2023 Annual Report

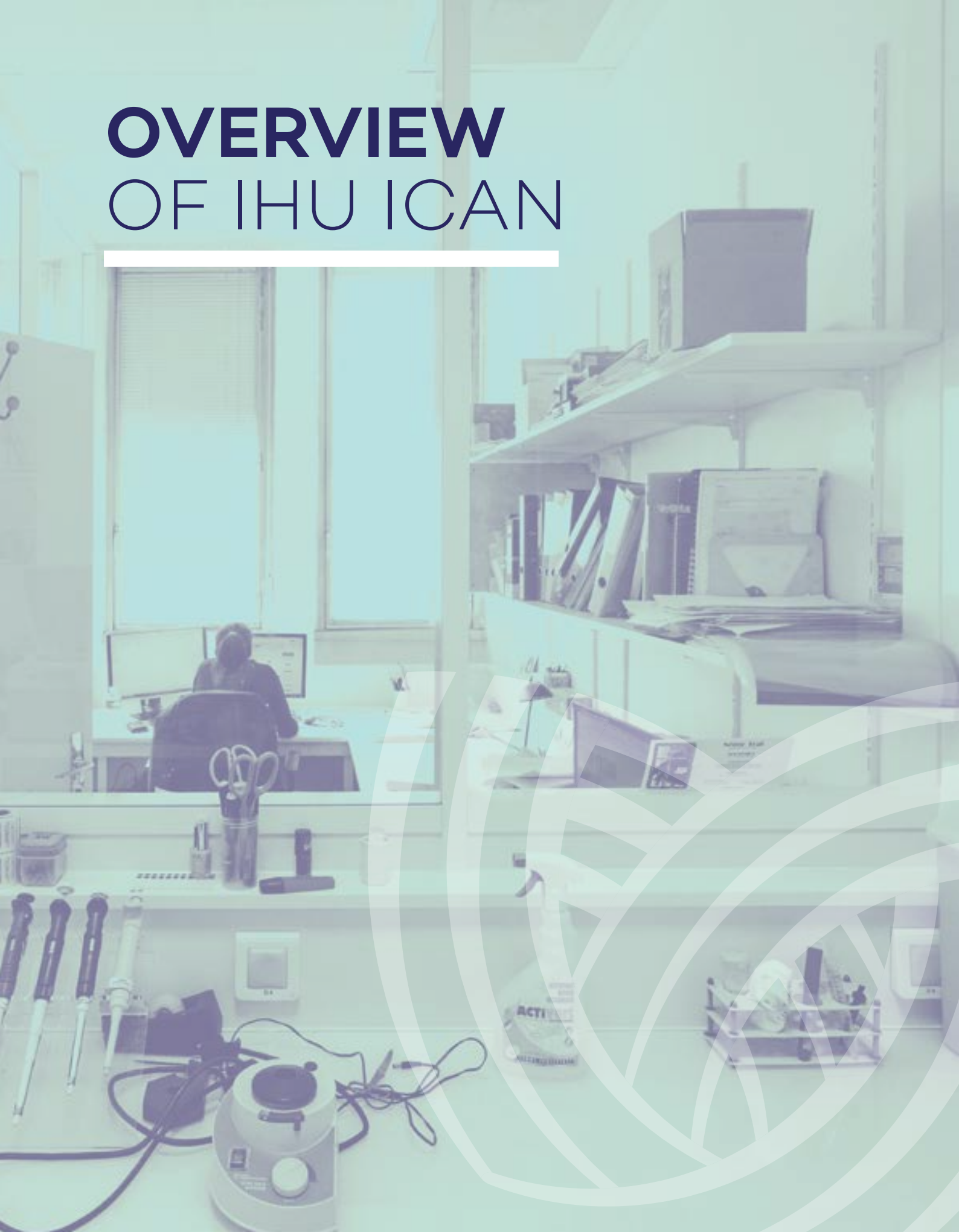
At the heart of health

IHU ican

Foundation for Innovation in Cardiometabolism and Nutrition

CONTENTS

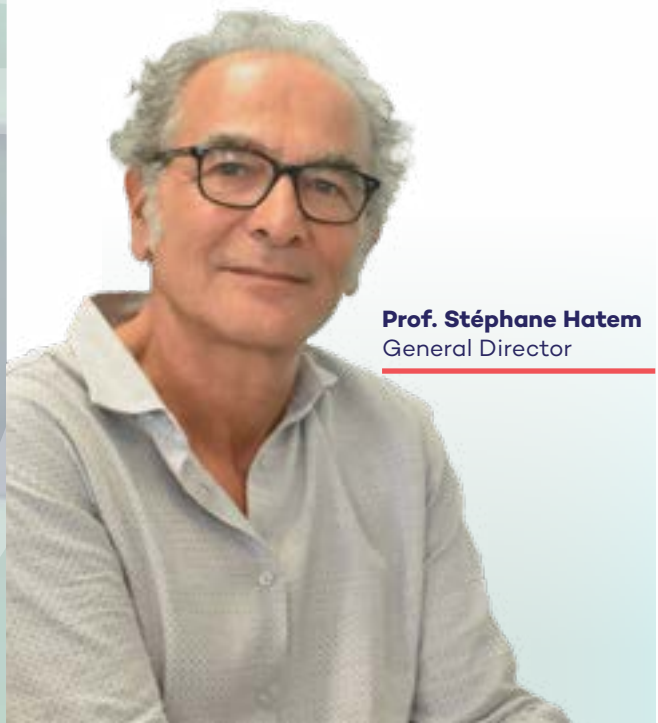
OVERVIEW
OF IHU ICAN



Editorial

Cardiometabolism is emerging as a new disciplinary field in medicine. Its definition, until recently limited to entanglements between diabetes, obesity, dyslipidaemia and atherosclerosis of the large arteries (atheromatous plaque, arterial stiffness), has been extended to include cardiac arrhythmias and heart failure.

There are several reasons why it is now viewed in this broader sense. The most notable of these is that drugs initially developed for diabetes or obesity, such as glucose transporter inhibitors and glucagon-like-peptide receptor agonists, have proven very effective for treating heart failure, and have therefore suddenly become part of cardiologists' therapeutic arsenal.
This has led learned cardiology societies to strongly recommended the use of SGLT2s in the treatment of heart failure.



Prof. Stéphane Hatem
General Director

In parallel to this, intense crosstalk has been discovered between organs involved in cardiometabolic diseases, with the microbiota, adipose tissue and liver – a genuine metabolic hub – all brought into play. Of course, there have also been biological advances within the fields of immunity, inflammation, genomics and epigenomics, which feed the research on cardiometabolic diseases.

There is now a sense, as there was in 2011 leading to the creation of IHU ICAN, that research needs to be scaled up and take a multidisciplinary approach based on a seamless exchange between basic and clinical research. Access to annotated, standardised, interoperable medical data that can be used by AI-generated algorithms represents a further key challenge.

> *"Intense crosstalk has been discovered between organs."*

Cardiometabolic diseases provide a paradigm for chronic diseases linked to interactions between the genome and environment, since these diseases last a lifetime, with onset potentially occurring very early, even in the foetal stage in the case of

so-called parental imprinting disorders. They progress unobtrusively over long periods. Even once they have taken hold, the only signs are risk factors such as high cholesterol, blood pressure and blood sugar. The boundary between preventive and curative medicine must be removed to prompt the emergence of personalised, precision medicine. New care pathways are needed in which patients are treated holistically under the leadership of healthcare staff trained to practise medicine in a way that combines elements of the major pathophysiological fields and incorporates social, economic and environmental factors. Several US universities have started cardiometabolic courses, unmistakable proof that this is the way forward.

An IFOP survey commissioned by IHU ICAN on a representative sample of the French population revealed the paradox that many people are unaware of the severity, health impact, prevention and even existence of these diseases that nevertheless affect us all and are rooted in our lifestyles and personal stories. The IFOP survey tells us that these diseases should not merely be viewed as a matter for the academic and medical sector, but as a cause and a fight involving all citizens.

“IHU ICAN now enjoys global recognition.”

In recent years, IHU ICAN has focused all its efforts on bringing about this profound change in the approach taken on cardiometabolic diseases. IHU ICAN has become a key stakeholder on cardiometabolic diseases and is strongly positioned within the French biomedical research ecosystem, thanks to its researchers' and clinicians' discoveries, the expertise its teams have developed, and the major research projects it has initiated. In short, IHU ICAN now enjoys global recognition in the fields of metabolic liver dysfunction, adipose tissue and cardiovascular diseases, and the genomics of cardiometabolic diseases (type 2 diabetes, obesity, fatty liver disease or metabolic steatosis, dyslipidaemia, coronary heart disease, arterial hypertension, metabolic syndrome and heart failure). It also built unique cohorts of patients with common or rare forms of cardiometabolic diseases including data with significant value for research (biological and imaging data, etc.). Moreover, the institute offers expertise on cardiovascular imaging, omics and AI-assisted data analysis. Finally, IHU ICAN’s community of scientists and healthcare staff coordinate its diligent communications aimed at educating and informing a wide audience about these diseases.

We hope you enjoy reading our 2023 annual report.

“These outstanding results demonstrate the value of the unique model of a cross-cutting IHU gradually developed by IHU ICAN.”

In 2023, IHU ICAN continued to step up its activity, winning around 20 competitive calls for proposals, including 5 European projects, with the support of its teams. **Over €10 M of multiannual funding was secured in relation to these projects in 2023, consolidating IHU ICAN's long-term position as a leading national and international stakeholder on cardiometabolic diseases,** a research field that is also experiencing significant growth.

These outstanding results demonstrate the value of the unique model of a cross-cutting IHU gradually developed by IHU ICAN with 1 cutting-edge research platforms and 2 expert data sourced from cardiometabolic patient cohorts 3.

1 ICAN's primary role is to bring together a community drawn from 5 research units (UMRs) and 13 clinical services and departments that includes almost 400 researchers and clinicians from a variety of disciplines. IHU ICAN's intention is not to encompass all the research activities of this multidisciplinary community, but to serve as a catalyst creating conditions in which funding can be secured and collaborative projects can be implemented to meet the challenges raised by cardiometabolic diseases. ICAN is an agile organisation with foundation status that encourages dialogue between disciplines, a strategy that has proven essential for taking action at multi-organ level, a key aspect of treating these diseases.

