European Heart Journal

New COST Action “EUropean network to tackle METAbolic alterations in HEART failure” (EU-METAHEART)

--Manuscript Draft--

Manuscript Number:	
Article Type:	CardioPulse
Section/Category:	Heart Failure and Cardiomyopathies
Keywords:	heart failure; metabolism; mitochondria; consortium; network; cardiomyopathies
Corresponding Author:	Christoph Maack, M.D. Universitätsklinikum Würzburg: Universitatsklinikum Wurzburg Würzburg, GERMANY
First Author:	Christoph Maack, M.D.
Order of Authors:	Christoph Maack, M.D.
	Gemma Vilahur
	Marisol Ruiz-Meana
	Derek Hausenloy
Abstract:	N/A

New COST Action "EUropean network to tackle METAbolic alterations in HEART failure" (EU-METAHEART)

Christoph Maack[1,2], Gemma Vilahur[3,4], Marisol Ruiz-Meana[5], Derek Hausenloy[6,7,8,9],

on behalf of the Core Group (see Appendix) and members of the management committee (MC) of EU-METAHEART (see online supplement for list of MC members)

1) Comprehensive Heart Failure Center, University Clinic Würzburg, Germany
2) Medical Clinic 1, University Clinic Würzburg, Germany
3) Research Institute - Hospital de la Santa Creu i Sant Pau, IIB-Sant Pau, Barcelona, Spain
4) Centro de Investigación Biomédica en Red Cardiovascular (CIBERCV), Instituto de Salud Carlos III, Madrid, Spain.
5) Vall d'Hebron Institut de Recerca (VHIR), Hospital Universitari Vall d'Hebron, Barcelona, Spain
6) The Hatter Cardiovascular Institute, University College London, London, UK
7) Cardiovascular & Metabolic Disorders Program, Duke-National University of Singapore Medical School, Singapore
8) National Heart Research Institute Singapore, National Heart Centre, Singapore
9) Yong Loo Lin School of Medicine, National University Singapore, Singapore

Correspondence to: Christoph Maack, MD; Comprehensive Heart Failure Center, University Clinic Würzburg, Am Schwarzenberg 15, 97078 Würzburg, Germany; Maack_c@ukw.de

Text

Cardiovascular diseases (CVD) are the main cause of morbidity and mortality in Europe, and heart failure (HF) is the terminal consequence of most CVD, making HF the largest disease burden in Europe. The prevalence of HF increases with age, and so does the prevalence of comorbidities. The most frequent comorbidities are chronic kidney disease, anemia and metabolic disorders, such as obesity and diabetes. Such metabolic (and also other) comorbidities adversely affect HF outcome and *vice versa*, HF induces metabolic alterations and predisposes to the development of diabetes and other comorbidities.[1] Therefore, HF is not a single-organ disease, but a systemic disease that requires an interdisciplinary approach towards prevention, diagnostics and treatment.

Major routes of communication between the heart and other organs are neuroendocrine activation, inflammation, and metabolism. Treatment of patients with HF has long been limited to drugs interfering with neuroendocrine activation, such as ACE inhibitors, β-blockers, aldosterone antagonists and angiotensin receptor/neprilysin inhibition. However, while these treatments are effective in patients with HF with *reduced* ejection fraction (HFrEF), they are not (or clearly less) effective in patients with HF with *preserved* ejection fraction (HFpEF).

In recent years, major breakthroughs were achieved in targeting metabolism in HF. Sodium-glucose co-transporter 2 (SGLT2) inhibitors improve morbidity and prognosis in HF of any EF,[2] and the glucagon-like peptide-1 (GLP-1) agonist semaglutide reduces body weight and improves quality of life in obese patients with HFpEF.[3] However, the mechanisms that underlie these benefits are not well understood, but likely involve improvements of systemic and cardiac metabolism. In addition, mitochondria-targeted therapies, such as nicotinamide adenine dinucleotide (NAD^+) precursors,[4] ketones, and compounds that interfere with mitochondria and oxidative stress improve cardiac function in preclinical studies, but their translation to the clinic is not yet accomplished.[5]

