

Mit  Care

2021

# MCJC 2021 - ZOOM

## Mito Circle Journal Club 2021 Summary

| Date   | Name            | 1 <sup>st</sup> au_last au: title_yr_journal                                                                                                                                         |
|--------|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Jan 11 | Michael (Young) | Atf-6 Regulates Lifespan through ER-Mitochondrial Calcium Homeostasis<br>Burkewitz et al. 2020 <i>Cell Reports</i>                                                                   |
| Jan 25 | Gyuri C         | ER membranes exhibit phase behavior at sites of organelle contact<br>King et al. 2020 <i>PNAS</i>                                                                                    |
| Feb 8  | Tom Neil        | Fission and fusion machineries converge at ER contact sites to regulate mitochondrial morphology. Abrisch et al. 2020 <i>J Cell Biol</i>                                             |
| Feb 22 | Biophysics      |                                                                                                                                                                                      |
| Mar 8  | Steve Hurst     | Mechanisms of EMRE-Dependent MCU Opening in the Mitochondrial Calcium Uniporter Complex. Van Keuren et al. 2020 <i>Cell Rep</i>                                                      |
| Mar 22 | Gyuri H         | Enhancing mitochondrial activity in neurons protects against neurodegeneration in a mouse model of multiple sclerosis.<br>Rosenkranz et al. 2021 <i>eLife</i>                        |
| Apr 5  | Benjamin        | Mitochondrial Safeguard: a stress response that offsets extreme fusion and protects respiratory function via flickering-induced Oma1 activation.<br>Murata et al. 2020 <i>EMBO J</i> |
| Apr 19 | Zuzana          | Correlation of organelle dynamics between light microscopic live imaging and electron microscopic 3D architecture using FIB-SEM.<br>Ohta et al. 2021 <i>Microscopy</i>               |
| May 3  | Dave Booth      | The mitochondrial calcium uniporter compensates for Complex I dysfunction. Balderas et al. preprint @ ResearchSquare                                                                 |
| May 17 | Elena           | The Mechanism of MICU-Dependent Gating of the Mitochondrial Ca <sup>2+</sup> Uniporter. Garg et al. 2021 BioRxiv                                                                     |
| Jun 7  | Mate            | Calcium channel ITPR2 and mitochondria–ER contacts promote cellular senescence and aging. Ziegler et al. 2021 <i>Nat Commun</i>                                                      |
| Jun 21 | Sergio (GH Lab) | Aberrant activity of mitochondrial NCLX is linked to impaired synaptic transmission and is associated with mental retardation.<br>Stavsky et al. 2021 <i>Commun Biol</i>             |

|        |                    |                                                                                                                                                                                                                                                                                                         |
|--------|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Aug 16 | Prottoy            | Distinct fission signatures predict mitochondrial degradation or biogenesis<br>Kleele et al 2021 <i>Nature</i>                                                                                                                                                                                          |
| Aug 30 | Arijita            | BOK controls apoptosis by Ca <sup>2+</sup> transfer through ERmitochondrial contact sites. Carpio et al 2021 <i>Cell Rep</i>                                                                                                                                                                            |
| Sep 13 | Ariele             | Superiority of focused ion beam-scanning electron microscope tomography of cardiomyocytes over standard 2D analyses highlighted by unmasking mitochondrial heterogeneity.<br>Heinen-Weiler et al. 2021 <i>J Cachexia, Sarcopenia Muscle</i>                                                             |
| Sep 27 | Veronica           | Long-lived mitochondrial cristae proteins in mouse heart and brain<br>Bomba-Warczak et al 2021 <i>J Cell Biol</i>                                                                                                                                                                                       |
| Oct 11 | Piyush             | VPS13D bridges the ER to mitochondria and peroxisomes via Miro.<br>Guill'en-Samander et al. 2021 <i>J Cell biol</i>                                                                                                                                                                                     |
| Oct 25 | Marilen (Sheu lab) | Defining the molecular mechanisms of the mitochondrial permeability transition through genetic manipulation of F-ATP synthase<br>Carrer et al. 2021 <i>Nat Commun</i>                                                                                                                                   |
| Nov 8  | Carmen             | Mitochondrial fatty acid synthesis coordinates oxidative metabolism in mammalian mitochondria. Nowinski et al. 2020 <i>eLife</i>                                                                                                                                                                        |
| Nov 22 | Cesar              | Na <sup>+</sup> controls hypoxic signalling by the mitochondrial respiratory chain<br>Hernansanz-Agustín et al 2020 <i>Nature</i>                                                                                                                                                                       |
| Dec 6  | RVS                | Mitochondrial calcium uniporter deletion prevents painful diabetic neuropathy by restoring mitochondrial morphology and dynamics.<br>George et al. 2021 <i>Pain</i>                                                                                                                                     |
| Dec 20 | Shey               | Mitochondrial Fission and Fusion Factors Reciprocally Orchestrate Mitophagic Culling in Mouse Hearts and Cultured Fibroblasts. Song et al. 2015 <i>Cell Metab.</i><br>Endogenous Drp1 Mediates Mitochondrial Autophagy and Protects the Heart Against Energy Stress. Ikeda et al. 2015 <i>Circ. Res</i> |

## MitoCircle 2021 ... another (mostly) Zoom edition

Carmen Mannella, Ph.D. Jan 19, 2021 Consequences of folding the chemiosmotic membrane

Tish Murphy, Ph.D. Feb 1, 2021 Role of mitochondria in Cardiovascular disease

John Lederer, Ph.D. Feb 15, 2021 Mitochondrial ATP production in the heart.

Paul Brookes, Ph.D. Mar 15, 2021 Mitochondria and Methylglyoxal Metabolism in Cardiac Ischemia

Mohamed Trebak, Ph.D. May 10, 2021 Coordinated functions of plasma membrane and organellar channel isoforms underlie the diversity of mammalian  $\text{Ca}^{2+}$  signaling events

John Lemasters, M.D., Ph.D. Jun 14, 2021 Aldehydes are the Culprit: A Unifying Paradigm for the Pathogenesis of Alcoholic and Non-Alcoholic Steatohepatitis

Andrew Thomas, Ph.D. (in person) Oct 19, 2021 Calcium signaling and fatty liver

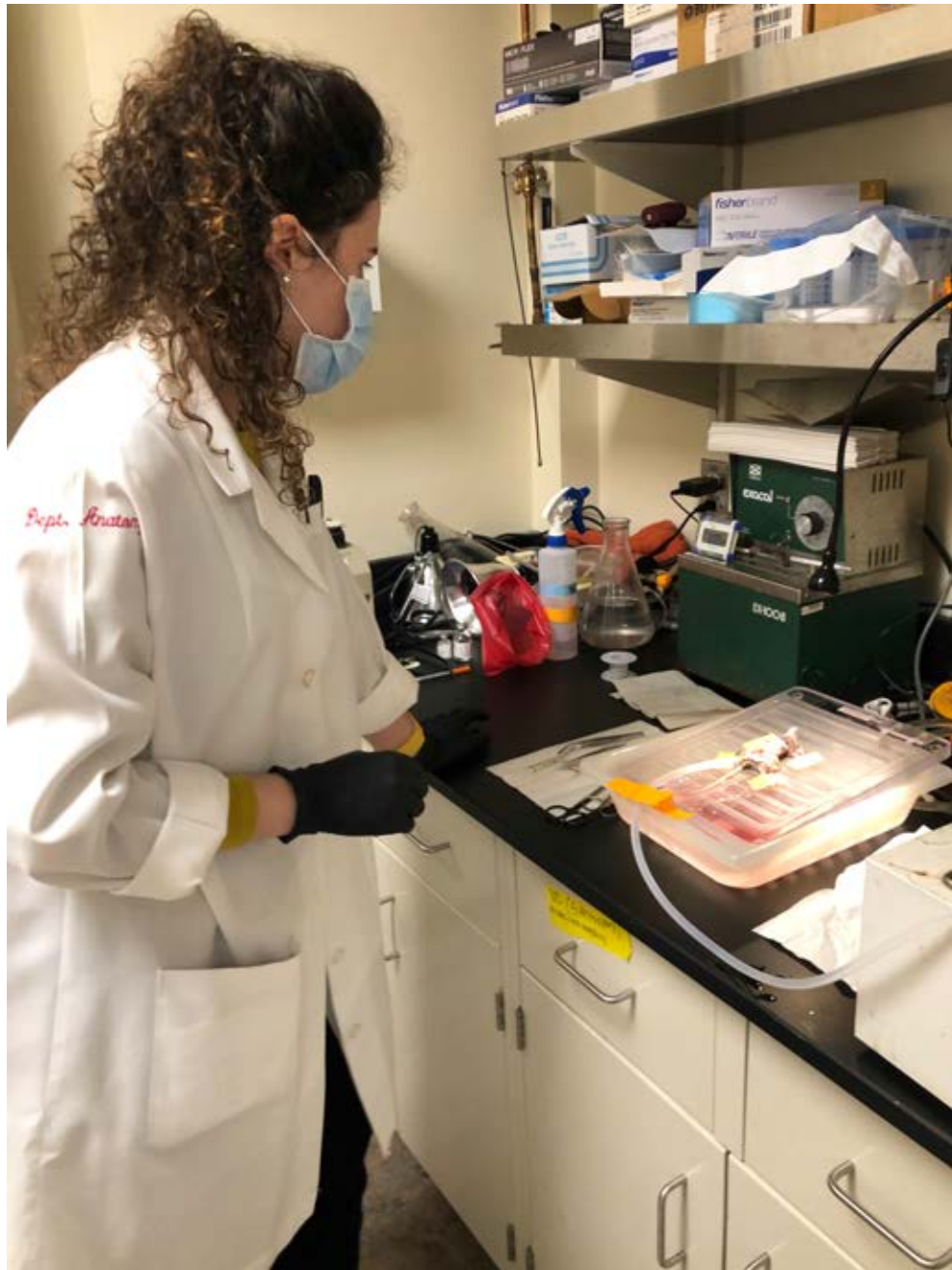
Ryan Cupo, Ph.D. (in person) Nov 4, 2021 Discovery of a human mitochondrial protein disaggregase, Skd3

# Structural, functional and molecular affairs at membrane contacts between SR/ER and mitochondria in the cardiac muscle.





