

Mitochondria and Us: from exploration to global collective

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The 'Mitochondria and Us' project embodies our ambition to break new ground by working across traditionally siloed disciplines and by co-creating innovative approaches to impact research and societal awareness. Our vision is to provide a paradigm shift of knowledge integration at all levels adopting a pandisciplinary cooperation in a crucial and emerging area of medicine impacting several incurable human diseases. We describe our efforts on this journey through a series of 'Crossover' workshops and webinars supported by the Biochemical Society and the Royal Society of Edinburgh, by bringing together mitochondria experts from the University of Glasgow and the University of Toronto together with designers from the Innovation School of the Glasgow School of Art, artists, patient groups, social scientists and bioethicists. The global Mitochondria Collective initiative has the vision to unite research, community voices and stakeholders to bring mitochondria to the forefront of medicine as a means of sustained impact on improved healthcare and quality of life.

Mitochondria are the sites in our cells responsible for making the energy needed to sustain life. They are involved not only in controlling the function of cells, but also in determining how cells die. Mitochondrial dysfunction underpins diseases like cancer, neurodegeneration and diabetes, and primary mitochondrial diseases are complex, incurable and often misdiagnosed. Mitochondrial research has provided seminal discoveries that span decades and have had broad ramifications for cellular health. Recent examples include advances in precise editing of the mitochondrial DNA, the important role of mitochondrial dynamics and modifications of internal mitochondrial architecture, the roles of mitochondria in signalling processes, the emerging role of mitochondria in infection and immunity and the malleability of mitochondrial biogenesis and links to cellular metabolism in response to stress. Many of these advances have resulted from an astute interdisciplinary approach, involving chemistry, physics and data science

and applying these to fundamental questions of mitochondrial biology with a view to provide therapeutic advances in mitochondrial medicine. This is an exciting time for mitochondrial research, spanning all aspects of how mitochondria are made, how they sustain life, how they underpin disease and how they control cell death. This research is impactful, international and highly interdisciplinary. This article reflects on a journey that explored this potential in creative and ambitious ways.

In summer 2019, the Innovation School (IS) at the Glasgow School of Art (GSA) was invited by the Biochemical Society (BS) to organize a 1-day interdisciplinary workshop between BS members close to or local to Glasgow and design researchers at the GSA. Elio Caccavale (Reader in Transdisciplinary Design Innovation, IS GSA) and Dr Michael Pierre Johnson (Creative Economy Leadership Fellow, IS GSA) were responsible for developing and delivering the workshop at GSA on 7 November 2019. The workshop was



Figure 1. Crossover workshop

attended by 16 participants, including design researchers and practitioners from GSA and biochemical scientists from the University of Glasgow (UofG), the University of Strathclyde (UofS) and Glasgow Caledonian University (GCU).

The event was titled 'Crossover' and explored the potential for exchanges between design and biochemical sciences. Specifically, it focused on sharing disciplinary expertise and perspectives to explore research opportunities for collaborative science and society projects. The workshop also provided the scope to initiate design and science dialogues to bring tangible form to the abstract and complex contributions of scientific research and its social implications (Figure 1).

The Crossover workshop aimed to act on clear motivations to communicate biochemical sciences in creative and engaging ways and to join up traditionally siloed scientific, policy, critical, communication and creative disciplines in ways that could stimulate new collaborations, new inquiries and innovative outcomes and reach new audiences. There was a clear sense from everyone involved that this type of initiative should happen again, so we explored opportunities for further transdisciplinary partnerships.

Professor Kostas Tokatlidis (Cathcart Chair of Biochemistry and Head of the Mitochondrial Biology Lab at the UofG) was one of the participants in the workshop and showcased the mitochondrial research (and applications to mitochondrial medicine) as a key area where such cross-over approaches can be pioneered to create new and impactful ways of engagement and innovative narratives to reach wider audiences. The critical and innovative concept brought to the foreground was to develop research in

a mitochondria-centric, disease-agnostic manner, by bringing mitochondria to the centre of medical research, transcending traditional disease-siloed approaches and going beyond the links to primary mitochondrial disease by exploring further the connection of mitochondrial dysfunction to common human disorders that affect millions (cancer, cardiometabolic disease and neurodegeneration). Towards this goal the University of Glasgow mitochondrial integrative research network aims to develop new cross-cutting research and novel tools, collaborate nationally and internationally to drive disruptive progress in fundamental mitochondrial mechanisms, diagnostics, precision mitochondrial delivery and therapeutic approaches together with the pharma industry, policy changes and in outreach/education. Amongst the many ideas discussed, three fundamental questions emerged for further exploration in the context of mitochondrial research and societal engagement:

- What do we know and still need to learn about mitochondria and how we as researchers in the field communicate scientific advances?
- What effects do mitochondrial dysfunction and disease have on people's lives?
- Who should we bring together to understand this and what it means for society?

