

COST Action

Progress Report at 24 months

(12/09/2016 to 12/09/2018)

CA15203: Mitochondrial mapping: Evolution - Age - Gender - Lifestyle - Environment

The Action was approved by the Committee of Senior Officials (CSO) on 26-2-2016 and has the MoU reference COST 003/16.

This report was submitted on 02-11-2018 by the Action Chair on behalf of the Management Committee in fulfilment of the requirements of the rules for COST Action Management, Monitoring and Final Assessment.

Action leadership and participants

Leadership positions

Position	Name	Contact details	Country*
Chair	Prof Erich Gnaiger	erich.gnaiger@i-med.ac.at +43512566796	Austria

Position	Name	Contact details	Country*
Vice Chair	Dr Elisa Calabria	elisa.calabria@univr.it +39458425146	Italy

Working groups

#	WG Title	# of participants	WG Leader	Country*
1	Standard operating procedures and user requirement document: Protocols, terminology, documentation	70	Dr Marko Vendelin markov@sysbio.ioc.ee	n/a
2	MITOEAGLE data repository in muscle and other tissues	55	Dr Pablo M. Garcia-Roves pgarciaroves@ub.edu	n/a
3	MITOEAGLE data repository on fat tissues and other tissues	30	Prof Jan Nedergaard jan@metabol.su.se	n/a
4	MITOEAGLE data repository for blood cells and cultured cells	70	Dr Nicoleta Moiso nicoleta.moiso@dmu.ac.uk	n/a

Other key leadership positions

Position	Name	Contact details	Country*
STSM Coordinator	Dr Magdalena Labieniec-Watala	magdalena.labieniec@biol.uni.lodz.pl	Poland
Science Communication Manager	Dr Marina Makrecka-Kuka	makrecka@farm.osi.lv	Latvia
GH Scientific Representative	Ms Melanie Schartner	melanie.schartner@student.i-med.ac.at	Austria

* The country displayed is: for the Action Chair, the country of the person's primary work affiliation; for the Vice Chair the country that nominated the person as a Management Committee Member, for all other leadership positions, if the person is a MC Member the country displayed is the country of nomination, otherwise it is the country of the person's primary work affiliation.

Participants

COST members having accepted the MoU

AT	23/03/2016	BE	02/05/2016	BA	08/01/2019	HR	06/04/2016	CZ	12/05/2016
DK	31/03/2016	EE	04/03/2016	FI	08/09/2016	FR	11/03/2016	DE	22/03/2016
EL	09/03/2016	HU	22/03/2016	IE	29/03/2016	IL	09/03/2016	IT	23/06/2016
LV	07/03/2016	LT	07/06/2016	MT	07/05/2016	NL	26/02/2016	NO	04/05/2016
PL	14/03/2016	PT	28/04/2016	RO	23/03/2016	RS	01/04/2016	SK	12/09/2016
SI	04/04/2016	ES	03/05/2016	SE	26/08/2016	CH	19/04/2016	TR	16/06/2016
UK	11/03/2016								

Other participants

Institution Name	Country
Zewail City of science and technology	Egypt
Translational Research Institute for Metabolism and Diabetes, Florida Hospital	United States
Birzeit University	Palestinian Authority

Summary

The main aim and objective of the Action is to

include Evolution, Age, Gender, Lifestyle and Environment (EAGLE) in studies of mitochondrial function. MITOEAGLE develops harmonisation protocols towards generating a data repository on mitochondrial respiratory function. A data management system will interrelate various study-results and set them into a multidimensional context, to better diagnose mitochondrial respiratory defects

During its first two years the Action progressed the achievement of this as described below

The Working Group and MC Meetings held in conjunction with the last MitoEAGLE Conference in Jurmala (LV) provided an excellent summary of the major results obtained in the course of COST Action 15203.

* WG1: MitoEAGLE protocols, terminology, documentation

Recommendations on terminology and an overview on normalization of mitochondrial and cellular respiration were published as a MitoEAGLE preprint on 'Mitochondrial respiratory states and rates' with 42 sequential open access versions and a track record on contributions and discussions among the nearly 400 co-authors:

** http://www.mitoglobal.org/index.php/MitoEAGLE_preprint_2018-02-08 and discussion page.

An overview on 'Mitochondrial respiratory control by fuel substrates and specific inhibitors of respiratory enzymes' was presented as Part 2 in the series of MitoEAGLE position papers:

** http://www.mitoglobal.org/index.php/Gnaiger_2018_MiP2018

Harmonisation protocols and a training programme for inter-laboratory proficiency tests were developed, as a basis for generating a data repository on mitochondrial respiratory function as influenced by Evolution, Age, Gender, Lifestyle and Environment (EAGLE).

A training and knowledge management concept is in an advanced state of development and will be put into action at the MitoEAGLE/MiPschool Tromsø-Bergen 2018:

** http://www.mitoeagle.org/index.php/MiPschool_Tromso-Bergen_2018

The report on ECI, ITC and gender balance in the COST Action MitoEAGLE was presented by Nina Krako Jakovljević, proudly summarizing the success in fully adhering to the COST guidelines in our expanding network.

