

## Subject | Minutes of the 13th Conference on Mitochondrial Physiology The role of mitochondria in health, disease and drug discovery- COST MitoEAGLE perspectives MIP2018 and MitoEAGLE WG and MC Meeting

Minutes prepared by Verena Laner and Marija Beno

### I. MITOEAGLE welcoming: 2018 September 18

#### Conference venue

Panorama hall, 10th floor, SemaraH Hotel Lielupe SPA

Bulduri prospect 64/68, Jurmala, Latvia

13:00 – 15:30 Registration

15:30 Welcome reception

### II. MITOEAGLE conference: 2017 September 18

#### 1. Welcome to participants

13:00 – 15:30 Registration

15:30 – 15:45 Opening and welcome by the conference organizers

The participants were welcomed by Dr. Marina Makrecka Kuka (Local Organiser)

#### 2. Participants

see Annex 1 – Attendance list

- Total: 93 COST participants (day 1: 63 - day 2: 66 - day 3: 65 – day 4:61)
- 103 total signed

#### 3. 15:45 – 17:30 Session A1: Mitochondria & basic science

Chair: Beatrice Chabi and Markus Keller

**Adam Chicco** *invited speaker:* [Defective cardiolipin remodelling and cardiac mitochondrial dysfunction: supercomplexes or just complex?](#)

**Markus Keller** *invited speaker:* The structural molecular diversity of mitochondrial cardiolipins

**Patrice X Petit:** [Decreasing cytosolic translation is beneficial to yeast and human Tafazzin-deficient cells with disrupted mitochondrial homeostasis \(Barth syndrome cell model\)](#)

**Maria Luisa Genova:** [Respiratory supercomplexes: evidence for separate though interconnected compartments of Coenzyme Q10 in mammalian mitochondria](#)

**Helene Lemieux:** [Plasticity of a critical regulator of energy production under hypothermia, the phosphorylation system](#)

**Thierry Arnould:** [Changes in mitochondria morphology in Brucella - infected cells: what is the impact for the bacteria and/or the host cell?](#)

**Mikhail Dubinin:** [The effect of triclosan on the permeability of mitochondrial membranes and lecithin liposomes](#)

**Ted Han:** [670nm Light Induced Decrease in Complex IV Function](#)

17:30 - 18:00 Coffee break



#### 4. 18:00 – 20:00 Session A2: 60 years since discovery of role of carnitine in fatty acid oxidation

Chair: Marina Makrecka-Kuka and Sean H Adams

**Maija Dambrova:** [Carnitine: from discovery to cardiometabolic risk marker](#)

**Sean H Adams** *invited speaker:* [Long-chain acylcarnitines: new perspectives on bioactivities and trafficking](#)

**Edgars Liepinsh:** [Mitochondrial and extramitochondrial effects of long-chain acylcarnitines](#)

**Kristine Volska:** [The accumulation of acylcarnitine during ischemia](#)

**Rob Wuest:** [Reduction of acylcarnitines restores electrophysiological abnormalities in VLCAD deficient hiPSC-cardiomyocytes](#)

**Carolina Doerrier:** [Evaluation of anaplerotic pathways to avoid artefacts in respirometric measurement of fatty acid oxidation](#)

**Marina Makrecka-Kuka:** [Fatty acid oxidation in brain: from aging to ischemia and sepsis](#)

20:00 Think&Drink session (welcome reception)

### III. MITOEAGLE conference: 2018 September 19

#### 1. 09:00 – 10:30 Session B1: Mitochondria & cancer

Chairs: Ljudmila Ounpuu and Uwe Schlattner

**Thomas Gorr:** [Myoglobin outside of muscle: new roles of an "old protein"](#)

**Germaine Escames:** Suppression of AKT/mTOR pathway and activation of mitophagy by melatonin via mitochondrial regulation in head and neck cancer

**Ljudmila Ounpuu:** [Metabolic plasticity of cancer stem - like cells](#)

**Uwe Schlattner:** [Intramitochondrial nucleotide regeneration by NME/NDPK proteins - roles in mitochondrial dynamics, signalling and metastasis](#)

**Gro Vatne Rosland:** Mitochondrial reshaping and suppression of succinate dehydrogenase C are integral parts of epithelial to mesenchymal transition in breast cancer

10:30 – 11:00 Coffee break

#### 2. 11:00 – 12:30 Session B2: Mitochondria & lifestyle

Chairs: Caronila Doerrier and Edgars Liepinsh

**Pavla Stankova:** [Impact of Western diet on energy metabolism in mouse liver](#)

**Pablo Miguel Garcia Roves Gonzalez:** [Mitochondrial signature and lifestyle modulation of metabolic plasticity](#)

**Elina Makarova:** [Plasma concentrations of fatty acids and acylcarnitines as biomarkers for diagnosis of insulin resistance in adipose and muscle tissues](#)

**Michael Nemeč:** [Three - month exercise modulates skeletal muscle mitochondria function health and memory of seniors](#)

**Adam Chicco** *invited speaker:* [Role of mitochondria in skeletal muscle acclimatization to high - altitude](#)

**Dominique Votion:** [Functional diagnosis of mitochondrial defects in equine atypical myopathy and targeted mitochondrial therapy: a preliminary study](#)

**Erkan Tuncay:** [Regulation of mitochondrial Zn<sup>2+</sup> level by Zn<sup>2+</sup> transporter ZIP7 effects sarco\(endo\)plasmic reticulum S\(E\)R-mitochondria coupling in hyperglycaemia](#)