Follow-on discussions led professor Kostas Tokatlidis to organize an international online event for Mitochondrial Disease Awareness Week (13–19 September 2020) together with Elio Caccavale and Dr Michael Pierre Johnson and with the support of the Royal Society of Edinburgh (RSE) who embraced this as part of the RSE's societal engagement and outreach activities.

WORLD MITOCHONDRIAL DISEASE WEEK 13 - 19 SEPTEMBER 2020

MITOCHONDRIA AND US

STORIES FROM SCIENCE AND SOCIETY ON THE POWERHOUSE OF THE CELL

THURSDAY 17 SEPTEMBER 2020 1pm - 3pm

FREE | OPEN TO ALL | ZOOM WEBINAR

University of Glasgow | INNOVATION SCHOOL THE GLASGOW SCHOOL OF ART | RSE The Royal Society of Edinburgh | Lily | Awareness Ribbon

Figure 2. Mitochondria and Us RSE webinar, online poster

The aim of the event was to co-curate a cross-over of interdisciplinary expertise, practice and personal experiences exploring the impact of mitochondrial research and related disorders on society. Mitochondria and Us: Interdisciplinary Stories from Science and Society on the Powerhouse CEO of the Cell highlighted stories from across scientific disciplines that shed light on how mitochondria are made, how they sustain cell life under stress and how they control cell death. The event was based on contributions from world experts of a variety of scientific disciplines that are integral to mitochondrial research (biology, chemistry, physics, data science and medicine). Importantly, it also brought together patient groups, the ‘women in mitochondria’ research group, social scientists, bioethicists and designers to share stories of what the understanding of mitochondria means for people and society. This online webinar was also part of the RSE Regional Champions event and was run in partnership with the UofG, the GSA and the Lily Foundation (the largest UK mito patient charity organization). It had a very wide reach with an attendance of over 350 people from all continents across the world.

Consecutively in 2021, the Biochemical Society, with the support of Dr Pedro Ferreira (Education, Public Engagement and Training Manager), sponsored a new-phase Crossover Project, co-funded by the RSE Young Academy of Scotland (YAS). The Crossover Project aimed to build further a network of interdisciplinary

exchange between science, society and design to develop transdisciplinary practices that creatively address complex challenges and opportunities that arise with the advancement of scientific knowledge and technology. To do this, the Crossover Project hosted a new series of three workshop programmes, with more focused contexts related to understanding and caring for invisible diseases and community STEM education.

The first of these workshops, Mitochondria and Us: Co-creating Science and Society Narratives of Mitochondrial Disease (Figure 2), built on partnership with professor Kostas Tokatlidis, took place online over Zoom and Miro on 25 February 2021. The workshop brought together 14 participants from a unique variety of expertise across biochemistry, design, social sciences and humanities to co-create stories that could support greater understanding of people’s experiences living with and working with mitochondrial diseases. Participants shared their perspectives through discussions and reflections across societal, experiential and biochemical levels (Figure 3) to co-create opportunities for collaboration across multiple disciplines that could challenge the current disease-siloed approach and build stronger connections across research, clinicians and patients.

With the momentum from these discussions, we were introduced to professor Ana Andrezza (Thomas C. Zachos Chair in Mitochondrial Research, University of Toronto) and Sonya Brijbassi (Associate Director,