* WG2: MitoEAGLE data repository in skeletal and cardiac muscle

An international 'Inter-laboratory proficiency test including harmonization of protocols for mitochondrial function evaluation in permeabilized muscle fibers' and 'Inter-laboratory study on human permeabilized myofibres: effects of fibre preparation, respiration buffer, and blebbistatin on mitochondrial respiratory capacity and oxygen limitation' were presented by Carolina Doerrier:

** http://www.mitoglobal.org/index.php/Doerrier_2018_MiP2018a

** http://www.mitoglobal.org/index.php/Doerrier_2018_MiP2018c

The Working Group 2 report on 'Generating mitochondrial respirometry reference values from permeabilized mouse soleus muscle fibers' was presented by Pablo Garcia-Roves:

** http://www.mitoglobal.org/index.php/Garcia-Roves_2018_MiP2018b

* WG3: MitoEAGLE data repository: adipose, liver, neuronal

Zuzana Cervinkova summarized the achievements on coordination of collecting data - WG3 liver tissue.

* WG4: MitoEAGLE data repository for blood cells and cultured cells

A manuscript on an 'Interlaboratory guide through procedures for mitochondrial respiratory studies with intact and permeabilized peripheral blood mononuclear cells and platelets' was prepared during a series of working group meetings, which will be extended by a summary of experimental results forming the foundation of a database:

** http://www.mitoglobal.org/index.php/MitoEAGLE_blood_cells_1

Nicoleta Moiso summarized the state on 'Integrating published data of mitochondrial function in cell lines as models of neurodegenerative disease'.

A data management system will interrelate various study-results and set them into a multidimensional context, to better diagnose mitochondrial respiratory defects.

Action website

<http://www.mitoglobal.org/index.php/MITOEAGLE>

Achievement of MoU objectives, deliverables and additional outputs/ achievements

MoU objectives

The Action reported the following progress in achieving its specific objectives.

MoU objective	Level of progress	Further information (hyperlink or other)
Intensify the dissemination of updated knowledge and know-how among the partners.	51 - 75%	<p>The MitoEAGLE COST action takes multiple measures to intensify the dissemination of updated knowledge and know-how.</p> <p>One major target is the education of Ph.D. students and ECIs, which is primarily achieved through public lectures of our senior COST members and the MitoEAGLE/MiP training schools. The action enables the COST members to actively participate in these meetings. Therefore, not only the experts and leaders in the field have access to the latest findings and discussions, but also the next generation. The lectures of COST members contribute furthermore to the spread of current knowledge and have proven to be highly helpful in the dissemination of the MitoEAGLE mission in general. Moreover, the Training schools make a substantial contribution to reaching our mission goals. The leading researchers give lectures and hold seminars with the focus on the most recent advances in the field. In addition, the Training schools offer excellent opportunities for the Ph.D. students and ECIs to present their own results and receive feedback. Beginners get an insight into the field and the importance of the topics which the COST action addresses.</p> <p>The dissemination of updated knowledge is also important for experienced researchers, especially regarding current projects. As all MitoEAGLE publications are open access, any interested researcher has immediate access to the results of the action and can benefit from it. The MitoEAGLE website is another useful tool to support the dissemination of knowledge, as it offers a large collection of relevant preprints, publications, and protocols, which are always up-to-date and therefore create a platform where recent know-how is accessible. Additionally, the current events and MitoEAGLE action papers are also published on the Facebook and the Research Gate page.</p> <p>Moreover, several projects are currently in the process of final manuscript preparation, such as harmonization of protocols, which not only help to create clear guidelines for other researchers but also lead to the exchange of know-how among the individual Working Groups. Currently, several international studies are running to unify procedures and create reference values and determining the best experimental approaches to mitochondrial respirometry in general.</p> <p>The exchange of know-how and the disclosure of the methods in use, lead to the identification of similarities and important check-points in each procedure, in addition to a critical evaluation and protocol improvement. Through the many actions (WG meetings, conferences, training schools), this know-how is spread far beyond the borders of Working Groups. The possibility of STSMs helps to further increase the spread of knowledge and know-how across COST laboratories and their partners with a special focus on ITCs.</p>
Build and improve collaborative relationships among the participating groups of the Action and interested end-users.	51 - 75%	<p>Up to now, the outstanding example of collaborative work during the COST MitoEAGLE Action, which builds and improves the relationship among MitoEAGLE member and interested end-user, is the MitoEAGLE preprint on "Mitochondrial respiratory states and rates: Building blocks of mitochondrial physiology". Close to 400 scientists from all over the world joint for this manuscript and the outcome can be tracked on the MitoEAGLE website and is therefore accessible for researchers and the public. After final corrections it will be submitted for journal publication. As for now, many co-authors are already using the preprint in their lectures.</p>

