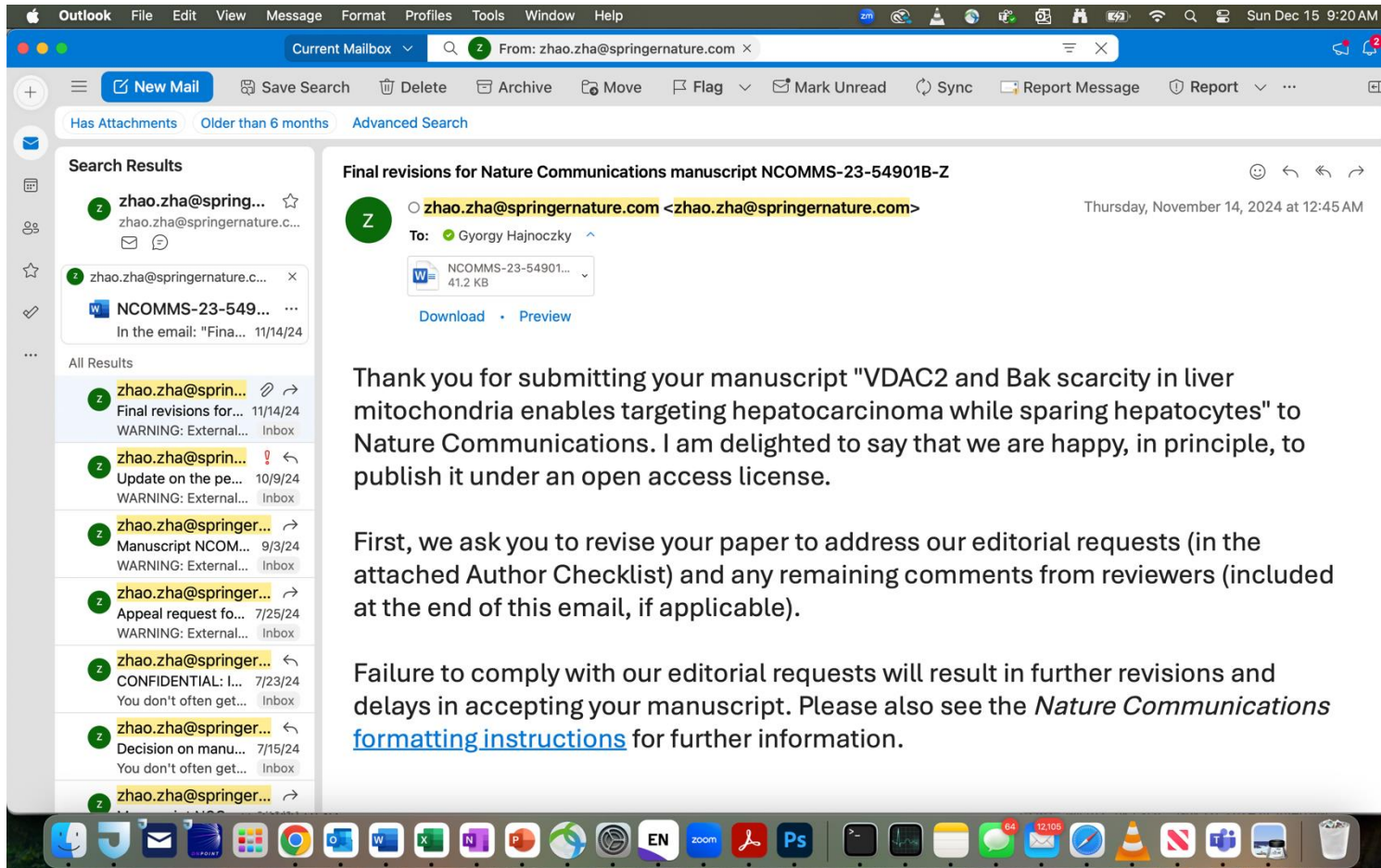


Mitochondrial DNA (mtDNA)-encoded RNA molecules undergo extensive processing to generate mature RNA, including removal of spurious poly-A tails by phosphodiesterase12 (PDE12). A new study by Van Haute and colleagues (Van Haute et al, [2024](#)) describes the first pathogenic variants in the human PDE12 gene. The 3 missense mutations that were identified each carry severe phenotypic consequences that correlate with the presence or not of residual PDE12 protein, show cell-type-specific adaptive responses, and specificity in the mtDNA-encoded electron transport chain subunits that are most affected. These new data demonstrate the necessity of PDE12 for life, and provide invaluable insights into RNA processing in mitochondria.