12:30 – 14:00 Lunch and Walk&Talk

### 3. 14:00 – 15:30 Session B3: Mitochondria & aging & neurological disorder

*Chairs: Nicoleta Moiso and Darioo Acuna-Castroviejo*

**Ivica Rubelj:** [Role of mitochondria in mammalian senescence and aging](#)

**Nicoleta Moiso:** [Mitochondria nucleus communication in age related neurodegeneration: Who talks first? Who talks louder?](#)

**Jan Nehlin:** [Aging biomarkers in multimorbidity patients](#)

**Lisa Chakrabarti:** [Fatty acid binding protein 3 regulation of mitochondrial lipids - A strategy for exceptional longevity in the Pipistrelle bat](#)

**Sentiljana Gumeni:** [Disruption of mitochondria dynamics induces proteome instability and promotes ageing](#)

**Natasha Kopitar-Jerala:** [The role of cystatins in metabolism and neuroinflammation](#)

**Dario Acuna-Castroviejo:** [Mitochondrial impairment, melatonin, and neuroinflammation in Parkinson's disease](#)

**Elena Marchesan:** Mitophagy and Parkinson's disease: the PINK1-Parkin link

**Gundega (Vikmane) Stelfa:** [Neuroprotective compound R-fenibut protects brain mitochondria against anoxia-reoxygenation damage in vitro](#)

15:30 – 16:00 Coffee break

### 4. Session B4: Mitochondria and drug discovery

*Chair: Maija Dambrova and Rob Wuest*

**Mark Bamberger:** [Discovery and development of elamipretide: targeting mitochondrial dysfunction in rare and common diseases](#)

**Alex Dyson** *invited speaker:* [Therapeutic utility of sulphide - donating thiometallates](#)

**Janis Kuka:** [The discovery of Methyl-GBB - the pharmacological potential of acylcarnitine lowering](#)

**Belma Turan:** [Role of Mitochondria-associated Oxidative Stress in Aging Heart Function](#)

**Cenk Aral:** [Effects of melatonin treatment on LETM1 silenced mouse embryonic fibroblast cells](#)

17:30 – 18:30 **MiPAssembly**

## IV. MITOEAGLE WG sessions: 2018 September 20

### MitoEAGLE Working Group Meetings (selected topics)

#### 1. 09:00 – 10:30 WG1: SOPs and user requirement document (URD): Protocols – Terminology – Reporting

*Chairs: Helene Lemieux and Pablo Miguel Garcia Rovés Gonzalez*

**1. Erich Gnaiger:** [Mitochondrial respiratory control by fuel substrates and specific inhibitors of respiratory enzymes: Building blocks of mitochondrial physiology Part 2](#)

Discussion: Explanation again on complete additivity for Marie Luisa Genova

Question Adam Chicco: Complexity of oxidation pathways upstream could also be influenced?

Genova Maria Luisa: Complete additivity not supercomplex but respirosome.

Gorr Thomas – comment: H<sub>2</sub>S, linked to COQ – only at suprphysiological levels. Physiological is a non competitive inhibitor of cyt c oxidase, concentration determines very much the fnction, ; comment Erich Gnaiger: malate of FAO substrates...

**2. Martin Laasmaa, Vendelin M:** Introducing open source platform for primary kinetics data analysis  
Pablo Garcia Roves – similar approach, how to put the data into the system? Cloud? Specialized person?  
Direct input by instrument, what about e.g. animal information? Martin Laasmaa: every preparation ID number, link it to experiment  
Do you use this as a labbook too? > no not yet, only comments so far by Laasamaa Martin; Rob Wüst: in theory it is possible to use it as a digital lab book? LM: yes  
Gorr Thomas: Planned as bioarchive or only data input export? Searching tool for biomaterials would be great?

**3. Ondrej Sobotka, Komlodi T, Doerrier C, Gnaige E:** [ROS measurement under hypoxia and unexpected methodological pitfalls of Amplex Red assay](#)

Chicco Adams: not ROS production but H<sub>2</sub>O<sub>2</sub> release for mitos; what makes it out into the media.. AmR is permeable,

10:30 – 11:00 Coffee break

## 2. 11:00 – 12:30 WG2: MitoEAGLE data repository on muscle tissues

*Chairs: Dominique Votion and Adam Chicco*

**1. Paul de Goede, Ritsema W, Wuest RCI, Kalsbeek A:** [Timing of Feeding Behavior Affects Daily Rhythms in Body Temperature and Muscle Mitochondrial Metabolism](#)

Gorr Thomas: Respiration goes down during active phase – puzzled by this result. ; Answer Paul de Goede: respiration should be highest in active phase. ;

EG: inactive phase – coming down, active phase – down; after active phase: inactive phase – up.

**2. Yusuf Olgar, Degirmenci S, Durak A, Turan B:** [Mitochondria -Targeted Antioxidants in Aging related functional changes in the heart and aorta: MitoTEMPO improves aged-cardiovascular performance](#)

**3. Rob Wuest, Held NM, Daal M, Baks-te Bulte L, Wiersma M, van Deel ED, Kuster DWD, Brundel BJJM, van Weeghel M, Coolen BF, Strijkers GJ, Houtkooper RH:** [The antibiotic doxycycline impairs cardiac mitochondrial and contractile function](#)

Chinopoulos Christos: Succinate effect; RC: downstream of CIV,

Vendelin Marco: life-style, did they investigate recovery – Rob Wüst: yes, increase growth again after taking away antibiotics.