		<p>http://www.mitoeagle.org/index.php/MitoEAGLE_preprint_2018-02-08</p> <p>Moreover, all generated data and the draft protocols of our Working Groups, which are continuously in progress, can be found online on the website. Thereby an easy access for all scientists is assured (beyond the group of MitoEAGLE members). In this way the Action improves the collaborative relationship between the end users and members. In various ongoing projects (such as preparation of a review manuscript on cardiac mitochondria; mitochondrial metabolism in human primary muscle cells; mitochondrial function in human muscle permeabilized fibers), both the scientific community and institutions working on mitochondrial function can use the results of these studies.</p> <p>During the Working Group meetings, which are organized in different laboratories, new collaborations are built, as some laboratory members and cooperation partner join the meeting and work together on specific topics of interest e.g. the mitochondrial function of skeletal muscle or blood cells. Additionally the Networking tools STSM or ITC Grant are an instrument for members to build up new collaborations.</p>
<p>Optimally harmonise protocols across research groups.</p>	<p>51 - 75%</p>	<p>The implementation of this objective was one major focus of the GP2. Therefore, three Working Group meetings were organized in order to proceed intensively with the harmonization of protocols across research groups and to compare protocols (sample preparation, experimental details).</p> <p>* http://www.mitoeagle.org/index.php/MitoEAGLE_Barcelona_2017</p> <p>* http://www.mitoeagle.org/index.php/MitoEAGLE_Obergurgl_2017</p> <p>* http://www.mitoeagle.org/index.php/MiP2017/MitoEAGLE_Hradec_Kralove_CZ</p> <p>Tested, standardized or harmonized protocols will help to facilitate the writing process for scientists and specifically, Ph.D. students and ECIs. Critical reviews of existing literature, as we are preparing in our WGs at the moment, will simplify the identification of potential discrepancies and diversity in our current methodologies, when assessing mitochondrial function in for example skeletal and cardiac muscle. The action is aiming to continue working on this issue in the future. Thereby, the inter-laboratory harmonization of protocols for mitochondrial function evaluation in for example permeabilized muscle fibers for mice and human and a joint review regarding cardiac mitochondrial function in diabetes is of particular interest. Furthermore, all WGs are working on a collection of protocols that different groups use as well as a comparison of experimentally obtained data is in progress. A publication on mitochondrial respiration in various cell cultures will be prepared as well. In addition, the WG meetings in Innsbruck, Poznan, and Lund along with a monthly E-Mail update to all participants moved the manuscript "An interlaboratory guide through procedures for mitochondrial respiratory studies with intact and permeabilized peripheral blood mononuclear cells and platelets" substantially forward.</p> <p>*WG2: http://www.mitoeagle.org/index.php/MitoEAGLE_Copenhagen_2018</p> <p>* WG4: http://www.mitoeagle.org/index.php/MitoEAGLE_Innsbruck_2018</p> <p>* WG4: http://www.mitoeagle.org/index.php/MitoEAGLE_Poznan_2018</p> <p>* WG4: http://www.mitoeagle.org/index.php/MitoEAGLE_Lund_2018</p>
<p>Foster coordinated research activities of scientific proposals in the European Research Area.</p>	<p>51 - 75%</p>	<p>The progress in the protocol harmonization is a perfect example for successful coordinated research activity in the European research area. All WGs participated and are preparing manuscripts in their respective field of interest. Thereby the knowledge of various laboratories and research groups all over Europe (and overseas) are combined. Furthermore, other studies that are currently being performed by our Action ensure the relevance of our activities and will provide preliminary results, which will support and trigger future scientific proposals. The</p>