VDAC2 and Bak scarcity in liver mitochondria enables targeting hepatocarcinoma while sparing hepatocytes

Shamim Naghdi^{1*}, Piyush Mishra^{1*}, Soumya Sinha Roy^{1*}, David Weaver^{1*}, Ludivine Walter¹, Erika Davies¹, Anil Noronha Antony¹, Xuena Lin¹, Gisela Moehren¹, Mark A. Feitelson¹, Christopher A. Reed², Tullia Lindsten³, Craig B. Thompson³, Hien T. Dang⁴, Jan B. Hoek¹, Erik S. Knudsen² and György Hajnóczky^{1†}
Nature Communications 2024 in press

A 20 year long project
reached a conclusion ...



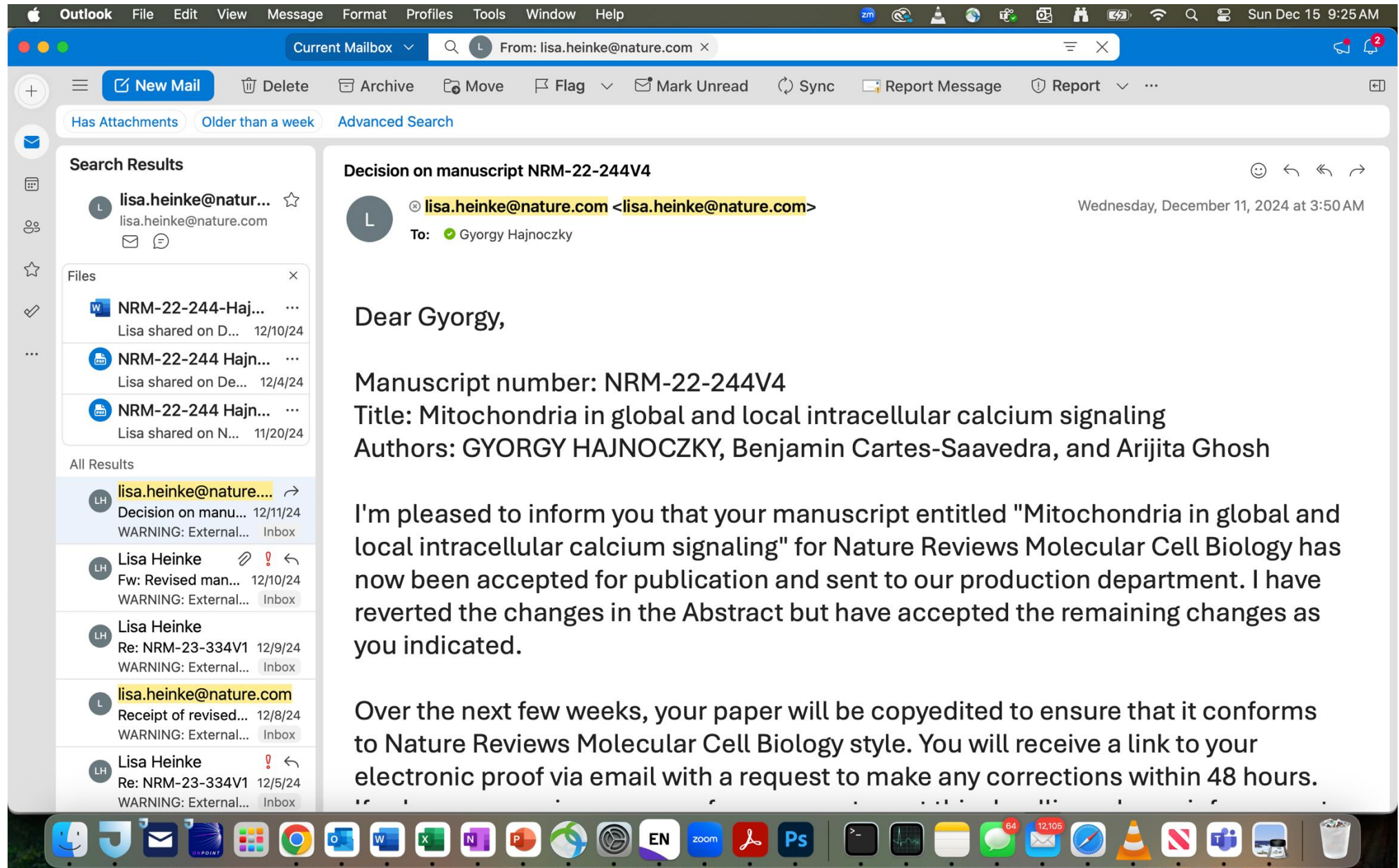
Mate Katona, a former postdoc at MC and current UPitt research associate, gives a talk at SfRBM
Khako and Emily joined him