2 IHU ICAN has spent over 10 years creating an infrastructure of research and clinical investigation platforms and honing them to meet new challenges raised by cardiometabolic research. As part of this work, ICAN has developed: advanced phenotyping platforms for lipidomics and metabolomics offering expert analysis of biological samples taken from patient cohorts with these diseases; iPS and liver tissue cellular platforms with unique expertise in this field; a biological resources centre, and more recently, a data sciences platform strongly integrated with Sorbonne University's artificial intelligence research ecosystem. Alongside this, the clinical investigation platforms offer the capacity to conduct around sixty clinical studies per year, over half of which are commercial studies and 25% are external academic studies, proving ICAN's major appeal within the international competitive field of clinical research.

Stéphane Barritault
General Secretary

Moreover, ICAN acquired a 1,5T MRI designed for cardiometabolic imaging in 2020, a research equipment that is unique within Greater Paris.

3 Finally, **IHU ICAN was forward-looking on the growing importance of health data secondary use,** creating several cohorts of patients with cardiometabolic diseases over the past years. As a result of IHU ICAN teams' specialised, expert approach to these diseases, **it has been possible to develop medical databases linked to very high-quality biological samples, incorporating innovative biomarkers from omics and multimodal imaging analysis** (MRI, ultrasound, CT), whose secondary reuse for research purposes is facilitated by anticipating regulatory requirements. These structured databases with deep phenotyping allow teams of researchers to use AI-based technologies that offer new opportunities in terms of patient care.

The research resources that IHU ICAN develops and supports in pursuit of its scientific programme are also backed up by a structured and transparent system of governance forged in close collaboration with its founders (Assistance Publique - Hôpitaux de Paris (AP-HP), Inserm and Sorbonne University), which is now covered by a ISO 9001 quality certification. This has proved instrumental in gaining the trust of patients, sponsors, doctors, researchers, and academic or industry partners, who are all working together to revolutionise the treatment of cardiometabolic diseases.

These pillars supporting the IHU ICAN model, as well as its **outstanding community of hospital and academic researchers**, are key factors in the successes achieved in recent years and major scientific discoveries within the discipline to which ICAN has contributed.

One of 6 first-wave IHUs set up in 2011 under the Investment for the Future Programme (PIA), **IHU ICAN can therefore look ahead confidently to the renewal of its IHU label for the 2025-2030 period.**

KEY FIGURES 2023

€8.5 million budget

61 employees

BASIC AND APPLIED RESEARCH

221 researchers

6 cutting-edge technological platforms

11 research teams

599 scientific publications

including 157 with an impact factor >10

31 patents in the portfolio

Over **€10** million raised through competitive grants

CLINICAL CARE AND RESEARCH

60 clinical studies ongoing

of which **34 are commercial** and **26 are academic**

- 16 hepatology studies
- 14 rhythmology studies
- 9 endocrinology/diabetes studies
- 11 cardiology studies
- 7 nutrition studies
- 3 other studies

1 clinical research division with

- 1 clinical investigation platform specialising in cardiometabolism and nutrition
- 1 cardiometabolic imaging platform (MRI and Core Lab)

168 doctors

13 clinical services

6 reference centres for rare diseases

A 12-year contribution to clinical research

With its roots in a groundbreaking vision, IHU ICAN has spent over 12 years since it was set up developing an interdisciplinary approach and forging synergies between basic and clinical research for the direct benefit of patients. **It has played a key role in our understanding of cardiometabolic diseases (CMDs) and the development of innovative therapeutic approaches for CMDs.**

Through active academic clinical research and industry-sponsored research, IHU ICAN has played a trailblazing role in elucidating the mechanisms involved in how newly discovered interfaces, such as the microbiota, adipose tissue and liver, work in the CMD development process. IHU ICAN has also been at the forefront of understanding interactions between metabolic diseases such as diabetes, obesity, metabolic dysfunction-associated steatohepatitis (MASH), dyslipidaemia and cardiovascular diseases, which has led to improvements in patient care and is now paving the way for novel, more personalised therapeutic approaches. These take account of both genetic and environmental factors, such as diet, exercise and living environment, when determining the care offered to individual patients so that they are given optimal treatment.

METACARDIS, one of this period's most noteworthy studies, focuses on the relationship between the gut microbiota and metabolic diseases, in particular obesity and cardiovascular diseases. This study, in

"IHU ICAN has been at the forefront of understanding interactions between metabolic diseases."

which 798 patients are enrolled in France (2,250 patients across Europe), has revealed how the gut microbiota affects the development of metabolic diseases and patients' response to treatment, thus providing some promising avenues for developing new drugs to treat CMDs and implement prevention strategies.

The EpOS-LT study, investigating **metabolic liver disease progression**, is another example of a large-scale clinical study conducted in the past 12 years. This single-centre cohort forms part of the largest histologically characterised international cohort of metabolic dysfunction-associated steatohepatitis (fatty liver disease) patients with longitudinal follow-up, and includes 664 patients (482 of the 6,986 patients on the LITMUS1a registry, 182 of the 2,526 patients on the LITMUS1b registry, and 30 of the 511 patients enrolled in the ancillary imaging study). Drawing on industry partnerships, it has led to the validation of biomarker candidates, some of which are now commercialised, such as NIS2+TM.

IHU ICAN has also garnered acclaim in the field of cardiovascular disease research for its emphasis of early diagnosis and treatment of disorders such as atherosclerosis and congenital heart disorders. **IHU ICAN researchers have combined clinical and translational approaches to help identify novel biomarkers, improve cardiometabolic imaging techniques, and develop innovative therapies**. All this progress opens up new avenues for devising innovative prevention strategies and developing tomorrow's medicine to improve the treatment of cardiometabolic diseases.

Since 2011...

188

clinical studies of which
107 commercial studies
81 academic studies

6,544

patients enrolled in studies

50

studies of phase III drugs

31

studies of phase IIa or IIb drugs

Over
42,000

patients included in cohorts

The IHU's ecosystem

RESEARCH UNITS

UMR 938 : Adipocyte, Lipodystrophy, Diabetes and Glucocorticoid

UMR 1138 : Metabolic Diseases, Diabetes and co-morbidities

UMR 1146 : Cardiovascular imaging and Artificial intelligence

UMR 1166 : Cardiomyopathy, Atherothrombosis, Cardiac arrhythmias and Lipid transportation Microbiota

UMR 1269 : Nutrition, Microbiota, Adipose tissue and Data Integration

CLINICAL TEAMS

DMU ARCHIMEDE (Medical-University Department)

Pitié Salpêtrière Hospital Group

- Cardiology Department
- Cardiovascular and thoracic surgery department
- Department of intensive care medicine
- Endocrinology department
- Diabetes department
- Endocrinology and reproductive medicine department
- Endocrinology, metabolism and cardiovascular disease prevention department
- Unit for thyroid disorders and endocrine tumours
- Internal medicine department
- Nutrition department

Saint-Antoine Hospital Group

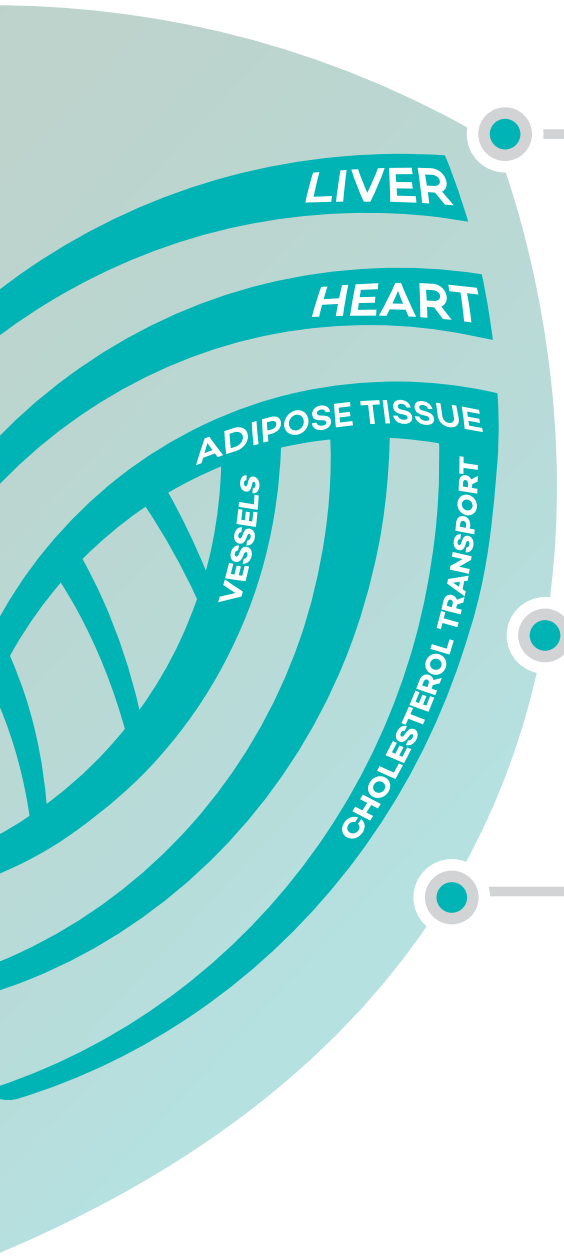
- Cardiology department
- Endocrinology, diabetes and reproductive medicine department

CARDIOVASCULAR AND THORACIC IMAGING UNIT (DIAMENT DMU)

REFERENCE CENTRES FOR RARE DISEASES

- Prader-Willi syndrome and other rare obesities - PRADORT
- Hereditary or rare cardiac diseases
- Rare insulin-secretion and insulin-sensitivity diseases
- Inflammatory diseases of the biliary tract and autoimmune hepatitis
- Rare endocrine diseases of growth and development
- Rare gynaecological diseases

IHU ICAN brings together a multidisciplinary community of basic and clinical research experts united in pursuit of a common goal: tackling cardiometabolic diseases.



6 CUTTING-EDGE SCIENTIFIC PLATFORMS

- **ICAN Omics** – Lipidomics
- **ICAN Omics** – Metabolomics
- **ICAN BioCollection** – Biobanking
- **ICAN BioCell** – iPS
- **ICAN BioCell** – Human Liver Biology
- **ICAN I/O** – Data Sciences

2 CLINICAL RESEARCH PLATFORMS

- **ICAN Clinical Investigation** – Cardiometabolic Diseases
- **ICAN Imaging** – MRI - Core Lab

- Innovation and Research Valorisation Division
- Legal, Compliance and Data Policy Division
- Administration, HR and Finance Division
- Communication and Sponsorship Division

CARDIOMETABOLISM AND NUTRITION FOUNDATION

IHU ICAN Foundation teams

Research and clinical teams

Research teams

Research Unit 1166 for Cardiovascular and Metabolic Diseases

Led by **Prof. Stéphane Hatem** and divided into 5 teams.