		<p>MitoEAGLE terminology preprint is worth mentioning under this objective. Especially in the field of mitochondrial terminology, where so much conflict regarding expressions and nomenclature existed and still partly persists, it is important to clarify the topic with a structured publication. This manuscript will facilitate particularly interdisciplinary cooperation across borders, as it helps to establish not only a common language but also clarifies concepts.</p> <p>In addition to the efforts mentioned above, personal meetings in Training Schools, conferences and meetings fostered coordinated research activities between participants, which otherwise might not have had the opportunity to take part. STSMs also play an important role in achieving this goal. Not only do they promote inter-European and international cooperation between different laboratories, but they also lead to a steady exchange of know-how. Projects that start with an STSM often end in a long-term cooperation and give rise to new projects and scientific proposals. For instance, the COST Action 15203 MitoEAGLE was explicitly mentioned in a H2020 SME Phase 1 proposal by one of the stakeholder partners Oroboros Instruments, which was funded and resulted in a recently submitted Phase 2 application, mentioning several MitoEAGLE members as key opinion leaders and potential first users.</p>
<p>Increase the number of active participants in the course of the COST Action.</p>	<p>76 - 100%</p>	<p>The number of participants is steadily increasing in the MitoEAGLE COST Action. The use of our numerous dissemination tools, such as our Facebook page, regular MitoEAGLE News circulars, the presence in ResearchGate and our MitoEAGLE website, MitoEAGLE bookmarks disseminated at various conferences (e.g. EBEC 2018) made a valuable contribution to this increase.</p> <p>Our action places special emphasis on the active oral dissemination of the action's agenda by the MitoEAGLE members, who are attending various conferences and meetings all over the world.</p> <p>A steady increase of members over the past two years can be demonstrated: In the starting phase of the COST Action MitoEAGLE in 2016, around 300 members joined. The first MC-Meeting held in Verona had 23 participants. In the next year, in 2017 the number of MitoEAGLE members started to increase initially by approximately 60 participants and later during the year by 140 new members, which made a total of 500 MitoEAGLE members. Also, the attendance rate of these participants increased during the second MC-Meeting in Barcelona to 96 COST participants with a further increase to 102 participants during the Meeting in Hradec Kralove (29 COST, 3 NNC, 4 IPC). Currently, we count 653 members in our address list and 400 members on the e-COST platform. The discrepancy is due to the many international and overseas participants who are encouraged to register on the COST platform (30 COST, 3 NNC, 7 IPC).</p> <p>* http://www.mitoeagle.org/index.php/MitoEAGLE_network</p> <p>In order to maintain the success achieved in this objective, the MitoEAGLE Action welcomes the policy of supporting and establishing Europe-wide centers of excellence in science. Furthermore, the action emphasizes the clearance of obstacles by creating cooperation opportunities for all participants, especially for ITCs, ECIs, and female researchers.</p>
<p>Form a unique well-coordinated network of senior researchers and young investigators.</p>	<p>51 - 75%</p>	<p>With our meet the expert groups we are coordinating a balanced network between young and senior scientists. This way we motivate senior researchers to mentor the younger investigators and also attract the young scientist to join meetings and ask questions they always wanted to ask. The idea of MitoEAGLE mentors is not only for MitoEAGLE events but also as an opportunity for students and ECIs to get in contact with a mentor at any time. A list of mentors can be found on the website:</p> <p>http://www.mitoeagle.org/index.php/MitoEAGLE_network#Members_in_the_MitoEAGLE_network</p> <p>In addition to the mentorship program, an active collaboration between students, ECIs and senior researchers is promoted by MitoEAGLE. Each WG or task</p>

		<p>involves a combination of experienced researchers and young scientist, working together on joint reviews, project applications, guidelines and data collection. This approach ensures an effective collaboration and not competition.</p>
<p>Include well established stakeholders.</p>	<p>51 - 75%</p>	<p>Many established researchers and professors, who are highly renowned in mitochondrial research, joined the MitoEAGLE action. These members help to achieve the goals of the COST action through active participation in research projects, mentorship or public lectures. In general, they support the action with their knowledge and promote the agenda of MitoEAGLE even further. In addition, we are able to welcome numerous universities and other institutions as members of our COST Action. Particularly noteworthy are the 56 institutions that act as STSM hosts.</p> <p>http://www.mitoeagle.org/index.php/Short-Term_Scientific_Missions_MitoEAGLE#MitoEAGLE_host_institutions</p> <p>The projects, which are promoted by MitoEAGLE, do not only have a positive impact on academic knowledge, but they also make an important contribution to companies and end-users. Thus, it encourages mutual cooperation with established companies. MitoEAGLE maintains for example collaborations with the two major players in the field of mitochondrial respirometry, Oroboros Instruments and Agilent Seahorse.</p> <p>Further attention is paid to the integration of other COST Actions, in our case a partnership with the COST Action CA16225 EU-CARDIOPROTECTION. This year's Training School will also specifically address the translation of basic mitochondrial physiology to cardiovascular health and disease:</p> <p>* http://www.mitoeagle.org/index.php/MiPschool_Tromso-Bergen_2018</p>
<p>Establish a spirit of mentorship and collaboration in contrast to fierce competition which characterised early decades of bioenergetics.</p>	<p>51 - 75%</p>	<p>Working on joint publications or data collections and writing joint guidelines ensures effective collaboration and not competition. Our current studies are an excellent example, as we inform all members via email newsletters about the current status of a manuscript or inform them about open calls in the Working Groups in order for them to contribute if interested. Therefore, if someone is interested in current studies, they can contact the WG-leaders or other listed members any time. Also, at our organized conferences, new collaborations are created every time, as scientists from all over the world exchange their interests and results and thus work together on solutions and effective research. As written in Obj. 6: Sharing experience works perfectly. Working on a joint review/project application, guidelines, data collections – ensures effective collaboration and not competition.</p> <p>To emphasize our goal of mentorship, the mentorship opportunities are specifically listed on:</p> <p>* http://wiki.oroboros.at/index.php/MitoEAGLE_Early_Career_Investigators</p>
<p>Initiate applications for funding to support international collaborative research projects.</p>	<p>26 - 50%</p>	<p>We are working to join forces among European groups (MitoEAGLE) and groups from USA (MoTrPAC) (Bret Goodpaster, Paul Coen) and other international countries. This cooperation will result in a review manuscript on mitochondrial function in permeabilized human muscle fibers. Moreover, an international study is carried out, involving several European and overseas laboratories who generate reference values for mitochondrial respiration in permeabilized skeletal muscle fibers.</p> <p>International collaborative research projects are working on the following: International study involving several European and overseas laboratories to generate reference values for mitochondrial respiration in permeabilized skeletal muscle fibers.</p> <p>An international study involving several European and USA laboratories to identify the best experimental approach to assess mitochondrial respiration in permeabilized human skeletal muscle fibers.</p>