# Kata & Mate: real and virtual lab moments

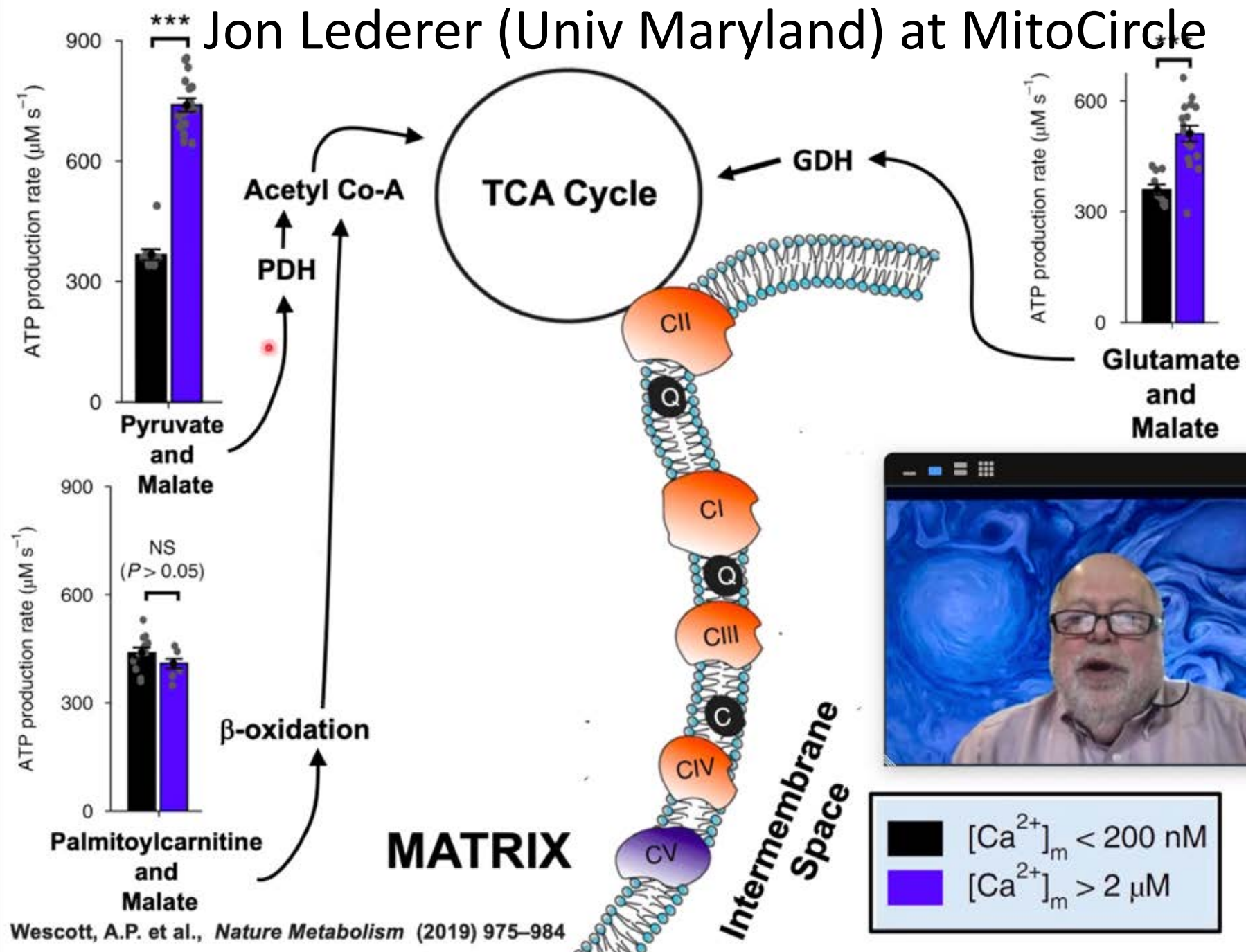


Belated receiving of  
a 2020 award at a  
virtual ceremony





# Jon Lederer (Univ Maryland) at MitoCircle

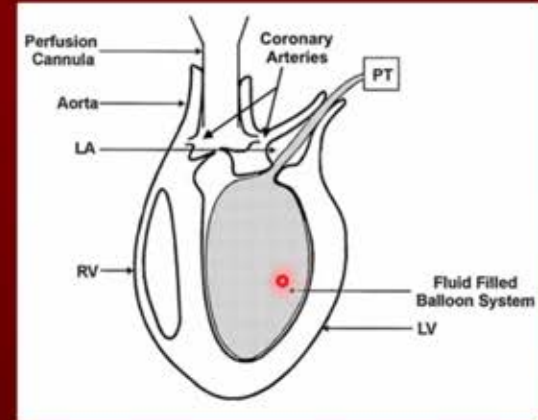


Attila Fonyo, who discovered the Phosphate Carrier beats COVID-19 and celebrates 93<sup>rd</sup> birthday with recalling his mitochondrial research experience in the 1960s