Team 1 - Genomics and Pathophysiology of Myocardial Diseases
Prof. Philippe Charron

Team 2 - Atherothrombosis and Applied Pharmacology
Dr Michel Zeitouni

Team 3 - Molecular and Cellular Plasticity in Cardiovascular Diseases
Sophie Nadaud and Elise Balse

Team 4 - Cellular and Systemic Lipid Metabolism in Cardiometabolic Diseases
Wilfried Le Goff

Team 5 - Mononuclear Phagocytes in Cardiometabolic Diseases
Philippe Lesnik

UMR 1146 - Biomedical Imaging Laboratory (LIB) CNRS - INSERM

Team - Cardiovascular Imaging
Nadjia Kachénoura

UMR 938 - Saint-Antoine Research Centre

3 of the 13 teams in this unit are part of IHU ICAN

Team 9 - Lipodystrophies, Metabolic and Hormonal Adaptations, and Ageing
Prof. Bruno Fève

Team 11 - Metabolic Fibro-inflammatory and Liver Bile Diseases
Jérémie Gautheron

Team 12 - IGF System, Foetal and Post-natal Growth
Prof. Irène Netchine

UMR 1138 - Cordeliers Research Centre

Metabolic Diseases, Diabetes and Co-morbidities team
Fabienne Foufelle

UMR 1269: Nutrition and Obesity: Systemic Approaches (Nutriomics)

Prof. Karine Clément

“The cardiovascular imaging team within the Biomedical Imaging Laboratory (LIB) includes researchers and doctors who produce innovative research combining cardiac and vascular image processing, artificial intelligence, and mathematical and haemodynamic modelling with in-depth knowledge of pathophysiological pathways. This cutting-edge research is extremely useful for ICAN projects involving imaging, as it provides bespoke tools that can be used to focus on key targets in various permutations of cardiovascular and cardiometabolic diseases. Our research also provides fertile ground for ICAN's medical and laboratory community, as it helps them formulate new hypotheses underpinning innovative research.”

Nadjia Kachénoura
Head of the Biomedical Imaging Laboratory (LIB) CNRS - INSERM Research Director

Early-career researcher profiles

Nadine Suffee

TEAM

UMR 1166 Team 3, Molecular and Cellular Plasticity in Cardiovascular Diseases

EDUCATION

Dr Nadine Suffee is a researcher specialising in the mechanisms of atrial cardiomyopathy development, with a focus on the role of progenitor cells, immune response and remodelling of epicardial adipose-fibrous tissue. Having graduated from Sorbonne Paris Nord with a degree in cell biology and experimental therapies, she went on to study neovascularisation induced by endothelial precursors modulated by biodegradable biomaterials. Her postdoctoral research on induced stem cells at the University of Saint-Etienne focused on corneal endothelium regeneration. At Sorbonne University, she explored the cellular and molecular mechanisms of atrial fibrillation, a common form of cardiac arrhythmia.

She subsequently specialised in macrophage-induced inflammatory response in atherosclerosis at PARCC/University of Cambridge, and is currently investigating the role of macrophages and epicardial precursors in atrial cardiomyopathy (ACM) in UMRS 1166/ICAN.

“Success is to be measured not so much by the position reached in life as by the obstacles overcome.”

Booker T. Washington

KEY PUBLICATIONS SEE PAGE 78

RESEARCH PROJECT

Atrial cardiomyopathy causes cardiac rhythm disorders such as atrial fibrillation (AF) and results in electrical and tissue remodelling of the atrium due to hypertension, valvular heart disease, cardiopathies and obesity. Epicardial adipose tissue (EAT) is a key factor in ACM. When it dysfunctions, due partly to obesity, adipo-fibrokines are secreted, causing fibrosis and electrical disturbances. Macrophages and epicardial progenitor cells (EPCs) play a key role in this remodelling, although understanding of this process remains limited. Her research project explores links between metabolism, immunoinflammatory response and adipo-fibrous remodelling in the atrial epicardium, with a focus on the role of macrophages, their deterioration in the event of obesity, and the impact of inflammation on EPCs. Her aim is to map the cellular actors of ACM linked to obesity and understand how they interact with myocardial remodelling and metabolic abnormalities.

AWARDS/DISTINCTIONS

2023 — **Best Poster Award**, ESC Working Group CBH&MF, Italy.

2023 — **Alain Castaigne Award**, French Society of Cardiology, France.

2020 — **Lefoulon-Delalande Foundation**, Postdoctoral Fellowship, PARCC France.

2012 — **Best Young Researcher Oral Award**, French Society of Cardiology, France.

2008 — **French Ministry of Research Grant,** Faculty of Science and Medicine, Sorbonne Paris Nord France.

SCAN FOR A FULL CAREER DESCRIPTION

Louis Parker

TEAM

UMR 1146 Louis Parker, Postdoctoral Fellow
Cardiovascular Imaging (iCV), Biomedical Imaging Laboratory (LIB)

EDUCATION

Louis Parker studied mechanical engineering at the University of Western Australia, where he developed an interest in biomechanics during his master's project at the VascLab. He applied digital fluid mechanics to blood flow analysis in aortic and iliac artery aneurysms. Fascinated by the diverse range of challenges relating to these research topics, he undertook a doctorate in aortic dissection before working as a postdoctoral fellow at KTH in Stockholm, collaborating with the extracorporeal resuscitation team at Karolinska University Hospital. The team he worked in used computational fluid dynamics (CFD) to optimise ECMO treatment, which proved crucial during the COVID-19 pandemic. This led Louis to realise the importance of imaging, particularly 4D MRI, in creating accurate models, prompting him to apply for a Marie Skłodowska-Curie postdoctoral fellowship at the Biomedical Imaging Laboratory (LIB) with Dr Nadjia Kachénoura.

"I'm excited to be in an interdisciplinary environment with cutting-edge systems and genuine imaging expertise. I'm looking forward to making my contribution, particularly in fluid mechanics!"

Louis Parker

RESEARCH PROJECT

The 'HiDDyn-AF' project combines computational fluid dynamics, 4D flow MRI, late gadolinium enhancement MRI and computerised tomography to create a new flow model for the left atrium (LA). This model will be used to study patients with atrial fibrillation (AF) before and after ablation with a view to developing personalised risk stratification and discovering new information on the pathophysiology of AF. In a departure from previous approaches, this project uses 4D flow MRI to develop a dynamic model of left atrial flow. Simulations will be performed on the Sorbonne University supercomputer (MeSU) using patient data (N=50) to determine the haemodynamics of the left atrium during atrial fibrillation and assess the impact of ablation. Researchers will also explore relationships between the haemodynamics of the left atrium, myocardial deformation and fibrosis.

AWARDS/DISTINCTIONS

2024 — **Marie Skłodowska-Curie Fellowship**
European Commission.

2023 — **Postdoctoral grant**
2020 for biomedical engineering.

2018 — **Mimics innovation award**.

2016 — **William and Marlene Schrader Scholarship**
for biomedical engineering.

KEY PUBLICATIONS
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SCAN FOR A FULL CAREER DESCRIPTION

Carine Beaupère

TEAM

UMR 938, PhD - Lipodystrophies, Metabolic and Hormonal Adaptations, and Ageing team,
Prof. Bruno Fève

EDUCATION

After graduating from Pierre and Marie Curie University, Carine Beaupère specialised in ageing at master's level. The topic of her PhD at the Saint Antoine Research Centre (CRSA), supervised by Jacqueline Capeau and Claire Lagathu, was bone ageing in patients with HIV. Following 4 years of postdoctoral research in Boston on lifespan regulation in a yeast model with multi-omics approaches, she joined Bruno Fève's team at the CRSA to take up a second postdoctoral research position.
In 2023, Carine was recruited as a researcher at Inserm. Her work is focused on metabolic ageing and strategies to delay this with a view to preventing various diseases. She is genuinely passionate about this research which offers both the freedom to explore her topic and a collaborative environment, something she considers particularly stimulating.

“The glucocorticoid receptor, particularly in adipocytes, is a therapeutic target with great potential for preventing age-related cardiometabolic disorders and promoting healthy ageing!”

RESEARCH PROJECT

Carine Beaupère specialises in metabolic ageing, particularly in response to glucocorticoids such as cortisol in humans. Glucocorticoids are steroid hormones that regulate the metabolism and inflammation. However, ageing leads to deregulated metabolic and pro-inflammatory responses that cause disorders such as diabetes, cardiovascular diseases, lipodystrophy and bone demineralisation. Endogenous glucocorticoid production changes with age, and overexposure to glucocorticoids increases the risk of ageing-associated metabolic diseases. Her project seeks to shed light on the impact of glucocorticoids on ageing, insulin sensitivity and cellular senescence, with a particular focus on the adipocyte glucocorticoid receptor as a means of preventing age-related cardiometabolic disorders and extending healthy life expectancy. Alongside this work, she is also investigating how ageing affects sensitivity to glucocorticoids, a key factor in treatment adjustment for patients aged over 65 receiving glucocorticoids with anti-inflammatory and immunosuppressive properties.

AWARDS/DISTINCTIONS

2022 — **Research grant from the Société Francophone du Diabète/ Lilly.**

2020 — **Research grant from the association Aide aux Jeunes Diabétiques.**

KEY PUBLICATIONS
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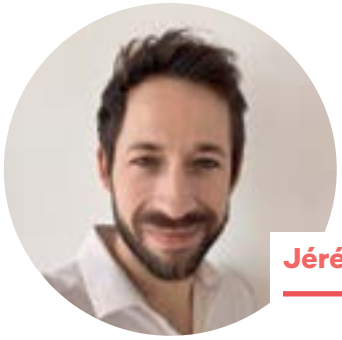
SCAN FOR A FULL CAREER DESCRIPTION

To improve is to change; to be perfect is to change often.