		<p>* http://www.mitoeagle.org/index.php/MitoEAGLE_Copenhagen_2018</p> <p>Some of our international partners who are actively working on results and publications within the MitoEAGLE network and are joining the Actions events with their own funds are Anthony Molina (USA), Charles Hoppel (USA), Paul Coen (USA), and Hong Kyu Lee (KR).</p> <p>In addition, funding was initiated for one student from Adam Chicco's Lab (USA), who will participate at the MitoEAGLE Training School in Tromsø-Bergen.</p>
Present and publish results of collaborative research projects within the COST Action, particularly related to STSMs supported by the Action.	26 - 50%	<p>The MitoEAGLE preprint #1 is the result of a large-scale collaboration of nearly 400 co-authors within the MitoEAGLE project. The present stage of the manuscript is close to final submission. We await last critical comments and input from additional co-authors. Further sections and other topics will be covered in subsequent parts of the MitoEAGLE position statements. After all, corrections are done, the preprint will be published. Editors have already been contacted. Moreover, the WG protocols are in progress and will be published in near future.</p> <p>STSMs were not only used to distribute the gained know-how but also to teach young scientists.</p> <p>This are some comments/projects which are mentioned in the STSM reports:</p> <ul style="list-style-type: none"> - Augustin Hidalgo and Lisa Chakrabarti are working on a manuscript together - Collaboration between Herve Dubouchaud and Isola Raffaella who are working with mouse heart tissue started - Andrea Dalmao worked during his STSM in Oslo with the hosts on different articles which will be published in his thesis. <p>Another collaborative project is, as mentioned previously, the cooperation between the COST MitoEAGLE Action and the COST CARDIOPROTECTION Action, where results will be shared and compared wherever possible.</p>
MITOEAGLE recommendations: The goal is to increase the value and reduce the noise in mitochondrial research. Prespecified and time-stamped protocols are needed in practice, and researchers need to be introduced into adhering to publicly deposited protocols in practice. MITOEAGLE recommendations will provide practical guidelines for students, scientists and stakeholders.	26 - 50%	<p>The harmonization of protocols across research groups and the comparison of protocols is only the beginning of the task to provide a guideline for all researchers and support them with future writing tasks. Moreover, the MitoEAGLE preprint #1 will bring a better understanding of the terminology in mitochondrial research. Therefore, it is very important to us to include opinions from scientists all over the world in order to ensure the accuracy of the content.</p> <p>* http://www.mitoeagle.org/index.php/MitoEAGLE_preprint_2018-02-08</p>
A monitored database – centres of excellence: The MITOEAGLE database will	26 - 50%	<p>Working Groups 2 and 4 have made excellent progress on collecting databases on preparation methods, protocols and reference values regarding mitochondrial function in permeabilized skeletal and cardiac muscle (WG2) and blood cells (PBMCs and platelets; WG4). Specific cell types isolated from blood offer a powerful model for diagnostic analysis of mitochondrial respiratory function. An</p>

<p>provide an invaluable tool for mitochondrial studies in the transition from exploratory preclinical research to clinical and pharmacological applications. Centres of excellence will emanate from the project's working groups providing training programmes and diagnostic services.</p>		<p>increasing number of studies show correlations between mitochondrial function and various diseases including cancer, diabetes, Alzheimers, Parkinsons, deep depression, and other neurodegenerative diseases.</p> <p>A training programme has been developed for instructors in proficiency training, allowing for the establishment of Centers of excellence based on inter-laboratory quality checks, to reduce the variability of data obtained and generate a database with solid reference values on mitochondrial respiratory function in different tissues and species.</p>
<p>Training: Enhance the rigorous training activities particularly for PhD students and young researchers (STSMs, Schools, Workshops, Conferences) in order to establish the practical guidelines introduced by MITOEAGLE and to enhance research results in the long term.</p>	<p>76 - 100%</p>	<p>Once a year a training school is organized where the participation of students and ECIs are financially supported and mitochondrial research is taught.</p> <p>* http://www.mitoeagle.org/index.php/MiPschool_Obergurgl_2017</p> <p>* http://www.mitoeagle.org/index.php/MiPschool_Tromso-Bergen_2018</p> <p>In general, ECIs and young researchers receive particular support for MitoEAGLE events. The overall aim is not only to provide financial assistance but also to spread the know-how by giving young scientists the opportunity to do STSMs in institutions they can choose for themselves and, as mentioned before, by organizing meet the expert sessions at every event.</p>