# Langendorff Perfused Mouse Heart



Paul Brookes (Univ Rochester)  
Presents at MitoCircle



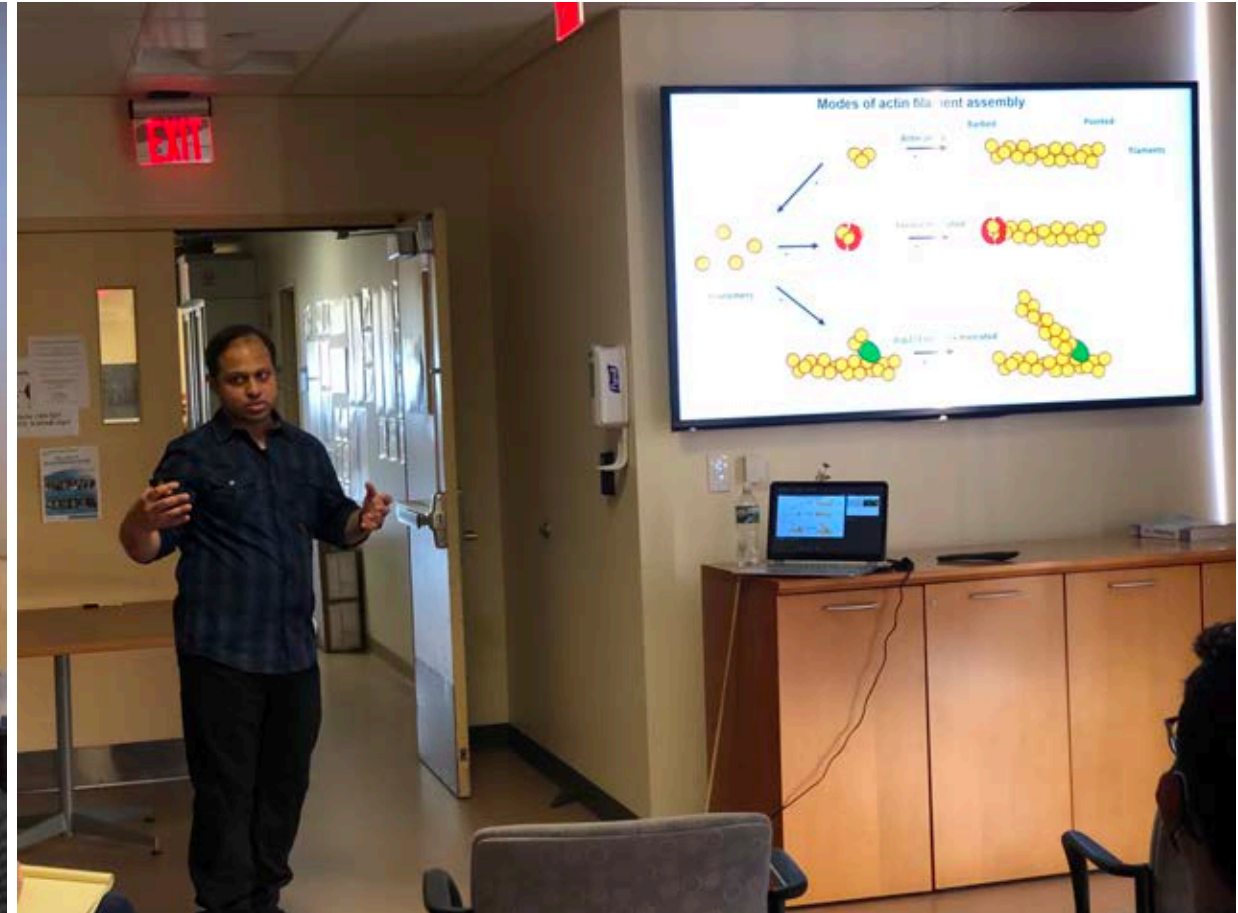
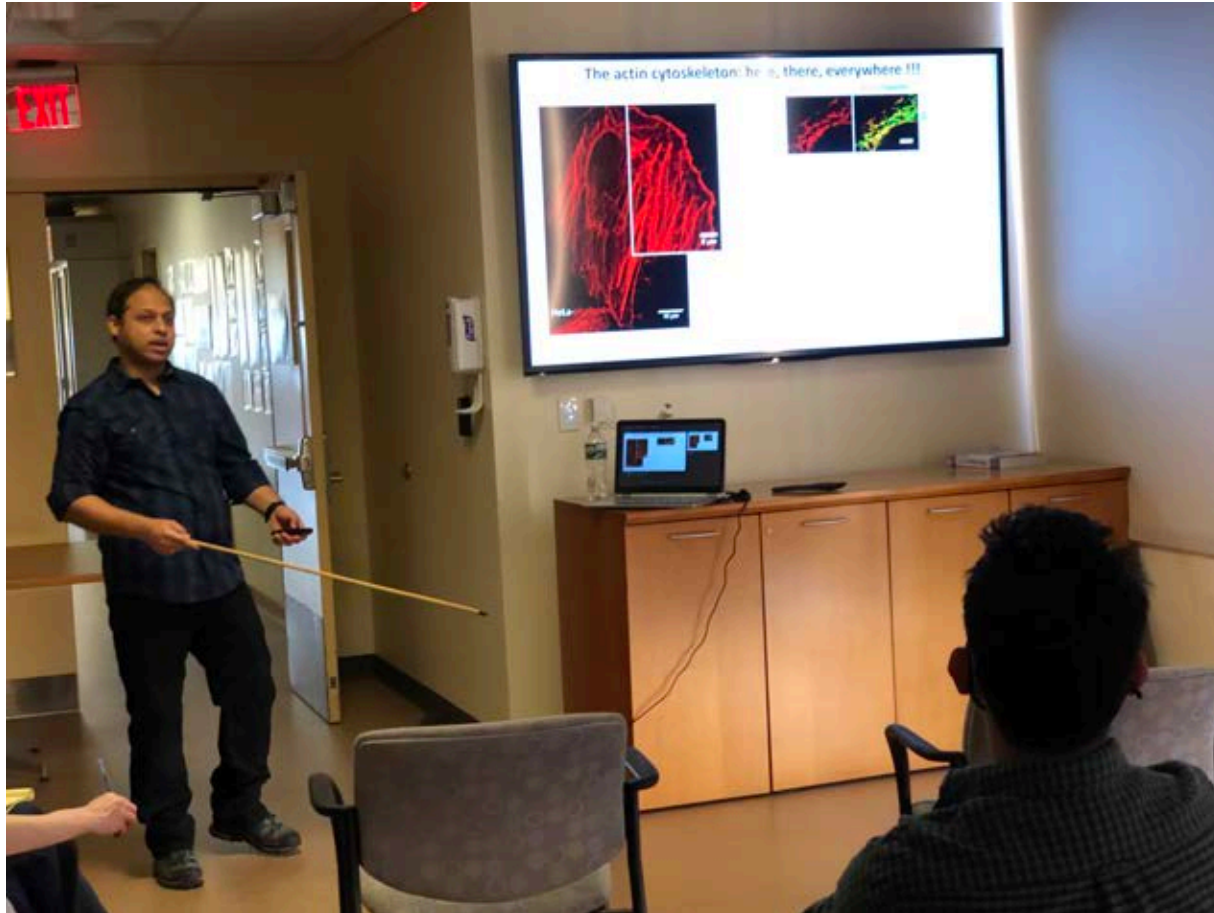
PAUL BROOKES



Marco's main postdoc work from NYU is printed!

[Nuclear sensing of breaks in mitochondrial DNA enhances immune surveillance.](#) **Tigano M**, Vargas DC, Tremblay-Belzile S, Fu Y, Sfeir A. Nature. 2021 Mar;591(7850):477-481. PMID: 33627873

# Rajarshi Chakrabarti visits MitoCare and presents at MitoCircle



# New MPI RO1 starts in April

**ER-mitochondrial communication in calcium signaling, energy metabolism and liver disease**

**Project Number 1R01DK125897-01A1**

**Former Number 1R01DK125897-01**

**Contact PI/Project Leader HAJNOCZKY, GYORGY**

**MPI CSORDAS, GYORGY**

**Awardee Organization THOMAS JEFFERSON UNIVERSITY**



Solana Rosalind Smith was born on May 8<sup>th</sup>  
as the 1<sup>st</sup> MitoCare baby in many years



Solana weighs 7 lbs 8 oz

Soon after we wished his father, David, good luck because he accepted a position to lead a CHOP OMICS facility

Zehnie Priyol Hasan arrives on May 12<sup>th</sup> and  
Prottoy happily treats the whole MC team