Winston Churchill



Jérémie Gautheron

TEAM

Inserm normal-class researcher (CRCN) with accreditation to supervise research (HDR), Team leader at the Saint-Antoine Research Centre. UMR 938, Biliary and Fatty Liver Diseases

EDUCATION

After graduating with a degree in cellular and molecular biology from Picardie Jules Verne University, Jérémie Gautheron successfully completed a two-year master's programme at Pierre and Marie Curie University. In 2008, he embarked on a PhD at Paris Descartes University (Paris V) focusing on ubiquitination in the NF-kappaB pathway. On completing his doctorate, he took up a postdoctoral position in Germany investigating necroptosis in liver diseases, during which time his team's work challenged the role of apoptosis in MASLD.
After returning to France in 2017, Jérémie led a research group demonstrating the potential of necroptosis inhibitors in the treatment of steatohepatitis. These discoveries led to a patent application. He also initiated studies on liver-adipose tissue interactions in lipodystrophy syndromes, leading to publications in prestigious journals. In 2022, Jérémie Gautheron was appointed joint team leader and became full team leader in September 2023.

KEY PUBLICATIONS
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SCAN FOR A FULL CAREER DESCRIPTION

RESEARCH PROJECT

Chronic liver diseases have a significant socio-economic impact and are characterised by a destructive inflammatory process, leading to fibrosis, cirrhosis and, in some cases, liver cancer. Cell death triggers an inflammatory cascade in which damaging signals are released, activating non-parenchymal cells and thus promoting fibrogenesis.
Current research is exploring the cellular and molecular mechanisms involved, from hereditary molecular defects to cancer development. His team's research projects combine human studies, mouse models and cell biology to translate these discoveries into therapies, identifying new molecular targets to devise innovative treatments.

AWARDS/DISTINCTIONS

2023 — **Winner of the G. & J-L. Smadja Award**, Société Francophone du Diabète (SFD).

2018 — **Winner of the Émergences programme** run by the City of Paris.

2017 — **Winner of the grant programme for returning French nationals run by the FRM**.

2015 — 2017 **Best article award** RWTH Aachen University.

2008 — 2017 **French Higher Education Ministry grant.**

Éloïse Giabicani

TEAM

Endocrine Functional Exploration
Saint-Antoine Research Centre:
Pathophysiology of Foetal Growth:
IGF System and Parental Imprinting.
CRESCENDO Reference Centre for Rare Endocrine Diseases of Growth and Development
Operational Unit (UF) for Molecular Endocrinology and Imprinting Disorders

RESEARCH PROJECT

Her most recent work involves the development of cell models for rare foetal growth disorders of epigenetic origin. Her team's approach focuses on induced pluripotent stem cells as well as stem cells derived from dental pulp that are differentiated into cell types involved in patients' phenotype.
The intention is to first gain an understanding of the underlying pathophysiology involved in these diseases and then use this to improve treatment for these patients, while also anticipating its long-term impact in individuals born with foetal growth restriction, which affects around 7% of infants born in France.
These individuals are exposed to an elevated risk of metabolic complications in adulthood which have been described in detail yet remain poorly understood.

EDUCATION

Dr Eloïse Giabicani is a paediatric specialist with expertise in paediatric endocrinology and holds a 2nd year master's degree in endocrinology and metabolism. Her dissertation explored the pathophysiological role of diseases subject to parental imprinting in growth and the IGF system.
In her career, she has combined basic research and clinical practice, with a focus on foetal growth restriction. She is committed to translating findings from basic research into tangible solutions for her patients. In her role treating patients with rare growth abnormalities, she applies a translational approach to improve their care.

“Thanks to patients, we are able to learn, experiment and understand, and they also benefit from being involved in this journey.”

AWARDS/DISTINCTIONS

2023 — **Young Investigator Award from the European Society of Pediatric Endocrinology** (ESPE), The Hague.

KEY PUBLICATIONS

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SCAN FOR A FULL CAREER DESCRIPTION

Clinical teams

Clinical teams at the ARCHIMEDE Medical-University Department have access to IHU ICAN's expertise on technological platforms and project set-up, enabling them to develop complex, innovative research programmes. IHU ICAN's strategic position at the interface between basic and clinical research, and also academic and commercial research, encourages a multidisciplinary approach that is vital for accelerating medical breakthroughs. These breakthroughs will change the way cardiometabolic diseases are treated in future.

Prof. Richard Isnard Cardiologist and Medical Director of the ARCHIMEDE DMU (Medical-University Department)

ARCHIMEDE MEDICAL-UNIVERSITY DEPARTMENT (DMU)

Prof. Richard Isnard

The ARCHIMEDE DMU combines clinical departments and units involved in the treatment and care of acute and chronic cardiovascular and metabolic diseases, as well as certain rare conditions.

Pitié-Salpêtrière Hospital Group Institute of Cardiology

Prof. Gilles Montalescot
Cardiology department

Prof. Pascal Leprince
Cardiovascular and thoracic surgery department

Prof. Alain Combes
Department of intensive care medicine

Prof. Laurent Chiche
Vascular surgery department

E3M Institute

Prof. Agnès Hartmann
Diabetes department

Prof. Philippe Touraine
Endocrinology and reproductive medicine department

Dr Antonio Gallo
Endocrinology, metabolism and cardiovascular disease prevention unit

Prof. Laurence Leenhardt
Unit for thyroid disorders and endocrine tumours

Prof. Zahir Amoura
Internal medicine department

Prof. Jean-Michel Oppert
Nutrition department

Saint-Antoine Hospital Group

Prof. Ariel Cohen
Cardiology department

Prof. Sophie Christin-Maître
Endocrinology, diabetes and reproductive medicine department

ICT - CARDIOVASCULAR AND THORACIC IMAGING UNIT (DIAMENT DMU)

Prof. Alban Redheuil

The ICT is the cardio-radiology unit at Pitié Salpêtrière, specialising in cardiac, vascular and thoracic imaging. The team is involved in research through the ICAN Imaging Platform.

Governance

BOARD OF TRUSTEES

The board of trustees, consisting of 16 members, 6 founding members, 5 qualified persons, 3 private-sector representatives and 2 representatives elected by associate professors, sets the IHU's overall policy.

President of the Board of Trustees **Catherine Boileau**, University Professor/Hospital Practitioner, Head of the Genetics Department, Bichat Hospital (replaced by **Anne-Marie Armanteras** on 20 June 2024).

Founders' Representatives

Nathalie Drach-Temam,
President of Sorbonne University

Nicolas Revel,
General Director of Assistance Publique - Hôpitaux de Paris (AP-HP)

Didier Samuel,
President and General director of Inserm

Permanent Invitees

Elli Chatzopoulou,
Director of Partnerships and External Relations, Inserm

Milan Lazarevic,
Head of Clinical Research and Innovation, AP-HP

Bruno Riou,
Dean of the Faculty of Medicine, Sorbonne University

Qualified Persons

Catherine Boileau, University Professor/Hospital Practitioner, AP-HP

Claudine Canale,
President of the Poids Plumes association

Ehrlich Dusko Stanislav,
Director of Research, INRAE

Jessica Leygues, CEO of MEDICEN, Paris Region (replaced by Julien Ettersperger in June 2024)

Private Sector Representatives

Laurence Comte-Arassus,
GE Healthcare, Executive director, FBFA zone, Representative for SNITEM

Pierre Sonigo,
SEBIA, Director, R&D and Medical Affairs

Philip Janiak,
Chief Executive of Corteria Pharmaceuticals

Representatives of Researchers and Associate Professors

Bruno Fève, Head of Research Unit 938

Corinne Frère, Lecturer/Hospital Practitioner, Biological Haematology, AP-HP

IHU BOARD

The IHU Board is chaired by the IHU General director and also includes the General Secretary; the Dean of Sorbonne University Faculty of Medicine; the directors and team leaders of the UMRs involved in ICAN; and the Medical Director and department heads of the ARCHIMEDE Medical-University Department (DMU).

Its objective is to strengthen cohesion within the IHU's medical and scientific community and to allow a flow of information between the teams to ensure overall consistency. The IHU Board provides a forum for discussing and sharing strategic priorities and the IHU's scientific policy.

EXECUTIVE COMMITTEE (COMEX)

The COMEX consists of the General Director, the General Secretary, the heads of the IHU's internal divisions and one community representative per key strategic area. The Director of the Pitié-Salpêtrière Hospital Group and the Medical Director of the ARCHIMEDE DMU are permanent invitees. The COMEX is tasked with helping the General director, in particular, to define the IHU's strategy and scientific priorities, and also with all other aspects of management.

"IHU ICAN provides a means of promoting cross-disciplinary interaction within our community, while also directly supporting research by actively helping to set up projects and providing access to technical and scientific platforms that form the basis of our commercial and academic collaborations."

Prof. Philippe Charron
Cardiology and Vascular Diseases
Coordinator of the Reference Centre for Hereditary or Rare Heart Diseases

Prof. Judith Aron-Wisnewsky,
Endocrinology and Metabolism

Dr Olivier Bourron, Diabetes

Loïc Carbadillo,
Director of Research, AP-HP. Sorbonne University

Prof. Philippe Charron, *new member*
Cardiology and Vascular Diseases

Prof. Alain Combes, Intensive Care Medicine

Dr Laurie Dufour, *new member*
Cardiology and Vascular Diseases

Prof. Bruno Fève, Director of Research Unit 938 - Saint-Antoine Research Centre

Dr Antonio Gallo,
Cardiovascular Disease Prevention

Prof. Estelle Gandjbakhch,
Cardiology and Vascular Diseases

Prof. Richard Isnard,
Cardiology and Vascular Diseases

Wilfried Le Goff,
Head of the Cellular and Systemic Lipid Metabolism in Cardiometabolic Diseases team

Prof. Irène Netchine,
Physiology - Paediatric Functional Investigation

Prof. Vlad Ratziu,
Gastroenterology and Hepatology

Prof. Alban Redheuil, Cardiovascular Imaging

SCIENTIFIC ADVISORY BOARD

The scientific advisory board offers expert, critical and constructive opinion on ICAN's scientific strategy. It consists of 6 external members who are highly recognised within the international scientific community in the fields of cardiometabolism and nutrition. This scientific governance body, appointed by the Board of Trustees, is consulted on the IHU's key scientific priorities and annual action program. 2023 saw a number of changes to the Scientific Advisory Board.
Prof. Roden and Prof. Hoyles were replaced by Prof. Michel Komajda and Prof. David Savage.

Prof. André Carpentier

Prof. Carpentier holds the Canada Research Chair in Molecular Imaging of Diabetes and is a professor and endocrinologist-lipidologist in the Université de Sherbrooke Department of Medicine, part of its Faculty of Medicine and Health Sciences. In December 2020, he took up post as the Scientific Director of the Sherbrooke University Hospital (CHUS) Research Centre. He has also served as Head of the Cardiometabolic Health, Diabetes and Obesity Research Network (CMDO) in Quebec (2012-2021).