Deliverables

The Action reported the following progress with achieving its deliverables

Deliverable	Month deliverable due	Delivery status	Further information (hyperlink or other)
Guidelines for future research and recommendations for the evaluation of respiratory characteristics in human respirometric samples (WG1).	46	Not delivered, but expected before end of Action	
A database on mt fitness evaluated with humans' cells and tissues (WG1).	47	Not delivered, but expected before end of Action	
Training of researchers towards improved reproducibility of sample preparation and respirometric evaluation (1/3 - WG1).	11	Delivered	http://www.mitoeagle.org/index.php/MiPSchool_Obergurgl_2017
Training of researchers towards improved reproducibility of sample preparation and respirometric evaluation (2/3 - WG1).	26	Delivered	http://www.mitoeagle.org/index.php/MiPSchool_Tromso-Bergen_2018
Training of researchers towards improved reproducibility of sample preparation and respirometric evaluation (3/3 - WG1).	35	Not delivered, but expected before end of Action	
Qualitative and quantitative evaluation of results obtained in ongoing studies by comparison with a reference sample (WG1).	44	Not delivered, but expected before end of Action	
An expanded MitoEAGLE database (WG1).	48	Not delivered, but expected before end of Action	
A joint publication documenting the results of the MitoEAGLE-PT (WG1).	42	Not delivered, but expected before end of Action	
A multi-authored publication towards a unification of concepts and nomenclature in mitochondrial physiology (1/3 - WG1).	15	Delivered	http://www.mitoeagle.org/index.php/MitoEAGLE_preprint_2017-09-21
A multi-authored publication towards a unification of concepts and nomenclature in mitochondrial physiology (2/3 - WG1).	26	Delivered	http://www.mitoeagle.org/index.php/MitoEAGLE_preprint_2018-02-08
A multi-authored publication towards a unification of concepts and nomenclature in mitochondrial physiology (3/3 - WG1).	35	Not delivered, but expected before end of Action	
A library of protocols for sample preparation and examination by respirometry (WG1).	39	Not delivered, but expected before end of Action	
A multi-authored publication with recommendations of comparable standard protocols and procedures (WG1).	45	Not delivered, but expected before end of Action	
Guidelines as to the optimum use of a reference sample for determination of respiration and related parameters of interest (WG1).	47	Not delivered, but expected before end of Action	
The MitoEAGLE data management system (WG1).	48	Not delivered, but expected within 2	

		years after the end of the Action	
A continuously updated MitoEAGLE database for the use as reference data and guideline towards application of optimised protocols, ultimately leading towards standardisation (WG1).	48	Not delivered, but expected before end of Action	
A joint publication on the use of the MitoEAGLE database and management system (WG1).	48	Not delivered, but expected before end of Action	
An education programme for the use of MitoEAGLE database and management system (WG1).	48	Not delivered, but expected before end of Action	
A MitoEAGLE database on muscle tissue from humans and model organisms (WG2).	38	Not delivered, but expected before end of Action	
A set of guidelines for future studies on mitochondrial bioenergetics in muscle tissue (WG2).	47	Not delivered, but expected before end of Action	
A draft of the review manuscript (WG2).	38	Not delivered, but expected before end of Action	
Guidelines for future research and recommendations for the evaluation of respiratory characteristics in fat tissue (WG3).	48	Not delivered, but expected before end of Action	
A database on mt-fitness evaluated with fat tissue from humans and model organisms and post-study reports (PubMed Commons) (WG3).	48	Not delivered, but expected within 2 years after the end of the Action	
A draft of the review manuscript (WG3).	44	Not delivered, but expected before end of Action	
SOPs for blood cell separation and respirometric characterisation open for the research community (WG4).	35	Not delivered, but expected before end of Action	
MitoEAGLE data repository for comparative data evaluation, planning of future studies data mining (WG4).	48	Not delivered, but expected before end of Action	
Publication with a set of reference data (WG4).	36	Not delivered, but expected before end of Action	

Additional outputs/ achievements

The Action reported 5 publications on the topic of the Action, co-authored by at least two Action participants from two countries participating in the Action, and for which the Action networking was necessary.

The Action has also produced the outputs/ achievements described below.