Genova Maria Luisa: CI or CI-III; RC: stability issue if you lack the ring of subunits

**4. Craig Porter, Ogunbileje JO, Fry CS, Bhattarai N, Rontoyianni VG, Capek KD, Bohannon FJ, Reidy PT, Finnerty CC, Suman OE, Rasmussen BB, Herndon DN:** [Skeletal muscle mitochondrial thermogenesis in hypermetabolic humans](#)

**5. Carolina Doerrier, Gama-Perez P, Garcia-Roves P, Gnaiger E:** [Inter-laboratory harmonization of protocols for mitochondrial function evaluation in permeabilized muscle fibers](#)

Discussion see below (Pablos presentation)

**6. Pablo Miguel Garcia Roves Gonzalez, Gama-Perez P, Dahdah N, Doerrier C, Gnaiger E, Lemieux H, Holody CD, Carpenter RG, Tepp K, Puurand M, Kaambre T, Dubouchaud H, Chabi B, Cortade F, Ost M, Pesta D, Calabria E, Casado M, Fernandez-Ortiz M, Acuna-Castroviejo D, Villena J, Grefte S, Keijer J, O'Brien K, Sowton A, Murray AJ, Campbell MD, Marcinek DJ:** [Generating reference values on mitochondrial respiration in permeabilized fibers of mouse soleus muscle. MitoEAGLE Working Group 2 report](#)

Rob Wüst: Fibre prep important, how to tease out fibre prep,

Pablo: video documentation, critical, try to keep 4-6 fibres together, not fully permeabilized,

Rob Wüst: sharp teasers

Pablo Garcia Roves: spezialied workshps for this for people working with PFI in future; SOP

Carolina Doerrier: permeabilization is key point, no diff. (Orlando) between fully separation (mech) or sticking together

Pablo Garcia Roves/Carolina Doerrier: strain from same company, standardized condition in the lab ...

Erich Gnaiger: permeabilization vs. preparation; we can separate with proficiency test (HEK cells); much effort: instrumental performance tests, then proficiency test, then go to skeletal muscle...

Doing that from scratch you gain a lot of if (time, money)... 60-80% should go to quality control

Patrice Petit: high costs to prepare chemicals every day, Caro clarifies:

ADP -80 is normal storage condition; can store at -20 for short time

Vendelin Marko: ADP speculation or approved?

Garcia Roves Pablo: operator the same, chemicals the same, animal not the same, kindof approved, adp newly prepared from BCN patch

12:30 – 16:30 Lunch and Excursion to Great Kemer Bog

### 3. 16:30 – 18:00 WG3: MitoEAGLE data repository on fat, neuronal and liver tissues

*Chairs: Zuzana Cervinkova and Craig Porter*

#### 1. **Filomena Silva Grilo Silva, Komlodi T, Garcia-Souza LF, Oliveira PJ, Gnaiger E:** [The unspecific effect of etomoxir on mitochondrial respiration](#)

Kuka Janis: incubator – not to use  $\mu\text{M}$  –

Filomena Silva: it depends on the model for the  $\mu\text{M}$  in etomoxir. No toxic effect with lower concentration.

#### 2. **Josep Villena, Castillo A, Pedriza I, Vila M, Pardo R, Camara Y, Nogueiras R:** [Lack of MTERF4 in brown adipocytes impairs mtDNA-encoded protein translation and leads to brown adipose tissue thermogenic dysfunction](#)

Genova Maria Luisa: How is the respiration affected in different complexes (succination)

Villena Josep: it has different respiration

Gorr Thomas: steady state concentration in theory could be increased – Villena Josep agrees that it is easy to increase.

#### 3. **Craig Porter, Herndon DN, Chondronikola M, Chao T, Saraf MK, Bhattarai N, Ogunbileje JO, Malagaris I, Rontoyianni VG, Clayton P, Bohannon FJ, Nunez Lopez O, Capek KD, Radhakrishnan RS, Sidossis LS:** [Evidence of functional UCP1 in subplatysmal and subcutaneous adipose tissue of hypermetabolic trauma patients](#)

Process of cosmetic surgeries – one year approximately work with the patients

Average of burning is 50-60%

#### 4. **Thierry Arnould, Demine S, Tejerina S, Bihin B, Thiry M, Reddy N, Raes M, Renard P, Jadot M:** [A form of autophagy triggers lipolysis in 3T3-L1 adipocytes exposed to a mitochondrial uncoupling](#)

Moiso Nicoleta: Is Ph measured to see if there are slight changes?

Thierry: Combine molecules to poison the liposomes

#### 5. **Christos Chinopoulos, Dobolyi A, Bago A, Palkovits M, Nemeria NS, Jordan F, Doczi J, Ambrus A, Adam-Vizi V:** [Exclusive neuronal expression of KGDHC-specific subunits in the adult human brain cortex despite pancellular protein lysine succinylation](#)

Adam Chicco: Real cells are like genes or how do they work with the protein, regulated so that they are bundled together?

Christos Chinopoulos: Explained how human and mice bundles are very different, and people sometimes assume wrong that it is similar.

#### 6. **Irina Shabalina, Gomez Rodriguez A, Talamonti E, Naudi A, Kalinovich A, Pauter AM, Barja G, Pamplona R, Dobrzyn P, Nedergaard J, Jacobsson A:** [Elovl2-ablation leads to mitochondrial phospholipid remodeling and reduced oxidative phosphorylation capacity in mouse liver mitochondria](#)

Adam Chicco: DHA high in mouse, exchanges in middleacid? (looking in muscle)

Irina Shabalina: Fatty acid composition – no change in liver, if it travels to muscle it is more leaking

Keller Markus: Easter lipid – much higher content of fatty acid that you study. Two versions – dyacyl – and also the fatty alcohol part

Irina Shabalina: it cannot be checked because it is very low. It is probably not what was discriminated also.

**7. Konstantin Belosludtsev, Belosludtseva NV, Talanov EYU, Starinets VS, Dubinin MV: [Effect of bedaquiline and delamanide on the functions of rat liver mitochondria](#)**

Genova Luisa: Show table with the activities decreases. Decrease of NHD to 72.1 if complexes don't change. Is there an interaction or how does that happen. It makes no sense and a better explanation is necessary. Defect in the essay is perhaps a reason.