Between 2012 and 2021, he was the Co-Scientific Lead of Diabetes Action Canada. His main research interests are:
1. the role of postprandial fatty acid metabolism in the development of type 2 diabetes and cardiovascular diseases;
2. the investigation of brown adipose tissue metabolism in humans;
3. the anti-diabetic mechanisms of bariatric surgery.

Since 2007, Prof. Carpentier has published over 180 peer-reviewed papers. He has received numerous awards, including the Canadian Society of Endocrinology and Metabolism Young Diabetes Researcher Award in 2011, the CDA and CIHR Young Researcher Award in 2012, and the Canadian Lipoprotein Conference Physician-Scientist Lectureship in 2014. He was elected Fellow of the Canadian Academy of Health Sciences (FCAHS) in 2015.

Prof. Arnold von Eckardstein

Professor of Clinical Biochemistry, Laboratory Medicine and Pathology, University Centre for Laboratory Medicine and Pathology (UZL), Switzerland.
Arnold von Eckardstein studied medicine in Giessen and Kiel, before going on to specialise in laboratory medicine and clinical chemistry in Frankfurt and Münster (Germany). Since 2001, he has held posts as Professor in the University of Zürich Faculty of Medicine and Head of the Institute of Clinical Chemistry at Zürich University Hospital. His main research interests are risk factors and biomarkers for cardiovascular and metabolic diseases, and the structure, function and metabolism of high-density lipoproteins (HDLs) and sphingolipids. He has published over 450 original and review papers in peer-reviewed scientific journals (Scopus h-index: 91).

Arnold von Eckardstein is currently Editor-in-Chief of *Atherosclerosis* and an editorial board member for *Arteriosclerosis, Thrombosis and Vascular Biology*, *BBA Molecular and Cell Biology of Lipids*, *Cardiovascular Research* and the *European Heart Journal*.

He has previously served as Chairman of the European Lipoprotein Club, the Swiss and German Atherosclerosis Societies and the Swiss Society of Clinical Chemistry, and is a former Secretary of the European Atherosclerosis Society.

Prof. Michel Komajda
New member

Between 1990 and 2017, Michel Komajda held the post of cardiology professor at Paris Sorbonne University, where he is now an emeritus professor. He is also a former Head of the Cardiology Department at Pitié Salpêtrière Hospital (Paris) and the Cardiometabolic Division (2006-2014).

He has been a member of the French National Academy of Medicine since 2012, where he chairs the cardiovascular committee, and he also chairs the executive board of Fondation Cœur et Recherche, a charity that has been raising funds for cardiovascular research since 2014.

Prof. Michel Komajda's main research interests are the pharmacology of heart failure, neurohormones in heart failure, and the genetics of dilated and

"ICAN is an ambitious, forward-looking, international centre of excellence at the cutting edge of cardiometabolic research. Its work in this field is highly relevant, given the current rise in obesity, diabetes and cardiovascular diseases. The ICAN approach is unique in that it focuses on communication between organs. The Scientific Advisory Board was particularly pleased to note the depth and scope of ICAN's research, which draws on advanced technological platforms to collect and use a multitude of data, linking basic and clinical research to optimise the application of results. Early and mid-career scientists who attended the meeting emphasised that the future of the ICAN mission is bright."

Prof. Karine Sipido Chair of the Scientific Advisory Board

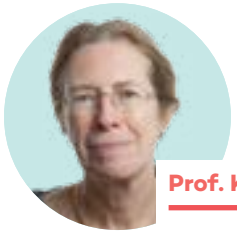
hypertrophic cardiomyopathy. He was the President of the European Society of Cardiology between 2010 and 2012. Furthermore, he co-chaired the *Euro Heart Failure Survey I* programme and was an executive committee member of the *Euro Heart Failure Survey II* programme.
He was also the President of the French Society of Cardiology between 2002 and 2003.

He is an editorial board member for the *European Heart Journal*, *European Journal of Heart Failure* and *Circulation*.

Michel Komajda is the author of over 500 peer-reviewed papers, mostly in the field of heart failure. He has worked with the steering committees, executive committees, adjudication committees and DSMBs of several international trials on heart failure and cardiovascular diseases (CARMEN, COMET, I-PRESERVE, HEAAL, RECORD, CORONA, SHIFT, PARADIGM HF, PARAGON, PARALLEL, RELAX AHF 2, PARADISE, COLCOT).

Prof. David Savage
New member

Professor David Savage is a clinician-scientist based at the University of Cambridge. He leads the national clinical service in England for patients with lipodystrophy and other syndromes associated with severe insulin resistance. His research is focused on understanding links between adipose tissue dysfunction and metabolic diseases. He is a world authority on lipodystrophy syndromes and has helped identify several monogenic forms of human lipodystrophy. His group applies cellular approaches, mouse models and detailed human physiological approaches to understand links between genetic variants and human metabolic diseases.



Prof. Karine Sipido

Chair of the SAB, Professor of Medicine and Head of Experimental Cardiology, University of Louvain, Belgium. Prof. Sipido conducts research on cardiac rhythm disorders and heart failure, identifying cellular and molecular mechanisms with translational potential. She is an expert in cellular electrophysiology and calcium imaging of cells and isolated tissues, using live cardiac myocytes and fibroblasts, isolated from animal models and human hearts.

Her functional studies draw on molecular studies of gene expression and regulation. She is an elected member of the Academia Europaea, European Society of Cardiology, American Heart Association and International Society for Heart Research.

She is actively involved in research policy and has held various posts at KU Leuven, both at European and international level. She is a former board member of the European Society of Cardiology and also led the Council on Basic Cardiovascular Science. She is a Founding Member and former President of the Biomedical Alliance in Europe.

Between 2015 and 2020, she chaired the European Commission's Scientific Panel for Health (SPH), a science-led expert group established under Horizon 2020. She is a member of the Scientific Advisory Board of ORE, the European Commission's open research platform.

Prof. Rozemarijn Vliegenthart

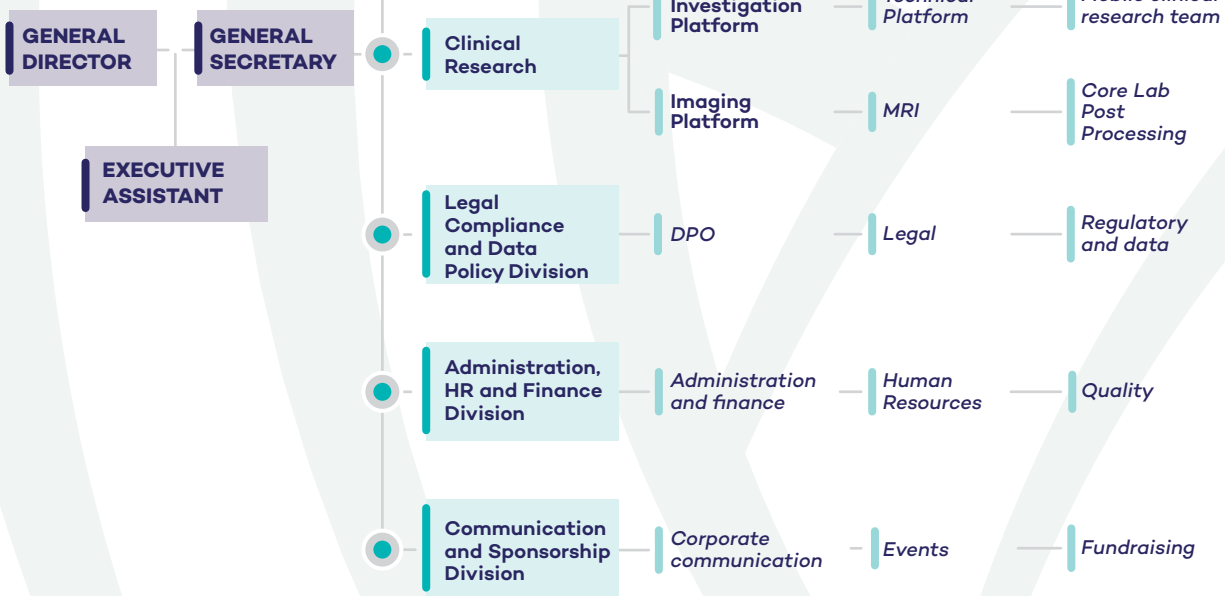
Radiologist and Professor of Cardiothoracic Imaging, University Medical Centre Groningen, Netherlands.
Her clinical and research interests are focused on the early detection of cardiopulmonary diseases, with a particular emphasis on imaging in cardiovascular diseases, lung cancer and COPD.

She has an interest in AI and works with the Data Science Center in Health (DASH) at UMCG as a cohort data expert. She is the PI for ImaLife, CONCRETE, NELSON-POP and B3Care. She has authored or co-authored 305 papers (h-index: 50) and is a Deputy Editor of the journal *Radiology*. She has been invited to give lectures at numerous international conferences, including the ECR and the RSNA and SCCT conferences. She is the current president of the European Society of Cardiovascular Radiology (ESCR)

SENIOR MANAGEMENT AND EXECUTIVE COMMITTEE

Prof. Stéphane Hatem has been IHU ICAN's general director since 2018. The general director oversees the general management of the IHU and is assisted by a general secretary, **Stéphane Barritault**, who is responsible for the operational management of the institute.

The general director and the general secretary are assisted by a steering committee with 6 members:
Stéphane Commans
Innovation and Research Valorisation Division
Maud Decraene
Legal, Compliance and Data Policy Division
Jeanne Haidar
Clinical Research Division
Ludovic Le Chat
Platforms and Business Development Division
Stéphanie Lapous
Administration, HR and Finance Division
Francine Trocmé
Communication and Sponsorship Division



HIGHLIGHTS

Big data and AI conference

On Friday 10 February 2023, IHU ICAN, the French Council of State, the French Data Protection Authority (CNIL) and the IHU France Alliance jointly organised a major conference on the use of data and artificial intelligence (AI) in the health sector.

This hybrid conference was attended remotely by 600 participants and in-person by approximately 100 people, including media representatives from 10 general national publications and specialist health and digital technology journals, who had come to watch discussions led by specialist speakers.

The event was opened by Didier-Roland Tabuteau (Vice-President of the French Council of State), **Marie-Laure Denis** (Chair of the CNIL) and **Prof. Stéphane Hatem** (General director of IHU ICAN) and consisted of 3 round-table discussions. Participants discussed issues regarding AI use in research and medical practice, the regulatory framework for health data, and the economic ecosystem for such data in France.