# Welcome to MitoCare babies 2021!





THE TIGANO LAB  
AT MITOCARE  
TIP. 1:  
IF YOU ARE IN A  
RUSH: DON'T RUSH

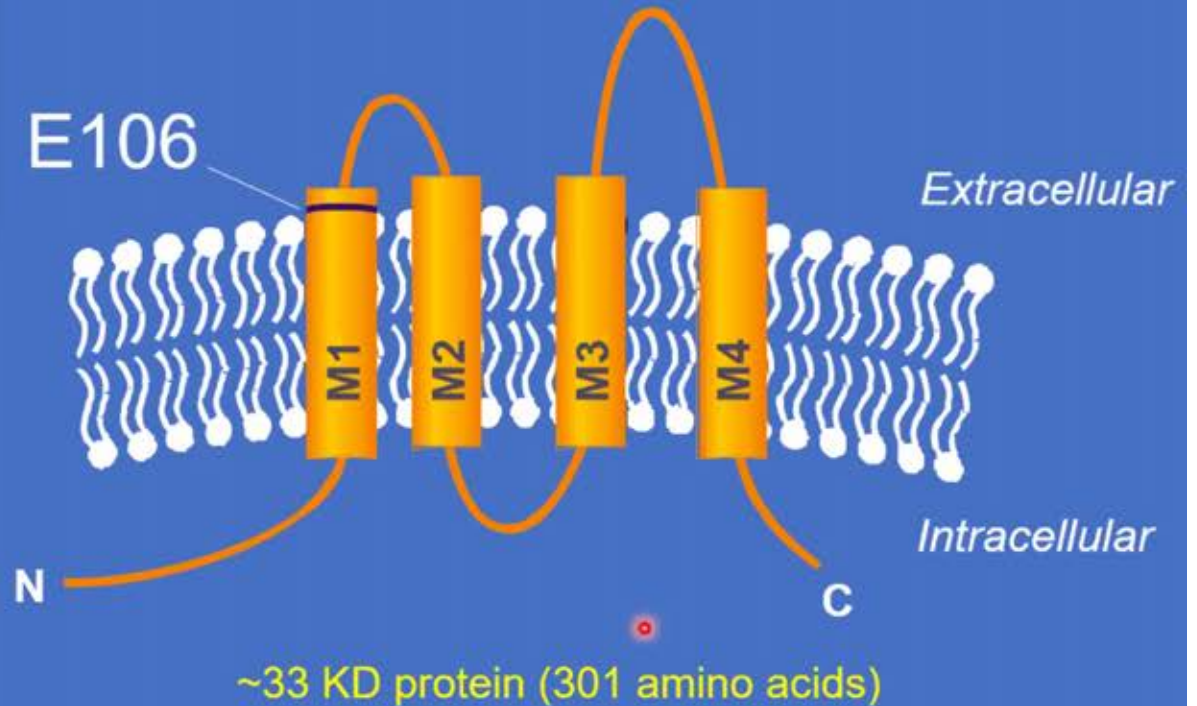


FIB-SEM arrives and fills  
the new facility



Mo Trebak  
from UPitt

ORAI1



dOrai

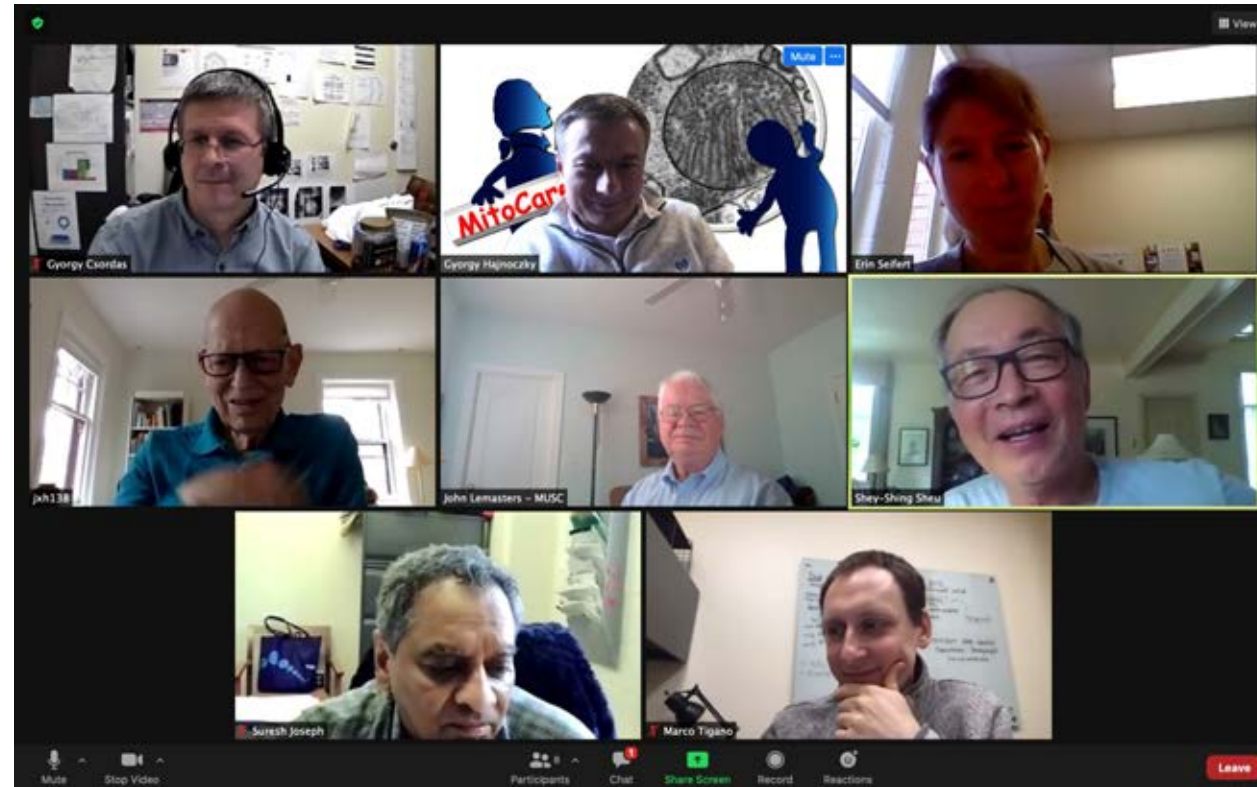
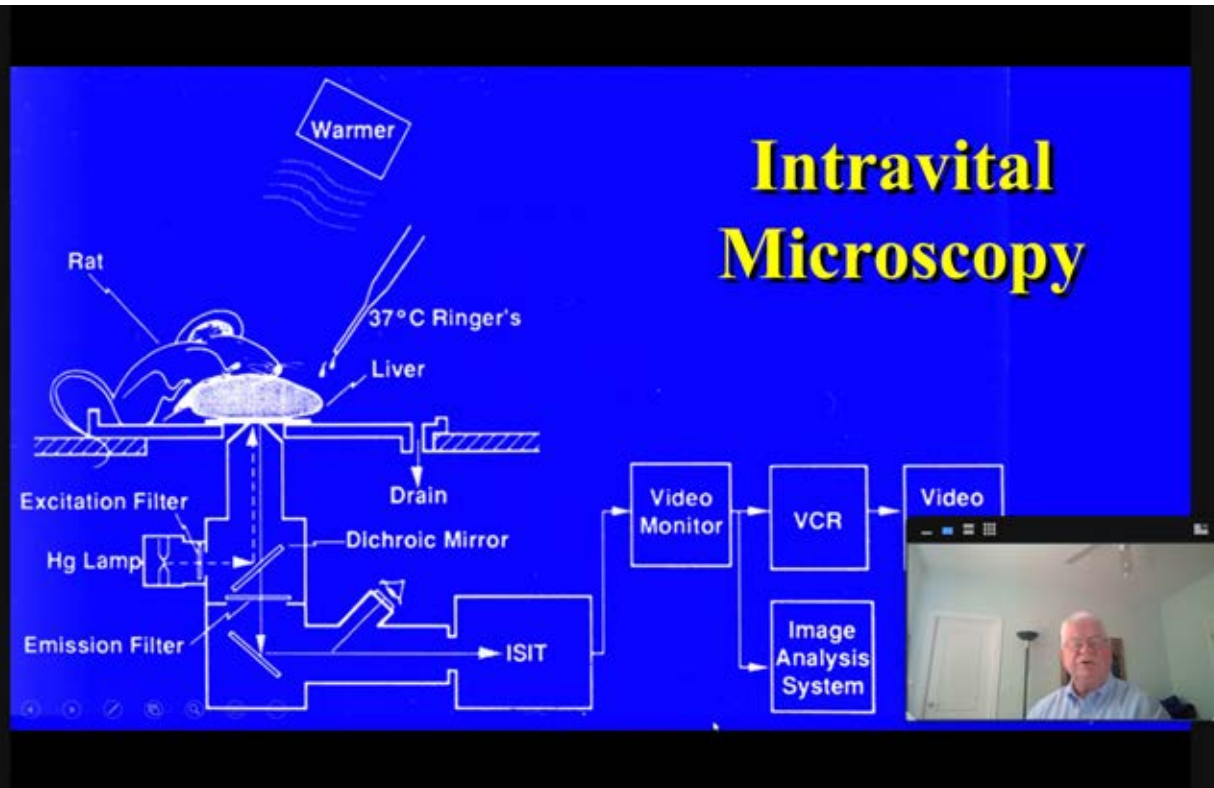
Hou et al. *Science*.  
2012. 338: 1308-13.





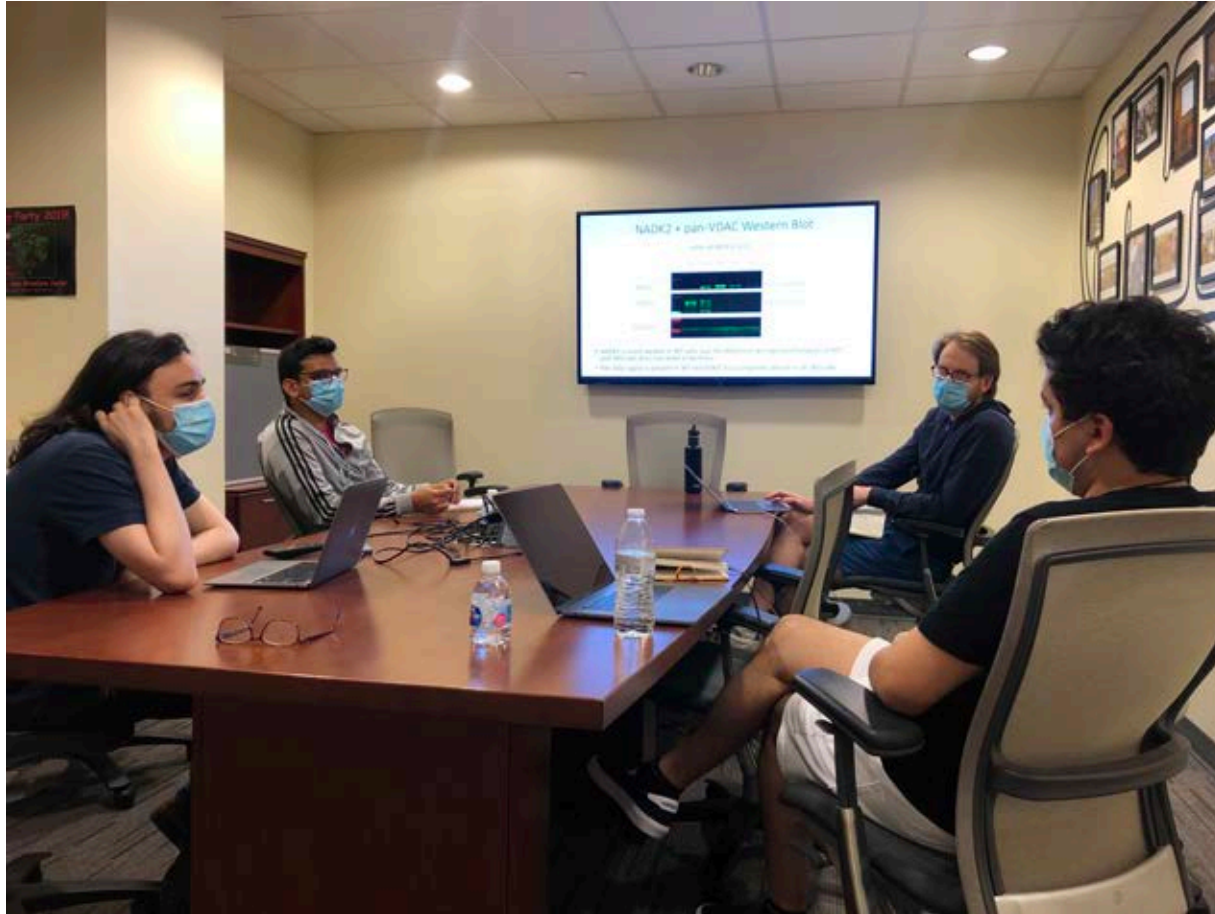
# John Lemasters (MUSC) in the MitoCircle