Konstantin Belosludtsev: Still working on this explanation.

18:00 – 18:30 Coffee break

**4. 18:30 – 20:00 WG4: MitoEAGLE data repository for blood cells and cultured cells**

*Chairs: Beata Cizmarova and Ondrej Sobotka*

**1. Adam Chicco, Obediat Y, Catandi GD, Carnevale EM, Chen T: [Maternal aging increases granulosa cell mitochondrial ROS release and reduces oocyte OXPHOS-linked respiration: implications for embryo development](#)**

Christos Chiopoulos: Why do not do Perfusion - 3 on inflow and outflow?

Adam Chicco: Idea of moving it across, one of the problems is that the enzyme oxidates did not handle it that is why they had to have it external

Rob Wüst: Chemical use for that?

Adam Chicco: clinically is there a metabolic profile which can be predicted? Screening tool - metabolism influence on drugs, and metabolic profile is predictive, evidence that higher oxygen consumption can be good or bad and they try to make a profile at what point it is good and the aim is to get actual numbers who can clearly demonstrate whether they are in a good stage or not

**2. David Carrageta, Silva AM, Alves CL, Almeida SP, Sousa M, Barros A, Alves MG, Oliveira PF: [Role of SIRT1 and SIRT3 in human sperm cells metabolism and bioenergetics](#)**

Develop main contraception? They want to make it more specific for medical facilities. Try improve invertibility.

Activators and oxidative stress is confusing

Po<sub>2</sub> is extremely low – hypoxia the fact that you see ROS production is no surprise. They should concentrate on that because they are not used to see that.

**3. Tereza Danhelovska, Zdrzilova L, Stufkova H, Sedlackova D, Rodinova M, Sladkova J, Honzik T, Hansikova H, Zeman J, Tesarova M: [The relevance of ACBD3 protein in energy metabolism in various cell lines](#)**

Moiso Nicoleta: What is the knock out type?

Lucia Zdrzilova: HEK and HELA

Adam Chicco: What is its role in helping holding together things in inner membrane. Is it participating in showeling in substrates?

Lucia Zdrzilova: Don't know if it is in the mitochondria, they are still researching this. It is not a stetogenic cell which is the problem.

**4. Dita Kidere, Makrecka-Kuka M, Stavusis J, Lace B, Liou CW, Inashkina I: [Cytoplasmic hybrid cells as a model to characterize the effect of the mtDNA mutations on the OXPHOS system](#)**

Found significant in ND, they will make new models, measure ATP levels in cells and grow them in a specific medium

No functional OXPHOS – they should try to block the Complex I and check if the mitochondrial

Membrane potential is an important aspect to investigate

**5. Andrea Evinova, Cizmarova B, Pilchova I, Brodnanova M, Racay P: [High resolution respirometry of neuroblastoma SH-SY 5Y cell line](#)**

Measure cell viability? Yes in the protocol – 96% and is stable

Too much cells have worse respiration, therefore they use bigger plates for the cells  
Always intact cells. Measurements without digitonin – according to protocol

**6. Vlad Florian Avram, Asander Frostner E, Hansson M, Muntean DM, Elmer E:** [Cell-permeable succinate bypasses statin-induced mitochondrial complex I inhibition in human platelets](#)

Concentrations? Clinically blood level around 1000 lower in nano molar, this is a study in healthy individual who take statins. In clinical trials they reselect the patients

Statin inhibit quinones. Higher concentration – they are relying on quinones – therefore add quinones as a possibility. To see what a succinate drug would do to the quinone.

**7. Gloria Keppner, Bayer F, Skurk T, Klingenspor M:** [Effects of cryopreservation of peripheral blood mononuclear cells](#)

FCCP reduction on respiratory rate – why is it not higher in the beginning than succinate? Is it uncoupled already?

Gloria Keppner: It was new for them as well, as usually it has a peak

Preservation medium has FCS

Try to use trehalose

**8. Nicoleta Moiso:** [Integrating published data of mitochondrial function in cell lines as models of neurodegenerative disease](#)

20:00 Dinner

## V. MC Meeting, 2018 September 21

Start: 09:00 – 10:30 **Management Committee Meeting**

1. Welcome to participants

- E. Gnaiger – Chair of the Action welcomed participants and thanked the local organizers for the organization of the successful meeting, then Marija Beno was leading through meeting.

2. Verification of the presence of two-thirds of the Participating COST Countries or, if applicable, a quorum

- 18 COST countries from 31 countries were present at the MC meeting, and additionally 2 more MC Members were added by Skype (Magda Labienic-Watala – representing Poland and Terje Larson for Norway) to the MC Meeting in order to vote according to the rules.
- 28 MC/MC-Sub in total: 20/55 MC, 8/40 MC-Sub  
65% ITC, 35% non ITC  
41% Male, 59% Female
- Present: AT, BE, CH, CZ, DK, EE, ES, FR, GR, IT, LV, NO, PL, SI, SK, TR, UK, RS, LT, HU,
- Not present: DE, EG, HR, FI, IE; IL, MT, PT, RO, SE, NL, IE
- Therefore two-thirds were present and all votings can and will be accepted.

3. Adoption of agenda – no adoption of the agenda required.

- The Working Group summaries/sessions (Point 8) were discussed in Session D in the morning and all the other points were discussed in the afternoon and according to the agenda. See programme: [http://wiki.oroboros.at/images/a/a5/MiP2018\\_MitoEAGLE\\_Jurmala\\_programme.pdf](http://wiki.oroboros.at/images/a/a5/MiP2018_MitoEAGLE_Jurmala_programme.pdf)

4. Approval of minutes and matters arising of last meeting

- Minutes from the WG and MC Meeting in Hradec Kralove were shown by M. Beno and approved by the MC members.

