The role of mitochondrial metabolism in health and disease
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Appendix
Abbreviations

Chapter 1

AMPK: AMP-activated protein kinase
AMP: adenosine triphosphate
BTHS: Barth syndrome
CL: cardiolipin
CLPP: caseinolytic peptidase P
CR: caloric restriction
ERAL1: Era G-protein-like 1
ETC: electron transport chain
FOXO: forkhead box O
GC-MS: gas chromatography-mass spectrometry
HARS2: histidyl tRNA synthetase 2
HSD17B4: Hydroxysteroid 17-Beta Dehydrogenase 4
IGF-1: insulin-like growth factor 1
IMM: inner mitochondrial membrane
LARS2: leucyl-tRNA synthetase
LHON: Leber’s hereditary optic neuropathy
MELAS: Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes
MLCL: monolysocardiolipin
mtDNA: mitochondrial DNA
mTOR: mammalian target of rapamycin
nDNA: nuclear DNA
NMR: nuclear magnetic resonance
OXPHOS: oxidative phosphorylation
RNAi: RNA interference
RNA-seq: RNA sequencing
WES: whole exome sequencing
3D: three dimensional
ROS: reactive oxygen species
TCA: tricarboxylic acid
Tet: tetracycline
UPRmt: mitochondrial unfolded protein response

Chapter 2

FH: fumarate hydratase
HIF-1: hypoxia-inducible factor 1
IDH2: isocitrate dehydrogenase 2
rtTA: reversed transactivation
SDH: succinate dehydrogenase subunits
TetO: Tet operator sequence
TetR: tetracycline repressor protein
tTA: tetracycline-controlled transactivator
VP16: Virus Protein 16

**Chapter 3**

CoQ10: Coenzyme Q10
FCCP: Carbonyl cyanide-p-trifluoromethoxyphenylhydrazon
GFP: green fluorescent protein
GTP: Guanosine triphosphate
MRPL54: mitochondrial ribosomal protein L54
MRPS22: mitochondrial ribosomal protein S22
MT-CO1: cytochrome \( \epsilon \) oxidase subunit 1
OCR: oxygen consumption rate
PS: Perrault syndrome
SDHA: succinate dehydrogenase complex, subunit A
BCAA: branched-chain amino acid
FA: fatty acid

**Chapter 4**

BCKD: branched-chain alpha-ketoacid dehydrogenase
BCKDK: Branched chain ketoacid dehydrogenase kinase
CDP-DAG: cytidine diphosphate diacylglycerol

DBT: Dihydrolipoamide Branched Chain Transacylase E2
DLD: dihydrolipoamide dehydrogenase
DLST: Dihydrolipoamide S-Succinyltransferase
KGDH: \( \alpha \)-ketoglutarate dehydrogenase
LETM1: Leucine Zipper And EF-Hand Containing Transmembrane Protein 1
MIB: mitochondrial intermembrane space bridging complex
MICOS: mitochondrial contact site and cristae organizing system
OGDH: oxoglutarate dehydrogenase
OPA1: Optic Atrophy Protein 1
PC: phosphatidylcholine
PE: phosphatidylethanolamine
PG: phosphatidylglycerol
SAM: sorting and assembly machinery
CS: citrate synthase
TAZ: tafazzin
TOM40: translocase of the outer membrane 40
VDAC: voltage-dependent anion-selective channel
Chapter 5

AA: amino acid
AAK-2: AMP-Activated Kinase 2
HPLC-MS: high-performance liquid chromatography-mass spectrometry
LOD: limit of detection
LOQ: limit of quantification
LPE: Lysophosphatidylethanolamine
MS: mass spectrometry
PCA: principal component analysis
PL: phospholipid
PS: phosphatidylserine
PUFA: polyunsaturated fatty acid
SM: sphingomyelin
UPLC-MS/MS: ultra-performance liquid chromatography-tandem mass spectrometry
5FU: 5-fluorouracil

Chapter 6

iPSC: induced pluripotent stem cell
shRNA: short hairpin RNA
Authors’ contributions

Chapter 2: Tetracycline antibiotics impair mitochondrial function and its experimental use confounds research

IAC, NMH, LM, JA and RHH wrote the manuscript.

Chapter 3: A homozygous missense mutation in **ERAL1**, encoding a mitochondrial rRNA chaperone, causes Perrault syndrome

IAC, MA, RHH, and ASP conceived and designed the project. IAC, MA, SGC, RZP, MAH, LM, JK, RO, FB, HRW, JNS, JA, and MMM coordinated, performed and interpreted experiments. IAC, MA, RHH, and ASP wrote the manuscript, with contributions from all other authors.