Post-presentation chat with the Faculty

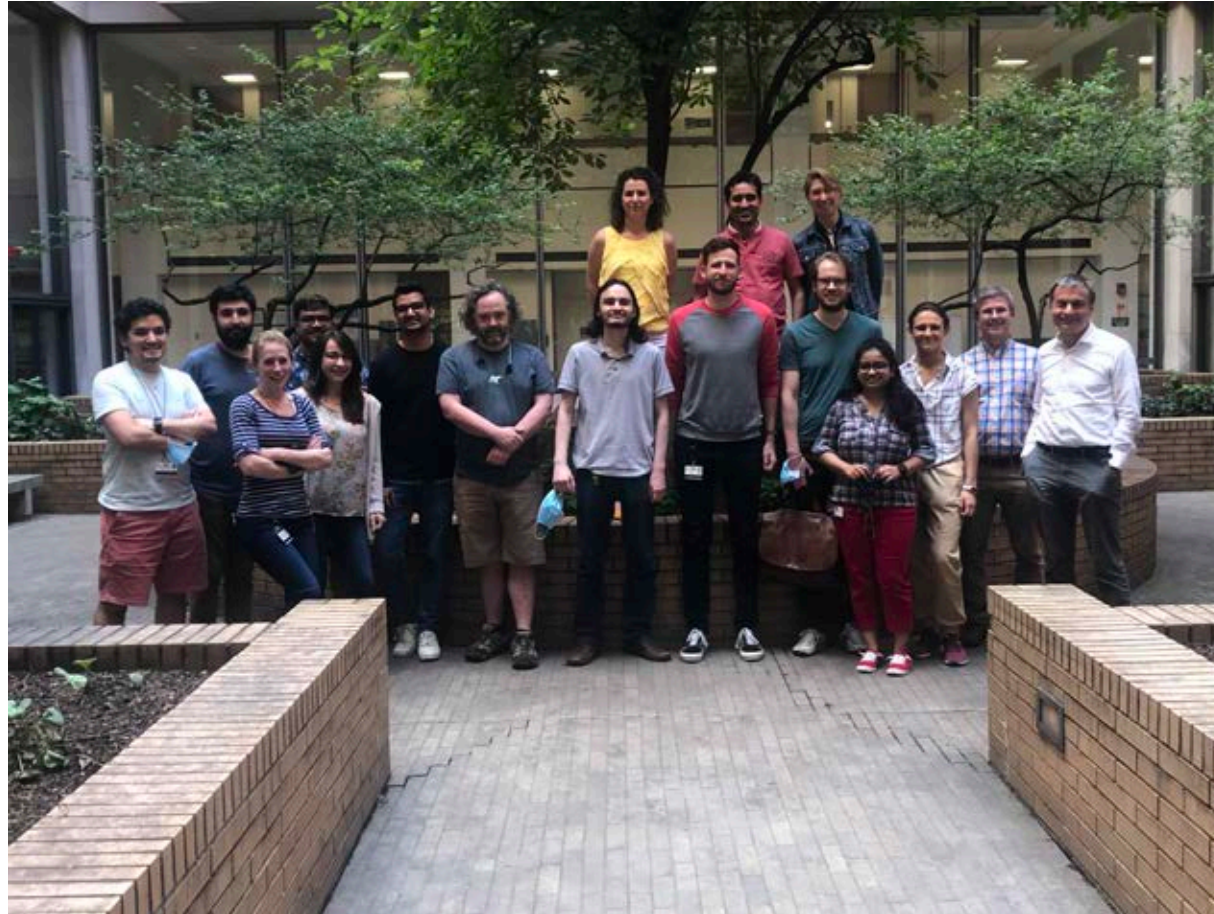




# Sergio's final VDAC labmeeting



Last group photo before Sergio, Mate & Kata depart





# Updated MitoCare Faculty Photo







Mate's final lab meeting presentation before heading to UPitt



2016-  
2021

MitCare





And another New MPI RO1 starts in September

**Ethanol Effects on the Transcriptional Regulatory  
Network in Liver Regeneration**

**Project Number**2R01AA018873-11A1

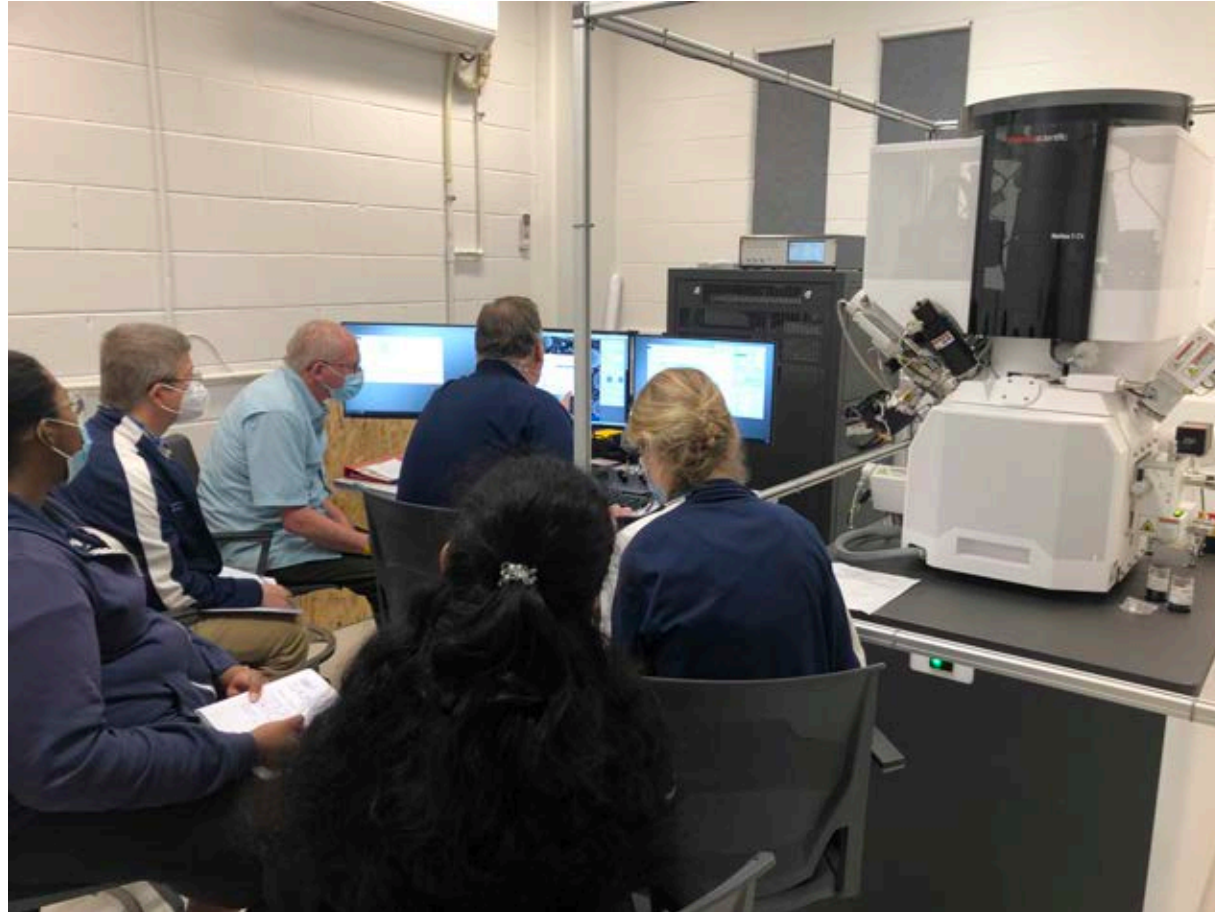
**Former Number**2R01AA018873-11

**Contact PI/Project Leader**HOEK, JOANNES B

**Awardee Organization**THOMAS JEFFERSON UNIVERSITY



# Learning the FIB-SEM instrument



# Csordas Lab submitted MS

## Enhanced mitochondria-SR tethering triggers adaptive cardiac muscle remodeling.

**Zuzana Nichtová PhD<sup>1</sup>, Yuexing Yuan PhD<sup>2</sup>, Celia Fernandez-Sanz PhD<sup>2</sup>, Sergio De La Fuente PhD<sup>2</sup>, Stephen Hurst PhD<sup>1</sup>, Sebastian Lanvermann PhD<sup>2</sup>, Hui-Ying Tsai MS<sup>2</sup>, Christopher Thompson<sup>3</sup>, Cedric Bouchet-Marquis PhD<sup>3</sup>, Péter Várnai MD, PhD<sup>4</sup>, Erin L Seifert PhD<sup>1</sup>, Gerald W Dorn II MD<sup>5</sup>, Shey-Shing Sheu PhD<sup>2</sup>, György Csordás MD<sup>1</sup>**