- The long term planning with a focus on the Working Groups, which was in the MC minutes was discussed during the meeting in Jurmala. MCs agreed on a additional WG4 workshop which should be held at end of October and a WG2 Workshop between Dezember and January in Innsbruck.  
» [http://www.mitoglobal.org/images/2/26/HradecKraloveMeeting\\_Minutes\\_CA15203.pdf](http://www.mitoglobal.org/images/2/26/HradecKraloveMeeting_Minutes_CA15203.pdf)

## 5. Update from the Action Chair

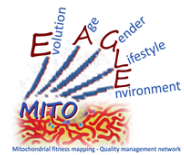
a) Status of Action: start 2016-09-12, end of Action: 2020-09-11, participating COST countries, participating NNC/IPC institutions and Specific Organisations:

- Start and end [dates](#) of Action: 2016-11-01 – 2020-09-11
- [Participating Countries](#) registered on e-COST:
- **31 COST countries:** AT, BE, CH, CZ, DE, DK, EL, EE, ES, FI, FR, GR, HR, HU, IE, IL, IT, LT, LV, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, TR, UK
- **3 NNC:** EG, PS, SA
- **7 IPC/Specific Organisation:** US, JP, KR, QA, AU, CA, CU, MX, RU

**Additional Countries** in our e-mail list but did not register on e-COST: BR, CN, GH, IN, IR, MK, MY, NZ, SG, TU, TW, UG, UY, ZA

b) [Short Term Scientific Missions \(STSM\)](#):

- Review of completed reports by Magdalena Labieniec-Watala presented by Beno Marija:



## STSM

### GP3 ... up to the end of April 2018

Until now we spent:

**12 520 euros (4000 euros ITC vs. 8520 euros non ITC)**

We still have:

**13 500 euros for ITC**  
**8 980 euros for non ITC**



Funded by the Horizon 2020 Framework Programme of the European Union

CA15203 MitoEAGLE - MC Meeting Jurmala

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Planning of next STSMs: For the WG2 and WG4 in Innsbruck STSM could be used, also an E-Mail will be sent to all members that there is budget left and that they can apply for STSMs

- We will suggest the same structure of the budget for STSM in GP4. MC members approved this decision  
Agreed: 20, disagreed: 0
- STSM should be more focused to target specific goals in MoU, devoted to direct manuscript-oriented tasks – also for manuscript writing

## 6. Update from the Grant Holder: Action budget status





- Action budget status presented by Maria Beno

| COST Networking Tool             | WBP          | Used               | Difference  | ITC        |
|----------------------------------|--------------|--------------------|-------------|------------|
| <b>Meetings</b>                  | € 50,238.00  | <b>€ 11,596.97</b> | € 38,641.03 | € 2,616.62 |
| <b>Training School</b>           | € 43,400.00  | <b>€ 0.00</b>      | € 43,400.00 | € 0.00     |
| <b>STSM</b>                      | € 34,650.00  | <b>€ 12,520.00</b> | € 22,130.00 | € 4,000.00 |
| <b>ITC Conference Grant</b>      | € 10,150.00  | <b>€ 2,430.00</b>  | € 7,720.00  | € 2,430.00 |
| <b>Dissemination</b>             | € 2,200.00   | <b>€ 0.00</b>      | € 2,200.00  | € 0.00     |
| <b>OERSA</b>                     | € 250.00     | <b>€ 0.00</b>      | € 250.00    | € 0.00     |
| <b>Total Science Expenditure</b> | € 140,888.00 | <b>26,546.97</b>   | 114,341.03  | 9,046.62   |
| <b>FSAC (15%)</b>                | € 21,133.20  |                    |             |            |
| <b>Total Grant</b>               | € 162,021.20 |                    |             |            |

- The column “Difference” shows the available budget and is therefore the current status of what can still be used.
- Additional budget in the COST Action – the ITC conference grant:  
There is still 2,216.00€ that can be used for ITC Grants. The suggestion is to send out a circular with upcoming conferences in order to attract some more ITC Grant applications. Suggestions for conferences which will be supported should be made by the MC Members.

Interested person for a Grant is: Tuncay Erkan for a Conference in USA

- The Work and Budget plan for GP4 was discussed. The Budget will be made on the basis of the GP3 WBP.

#### 7. Update from the COST:

- Marija Beno informed about General Data Protection Regulation (GDPR) documents that were uploaded on the MitoEAGLE webpage :  
[http://wiki.oroboros.at/images/d/da/FAQs\\_GDPR\\_for\\_COST\\_Actions.pdf](http://wiki.oroboros.at/images/d/da/FAQs_GDPR_for_COST_Actions.pdf)

#### 8. Monitoring of the Action:

- The Action is monitored in detail on the website (<http://www.mitoeagle.org/index.php/MitoEAGLE>)
- Meeting minutes are available on the website for each meeting on the page of the meeting.
- Summary of WG progress for each WG could be found in minutes from each meeting and also on each Working Group webpage.
- The suggestion to better organize the WG pages was considered and the pages were updated. The summaries of WG meetings are added to the page of each WG under Next steps.