Chapter 4: Barth syndrome cells display widespread protein complex destabilization and impaired metabolic flux distribution

IAC and RHH conceived and designed the project. IAC, SGC, NMH, JPNR, SWD, LIJ, RJW, MvW, SF, and FMV coordinated, performed and interpreted experiments. IAC, SGC, NMH, UB and RH wrote the paper with contributions from all other authors.

Chapter 5: A sensitive mass spectrometry platform identifies metabolic changes of life history traits in *C. elegans*

IAC, AWG, and RHH conceived and designed the project. IAC, AWG, RK, YJL and RS performed experiments and interpreted data, HvL, AvC, MATV and FMV coordinated and interpreted mass spectrometry experiments. KH, ACL, MLPR and AvK performed bioinformatics. IAC, AWG, and RHH wrote the manuscript, with contributions from all other authors.

Chapter 6: **Acl-3** knockdown in *C. elegans* mimics lipid disturbance in Barth syndrome patients and causes widespread transcriptional changes

IAC and RHH conceived and designed the project. IAC, MM, RK and AWMI coordinated, performed and interpreted experiments. MATV, MvW, HvL, FMV and RJW coordinated and interpreted mass spectrometry experiments. TS, MvW, GEJ, ACL, MLPR, AvK and RJ performed bioinformatics. IAC and RHH wrote the manuscript, with contributions from all other authors.
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List of publications


*Equal contribution
Manuscripts in preparation


*Equal contribution
# PhD portfolio

## 1. PhD training

### General Courses/Transferable Skills

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<thead>
<tr>
<th>Course</th>
<th>Year</th>
<th>Workload (ECTS)</th>
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<td>Scientific Writing</td>
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### Specific Courses/Scientific Methods

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<td>Bioinformatics</td>
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### Seminars, workshops and master classes

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<td>Ruysch Lectures, AMC, Amsterdam (NL)</td>
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<td>Tager Lectures, AMC, Amsterdam (NL)</td>
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<td>XF24 &amp; XF96 Seahorse Technology Training, Copenhagen (DK)</td>
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<td>CRISPR-Cas9 workshop, AMC, Amsterdam (NL)</td>
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<td>Time management workshop, AMC, Amsterdam (NL)</td>
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### Presentations

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<td>Oral presentation, ACM-MDL meeting, Lunteren (NL)</td>
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<tr>
<td>Oral presentation, Dutch Worm Meeting, Groningen</td>
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**International conferences**

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<td>2013</td>
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<tr>
<td>Ageing-Research@NL, Den Haag (NL)</td>
<td>2013</td>
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<td>ACM-MDL meeting, Lunteren (NL)</td>
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<td>Dutch Worm Meeting Groningen (NL)</td>
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<td>Dutch Worm Meeting, Wageningen (NL)</td>
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<td>NVBMB symposium for Metabolic control of age-related disease, Amsterdam (NL)</td>
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<tr>
<td>AMGRO meeting, Lemmer (NL)</td>
<td>2015</td>
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<td>ACM-MDL meeting, Lunteren (NL)</td>
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<td>2016</td>
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<td>AMGRO meeting, Lemmer (NL)</td>
<td>2016</td>
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<tr>
<td>Cell symposium: Aging and Metabolism, Sitges (ES)</td>
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Other

Research department meetings, AMC, Amsterdam (NL) 2012-2016 2.0

Journal club, AMC, Amsterdam (NL) 2012-2016 1.50

2. Teaching

Supervising 3-month post-master’s internship of Eileen Daniels, MSc 2015 0.5

3. Parameters of Esteem

Grants

AMC PhD Scholarship 2012

Awards and Prizes

Selection for oral presentation at Keystone Symposia 2015

Keystone Symposia Future of Science Fund scholarship 2015

Best abstract award at ACM-MDL meeting 2015
Curriculum Vitae

Iliana Antonia Chatzispyrou was born on 3 January 1986 in Thessaloniki, Greece. In 2003 she completed her secondary education at the 17th Lyceum of Thessaloniki and participated in the national-level examinations for admission to higher education. In 2009 she received her BSc degree in Biology from Aristotle University of Thessaloniki. During her last years of undergraduate studies she followed the specialization track of Molecular Biology, Genetics and Biotechnology. Having received a grant from the European student exchange program ‘Erasmus’, she conducted part of her studies at the Free University of Berlin, Germany during the spring semester of 2007. After receiving her BSc degree, she conducted a three-month internship at the Department of Physiology of the University Medical School of Thessaloniki. In the fall of 2010 she moved to the Netherlands to attend the MSc program in Biomedical Sciences at the University of Amsterdam and received her MSc degree in early 2013. During the first year of her Master’s studies she conducted a research internship at Tytgat Institute for Liver and Intestinal Research of the Academic Medical Center, working on the identification of transcription factors that are crucial for the induction of hepatocyte differentiation. She wrote her Master’s literature thesis on the evolution of mitochondrial DNA. In the beginning of 2012 she started her second research internship at Swammerdam Institute for Life Sciences of the University of Amsterdam, where she studied the effect of anti-HIV drugs in mitochondrial function using C. elegans as a model organism. In the fall of 2012, having won an AMC PhD scholarship, she started her doctoral studies at the Laboratory of Genetic Metabolic Diseases of the Academic Medical Center under the supervision of her promotor Prof. dr. Ronald J. A. Wanders and co-promotor dr. Riekelt H. L. Houtkooper. During her PhD research she studied the role of mitochondrial function in rare metabolic diseases, and introduced C. elegans as a model for mechanisms related to metabolic deregulation. The results this research are presented in this doctoral thesis.
Acknowledgements