Co-authored Action publications - peer-reviewed

1. [doi:10.1038/s41598-017-02789-8](https://doi.org/10.1038/s41598-017-02789-8)

Title	Remodeling pathway control of mitochondrial respiratory capacity by temperature in mouse heart: electron flow through the Q-junction in permeabilized fibers
Authors	Hélène Lemieux; Pierre U. Blier; Erich Gnaiger
DOI	doi:10.1038/s41598-017-02789-8
Type	Journal article
Published in	Scientific Reports
Published by	Springer Nature
ISSN	2045-2322
Links	http://www.nature.com/articles/s41598-017-02789-8.pdf ; http://www.nature.com/articles/s41598-017-02789-8

2. [doi:10.3390/antiox7010001](https://doi.org/10.3390/antiox7010001)

Title	Biological Implications of Differential Expression of Mitochondrial-Shaping Proteins in Parkinson's Disease
Authors	Sara Rocha; Ana Freitas; Sofia Guimaraes; Rui Vitorino; Miguel Aroso; Maria Gomez-Lazaro
DOI	doi:10.3390/antiox7010001
Type	Journal article
Published in	Antioxidants
Published by	MDPI AG
ISSN	2076-3921
Link	http://www.mdpi.com/2076-3921/7/1/1/pdf

3. [doi:10.1016/j.freeradbiomed.2018.04.353](https://doi.org/10.1016/j.freeradbiomed.2018.04.353)

Title	The alteration of mitochondrial function is associated with the induction of endoplasmic reticulum stress autophagy and apoptosis by Sorafenib in liver cancer cells
Authors	Angeles Rodriguez-Hernández; Pavla Staňková; Raúl González; Ángel José De la Rosa; José María Álamo-Martínez; Luis Miguel Marin-Gómez; Ondřej Sobotka; Otto Kučera; Francisco Javier Padillo; Zuzana Červinková; Jordi Muntané
DOI	doi:10.1016/j.freeradbiomed.2018.04.353
Type	Journal article
Published in	Free Radical Biology and Medicine
Published by	Elsevier BV
ISSN	0891-5849
Subjects	Physiology (medical); Biochemistry
Links	https://api.elsevier.com/content/article/PII:S0891584918305185?httpAccept=text/xml ; https://api.elsevier.com/content/article/PII:S0891584918305185?httpAccept=text/xml

[84918305185?httpAccept=text/plain](https://doi.org/10.1101/151480)

4. [doi:10.1101/151480](https://doi.org/10.1101/151480)

Title	Impairment of mitochondrial respiratory function as an early biomarker of apoptosis induced by growth factor removal
Authors	Helene Lemieux ; Patrick Subarsky; Christine Doblander; Martin Wurm; Jakob Troppmair ; Erich Gnaiger
DOI	doi:10.1101/151480
Type	Posted content
Published by	Cold Spring Harbor Laboratory
Link	https://syndication.highwire.org/content/doi/10.1101/151480

5. [doi:10.1155/2018/1391387](https://doi.org/10.1155/2018/1391387)

Title	Intracellular and Intercellular Signalling Mechanisms following DNA Damage Are Modulated By PINK1
Authors	Mihaela Temelie; Diana Iulia Savu ; Nicoleta Moiso
DOI	doi:10.1155/2018/1391387
Type	Journal article
Published in	Oxidative Medicine and Cellular Longevity
Published by	Hindawi Limited
ISSNs	1942-0900 ; 1942-0994
Subjects	Cell Biology; Biochemistry; Ageing; General Medicine
Links	http://downloads.hindawi.com/journals/omcl/2018/1391387.pdf ; http://downloads.hindawi.com/journals/omcl/2018/1391387.xml

Proposals/ projects

The Action reported 1 project(s) and 4 proposal(s) resulting from the Action networking.

Key details of the projects are shown below:

1. NextGen-O2k H2020 SME Phase 1 (H2020)

Other outputs / achievements

The following other outputs/ achievements contributing to the COST mission resulted from the Action:

1. As direct output results of the COST Action the following achievements can be considered: Preprint, Impact Flyer (will be published shortly after the MitoEAGLE Preprint), Website, Harmonization protocols of working groups, continuous exchange of knowledge and methods during meetings and passing on of know-how during STSMs.

Impacts

The Action reported the following impact(s):

Description of the impact, i.e. what will change, and for whom, as a result of what the Action achieved	Type of impact	Timing of impact
<p>STSMs at working group meetings, where the participants were doing experiments and working on the protocols will have an impact on all participants who can share their know-how and/or expand their knowledge.</p> <p>Also, other impacts are that new collaborations within the COST MitoEAGLE Action result in opportunities such as lectures at various events, e.g.:</p> <p>Prof. Charles Hoppel gave a lecture at the Charles faculty in November</p> <p>Dr. Nicoleta Moisoi gave a lecture at: Dementia Conference 17th of May 2017</p> <p>Dr. Nicoleta Moisoi and Dr. Lisa Chakrabarti gave a lecture at: Parkinson's UK East Midlands - Researcher's Meeting</p> <p>Dr. Erich Gnaiger plenary lecture at: EBEC 2018, Budapest, Hungary</p>	<ul style="list-style-type: none"> Scientific / Technological 	<p>Achieved</p>

Dissemination and exploitation of Action results

Dissemination and exploitation approach of the Action

The Action's dissemination and exploitation approach as well as all activities undertaken to ensure dissemination and exploitation of Action results and the outcomes of these activities are described below.