Renaud Vedel (Chief of Staff for **Jean-Noël Barrot**, Minister Delegate for Digital Transition and Telecommunications) and **Thierry Tuot** (Vice-President of the Council of State office for internal affairs) closed these discussions that yielded numerous proposals.

The intention is to continue the work initiated at this conference within the IHU France Alliance in order to develop a new model for using health data in research in France. In collaboration with the CNIL and with support from the Council of State and government, the IHU France Alliance will seek to create a new experimental space in which to identify solutions to the various economic, social and medical issues raised by the use of artificial intelligence and research data in the health sector. This will be done in a way that is fully transparent to the public, patients and press.

SCAN HERE FOR A CONFERENCE ROUND-UP AND REPLAY ON THE IHU ICAN WEBSITE

MoU signed with SEHA

IHU ICAN has signed a memorandum of understanding with SEHA (*Abu Dhabi Health Services*) to help tackle cardiometabolic diseases in the United Arab Emirates.

The incidence of cardiometabolic diseases has been constantly rising in recent decades, making them the world's leading cause of death and a major public health problem in the United Arab Emirates. SEHA and IHU ICAN are well aware of this issue, which prompted them to sign a memorandum of understanding on 6 November 2023 to develop innovative AI-based tools aimed at tackling these diseases.

This strategic collaboration between France and the United Arab Emirates is focused on two key projects: **a local arm of the MAESTRIA European project coordinated by Prof. Stéphane Hatem** aimed at early detection of atrial fibrillation, a major cause of death and disability, and an **advanced study of fatty liver disease, whose prevalence is rapidly increasing** and now affects a quarter of the world's population, with 30.2% of Emiratis expected to have the disease by 2030. The purpose of the collaboration is to improve prevention, diagnosis and medical care; stimulate the growth of a patient-focused high-tech medical ecosystem; and encourage local production of pharmaceutical and medical products.

It also seeks to include the United Arab Emirates in major European projects, thus promoting collaboration and progress in the field of cardiometabolic diseases.

Stéphane Hatem
General director of IHU ICAN

International cooperation on research development is vital if we are to improve prevention, diagnosis and treatments, and ensure that as many people as possible benefit. Given the prevalence of cardiometabolic diseases, the United Arab Emirates appreciates the importance of developing cutting-edge personalised medicine based on digital technologies and the expertise accumulated by IHU ICAN teams in this field. The collaboration between SEHA and IHU ICAN was therefore a natural step aimed at jointly developing innovative research projects to tackle cardiometabolic diseases and sharing the benefits of cutting-edge research conducted in France and Europe for the past several years with a wider population.

Antonio Gallo MD, PhD
Lecturer, Lipidology and Cardiovascular Prevention Unit

IHU ICAN views MEDITWIN as an ambitious project encompassing various factors such as drug therapies, living environment and cardiovascular risks. Its aim is to improve clinical management by personalising care and anticipating changes in patients' health using breakthroughs in digital twin technology.

French scientific and technological excellence driving improvements to care

The MEDITWIN consortium was launched on 11 December 2023 in the presence of the French President. This project involves 7 Hospital-University Institutes, Nantes University Hospital, Inria, a number of startups and Dassault Systèmes. The aim of MEDITWIN is to develop digital twins to improve medical care, with applications in neurology, cardiology and oncology. Digital twins developed for the project will be used to simulate medical scenarios for patients, with seven new virtual health products to be commercialised on an industrial cloud platform. The project will be conducted over a 5-year period from 2024 to 2029 and receive financial support from the government through the France 2030 programme.

IBiSA label renewed for the omics platform

Metabolomics and lipidomics are disciplines enabling the discovery of valuable biomarkers and potential therapeutic targets, as seen in atherosclerosis, where serum lipid profile is linked to risk of progression. IHU ICAN uses advanced technology such as chromatography and mass spectrometry to analyse these complex molecular signatures.

In 2023, the IBiSA label was renewed for the ICAN Omics Platform, providing €80,000 of funding for new mass spectrometry equipment. This highlights the facility's key role in biomedical research in France. IHU ICAN will use this official and financial recognition to advance its research and maintain its position of excellence in the field of big data applied to health.

Marie LHOMME
Head of the Omics Lipidomics platform

It's crucial for our platform that the IBiSA label has been renewed. This provides the platform with visibility at national level, facilitates discussions with experts, co-funds technology replacement and provides key training, particularly on data management and carbon footprint.

Eric Thibaut
Head of Research Valorisation

The GEAT patent provides a new imaging biomarker (MRI, CT) for assessing cardiovascular and cardiometabolic risk (diabetes). It sends a strong message to the health industry that ICAN is keen to support innovation in health.

Patent – a new cardiomyopathy biomarker: GEAT

In June 2023, the IHU ICAN Core Lab team (Prof. Alban Redheuil and Khaoula Bouazizi-Verdier [Inserm-IHU ICAN]) and Prof. Stéphane Hatem, with the support of the Biomedical Imaging Laboratory (LIB) and assisted by Dr Nadjia Kachénoura and Maharajah Ponnaiah (IHU ICAN Data Scientist), revealed a significant correlation between diabetic patients and groove epicardial adipose tissue (GEAT) quantity based on cardiac MRI.

The groove is a stable anatomical marker ensuring sampling consistency and comparability between examinations and patients. Patent PCT/FR2023/051602 was filed in 2023 for exclusively epicardial groove adipose tissue (GEAT biomarker) used to diagnose predisposition to cardiomyopathy.

IHU ICAN expands its training catalogue (Al-Ain, United Arab Emirates)

In 2023, IHU ICAN offered young researchers from its community the chance to take part in the first autumn camp organised through the young researcher training programme in Al-Ain (United Arab Emirates) in partnership with the United Arab Emirates University (UAEU). This unique camp focusing on food sustainability and cardiometabolic health provided PhD students and postdoctoral fellows from the community with a new opportunity to discover breakthroughs in basic and clinical research in the UAE.

The programme included:

- New perspectives on sustainable food consumption and tackling obesity
- Development of artificial intelligence to tackle cardiometabolic diseases
- Talks by Canadian and French nutrition specialists
- Valuable opportunities to discover a different culture

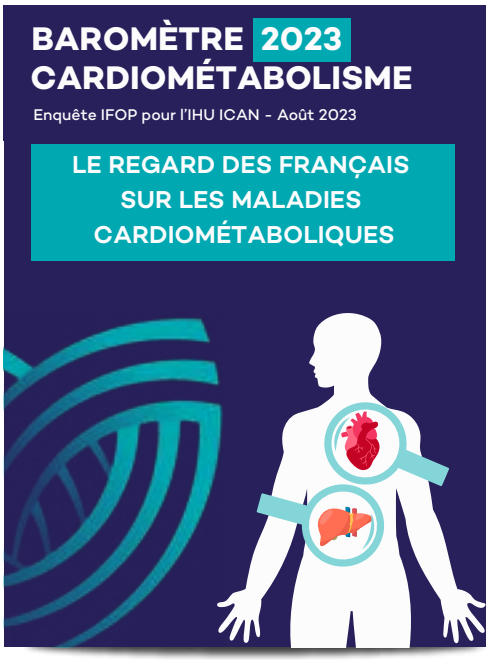
First edition of the survey on cardiometabolic diseases

Public awareness of cardiometabolic diseases (CMDs) in France is limited despite their prevalence and significant impact on health.

According to a survey conducted by IHU ICAN in collaboration with IFOP in November 2023, **only 38% of French people had heard** of CMDs, and of this subgroup, only 10% knew exactly what they were. This lack of awareness is concerning, since these diseases are among the world's leading causes of death, although only 15% of respondents perceived them as such, often incorrectly believing them to be curable.

The survey also revealed that **57% of respondents were unaware that CMDs are chronic diseases** with severe consequences for patients' quality of life and the potential to result in emergency hospital admissions. Moreover, less than half of those who had heard of CMDs were aware that these diseases include conditions such as obesity (49%), hypercholesterolaemia (47%) and diabetes (37%). **Even fewer respondents recognised metabolic dysfunction-associated steatohepatitis (MASH) as a metabolic disease.**

IHU ICAN has responded to this troubling situation by stepping up its awareness-raising and information-providing activities. Its aim is to ensure that the public is better informed about the severity and prevalence of CMDs and the vital importance of improving early diagnosis and treatment of these diseases. **These measures seek to reduce the impact of CMDs by improving prevention.**



62%

of French people have never heard of cardiometabolic diseases (CMDs)

57%

are unaware that they are chronic diseases and believe it is **possible to cure a CMD**

15%

consider them to be **one of the main causes of death in France**

In fact, cardiometabolic diseases are the biggest cause of death in women and the second biggest cause of death in the French population in general. (source: CépiDC)