It has been a long-held concept that the failing heart is an engine out of fuel.[6] However, it is still difficult to decipher whether the alterations in substrate utilization and the energetic deficit are sufficient to cause contractile dysfunction in their own right, or rather the associated alterations in metabolic *intermediates* through inducing maladaptive cardiac remodeling.[5] This latter hypothesis stems from the growing recognition that such metabolic intermediates can induce post-translational modifications of cytosolic and nuclear proteins, modifying their interactome and function in cardiac myocytes (**Figure 1**).[5] Furthermore, coupling of cardiac mechanics to metabolism, mediated by cytosolic and mitochondrial ion handling and adenosine diphosphate, is disrupted in various forms of HF, increasing mitochondrial reactive species that hamper excitation-contraction coupling and activate redox-sensitive, maladaptive signaling pathways (**Figure 1**).[5, 7]

Metabolic diseases are also important risk factors for vascular dysfunction. While macroangiopathy with myocardial ischemia and infarction typically leads to HFrEF, microvascular dysfunction is particularly relevant in patients with HFpEF.[1] In both scenarios, the relationship between coronary blood flow and the failing heart is bidirectional, as reduced coronary blood flow impairs contractile function, and *vice versa*, HF impairs coronary blood flow.[8] Finally, there is a tight interplay between metabolism and immunity, and inflammation plays an important role in atherosclerosis, but also myocardial remodeling during HF development (**Figure 1**).

Hence, it is essential to analyze perturbations of cardiac metabolism in an *integrative* fashion, taking into account the tight interplay of metabolism with cardiac and vascular function. Despite the substantial advancements in basic and clinical research in recent years, scientific progress has been hampered by the complexity of metabolism *per se* and the fact that the interdependence of the mechanisms controlling metabolism (**Figure 1**) often supersedes the capacity of single-discipline researchers and institutes to address the functional impact of dysregulated metabolic pathways and networks.

Therefore, the new COST Action EU-METAHEART (CA22169; https://www.cost.eu/actions/CA22169/) will facilitate interdisciplinary dialogue, knowledge and technology transfer to improve our understanding of metabolic alterations in HF and identify biomarkers and treatment targets for the benefit of patients with this devastating syndrome. At the same time, the Action will train the next generation of scientists to tackle the challenges imposed by the ever-growing burden of metabolic and cardiovascular disease.

COST stands for “European Cooperation in Science and Technology” and is a funding organization for research and innovation networks (https://www.cost.eu/). COST “Actions” help connect research initiatives across Europe and beyond and enable researchers and innovators to grow their ideas in any science and technology field by sharing them with their peers. COST Actions are bottom-up networks with a duration of four years that boost research, innovation and careers. COST Actions are typically made up of researchers from academia, small and medium-sized enterprises (*SMEs*), public institutions, and other relevant organizations or interested parties (https://www.cost.eu/cost-actions/what-are-cost-actions/).

COST Actions fund the expenses of networking activities rather than specific research projects. The Actions support conferences, short-term scientific missions (STSMs), training schools, communication activities, and virtual networking tools. In this context, COST Actions promote especially young research investigators (YRIs) by involving them in activities, for instance by giving them the opportunity to visit labs where they can learn new techniques (with STSMs), perform experiments and gain a broader expertise (https://www.cost.eu/what-do-we-fund/).

For our COST Action, we identified four major research areas that are crucial for the investigation of metabolic and mitochondrial dysfunction in HF that will be addressed in four working groups (WGs; 1-4; **Figure 1**):

- WG1: Substrate and intermediary metabolism in failing cardiomyocytes
- WG2: Metabolic impact of coronary vascular dysfunction
- WG3: Immunometabolism
- WG4: Mechano-energetic uncoupling and mitochondrial redox alterations