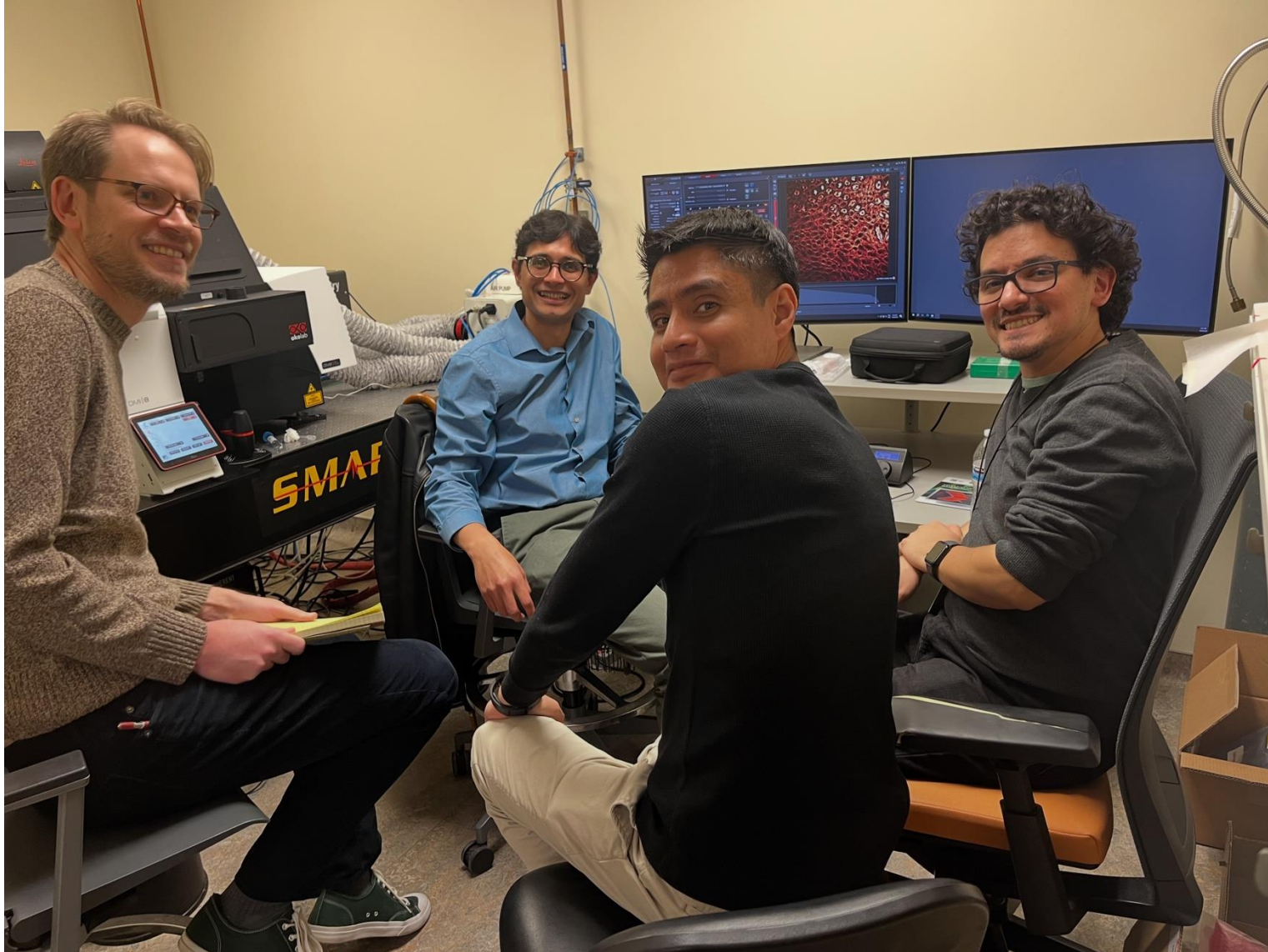
Ryan Cupo visits MitoCare as a post-doc and presents his current work at MitoCircle



A comprehensive review resulted from the diligent efforts of Arijita & Benjamin:



First testing of the Leica FLIM



FLIM is funded
by the Hayne
Donation

Jorge Mondejar,
a PhD student from
Valladolid, Spain,
becomes Master
Segmenter and
Proofreader
during a 3-month
training with
Gyuri C



Another potential function for ER-mitochondrial tethering:

Received: 22 July 2024 | Revised: 24 September 2024 | Accepted: 21 October 2024

DOI: 10.1002/alz.14417

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

RESEARCH ARTICLE

Stabilization of mitochondria-associated endoplasmic reticulum membranes regulates Aβ generation in a three-dimensional neural model of Alzheimer's disease