#### 9. Implementation of COST policies on:

##### a) Promotion of gender balance and Early Career Investigators (ECI)

- Gender:** balanced and will be furthermore maintained in all MitoEAGLE events
- ECI:** ECIs in leadership positions has increased. 3 horizontal leadership positions are ECIs
  - ECIs, ITCs and gender balance Coordinator: Nina Krako (RS);
  - ECIs, ITCs and gender balance Substitute: Tomaz Mars (SI)
  - Dissemination coordinator: Marina Makrecka-Kuka is ECI from ITC (LV)

- Currently approx. 16% of all Action members are ECIs – information of many participants still missing. Dr. Gorr suggested to start a “Doodle” Action which every member has to fill out and this is how we will get the ECI information.
- A list for ECI was created on the website – which can be found on the website: ([http://www.mitoeagle.org/index.php/MitoEAGLE\\_network](http://www.mitoeagle.org/index.php/MitoEAGLE_network))
- Plans to increase the involvement of ECIs and to maintain and monitor gender balance:
  1. Encourage: Consider ECIs and gender balance in their nominations as new MC Members. (Suggestion Gloria Keppner as next MC Member for Germany)
  2. Support MC members to rotate in exchange of ECIs and to consider gender balance in replacement nominations. (Suggestion Thierry Arnould as MC Member for BE)
- Suggestion to send a circular to all participants again introduce the doodle system which will let us know who is an ECI.

b) Inclusiveness and Excellence (see below list of Inclusiveness Target Countries)

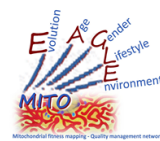
- Leadership roles in CA15203 = 38% ITC
  - 3 ITC in WGs (Marko Vendelin, Vilma Borutaite, Zuzana Cervinkova)
  - 5 ITC in other horizontal roles like STSM (Magda Labieniec-Watala), ECIs, ITCs and gender balance (Nina and Tomaz), Training schools (Ayse Basak Engin) and Disseminations (Marina Makrecka-Kuka)
- 5 possible ITC countries not yet involved in the MitoEAGLE project: Bosnia-Herzegovina, Bulgaria, Cyprus, Luxembourg, Montenegro. (the former Yugoslav Republic of Macedonia joined MitoEAGLE in GP3)
- Increase networking in order to involve the 5 remaining ITCs.

10:30 – 11:00 Coffee break

10. Follow-up of MoU objectives:

- [MoU objectives](#) and grant period goals (red=not achieved yet, green=done):

## Progress of GP Goals



- GAPG 1: Publication of paper on concepts and terminology: **Dissemination of preprint** and **journal submission of final manuscript**
- GAPG 2: **Upload** of datasets **generated through WG 2 and 4** in internal lab developments, results of the proficiency ring test (generated but not uploaded yet), and during application module developments.
- GAPG 3: **Reports** with specific results on muscle fibres in comparison with an anonymous data summary, and **joint publication**.
- GAPG 4: Muscle sample selection, **ring test experiments** including **MitoEAGLE-proficiency training**, **data analysis by experimenters** and **MitoEAGLE proficiency test manager**.
- GAPG 5: **Testing of newly developed software** modules regarding functionality and usability during proficiency tests and **experimental optimization of OXPHOS protocols**.

## Progress of GP Goals



- GAPG 6: Develop **recommendations for data reporting** and data **sharing** beyond the published record
- GAPG 7: Provide a **summary on education programme** for MitoEAGLE
- GAPG 8: **Guidelines for future research and recommendations for the evaluation of respiratory characteristics in human blood**
- GAPG 9: **Guidelines** for future research and recommendations for the evaluation of respiratory characteristics in **(human)** muscle biopsies samples
- GAPG 10: **Training of researchers towards improved reproducibility of sample preparation and respirometric evaluation**



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- DONE: The list of host institutions for STSM should be updated on the website and sorted alphabetically:  
([http://www.mitoeagle.org/index.php/Short-Term\\_Scientific\\_Missions\\_MITOEAGLE](http://www.mitoeagle.org/index.php/Short-Term_Scientific_Missions_MITOEAGLE))
- DONE: The participants were asked to contact M. Beno for adding their name to mentor list and their institution to the list of host institutions
- To GAPG3:
  - WG2 Retreat planned at the beginning of January 2018 in Innsbruck. – the final date will be announced.

### The progress report of the working groups was reported by the WG leaders:

Erich Gnaiger (WG1)  
Pablo Miguel Garcia-Roves and Marina Makrecka-Kuka (WG2)  
Zuzana Cervinkova and Thierry Arnould (WG3)  
Nicoleta Moiso (WG4 cell lines)

### MitoEAGLE Working Group 1

- [WG1 summary](#) presented by Erich Gnaiger:  
Introduction and welcome words by Erich Gnaiger.  
All participants are invited to submit comments and improvements, and those who are not yet included as co-authors are invited to join. Discussion about authorship, Arnould Thierry will join, as well as the Theresa Merz from Ulm.

Arnould Thierry started discussion about textbooks and graphics; Schlattner Uwe mentioned that we should make the PPT files from graphics accessible; Arnould: textbooks not edited every year – consider that. Genova Maria Luisa is writing letter for textbooks to be sent to the Editors. Gnaiger Erich informed that the MitoEAGLE preprint can be used as a teaching material. The figures are available in the web.

For graduate students who need a general introduction on mitophysiology the publication might be too difficult to understand.

Schlattner: Offer different figures on different complexity levels, eliminate stuff –, if we do work upfront many people will take our figures, deliverable of consortia. This makes it easier for teachers to use it in their lectures. Suggestion to make another review which explains this better. Separate teaching material should be uploaded on the website. Take the preprint and put it in this basic teaching mode. Structured in different parts.

Couplig figure as an example

- [ECI and Gender balance](#) presented by Nina Karko-Jakovljevic:

## MitoEAGLE Working Group 2

- **WG2 summary** presented by Pablo Garcia-Roves:  
[http://wiki.oroboros.at/images/0/04/Summary\\_WG2.pdf](http://wiki.oroboros.at/images/0/04/Summary_WG2.pdf)

Human vastus lateralis pfi study: Is an ongoing project, which will for sure will be ongoing as more information will be given and will be necessary. A meeting is required for data analysis and interpretation. Afterwards, the manuscript comparing O2 regime, buffers and blebbistatin can start.