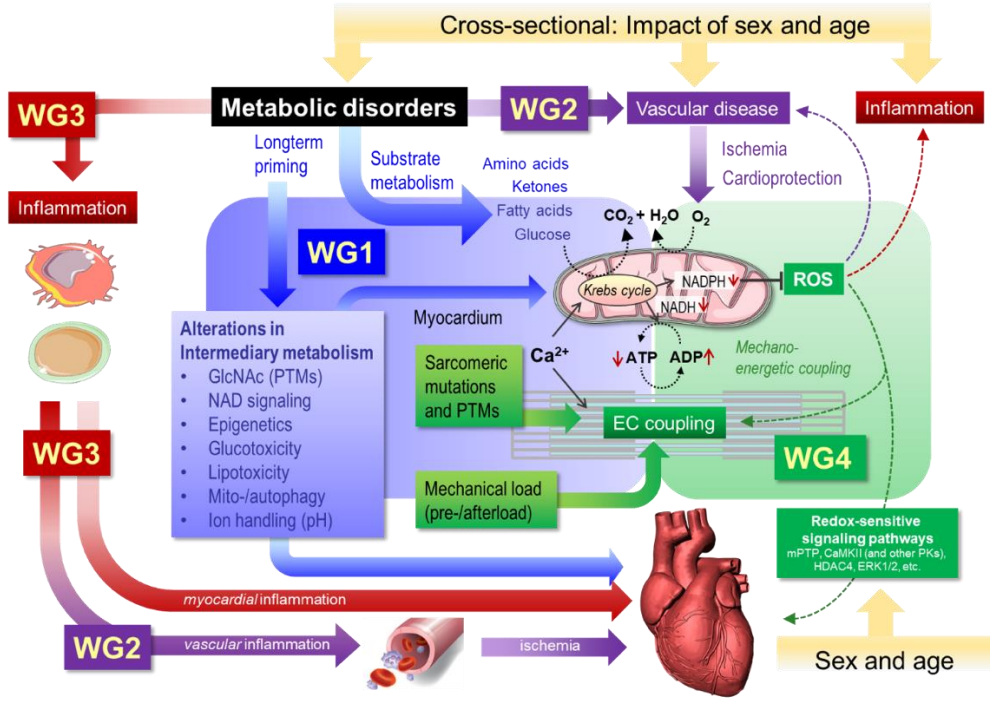

Figure 1: Pathophysiological concept of EU-METAHEART consortium. Four distinct fields of research covering metabolic aspects in HF are integrated towards a comprehensive approach to gain deeper understanding of HF pathophysiology and identify novel treatment targets. In all areas, sex- and age-related aspects will be integrated as key influencing factors. PTM, post-translational modifications; NAD, nicotinamide adenine dinucleotide; mPTP, mitochondrial permeability transition pore; CaMKII, Ca^{2+}/calmodulin-dependent protein kinase II; HDAC4, histone deacetylase 4; ERK1/2, Extracellular-signal regulated kinases 1/2. From https://www.cost.eu/actions/CA22169/.

EU-METAHEART will bring together excellent European researchers, who share a broad spectrum of scientific expertise and cutting-edge technologies to build a platform to exchange ideas, technologies and education, fostering breakthroughs in science that move the field forward and towards improving the treatment of patients with HF. The Action will harness recent advances and breakthroughs in scientific methodologies, such as in

- omics-based technologies,
- *in vitro* technologies to assess mechano-energetic coupling in isolated cardiac myocytes,
- small and large animal models for HFpEF and HFrEF, but also hereditary cardiomyopathies,
- *in vivo* functional, metabolic and immunological imaging,
- well-characterized and –phenotyped cohorts of patients with HF and hereditary cardiomyopathies, and
- metabolically and functionally maturated human induced pluripotent stem cell (hiPSC)-derived cardiac myocytes from patients with hereditary cardiomyopathies.

These complementary resources will develop harmonized integrative approaches that span from bench to bedside, providing fresh insights into metabolic aspects of HF and identifying novel treatment targets and biomarkers. At the same time, EU-METAHEART makes these achievements broadly accessible for laboratories across Europe and its near-neighbouring- and less privileged countries.