The effectiveness of the dissemination activities stated before can be explained as follows: ResearchGate and MitoEAGLE website: open access tool which can be used by another end-user. Attracts new users, everybody can take part at MitoEAGLE meetings to discuss their results or problems and work join the MitoEAGLE action to work on solutions and progress steps in order to achieve the Actions goals. Also, all presentations and reports which summarize the results of the Action can be found online on the MitoEAGLE website. Dissemination at various conferences: Results are shared during the oral or poster presentations.

Dissemination

Dissemination meetings funded by the Action

The Action did not fund any Dissemination Meetings

Other dissemination activities

The Action also undertook the following dissemination activities:

Activity	MitoEAGLE website ensures continuous dissemination of the MitoEAGLE Action progress. http://www.mitoglobal.org/index.php/MitoEAGLE
Target	The target audience is everyone who is interested in knowledge on mitochondrial function in health and disease related to Evolution, Age, Gender, Lifestyle, and Environment.
Outcome	The open access of the website leads to a steadily growing MitoEAGLE network. In particular, the active members work together on harmonization of protocols and improving the knowledge on mitochondrial research.
Link	http://www.mitoeagle.org/index.php/MitoEAGLE

Activity	Participation at various events worldwide, not only by the Chair of the Action but also by the members. Our COST Action members disseminate the actions aims and objectives, which motivates new participants to join as members and will help us to reach out to stakeholders.
Target	Conference and Meeting participants who are interested in mitochondrial research.
Outcome	New cooperations were established, new members joined the action, received opinions from scientists all over the world on MitoEAGLE topics in order to fight the reproducibility crisis and to establish advanced standards in mitochondrial functional diagnostics.
Link	http://www.mitoglobal.org/index.php/MitoGlobal_Events

Activity	Another tool used by our dissemination coordinators is Facebook, where current events, project results and general ideas related to MitoEAGLE are announced.
Target	Again MitoEAGLE members and also friends of MitoEAGLE members who can see shared MitoEAGLE posts.
Outcome	Steadily growing MitoEAGLE network and interested new members who want to participate in events or open calls.
Link	https://www.facebook.com/costmitoeagle/?ref=bookmarks

Activity	The Research gate website is used to disseminate the MitoEAGLE Action, where other members can add
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	their publications.
Target	Scientists who are registered on Research gate and can access the MitoEAGLE page.
Outcome	Exchange by MitoEAGLE members who share their work on the Research gate website.
Link	https://www.researchgate.net/project/Cost-Action-MITOEAGLE-Evolution-Age-Gender-Lifestyle-Environment

Activity	Our MitoEAGLE website is mentioned on several MitoEAGLE member institution web pages or on conference websites who organized MitoEAGLE sessions, such as EBEC2020, WISE3 in Szeged or MitoEST in Estonia.
Target	Members and cooperation partners from different MitoEAGLE member institutions and also participants from conferences which are organized by MitoEAGLE members and disseminate the MitoEAGLE Action.
Outcome	New members joined the MitoEAGLE network. New cooperations between MitoEAGLE members and conference attendees were a result which also lead to new members.
Link	http://portal.research.lu.se/portal/en/projects/eu-fp-horizon-2020-cost-action-ca15203-mitoeagle(06fb61a9-eeef-49de-beeb-fea139bb6b28).html

Exploitation activities

The Action undertook the following activities to ensure exploitation (use, in particular in a commercial context) of the Action's achievements:

Activity	Interlaboratory testing of mitochondrial diagnostic protocols sets new standards for quality control, based on instrumental platforms developed and distributed by participating companies. These companies benefit from the multi-author reports and publications which present instrumental applications on an international and unbiased basis.
Target	Researchers who are interested in improving our knowledge on mitochondrial function in health and disease with regard to Evolution, Age, Gender, Lifestyle, and Environment. The training schools help to introduce instrumental platforms used for diagnosis of mitochondrial function to a specifically targeted audience.
Outcome	The large MitoEAGLE network provides strong support to increase the scientific and public awareness on the importance of mitochondrial functional diagnostics, which helps all involved commercial stakeholders in their marketing strategies. Interrelating results of studies performed world-wide with the help of a MitoEAGLE data management system. Providing standardized measures to link mitochondrial and physiological performance to understand the myriad of factors that play a role in mitochondrial physiology.

Action Expenditure

The table below shows the budget allocated to the Action for each Grant Period (funds allocated for the first meeting of the Action and any Final Action Dissemination are not included):

#	Grant Period	Start Date	End Date	Budget allocated to Action (EUR)
1	AGA-CA15203-1	1-11-2016	30-4-2017	70,518.00 (EUR)
2	AGA-CA15203-2	1-5-2017	30-4-2018	165,044.44 (EUR)
3	AGA-CA15203-3	1-5-2018	30-4-2019	187,329.60 (EUR)
4	AGA-CA15203-4	1-5-2019	30-4-2020	159,383.10 (EUR)