<sup>1</sup>MitoCare, Pathology, Anatomy and Cell Biology, TJUH, Philadelphia, PA, USA

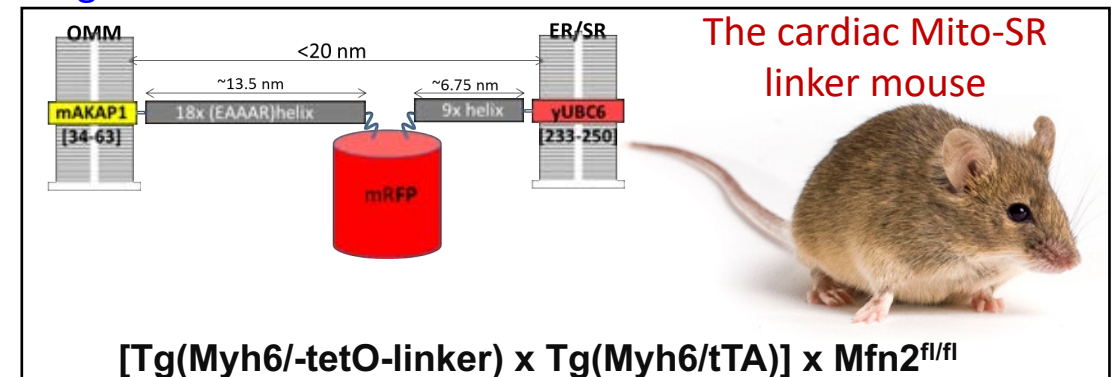
<sup>2</sup>Center of Translational Medicine, TJUH, Philadelphia, PA, USA

<sup>3</sup>Thermo Fisher Scientific, Hillsboro, OR, USA

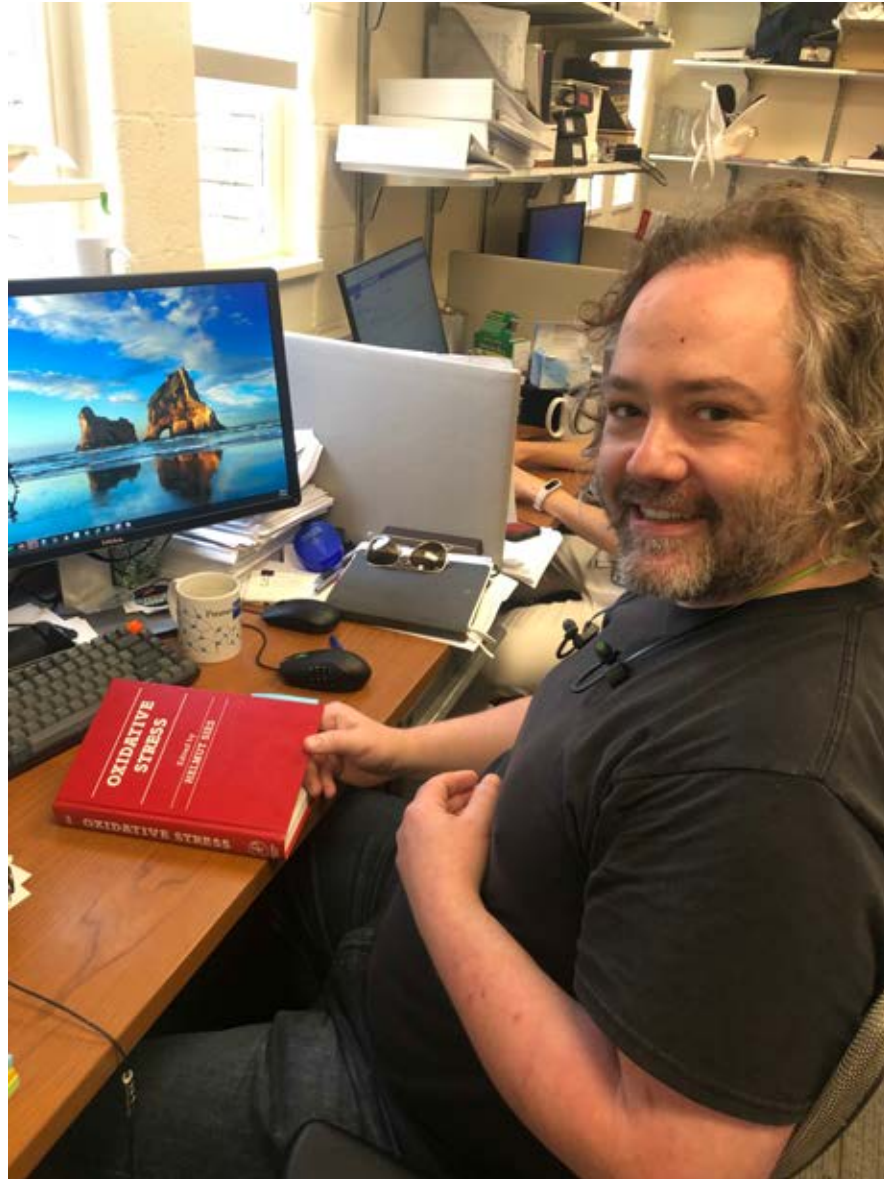
Under revision to *Circulation Research*



Csordas' Lab  
Sheu's Lab

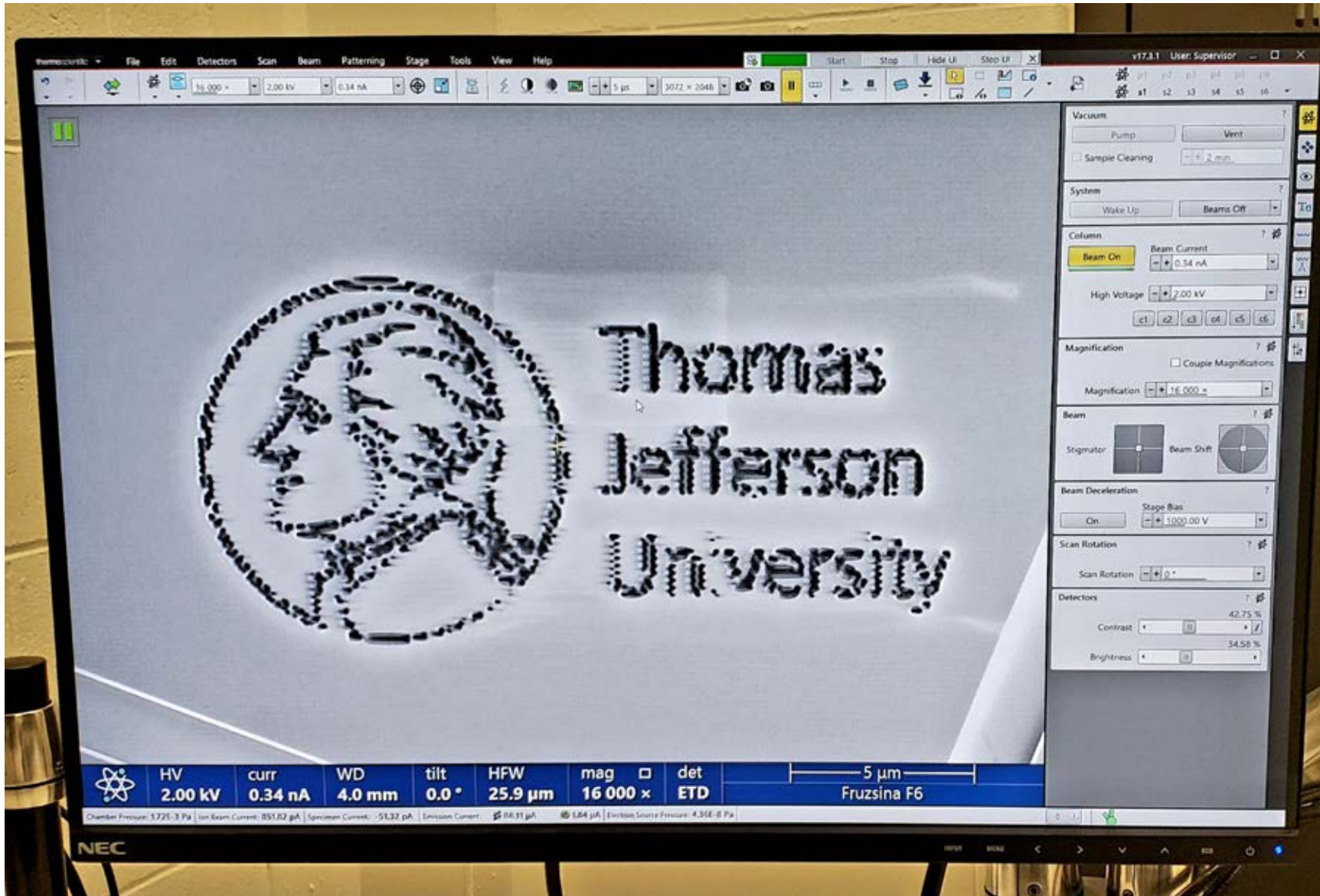


Dave's new reading material is the redox book of Helmut Sies





# Jefferson - @ microscale (pattern milling via FIB-SEM)



Marco's 1<sup>st</sup> assistant, Andrew  
arrives



# Mitocare.org brought to life by Marco!

Donate here!