An important aspect of a COST Action is the transfer of knowledge. To this end, a 5th WG will guide and foster transfer of knowledge via a broad array of channels:

- Training schools periodically organized to facilitate transfer of skills and technologies;
- STSMs to encourage mobility of young scientists among European research institutions;
- workshops and scientific conferences to enable discussion of the generated knowledge and resources between partners, and
- publications on new results, methodologies, consensus documents and practical guidelines.

To increase disease awareness of the general public, communication on the main achievements of the Action will be through a COST Action website, newsletters, press releases and social media. Finally, the Action will take great care of training YRIs in all the dimensions of the Action, including scientific publications, conferences, mentoring sessions, workshops, training schools and mobility programs (such as STSMs) that can lead to joint projects.

EU-METAHEART builds on achievements of previous COST Actions, such as MitoEAGLE (https://www.cost.eu/actions/CA15203/), a mitochondrial data management system that allows to analyse the impact of age, gender, lifestyle and environment on mitochondrial function,[9] and EU-CARDIOPROTECTION (CA16225) that focussed on strategies to protect the myocardium from ischemia/reperfusion damage.[10]

On October 18th, 2023, EU-METAHEART held its kick-off meeting in Brussels (**Figure 2**). As of February 2024, the Action has more than 250 members from 36 countries. The list of the members of the management committee can be found in the online supplement, and the core group (consisting of working group leaders and officer positions) is listed in the appendix. It is possible to apply for WG membership anytime at https://www.cost.eu/actions/CA22169/.

Figure 2: Members of COST Action EU-METAHEART (CA22169) during the kick-off meeting at the COST office in Brussels, Belgium on October 18th, 2023.

References

1. Maack C, Lehrke M, Backs J, Heinzel FR, Hulot JS, Marx N, Paulus WJ, Rossignol P, Taegtmeyer H, Bauersachs J, Bayes-Genis A, Brutsaert D, Bugger H, Clarke K, Cosentino F, De Keulenaer G, Dei Cas A, Gonzalez A, Huelsmann M, Iaccarino G, Lunde IG, Lyon AR, Pollesello P, Rena G, Riksen NP, Rosano G, Staels B, van Laake LW, Wanner C, Farmakis D, Filippatos G, Ruschitzka F, Seferovic P, de Boer RA and Heymans S. Heart failure and diabetes: metabolic alterations and therapeutic interventions: a state-of-the-art review from the Translational Research Committee of the Heart Failure Association-European Society of Cardiology. *Eur Heart J*. 2018;39:4243-4254.
2. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F and Skibelund AK. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023;44:3627-3639.
3. Kosiborod MN, Abildstrøm SZ, Borlaug BA, Butler J, Rasmussen S, Davies M, Hovingh GK, Kitzman DW, Lindegaard ML, Møller DV, Shah SJ, Treppendahl MB, Verma S, Abhayaratna W, Ahmed FZ, Chopra V, Ezekowitz J, Fu M, Ito H, Lelonek M, Melenovsky V, Merkely B, Núñez J, Perna E, Schou M, Senni M, Sharma K, Van der Meer P, von Lewinski D, Wolf D and Petrie MC. Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity. *N Engl J Med*. 2023;389:1069-1084.
4. Diguet N, Trammell SAJ, Tannous C, Deloux R, Piquereau J, Mougenot N, Gouge A, Gressette M, Manoury B, Blanc J, Breton M, Decaux JF, Lavery GG, Baczkó I, Zoll J, Garnier A, Li Z, Brenner C and Mericskay M. Nicotinamide Riboside Preserves Cardiac Function in a Mouse Model of Dilated Cardiomyopathy. *Circulation*. 2018;137:2256-2273.
5. Bertero E and Maack C. Metabolic remodelling in heart failure. *Nat Rev Cardiol*. 2018;15:457-470.
6. Neubauer S. The failing heart--an engine out of fuel. *N Engl J Med*. 2007;356:1140-51.
7. Aksentijević D, Karlstaedt A, Basalay MV, O'Brien BA, Sanchez-Tatay D, Eminaga S, Thakker A, Tennant DA, Fuller W, Eykyn TR, Taegtmeyer H and Shattock MJ. Intracellular sodium elevation reprograms cardiac metabolism. *Nature Commun*. 2020;11:4337.
8. Heusch G. Coronary blood flow in heart failure: cause, consequence and bystander. *Basic Res Cardiol*. 2022;117:1.
9. Gnaiger E and Group MT. Mitochondrial physiology. *Bioenerg Commun*. 2020;1.
10. Davidson SM, Ferdinandy P, Andreadou I, Bøtker HE, Heusch G, Ibáñez B, Ovize M, Schulz R, Yellon DM, Hausenloy DJ and Garcia-Dorado D. Multitarget Strategies to Reduce Myocardial Ischemia/Reperfusion Injury: JACC Review Topic of the Week. *J Am Coll Cardiol*. 2019;73:89-99.