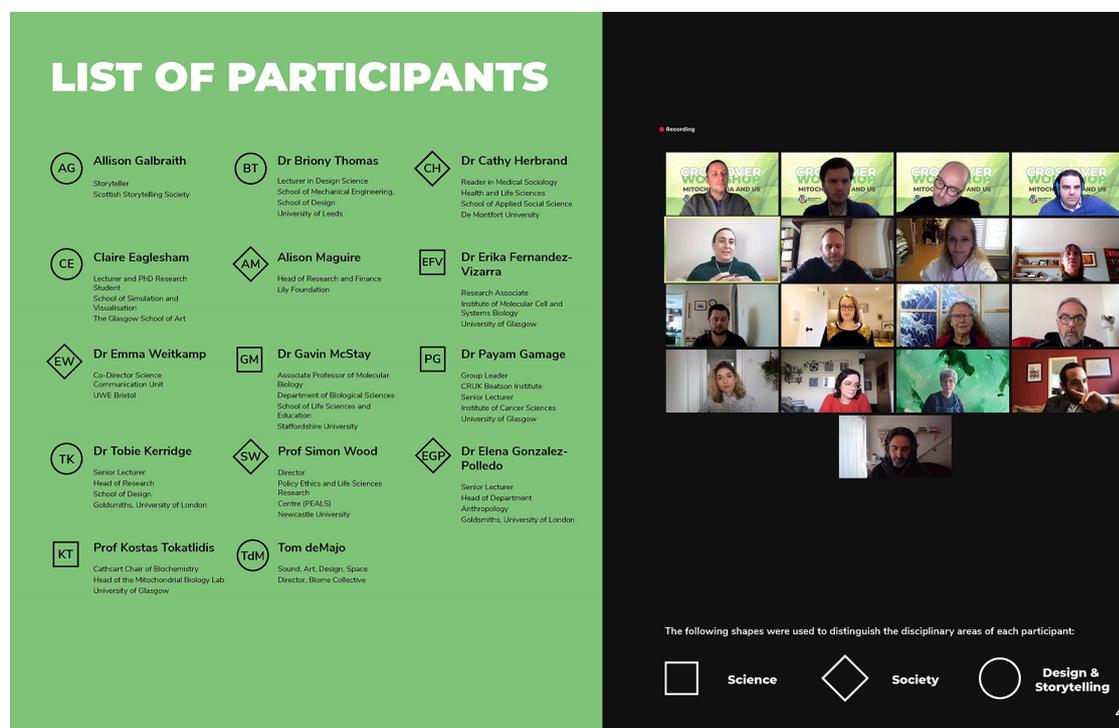


Figure 3. Mitochondria and Us workshop, List of Participants

Lifelong Learning

Strategy & Partnership for Mitochondrial Innovation Initiative (MITO2i)); at the University of Toronto, who had also been pioneering engaging forms of collaboration across research, industry and patient groups.

Mitochondrial dysfunction has a direct impact on patients' lives. In 2014, a mother to a living son with bipolar disorder (and two deceased children

with mitochondrial disease) participated in a webinar discussing mitochondrial dysfunction in relation to bipolar disorder; afterward, she contacted professor Andrezza to ask if these two diseases were linked and, if so, how. Enquiries like these, and growing support in the literature, led to the creation of MITO2i – a network of researchers, clinicians, patient



Figure 4. Mitochondria and Us workshop, brainstorming Session

advocates and partners with a mission to transform our understanding of the role of mitochondria in human health and disease. Researchers and medical professionals recognize that mitochondrial dysfunction plays a significant role in common, chronic diseases, including neurodevelopmental, neuropsychiatric, neurodegenerative disorders and multiple metabolic disorders. MITO2i's *vision* is to innovate mitochondrial medicine and research through global community building, interdisciplinary research and development of novel tools and platforms. MITO2i's *goal* is to transform the understanding of mitochondrial health and disease, leading to better diagnoses and treatments that enhance the quality of human life, ultimately transforming healthcare by integrating mitochondrial health into routine care. The relationship between mitochondrial dysfunction and severe mitochondrial disease has long been known. More recent research has established links to a broad range of neurodegenerative and metabolic disorders. This is a game-changer. Unveiling how mitochondrial dysfunction is implicated in multiple diseases will transform medical diagnoses, technologies and drug delivery systems, leading to a paradigm shift in the prevention, diagnosis and treatment of disease. MITO2i is delivering a collaborative hub that engages all stakeholders in advancing science in the field of mitochondrial medicine and research and engaging in global collaborative efforts like the one developed with UofG and GSA.

In our discussions, the idea of forming a Global Mito Collective emerged to provide a mito-centric approach to bridge new collaborations that can help build a new

understanding on the role mitochondria play in our lives. An essential aspect identified for such a collective was to empower scientific collaboration across mitochondrial research disciplines, by generating an interdisciplinary 'collective' of international scientists, social scientists, bioethicists, patient groups, clinical groups and design researchers that seek to contribute to the understanding and caring for mitochondrial diseases and dysfunctions using innovative approaches.

We co-developed and co-presented a proposal for the Global Mito Collective, first as an online panel discussion with mitochondrial disease foundations at the World Mitochondrial Disease Awareness Week 2021 programmed in partnership with the Biochemical Society and organized by professor Kostas Tokatlidis, professor Ana Andreazza, Sonya Brijbassi, Dr Michael Pierre Johnson and Elio Caccavale and facilitated by Gaston Welisch (Research Associate, IS GSA). This was followed by a second discussion at the Mito2021 Conference organized and co-hosted by MITO2i, MitoCanada and the Brain and Mind Institute at the University of Ottawa .

Both events enabled discussion and input on what such a Global Mito Collective should do (Figure 4), as well as what the benefits could be, building towards a series of aims that could shape forms of collaboration and value creation moving forward.