Mitocare

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MAKING THE INVISIBLE VISIBLE SINCE 2013

## — MISSION —

innovate, create, and use advanced technologies  
in a programmatic context  
to study mitochondria in health and disease.



## — WHY MITOCHONDRIA —

For a long time, we thought  
mitochondria were just the powerhouses of the cell.



2021 Postdoctoral  
Symposium with the  
participation of Arijita,  
Elena & Benjamin.  
Arijita brings home  
one of the awards!



# 2021 EMBO meeting on Mitochondria - the first in person meeting in 20 months!





Andrew Thomas stops by to  
present at MitoCircle and to  
catch up with friends





# FASEB Calcium Meeting (Oct 26-28, 2021) moves on-line .... and in-house





FIB-SEM with open chamber for the users' training





Lot of smiles and  
sadness as  
Ji leaves to take on a  
new challenge





# Ryan Cupo, Ph.D. presents at MitoCircle Nov 2021



... with an opportunity for an after party,  
and seeing George Purkins

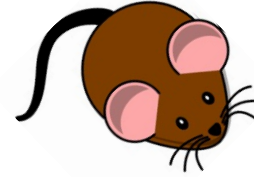




Inspecting the new mouse house ...  
and welcome to the IP3R mouse gang



IP3R TKO floxed



IP3R1 floxed



IP3R2 floxed



# First Photo with TJ for Marite & Mom



November 18:

Marco scores a 2-yr Landenberger Foundation award a day after Lillian, his wife is accepted to the Class 2026 of SKMC!



# Michael's “big paper” from his PhD studies is out

Young MP, Schug ZT, Booth DM, Yule DI, Mikoshiba K, Hajnóczky G, Joseph SK.  
Metabolic adaptation to the chronic loss of  $\text{Ca}^{2+}$  signaling induced by  
KO of  $\text{IP}_3$  receptors or the mitochondrial  $\text{Ca}^{2+}$  uniporter. J  
Biol Chem. 2021 Nov 19;298(1):101436. doi: 10.1016/j.jbc.2021.101436. Epub ahead  
of print. PMID: 34801549; PMCID: PMC8672050.

Bradley joins  
as the first  
human team  
member in  
Marco's lab:



# Gyuri & Shey succeed with a multiPI NIH grant!

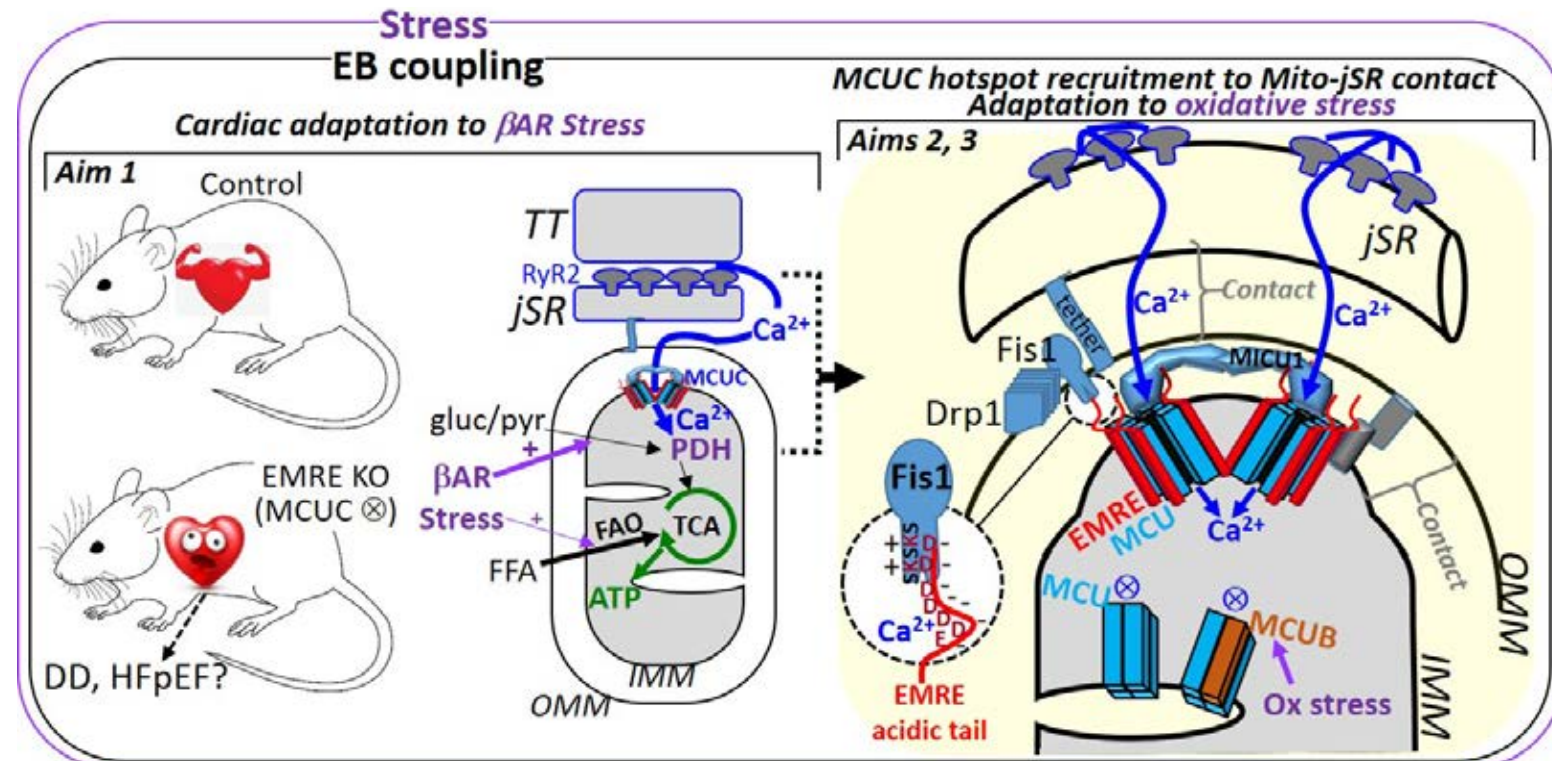
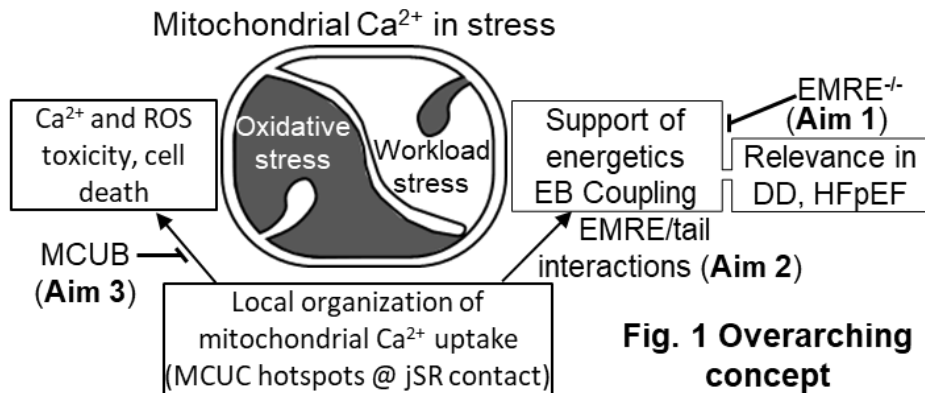


Department of Health and Human Services  
National Institutes of Health  
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Notice of Award  
FAIN# R01HL122124  
Federal Award Date  
12/06/2021

## 14. Federal Award Project Title

Mitochondria-SR Tethering: Its Role in Cardiac Bioenergetics and Ca<sup>2+</sup> Dynamics





# Visiting the Mitochondria & Metabolism Center



How many MitoCare friends can you recognize on the photos?