Word count excluding references: 1.412 (excluding legends: 1.312)

Appendix:

The article was written on behalf of the Core Group of the COST Action EU-METAHEART (CA22169), which consists of the following members:

Dunja **Aksentijevic,** Queen Mary University of London, United Kingdom; Ioanna **Andreadou,** National and Kapodistrian University of Athens, Greece; Inês **Falcao-Pires,** Faculdade de Medicina da Universidade do Porto, Portugal; Jeremy **Fauconnier,** INSERM, France; Alessandra **Ghigo,** University of Torino, Italy; Derek **Hausenloy,** University College London, United Kingdom; Lisa **Heather,** University of Oxford, United Kingdom; Gerd **Heusch,** University of Essen, Medical School, Germany; Georgios **Kararigas,** University of Iceland, Iceland; Petra **Kleinbongard,** University of Essen, Medical School, Germany; Luca **Liberale,** Universita Degli Studi Di Genova, Italy; Christoph **Maack,** University Clinic Würzburg, Germany; Mathias **Mericskay,** Universite Paris Saclay, France; Melanie **Paillard,** INSERM, Université Claude Bernard Lyon-1, France; Bruno **Podesser,** Medical University of Vienna, Austria; Marisol **Ruiz-Meana,** Vall d'Hebron University Hospital, Autonomous University of Barcelona, Spain; Gabriele **Schiattarella,** Charité Universitätsmedizin Berlin, Germany; Marie **Schroeder,** Novo-Holdings, Hellerup, Denmark; Simon **Sedej,** Medizinische Universität Graz, Austria; Katrin **Streckfuss-Bömeke,** Institute of Pharmacology and Toxicology, University Würzburg, Germany; Gemma **Vilahur,** Research Institute - Hospital de la Santa Creu i Sant Pau, IIB-Sant Pau, Spain.