40%

are not concerned about developing a CMD

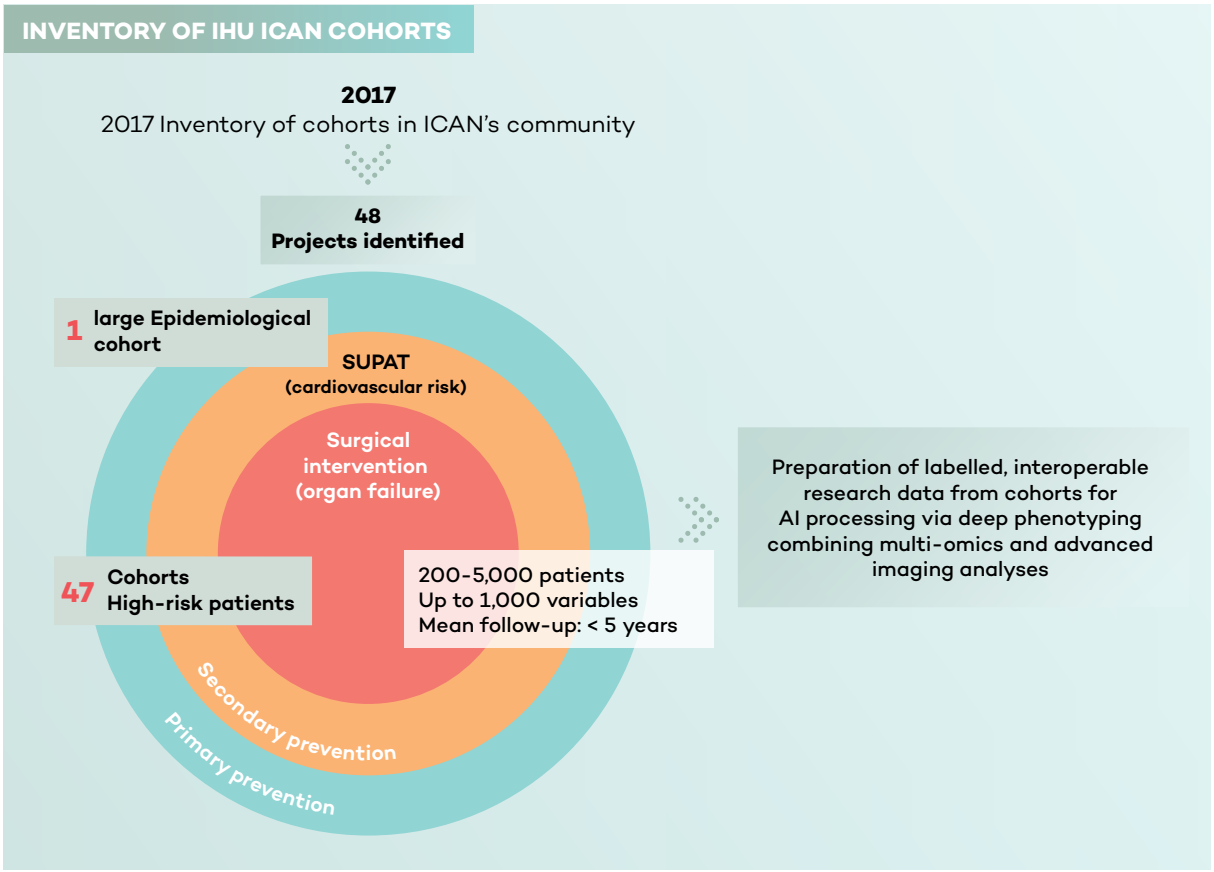
INNOVATION IN **RESEARCH**

A cohort strategy to support the scientific and medical community

Cardiometabolic diseases typically progress slowly and asymptomatically, which means it generally takes decades to clinically detect them using a set of diagnostic tools combining blood biomarkers with medical imaging and/or electrocardiograms. In most cases, patients exhibit several risk factors and progression may continue slowly after diagnosis in terms of clinical event incidence. Effective alternative markers are therefore needed to identify patients most at risk of developing severe, quickly progressing forms.

Cohorts represent a key research tool for accelerating innovation in biomedical science through evidence-based medicine. They have therefore become a **cornerstone of translational research developed within the ICAN community to improve understanding of cardiometabolic diseases.** In order to be usable, these cohorts must meet strict criteria in terms of regulatory compliance and the quality of data and biological samples. While various teams in the IHU have put together sample collections and associated databases over the years, there has never been a framework to enable satisfactory reuse and valorisation. Since it was founded, **ICAN has therefore pursued an active policy of structuring and consolidating these cohorts to allow their use in national and international academic and commercial research projects**. This work is in addition to hospitals' efforts to structure health data warehouses (HDWs).

	HDW	Cohorts
Size	> 100,000	500 - 10,000
Diseases	All	Focused
Data source	Care	Care + Research
Phenotyping depth	Low	**High**
Data quality	+	**+++**
Innovative value	+	**+++**
Cost per subject	+	**+++**



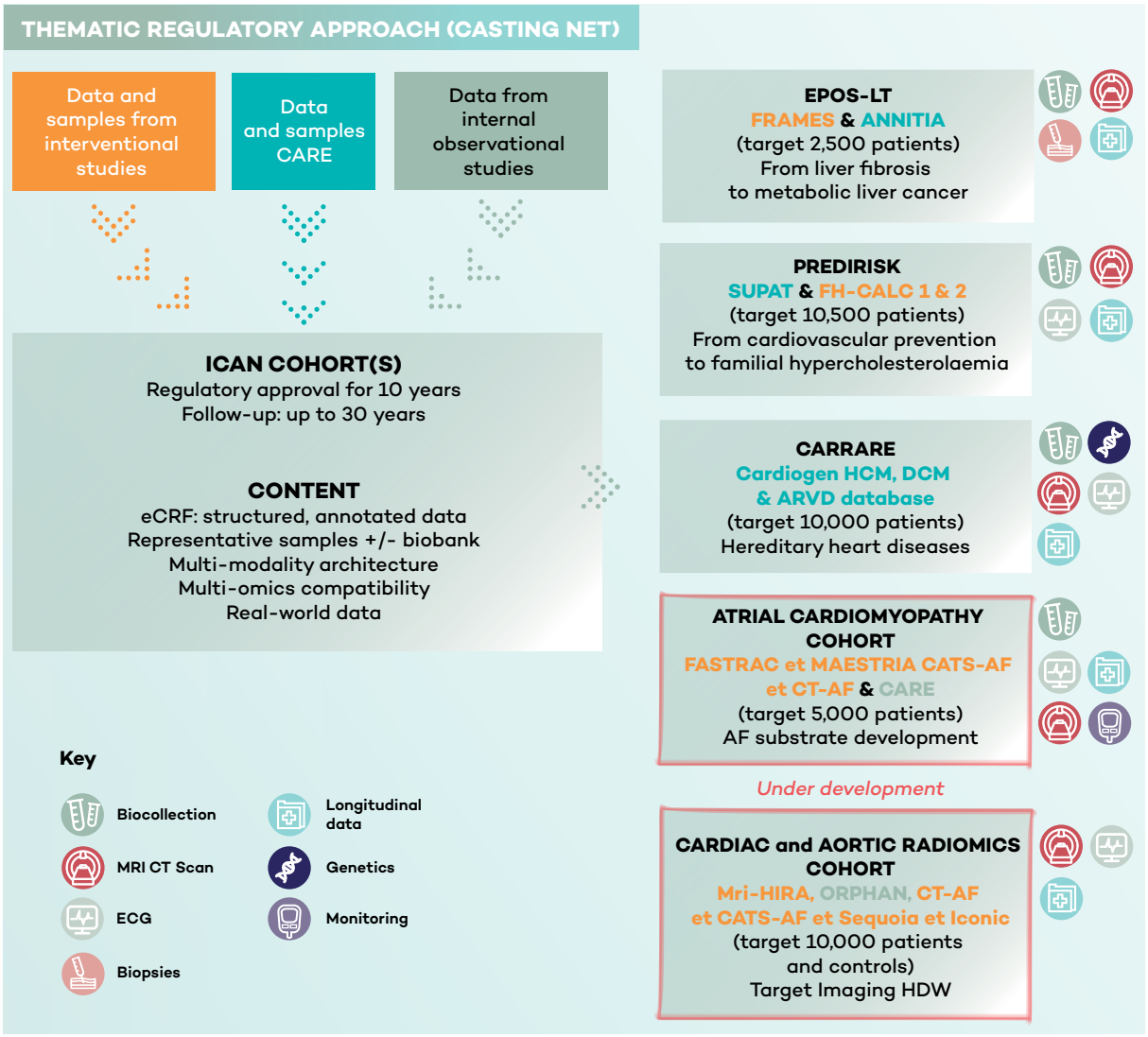
IHU ICAN considers cohorts to be critical to innovation due to their targeted objectives combined with deep phenotyping, which can only be achieved by investigating specific patient groups using the latest available 'omics' research tools and imaging equipment. Discoveries made through cohorts can then be tested in real-world conditions using hospitals' health data warehouses."

Stéphane Commans
Head of the Innovation and Research Valorisation Division

Initially, in 2014, following the creation of the **METACARDIS** cohort, IHU ICAN, developed 4 new specific prospective cohorts (**BARICAN, FIFA, Myocard-ICAN and ACS-APPROACH**). In 2017, conscious of the innovative value of big data in health combined with developments in AI-based decision-making algorithm technology in medicine, ICAN launched a cohort plan to identify, inventory, structure and classify retrospective cohorts created by researchers in its community.

48 clinical projects were identified:

- A broad epidemiological cardiovascular risk cohort seen in primary prevention clinics with an existing biocollection and imaging data (CT or ultrasound) including over 7,000 patients providing longitudinal data covering the past 20 years.
- 47 cohorts of high-risk groups including 200 to 5,000 patients with average follow-up of less than 5 years, mostly without biological collections but with imaging data relating to care procedures (such



as AF ablations, bariatric surgery, liver resections, transplants, etc.) or genetic diseases (lipodystrophy, obesity, cardiomyopathies, familial hypercholesterolaemia, etc.).

Since 2021, IHU ICAN has been integrating these projects by:

- **applying a casting-net approach** to group data and samples from potentially compatible projects and clinical studies under broader unifying regulatory frameworks to enable the recovery of complex data and anticipate translational research and the development of AI-based IT solutions, while also helping with diagnosis and facilitating data use for subsequent partners.
- **creating pipelines enabling its technical platforms (ICAN Imaging, ICAN Omics and ICAN I/O) to recover and analyse complex data** by prioritising projects with available biocollections enabling the discovery of biomarkers.
- **conducting an imaging study with a significant population** (the ICONIC project) enabling future case-control validation studies.

Cohorts

Deep phenotyping and accurate data on patients at advanced stages of their diseases.

POPULATION AT CARDIOMETABOLIC RISK

Identification
by non-hospital practitioners

PATIENTS DIAGNOSED

Hospital-based
management

SUPAT-PCV
25,000 patients
(cardiovascular prevention)

National CARDIOGEN network
2,660 patients with HCM
(hypertrophic cardiomyopathy)

3,210 patients with DCM
(dilated cardiomyopathy)

1,000 patients with ARVD
(arrhythmogenic right ventricular dysplasia)
ERN European extension

FASTRHAC cohort
300 patients
(atrial fibrillation)

FH-CALC cohort
270 patients
(hypercholesterolaemia)

FRAMES cohort
600 patients
(metabolic steatosis)
European extension
EpOS/Litmus
> 10,000 patients

METACARDIS cohort
800 patients
European extension
> 2,000 patients

PATIENTS WITH SEVERE CONDITIONS

Surgical intervention necessary

Transplant cohort
> 1,000 patients
(heart and liver)

DATABRAVE cohort
200 patients
(vascular surgery)

ATLANTIS cohort
1,500 patients
(transcatheter aortic valve implantation)

LIVERBASE cohort
2,200 patients
(liver surgery)

Over 42,000 individuals included in cohorts, registries or clinical trials

Key

- Metabolic
- Cardiovascular
- Optics
- Monitoring
- MRI CT Scan
- Ultrasound
- Nutrition
- Longitudinal data
- Biocollection
- Biopsies
- ECG

FOCUS
Atrial cardiomyopathy

Atrial fibrillation (AF) is the most common cardiac rhythm disorder. Its incidence and prevalence are rising quickly, largely due to population ageing. In France, approximately 750,000 people suffer from atrial fibrillation. The estimated cost of care for the disease is €2.5 billion per year.