MITO RESEARCH – for a shared understanding of cell health

MITO VOICES – to share experiences of those affected by or working with mitochondria



Figure 5. The Mito Collective initiative uniting research and community voices and bringing mitochondrial and metabolism to the forefront of medicine

MITO COURSES – to develop skills in research and clinical impact

MITO MEDICINE – as part of everyday treatment and advice

MITO MATTERS – for collective dialogue on the urgent matters for development

Steps have since taken place to contribute to focused developmental discussions with diseases foundations, mitochondrial research centres, industry and healthcare stakeholders, with a view to present and launch a developed proposal for the Global Mito Collective during the World Mitochondrial Disease Week 2022.

Globally, there are many excellent research centres with their own focus on some aspects of mitochondrial research and with their own expertise, often built over many years of frontier research achievements. Some examples in the UK are the MRC Mitochondrial Biology Unit and the Wellcome Trust Mitochondrial Research Centre as well as centres in Oxford and London. Relevant networks include the North American Disease consortium, the Mitochondrial Medicine Society and several patient advocate groups and charities like the Lily

foundation and MyMitoMission in the UK, the United Mitochondrial Disease Foundation (UMDF) in the USA and several other foundations across the world (some with broader remit like Alzheimer's and Parkinson's disease foundations). Funding organizations supporting high-risk, high-reward projects to a better society and improve the field of medicine (Michael J Fox Foundation, Bill & Melinda Gates Foundation and others) have funded and can play a critical role in supporting highly innovative mitochondrial research, which also has the potential to attract eventually investment from pharma to develop new therapeutics that target mitochondrial function.

While all of the above is critical to obtain an in-depth understanding of specific human diseases and mitochondrial dysfunctions, there is increasing awareness that expanded collaborations are critical to develop a more holistic, mitochondria-focused, but disease-agnostic approach to mitochondria research. This is an ambitious vision, but aligns well with the idea of the Mito Collective (Figure 5) along the lines we have highlighted in this article. ■



Elio Caccavale is a Reader in Transdisciplinary Design Innovation at The Glasgow School of Art. His research is an exploration into new visual and three-dimensional design vocabularies for thinking about ethical and social issues in the sciences, and he aims to contribute to the on-going methodological debates in bioethics, science communication and the sociology of emerging scientific knowledge.



Michael Pierre Johnson is an AHRC-funded Innovation Leadership Fellow at The Glasgow School of Art. His research interests include making the effects and viability of design innovation approaches and the preferable changes they seek to serve, more explicit within complex collaborative contexts through visual mapping methods.



Sonya is the Associate Director of the Mitochondrial Innovation Initiative, a strategic initiative out of the University of Toronto. She has a Master of Science Degree in biochemistry from the University of Western Ontario and an undergraduate degree in human biology from the University of Toronto. Sonya joined the University of Toronto at the Innovations & Partnerships Office (IPO), a division of the VPRI in 2007 as a Commercialization Manager for the Life Sciences team. In 2013, she took on another role at IPO as Business Development Officer, Industry Partnerships, to support sponsored research, facilitate interactions and negotiations with industry partners and create long-term strategic partnerships and collaborations for the university with external organizations.



Ana C. Andreazza is a Professor in the Departments of Pharmacology & Toxicology and Psychiatry at the University of Toronto and holds a Tier II Canada Research Chair in Molecular Pharmacology of Mood Disorders and the Thomas C. Zachos Chair in Mitochondrial Research. Her research focuses on the effects of mitochondrial dysfunction on neurotransmission phenotypes, to unveil the brain's mitochondrial signatures and advance discovery of novel and effective treatments for complex brain illnesses. To accelerate discovery and accelerate translation, she founded the Mitochondrial Innovation Initiative, MITO2i, a strategic initiative at the University of Toronto bringing together a network of researchers, trainees, clinicians, patients and partners working together with a common mission – to transform our understanding of the role of mitochondria in human health and disease.



Kostas Tokatlidis is the Cathcart Chair of Biochemistry, Director of Research of the School of Molecular Biosciences and Head of the Mitochondria Biology laboratory in the University of Glasgow. He is an elected Fellow of the Royal Society of Edinburgh, of the Royal Society of Chemistry and of the Royal Society of Biology and an elected member of the European Molecular Biology Organisation (EMBO). His research over 25 years has focused on understanding mitochondrial biogenesis, structure and function and how these underpin cell homeostasis and human disease. He is leading a new integrative mitochondrial network at the University of Glasgow, bringing together mitochondrial research in cancer, cardiovascular disease, ageing, parasite biology, structural/chemical biology and immunology. Email: Kostas.tokatlidis@glasgow.ac.uk