Jacob C. Zellmer¹ | Marina B. Tarantino¹ | Michelle Kim¹ | Selene Lomoio² |
Masato Maesako³ | György Hajnóczky⁴ | Raja Bhattacharyya¹

¹Genetics and Aging Research Unit, MassGeneral Institute for Neurodegenerative Disease, Henry and Allison McCance Center for Brain Health, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Charlestown, Massachusetts, USA

²Department of Neuroscience, Tufts University School of Medicine, Boston, Massachusetts, USA

³Alzheimer's Disease Research Unit, MassGeneral Institute for Neurodegenerative Disease, Massachusetts General Hospital/Harvard Medical School, Charlestown, Massachusetts, USA

⁴MitoCare Center, Department of Pathology, Anatomy & Cell Biology, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Abstract

INTRODUCTION: We previously demonstrated that regulating mitochondria-associated endoplasmic reticulum (ER) membranes (MAMs) affects axonal Aβ generation in a well-characterized three-dimensional (3D) neural Alzheimer's disease (AD) model. MAMs vary in thickness and length, impacting their functions. Here, we examined the effect of MAM thickness on Aβ in our 3D neural model of AD.

METHODS: We employed fluorescence resonance energy transfer (FRET) or fluorescence-based MAM stabilizers, electron microscopy, Aβ enzyme-linked immunosorbent assay (ELISA), and live-cell imaging with kymography to assess how stabilizing MAMs of different gap widths influence Aβ production and MAM axonal mobility.

RESULTS: Stabilizing tight MAMs (~6 nm gap width) significantly increased Aβ levels, whereas basal (~25 nm) and loose MAMs (~40 nm) maintained or reduced Aβ levels,

A new manifestation of MitoCare productivity,
for the end-of-year holidays



Thanks to all members of the 2024 MitoCare crew for their efforts throughout the year:

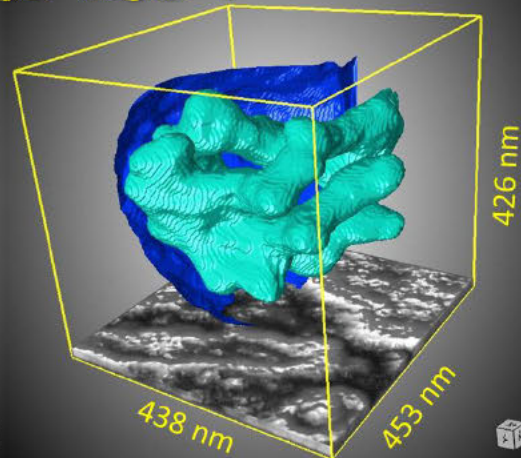
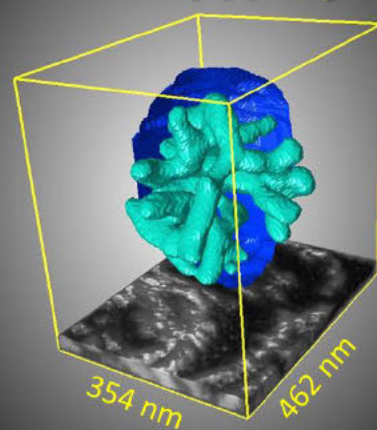
- Aron Andresi
- Faiza Ansari
- Samieh Asadian, PhD
- Prashant Badgujar
- Ariele Baggett
- Brittney Blackburne
- Dave Booth PhD
- Benjamin Cartes Saavedra, PhD
- Marite Castromonte
- Rajarshi Chakrabarty, PhD
- Sourav Chattopadhyay, PhD
- Amanda Collins
- György Csordas, MD
- Marilen Federico PhD
- Amy Ghosh
- Arijita Ghosh PhD

György Hajnóczy, MD, PhD
Prottoy Hasan, PhD
Joannes Hoek, PhD
Steven Hurst, PhD
Victoria Jackson
Joanie Johnson
Suresh K. Joseph, PhD
Shannon Lynch
Peter Nelson
Piyush Mishra, PhD
Jorge Mondejar
Zuzana Nichtova PhD
Joshua Okletay
Davide Pantaleoni
Selin Seckin

- Erin L. Seifert, PhD
- Karan Shah,
- Mehak Shaik
- Dhavalkumar Shukal PhD
- Raghavendra Singh PhD
- John Sanchez-Siguenza
- Marco Tigano, PhD
- Hui-Ying Tsai
- Sidney Tsiong
- Victor Sanchez Vasquez PhD
- Maite Raquel Zavala PhD
- David Weaver
- Michael Young, PhD
- Chenxiao Yu MD
- Yuexing Yuan PhD,

and to our superb Collaborators.

Happy Holidays
and 2025!



MitCare