One of the ongoing projects tries to establish reference values of mitochondrial respiration for skeletal muscle permeabilized fibers (pfi). Moreover, this values will allow to evaluate if the skills for muscle preparations are reached. Open call deadline is extended in order to have more groups on board:

Adam Chicco: O2 dependence seen in study? Carolina Doerrier: In pilot studies we observed an O2 dependence which is higher in mouse model. In the human study (vastus lateralis) an individual reanalysis is required, making special attention in O2 reoxygenations; O2 dependence higher in mouse than in human muscle

Marina Makrecka-Kuka outlining programme  
Pablo Garcia Roves presentation – talking about call

Vendelin Marco questions whether the main discrepancies for the Copenhagen data was due to normalization. Normalization only to wet weight? Carolina Doerrier: yes

Microscopy on the samples before and after experiment was done.

Rob Wüst: Variation can also come from fibre distribution?

Carolina Doerrier: Source of variability is also the tool of the separation. Moreover, marks taken can also make difference, have to go through all the data again

Pablo Garcia Roves: aware of two things: a lot of variability, but also outliers, , but still they do not want to put away the wrong data, they just want to keep it to see if they can find tools that are able to fix the wrong measures still and that it is not useless anymore.

Tools can be a source of variation (needle vs. forceps)

Adam Chicco: better to exclude give an example how a fibre looks like etc., common pitfalls  
Explanation on MitoFit proficiency test, data from mouse muscle study is not yet separated by experienced and not experienced scientists

Petit Patrice: explanation on the proficiency test -people get started with frozen cells and then have to do do cell cultures? ... Erich Gnaiger: viability tests (multiple tests, not relying on one opinion if one test is good or not; 2 years tests...) viability: 90%.

Erich Gnaiger: Question if cultured cells are used, Erich Gnaiger explained that no cultured cells are used because there are no changes in the outer membrane. Viability test – with several tests that

where done during two years the viability was confirmed. Training courses are necessary to achieve the expertise and are the key to evaluate experience.

Suggestion in general WG2: Skeletal muscle review to look at literature of different biological species. Dominique Votion and Helene Lemieux as leaders for this new project in WG2.

[WG2 summary](#) presented by Marina Makrecka-Kuka:

WG2 for heart: is going smoothly – of course it is always open for new interested persons

### MitoEAGLE Working Group 3

- [WG3 summary](#) presented by Irina Shabalina:  
Erich Gnaiger: which substrate combinations?  
Brown adipose tissue, UCP2 activity is seen, this is what has been shown, not for liver; additional substrate...  
Adam Chicco Succinate conflict- if they add the acid after the succinate it? gets really high. UCP1 substrate gives huge reactions., Oct after S,  
  
Continuation is the only huge problem – first remove lipids. There should no free acids around. They work like a detergent.  
  
Credibility of study? Reproducing is quite difficult. They hope for nice data, Irina Shabalina is in collaboration with other scientists to achieve some results. Not enough tissue to actually isolate mitochondria.  
  
Thomas Gorr: synthesized fat in the mitochondria have you heard before? Patrice Petit confirmed
- [WG3 summary](#) presented by Thierry Arnould:  
Thierry Arnould: will be added to WG3 as he started with this research field.  
Thierry Arnould -difficulties; invitation from R. Rossignol for review on coupling system – asked if someone has input on this.  
Reactivate F. Bouillaud (mentioned by Patrice).
- [WG3 summary](#) presented by Zuzana Cervinkova:  
Only few samples because it is difficult to get them and therefore the progress is not as far as in the other working groups.  
Each liver we investigate 1st biopsy when it comes to the surgeons, preservation period of 1 part – parallel run on ice ... after period from cold stored liver, then implanted, after further period biopsy from recipient  
From proficiency test to mouse liver now involved  
In our case: healthy liver, in Zuzana's case: liver affected  
We expect 400 livers  
Source is liver biopsy from surgeons, then preservation period on ice with organ perfusion, and after measurements from cold stored liver and implanted and after period of time again a biopsy of patient  
Healthy livers are used for above, but they also use affected livers.  
Work with Jordi Muntane – using hepatocytes - Nina Krako can give data that she already analyzed to the WGs  
Nina Krako Jakovljevic: Hepato cellcarcinoma, HepaG and HepG2 by Zuzana (H2H7 – Nina)  
  
Human samples fasting is very big factor, liver is transported before isolation – which influences the myocytes more. It was cruel to starve the animal and it has to stop because it is already great quality with not fasted mice. Adam Chicco suggests to just leave it for 4 hours to fast. It is hard to unify because the mice are not all the same fasted.

## MitoEAGLE Working Group 4

- [WG4 cell lines summary](#) presented by Nicoletta Moisi:

Erich Gnaiger: Hepatocytes from rats in routine state you can boost their respiration.

Tissue specific studies are more important than cell lines themselves.

Stem cells need special components otherwise they get old very quick. All components have contributions and it is not clear now how they affect the cells. A lot of cells are necessary for the analysis. Muscle cells get old really quick. Perhaps a new Action on that topic? Nutrition is cell culture.

Nehlin Jan: Senescence, special component needed to be added to drive cells further, a lot of work to find out the combinations etc.

Gorr Thomas: how you control co-founding factors?