Figure 1

Click here to access/download;Figure;Figure 1.png

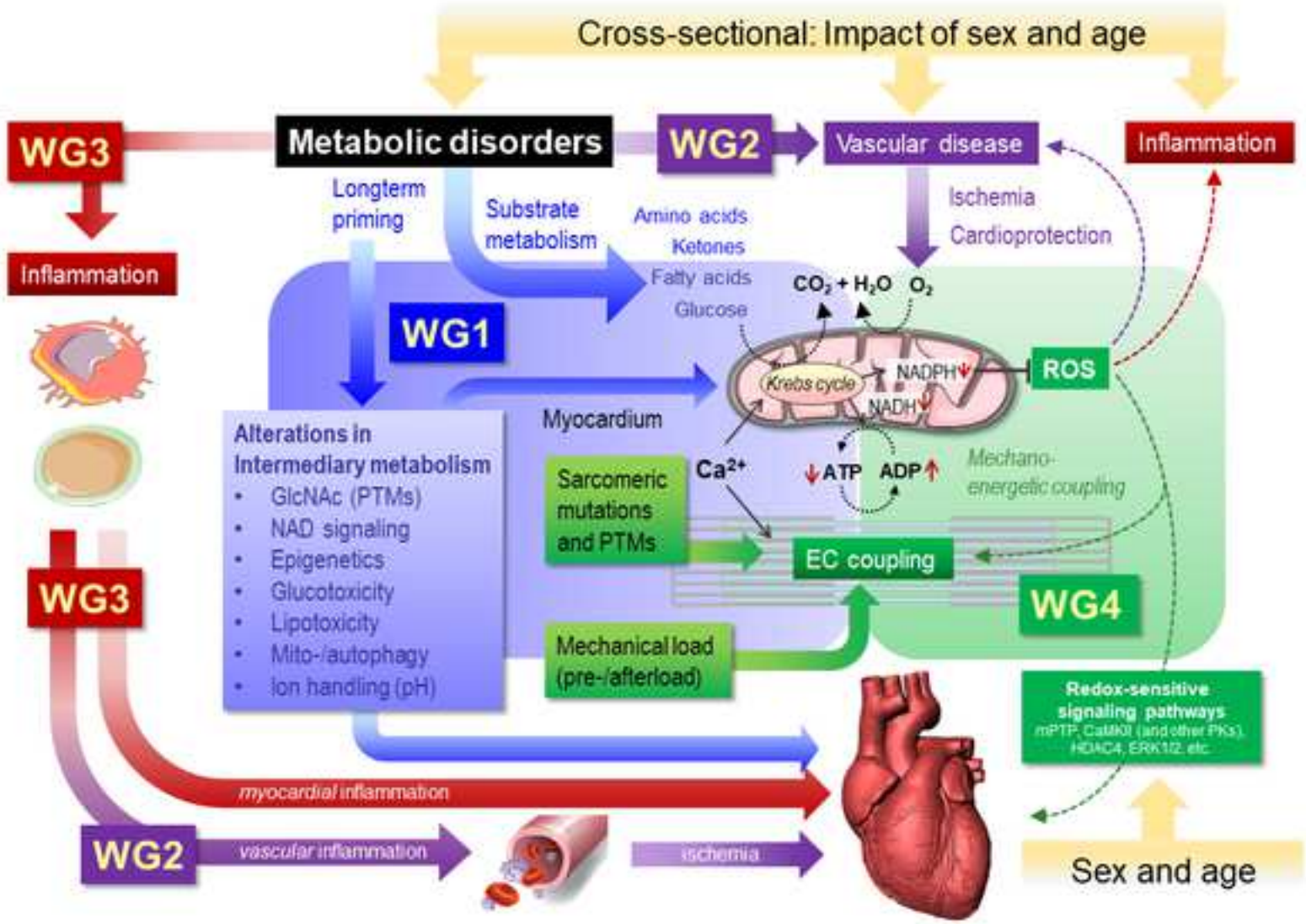

Figure 2

Click here to access/download;Figure;Figure 2 Group photo.JPG

Supplementary Information

List of members of the Management Committee of COST Action EU-METAHEART (CA22169)