# Jan's 2021 in publications

Verma A, Manchel A, Narayanan R, Hoek JB, Ogunnaike BA, Vadigepalli R. A

Spatial Model of Hepatic Calcium Signaling and Glucose Metabolism Under Autonomic Control Reveals Functional Consequences of Varying Liver Innervation Patterns Across Species. *Front Physiol.* 2021 Nov 26;12:748962. doi: 10.3389/fphys.2021.748962. PMID: 34899380; PMCID: PMC8662697.

Parrish A, Srivastava A, Juskeviciute E, Hoek JB, Vadigepalli R.

Dysregulation of miR-21-associated miRNA regulatory networks by chronic ethanol consumption impairs liver regeneration. *Physiol Genomics.* 2021 Dec 1;53(12):546-555. doi: 10.1152/physiolgenomics.00113.2021. Epub 2021 Nov 19. PMID: 34796728.

Gaspers LD, Thomas AP, Hoek JB, Bartlett PJ.

Ethanol Disrupts Hormone-Induced Calcium Signaling in Liver. *Function (Oxf).* 2021 Jan 8;2(2):zqab002. doi: 10.1093/function/zqab002. MID: 33604575; PMCID: PMC7875097.

Rottenberg H, Hoek JB.

The Mitochondrial Permeability Transition: Nexus of Aging, Disease and Longevity. *Cells.* 2021 Jan 6;10(1):79. doi: 10.3390/cells10010079. PMID: 33418876; PMCID: PMC7825081.

# Seifert Lab 2021

The whole crew participated in the Frataxin theme:

**First paper of the Frataxin theme:**

**Adaptation of the heart to Frataxin depletion: Evidence that integrated stress response can predominate over mTORC1 activation**

[César Vásquez-Trincado](#)<sup>1</sup>, [Monika Patel](#)<sup>1</sup>, [Aishwarya Sivaramakrishnan](#)<sup>1</sup>, [Carmen Bekeová](#)<sup>1</sup>, [Lauren Anderson-Pullinger](#)<sup>1</sup>, [Nadan Wang](#)<sup>2</sup>, [Hsin-Yao Tang](#)<sup>3</sup>, [Erin L Seifert](#)<sup>1</sup> Human Molecular Genetics. 2021 Sep 22;ddab216. Online ahead of print.

**Second Frataxin paper submitted (A Jefferson (Seifert, Csordas)-Penn-CHOP collaboration):**

**Frataxin deficiency lowers lean mass and triggers the integrated stress response in skeletal muscle**

Cesar Vasquez-Trincado<sup>1</sup>, Julia Dunn<sup>2</sup>, Ji In Han<sup>1</sup>, Briyanna Hymms<sup>1</sup>, Jaclyn Tamaroff<sup>2</sup>, Monika Patel<sup>1</sup>, Sara Nguyen<sup>2</sup>, Anna Dedio<sup>2</sup>, Kristin Wade<sup>2</sup>, Chinazo Enigwe<sup>2</sup>, Zuzana Nichtova<sup>1</sup>, David R. Lynch<sup>3,4</sup>, Gyorgy Csordas<sup>1</sup>, Shana E. McCormack<sup>2,5</sup>, Erin L. Seifert<sup>1\*</sup>. Under review at JCI Insight

Submission of 2 R01s: Another big effort from the whole team!

Cesar was invited for an oral presentation:

XXXVI Annual Meeting of the Chilean Society for Physiological Sciences (Chile)

Topic: Frataxin depletion in the heart

Carmen: Exciting opportunity: JO2 in previously frozen human heart, in Collaboration with Prottý (Hajnoczky lab)

Bye to Ji, wishing her all the best in the next steps







-Monteith AJ, Miller JM, Beavers WN, Maloney KN, Seifert EL, Hajnoczky G, Skaar EP. Mitochondrial calcium uniporter affects neutrophil bactericidal activity during *Staphylococcus aureus* infection. Infect Immun. 2021 Dec 6:IAI0055121. doi: 10.1128/IAI.00551-21. Epub ahead of print. PMID: 34871043.

-Young MP, Schug ZT, Booth DM, Yule DI, Mikoshiba K, Hajnoczky G, Joseph SK. Metabolic adaptation to the chronic loss of Ca<sup>2+</sup> signaling induced by KO of IP<sub>3</sub> receptors or the mitochondrial Ca<sup>2+</sup> uniporter. J Biol Chem. 2021 Nov 19;298(1):101436. doi: 10.1016/j.jbc.2021.101436. Epub ahead of print. PMID: 34801549; PMCID: PMC8672050

-Berezhnaya E, Hajnoczky G. How do MICUs gate the mitochondrial calcium uniporter? Cell Calcium. 2021 Dec;100:102497. doi: 10.1016/j.ceca.2021.102497. Epub 2021 Nov 2. PMID: 34775300.

-Booth DM, Várnai P, Joseph SK, Hajnoczky G. Oxidative bursts of single mitochondria mediate retrograde signaling toward the ER. Mol Cell. 2021 Sep 16;81(18):3866-3876.e2. doi: 10.1016/j.molcel.2021.07.014. Epub 2021 Aug 4. PMID: 34352204; PMCID: PMC8455442.

-Kohlschmidt N, Elbracht M, Czech A, Häusler M, Phan V, Töpf A, Huang KT, Bartok A, Eggermann K, Zippel S, Eggermann T, Freier E, Groß C, Lochmüller H, Horvath R, Hajnoczky G, Weis J, Roos A. Molecular pathophysiology of human MICU1 deficiency. Neuropathol Appl Neurobiol. 2021 Oct;47(6):840-855. doi:10.1111/nan.12694. Epub 2021 Feb 22. PMID: 33428302.

-Márta K, Hasan P, Rodríguez-Prados M, Paillard M, Hajnoczky G. Pharmacological inhibition of the mitochondrial Ca<sup>2+</sup> uniporter: Relevance for pathophysiology and human therapy. J Mol Cell Cardiol. 2021 Feb;151:135-144 PMID: 33035551

## OPA1 Modulates Mitochondrial Ca<sup>2+</sup> Uptake Through ER-Mitochondria Coupling

Benjamin Cartes-Saavedra<sup>1</sup>, Duxan Arancibia<sup>1</sup>, María E. Andrés<sup>1</sup>, Patrick Yu-Wai-Man<sup>2,3,4,5</sup>, György Hajnoczky<sup>6</sup> and Verónica Eisner<sup>1\*</sup>

Benjamin's PhD work in  
Verónica Eisner's lab



# Our COVID conscious Holiday Party

ER-mito  
Contact  
Cake  
By Arijita



The Trivia Master



Question checking



Pisco Sour team



Joanie & Marja  
Food inspection



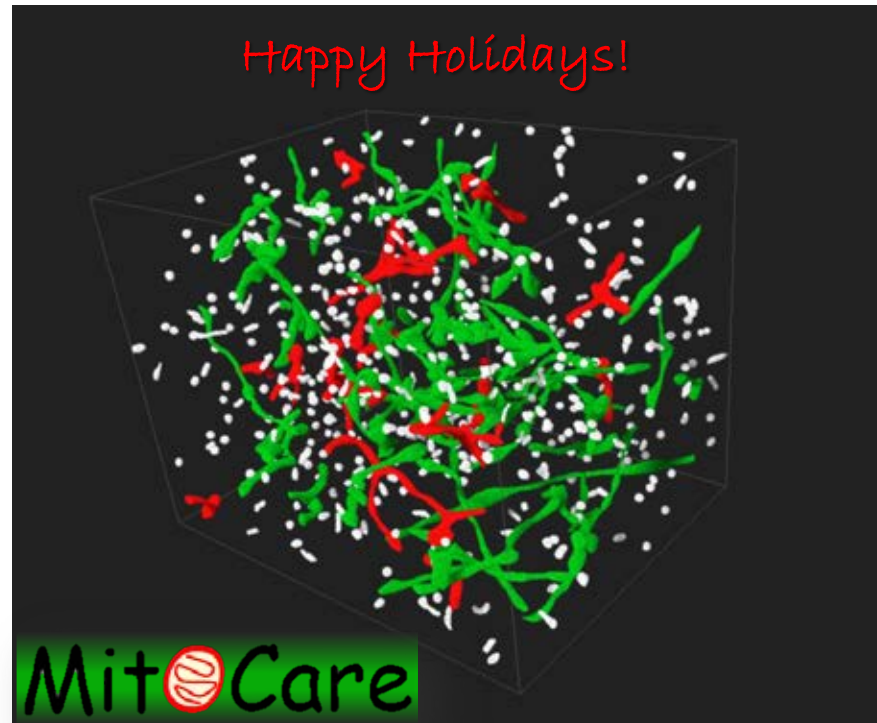
Shamim  
visit



The 2021 Trivia Champions

The MitoCare team members thank you for your support throughout the challenges of 2021.

We wish you and yours  
a happy and healthy Holiday Season  
and the very best for 2022!



**Mitochondrial diversity in brain cortex visualized by FIB-SEM**

A selection of 600 mitochondria—from approximately 6,000 total—in a  $23 \times 19 \times 19$   $\mu\text{m}$  volume of mouse brain. 500 small mitochondria are shown in white, 85 large elongated in green and 15 large branched in red.