This thesis would not have been completed without the invaluable contribution and support of many people.

First of all, I would like to thank my supervisors for their guidance and support throughout my PhD studies and for giving me the chance to conduct my research in lab GMZ. Dear Riekelt, thank you for trusting me with the amazing opportunity of writing a proposal for the PhD scholarship grant that enabled me to work with you, especially as I would be the first PhD student of your group in lab GMZ. It has been a great experience, and I am grateful for everything I have learned from you both on a scientific and mentorship level, and for your constant presence and support, even under the pressure of your increasing responsibilities and busy timetable. Dear Ronald, you have been an inspiring and positive figure, always encouraging dialogue and expressing enthusiasm about new ideas and research projects. Thank you for your valuable feedback and for making me feel welcome in the lab from the very beginning.

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Moreover, I am very thankful to everyone from Lab GMZ for your support as well as for the fun occasions of borrels and lab days. I would like to thank very much in particular Hans, Sacha, Fred, Rob O., Mia, Janet K., Jos, Martin V., Henk, Arno and Femke S. for your scientific contribution. Also, many thanks to Petra and Patricia for help with cell culture issues, to Gerrit-Jan, Maddy, Carin, Martin A. and Anneliese for kindly taking care of all administrative and ordering matters, and Rutger, René and Jeroen R. for your useful lab tips and the funny and interesting conversations. Special thanks to Carlo, it was very nice to share the same office, thank you for your enthusiasm about science but also music.

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Auwerx. Many thanks to Sergio Guerrero-Castillo, Hans Spelbrink and Ulrich Brandt from the Department of Pediatrics at Radboud Institute for Molecular Life Sciences in Nijmegen. Finally, thanks to Toon Santermans and Rob Jelier from the Centre of Microbial and Plant Genetics at the University of Leuven, Belgium.

The AiO group was a very important part of my PhD, I had a great time with all our trips, dinners and drinks, and would like to thank you all including of course the non-mitos! Dear Iedan, it was very nice to be roomies, you were always eager to express ideas about our projects, participate in group activities and we all had a great time with the AiO Sinterklaas dinner at your place, thank you. Dear Olga M. thank you for your good company in the AiO room, it was a pleasure. Dear Kim, it was lovely chatting about our projects and hanging out together in Amsterdam, and my capacity for drinking beer has greatly increased since I met you, for which I am thankful and fully appreciate. Dear Kathi, thank you for your valuable help with all the heat map versions for our worm paper, as well as for your company during many AiO activities. Dear Femke, I appreciate your enthusiasm to guide us through the quickest way to Efteling rides, it was lots of fun. Dear Clair, although we didn’t spend much time together in the lab, it was nice to chat with you, and I am still grateful that you introduced me to the lovely Greek taverna close to your place in De Pijp. Many thanks also to all AiOs that were in the lab some time ago: Sandra, Eveline, Olga P., Kevin, Martin, Max, Catherine, it was great to have met you, you were good company. I would like to warmly congratulate all of my fellow AiOs that have already defended their theses, and I wish the best of luck to the rest of you for the successful completion of your doctorate. And of course I wish to everyone all the best for the future. Many thanks and best of luck also to all current and previous students of the lab.

Life outside the lab, though at times limited, has been equally important for keeping the balance throughout my PhD, and I am grateful for all the wonderful moments spent with dear friends for drinks, house parties, dinners, concerts and even long Skype calls. Special thanks to my dear Greek friends in Amsterdam Αρέτη και Ελεωνόρα (and your lovely partners Marco and Jochem) για όλη σας την υποστήριξη, and together with Florance, our unique French in our lives, our girl nights in-house and outside. Also, many thanks to my Greek friends that unfortunately have moved out of Amsterdam: Γιώργος, Σπύρος Γ., Δήμητρα, Αθηνά, Θοκάση και Σπόρος Π., οι συναντήσεις μας ήταν πάντα απολαυστικές, με κέφι και καταπληκτικό φαγητό, μου έχετε λείψει πολύ.

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For anyone whose name I have failed to mention, my sincerest apologies; the omission is likely due to the heavy demands of a long, yet rewarding, marathon…

Best wishes,

Iliana