First Name	Last Name	Affiliation	Country
Gohar	**Tsakanova**	Institute of Molecular Biology NAS RA	Armenia (AM)
Erich	**Gnaiger**	OROBOROS INSTRUMENTS GmbH, Graz	Austria (AT)
Simon	**Sedej**	Medizinische Universitat Graz	Austria (AT)
Luc	**Bertrand**	Université catholique de Louvain, Brussels	Belgium (BE)
Christophe	**Beauloye**	Université catholique de Louvain, Brussels	Belgium (BE)
Lana	**Nežić**	University of Banja Luka	Bosnia and Herzegovina (BA
Jelena	**Jovanic**	University clinical centre of Republic of Srpska, Banja Luka	Bosnia and Herzegovina (BA
Jasna	**Marinovic**	University of Split School of Medicine	Croatia (HR)
Marija	**Ljubojević**	Institute for Medical Research and Occupational Health, Zagreb	Croatia (HR)
Evelina	**Charidimou**	University of Nicosia - University of Cyprus	Cyprus (CY)
Eleftheria	**Galatou**	University of Nicosia - University of Cyprus	Cyprus (CY)
Frantisek	**Kolar**	Czech Academy of Sciences - Institute of Physiology, Prague	Czech Republic (CZ)
Hans Erik	**Botker**	Aarhus University	Denmark (DK)
Marie	**Schroeder**	Novo Holdings	Denmark (DK)
Marko	**Vendelin**	Tallinn University of Technology	Estonia (EE)
Florencia	**Cabrera Cabrera**	Tallinn University of Technology	Estonia (EE)
Olga	**Kofanova**	Luxembourg Institue of Health - Integrated Biobank of Luxembourg	European Commission and
Risto	**Kerkelä**	University of Oulu	Finland (FI)
Suvi	**Linna-Kuosmanen**	University of Eastern Finland, Joensuu, Kuopio	Finland (FI)
Ebba	**Brakenhielm**	INSERM - Inserm, Faculté de Médecine-Pharmacie de Rouen	France (FR)
Mathias	**Mericskay**	Universite Paris-saclay	France (FR)
Gerd	**Heusch**	University of Essen Medical School	Germany (DE)
Ioanna	**Andreadou**	National and Kapodistrian University of Athens	Greece (EL)
Antigone	**Lazou**	Aristotle University of Thessaloniki	Greece (EL)
Péter	**Ferdinandy**	Semmelweis University, Budapest	Hungary (HU)
Zoltan	**Papp**	Pharmahungary 2000 ltd - Pharmahungary 2000 kft	Hungary (HU)
Georgios	**Kararigas**	University of Iceland	Iceland (IS)
Roisin	**Kelly-Laubscher**	University College Cork	Ireland (IE)
Aamir	**Hameed**	Royal College of Surgeons in Ireland - RCSI University of Medicine and Health Sciences, Dublin	Ireland (IE)
Nina	**Kaludercic**	University of Padua	Italy (IT)
Alessandra	**Ghigo**	University of Torino	Italy (IT)
Maija	**Dambrova**	Latvian Institute of Organic Synthesis, Riga	Latvia (LV)
Reinis	**Vilskersts**	Latvian Institute of Organic Synthesis, RIga	Latvia (LV)
Vilmante	**Borutaite**	Lithuanian University of Health Sciences, Kaunas	Lithuania (LT)
Jelena	**Celutkiene**	Vilnius University	Lithuania (LT)
Joanna	**Vella**	UNIVERSITA TA MALTA	Malta (MT)
Emir	**Muzurovic**	Clinical Center of Montenegro	Montenegro (ME)
Coert	**Zuurbier**	university of amsterdam, academic medical center	Netherlands (NL)
Jolanda	**van der Velden**	Amsterdam UMC - Jolanda van der Velden	Netherlands (NL)
Marija	**Vavlukis**	Medical Faculty, University Ss' Cyril and Methodius in Skopje	North Macedonia (MK)
Hristo	**Pejkov**	Faculty of medicine, University Ss Cyril and Methodius, Skopje, North Macedonia	North Macedonia (MK)
neoma	**boardman**	UiT-Arctic University of Norway, Tromso	Norway (NO)
Ida Gjervold	**Lunde**	Oslo University Hospital	Norway (NO)
STEFAN	**CHLOPICKI**	Jagiellonian University, Krakow	Poland (PL)
Ewa A.	**Jankowska**	Wrocław Medical University	Poland (PL)
Henrique	**Girão**	Faculty of Medicine University of Coimbra	Portugal (PT)
Inês	**Falcao-Pires**	Faculdade de Medicina da Universidade do Porto	Portugal (PT)
Daniela Mirela	**Muntean**	"Victor Babes" University of Medicine and Pharmacy of Timisoara	Romania (RO)
Alina	**Scridon**	universitatea De Medicina, Farmacie, Stiinte Si Tehnologie "george Emil Palade" Din Targu Mures	Romania (RO)
DRAGAN	**DJURIC**	Faculty of Medicine, University of Belgrade - Institute of Medical Physiology, Faculty of Medicine	Serbia (RS)
VLADIMIR	**JAKOVLJEVIC**	Faculty of Medical Sciences, University of Kragujevac	Serbia (RS)
Tanya	**Ravingerova**	Slovak Academy of Sciences - Institute for Heart Research, Bratislava	Slovakia (SK)
Monika	**Bartekova**	Institute for Heart Research, Centre of Experimental Medicine, Slovak Academy of Sciences, Bratislava	Slovakia (SK)
Manuel	**Ruiz-Meana**	Vall d'Hebron University Hospital, Autonomous University of Barcelona - Vall d'Hebron Institut de Recerca (VHIR)	Spain (ES)
Gemma	**Vilahur**	Research Institute - Hospital de la Santa Creu i Sant Pau, IIB-Sant Pau	Spain (ES)
Sara	**Liin**	Linköping University	Sweden (SE)
Brenda	**Kwak**	University of Geneva	Switzerland (CH)
Sarah	**Longnus**	Inselspital, Bern University Hospital and University of Bern	Switzerland (CH)
BELMA	**TURAN**	Faculty of Medicine Department of Biophysics, Ankara University	Türkiye (TR)
Saime	**Batirel**	Marmara University, Faculty of Medicine, Department of Medical Biochemistry - Marmara University, Faculty of Medicine	Türkiye (TR)
Oleksii	**Korzh**	Kharkiv National Medical University	Ukraine (UA)
Derek	**Hausenloy**	University College London	United Kingdom (UK)
Dunja	**Aksentijevic**	Queen Mary University of London	United Kingdom (UK)