ATP in monocyte are coming from external mitochondria – just measure respiration is perhaps not enough. Some cells also don't respond,

Moisi Nicoletta: blood cells highly glycolytic

STSM needed for comparison of isolation methods (Erich Gnaiger)

Krako Nina Jakovljevic: Glycolysis in cell lines

If ATP doesn't change you start assuming. But there is no concrete proof. Glycolysis should not be confused with acidification.

Microcalorimetry (Erich Gnaiger) mentioned by Irina Shabalina

IT is unclear how much you can trust all this data but still in the end when you compare you actually do have data that is most probably correct. Next step is to try to analyze them  
Idea is to collect the data now.

### 11. Scientific planning:

#### a) Scientific strategy (MoU objectives, GP2 goals, WG tasks and deliverables)

Next WG tasks are listed in WG summaries (see above)

#### b) Action Budget Planning: Work and Budget Plan Summary:

We will keep the same structure for the budget plan as for the GP2.

Votes: agreed 20, disagreed: 0.

#### c) Long-term planning (including anticipated locations and dates of future activities)

- MiP2018/MitoEAGLE Meeting in September-October 2018 in Belgrade will be organized by Nina Krako Jakovljevic, the dates and place will be announced soon (presented at MC Meeting)  
4 suggested days, overlap with ASMRM therefore option 3 or 4. Go for option 4: Oct 13-16  
Mare Luise Genova: check if hotel is more expensive. Benefits for participants if everything is at one place.  
Discussion what is included in the LOS  
Caro: Time for individual working groups should be allocated, not only for presentations.  
MiPsociety will be involved in the organization of the meeting.
- MiPschool 2018– two ideas were presented (Greece and Portugal) decision was for Portugal, therefore it will be organized by Carlos Palmeira in Coimbra – the final date will be coordinated with Nina Krako Jakovljevic and Pable Garcia Roves (Meeting in Barcelona) and other organizers to avoid overlaps with the other meetings.  
Greece: dates too close to MC meeting, input from Cervinkova: Greece is too expensive  
  
Pablo: MC Meeting – teaching is in October, MC meeting can be moved to another time period?  
December would be better – Nina will check alternative dates.

d) Dissemination plan (Publications and outreach activities):

- COST Action should be acknowledged in our publications. The example how to acknowledge is in the preprint terminology publication.
- Publications with authors from at least three COST countries will count as a contribution to the Cost Action MitoEAGLE. We need to list all such publications for final report.
- We need to list and document all outreach activities presenting our COST Action MitoEAGLE: seminars, meetings. Participants were asked to send the documentation about their outreach activities, photos are welcome for documentation. Everything will be listed on MitoEAGLE website.

12. New members of the COST Action MITOEAGLE:

a) COST countries

b) Institutions in Near Neighbouring Countries, International Partner Countries, and/or Specific Organisations:

- 5 COST countries are not yet members of our COST Action MitoEAGLE

\_There was no request to join our Action

- The participants were asked to contact (with E.Gnaiger in CC) the collaborators from the COST countries, will contact Contacts which are not members of our Action yet, to join MitoEAGLE

13. Any Other Business (AOB)

- New structure of the MitoEAGLE Website. The events and general information are separated in order to make the website more logical and to make it easier for members to find upcoming events and also find recent news better.
- Progress report: Discussed with MC Members and asked for input on

1) Dissemination: Genova – will put a link to the COST Action on her university page

2) Fostering research activities: Nicoleta Moiso is involved in a ITN related to (mitochondria and stress signaling), cell models, animal models, samples from patients, how mitos impact, chaperons protein...? – January 15th Application deadline

3) Initiate applications: Are there special funds for running training schools?

Liepins: Training is in ITN included, Fat in Brain project included, include reference in the applications

4) MitoEAGLE publications with acknowledgements: co-authors from 3 countries at least

5) Cardioprotection COST Action

- MitoEAGLE in Google > first hit is the facebook page and not the website – Christos can help

14. Location and date of next MC meeting

- MC Meeting in Belgrade, Serbia in autumn 2019 – date to be announced
- Training School in Coimbra, Portugal in July 2019 – date to be announced

15. Summary of MC decisions:

MC members and Substitutes voted for these points:

1. The remaining money from the conference in Jurmala will be used for the WG2 Meeting  
Agreed: 20, disagreed: 0
2. The remaining money from the event in Jurmala will be shifted to the costs for the Workshop –  
WG 4 blood cells workshop  
Agreed 20, disagreed: 0
3. Approval that conferences that are listed in the MitoGlobal Calendar or suggestions of  
conferences that will be sent to us by MC Member will be accepted for ITC Grants  
Agreed: 20, disagreed: 0
4. The next Training School will take place in Portugal and will be organized by Carlos Palmeira and  
the MC Meeting will take place in Serbia and will be organized by Nina Krako-Jakovljevic  
Agreed 20, disagreed: 0.
5. The same structure for the budget plan as for the GP2 will be proposed.  
MC members approved this decision.  
Agreed 20, disagreed: 0.
6. The WG1 Leader role will be switched: Kathrin Renner-Sattler will be replaced by Marko Vendelin  
and Domink Pesta as WG1 Co-leader  
MC members approved this decision.  
Agreed 19, disagreed: 1

16. Closing: The meeting was closed by the Chair Erich Gnaiger and local organizer Marina Makrecka-Kuka at 14:45.

## LIST OF ANNEXES AND LINKS

### Annex 1 – [Attendance List](#)

#### Links:

Abstracts, presentations and agenda:

[http://www.mitoeagle.org/index.php/MiP2018/MitoEAGLE\\_Jurmala\\_LV#Abstracts.2FParticipants\\_-\\_alphabetical\\_order](http://www.mitoeagle.org/index.php/MiP2018/MitoEAGLE_Jurmala_LV#Abstracts.2FParticipants_-_alphabetical_order)