New COST Action “EUropean network to tackle METAbolic alterations in HEART failure” (EU-METAHEART)

Christoph Maack, Gemma Vilahur, Marisol Ruiz-Meana, Derek Hausenloy

The authors do hereby declare that all illustrations and figures in the manuscript are original and not require reprint permission.

European Heart Journal

Declarations Form

Instructions

1. The Journal requires the submitting author to provide a completed declarations form with each submission.

2. Refer to the table below to identify the minimum declarations required for your article type.

Article type	Disclosure of Interest	Data Availability Statement	Funding Statement	Ethical Approval Statement	Pre-registered Clinical Trial Number
Clinical Research Fast Track Meta-analysis Rapid Communications Translational Research					
CardioPulse Discussion Forum Editorial Great Debate Issue @ a Glance Viewpoint Weekly Journal Scan			See note*		
Special Article State of the Art Review					
Cardiovascular Flashlight			See note*		

*A funding statement is not required, but if you have funding to declare you should include this section in your declaration.

3. Enter or select your declarations under the headings on page 2 of this form.

4. Delete any text on page 2 that does not apply to your manuscript. For example, if you do not need to provide a data availability statement, you should delete the heading and text for this section on page 2. **After this step, Page 2 should only contain the headings and wording applicable to your article. Any text included on Page 2 will be typeset with your manuscript.**

5. Upload page 2 of the form only to Editorial Manager under the heading 'Declarations' when you submit your manuscript.

6. If you have any questions, please email ehj@unicatt.it.

Useful links for authors submitting to *European Heart Journal*

- EHJ Instructions to authors
- Guidance on data availability statements
- Guidance on disclosure of interest
- Guidance on funding

Declarations

Disclosure of interest

Christoph Maack received honoraria for presentations or consultancy from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Edwards, Novo Nordisk, Novartis, Pharmacosmos and Servier.

Derek Hausenloy has received consultant fees from Faraday Pharmaceuticals Inc. and Boehringer Ingelheim International GmbH, honoraria from Servier, and research funding from AstraZeneca, Merck Sharp & Dohme Corp and Novo Nordisk.

Gemma Vilahur has received research funding from Astra Zeneca and honoraria from Astra Zeneca and Ferrer.

Marisol Ruiz-Meana: None

Data availability

No data were generated or analysed for or in support of this paper.

Funding

Funding for this consortium is received from COST for COST Action EU-METAHEART (CA22169).

Pre-registered clinical trial number

Not applicable.