The MAESTRIA (Machine Learning and Artificial Intelligence for Early Detection of Stroke and Atrial Fibrillation) project is run by a consortium of 18 partners in Europe, the United States and Canada that responded to an H2020 call for proposals on digital diagnosis aimed at developing and validating the first digital integrative diagnosis platform for atrial cardiomyopathy.

MAESTRIA CONSORTIUM MEETING IN MADRID

In October, the third consortium general meeting was held at the CNIC (Centro Nacional de Investigaciones Cardiovasculares Carlos III) in Madrid with over 60 participants.

LAUNCH OF THE MAESTRIA-AFNET 10 EUROPEAN PROSPECTIVE STUDY

On 12 March 2023, the first patient was recruited to the MAESTRIA-AFNET 10 cohort which represents a cornerstone of the consortium's work, since data from the cohort will be used to roll out a digital diagnosis platform. **The MAESTRIA-AFNET 10 cohort will play an essential role in refining risk stratification in AF patients based on cutting-edge imaging techniques, electrophysiological investigations and AI-based approaches.** It will contribute to the development of a set of precision medical tools enabling AF and strokes to be managed simultaneously in Europe and beyond.

MAESTRIA-AFNET 10 is an international, multi-centre, non-interventional observational cohort that will provide a representative sample of AF patients in Europe, allowing detailed analysis of relevant clinical parameters (digitised ECG, cardiac imaging, blood biomarkers). Research derived from this cohort may eventually be used to change clinical practices for diagnosing atrial cardiomyopathy and related risks. Data sets will be evaluated using various

MAESTRIA consortium meeting in Madrid

MAESTRIA consortium meeting at the CNIC

methods, including the application of AI algorithms to characterise specific AF subgroups and define new risk predictors.

At the end of 2023, 93 patients were already enrolled in Germany and sites in Spain, France (2 sites: Pitié-Salpêtrière Hospital and Saint-Antoine Hospital) and the Netherlands were preparing to begin enrolments. ECG and imaging data are sent to a data hub set up for MAESTRIA, so that they can be analysed by various Core Labs experts.

Louise Meyfroit
Scientific Operations Manager - IMAGING

ICAN teams play a key role in the MAESTRIA project and are involved to various degrees in all the work packages, particularly in the cross-cutting area of data (transfer, use and reuse, regulatory compliance, governance, quality) and also in developing the digital platform, designing useful algorithms, follow-up of clinical studies, and scientific and organisational coordination. The MAESTRIA-AFNET cohort raises several data-related challenges. For instance, imaging data will be combined with physiological data (omics, clinical data, etc.) from patients in this cohort to enable the digital platform created through the project to identify new therapeutic targets in order to improve diagnostic accuracy in atrial cardiomyopathy.”

THIS PROSPECTIVE COHORT SPONSORED BY AFNET AIMS TO RECRUIT

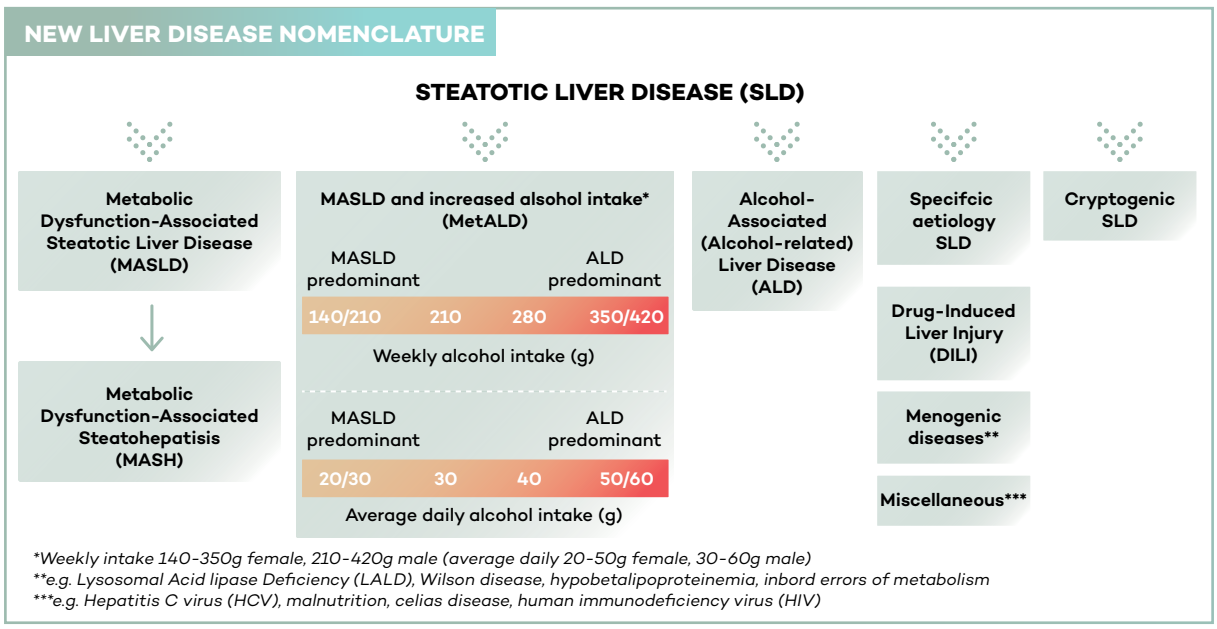
- **200 patients with paroxysmal AF**
- **200 patients with persistent AF**
- **200 patients with permanent AF**

FOCUS
Metabolic dysfunction-associated steatohepatitis

Non-alcoholic fatty liver disease (NAFLD) is currently assessed by liver biopsy, an invasive, expensive and risky procedure that does not predict the individual rate of disease progression. A lack of non-invasive biomarkers raises challenges for conducting clinical trials, thus hampering patient care and drug development. Drawing on one of the oldest and largest European single-centre NAFLD cohorts, **IHU ICAN is playing a key role in the development, validation and qualification of novel non-invasive biomarkers through multiple international public-private partnerships (FLIP, EpOS, LITMUS)** which offer the potential to determine the validity of these new biomarkers for NAFLD, while also supporting drug development and efforts to target medical care and limited health resources on those who most need it.

DELPHI CONSENSUS ON CHANGES TO THE NOMENCLATURE

The key issue with NAFLD and NASH is that they are confusing, exclusive and potentially stigmatising terms. A modified Delphi process was conducted by three major international associations. An independent committee of experts outside the nomenclature process made the final recommendation on the acronym and its diagnostic criteria. A total of 236 panellists from 56 countries took part in 4 online surveys and 2 hybrid meetings. 74% of the individuals questioned stated that the current nomenclature is sufficiently imperfect to consider a change of name. The terms "non-alcoholic" and "fatty" were considered stigmatising by 61% and 66% respectively of the individuals questioned. **"Steatotic liver disease" was chosen as an umbrella term for the various aetiologies of steatosis.** The term "steatohepatitis" was deemed an important pathophysiological concept that should be retained. **The term chosen to replace NAFLD was "metabolic dysfunction-associated steatotic liver disease" (MASLD).** There was consensus on changing the definition to include at least one of the five cardiometabolic risk factors. Patients presenting with no metabolic parameters and no known cause were considered to be suffering from cryptogenic steatotic liver disease. A new category distinguished from pure metabolic dysfunction-associated steatotic liver disease, defined as metabolic dysfunction- and alcohol-associated liver disease (MetALD), was chosen to describe individuals



suffering from steatotic liver disease associated with metabolic dysfunction, whose weekly alcohol consumption is towards the higher end (140 to 350 g per week for women and 210 to 420 g per week for men). **The new non-stigmatising nomenclature and diagnostic criteria may improve awareness and patient identification.**

2023 WAS A VERY SUCCESSFUL YEAR WITH 4 NEW EUROPEAN PROJECTS AWARDED, INVOLVING Prof. VLAD RATZIU AND Dr RALUCA PAIS FROM IHU ICAN

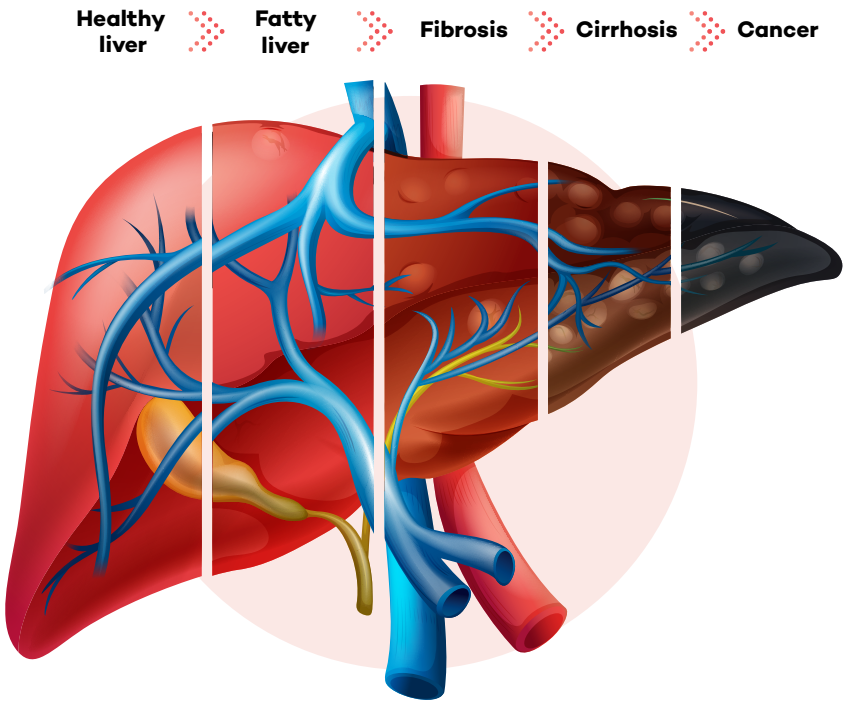
EDC-MAFLD
which will focus on investigating the impact of environmental exposure to endocrine disruptors on the internal exposome (metabolome, gut microbiome, epigenome, proteome, immunome) and the severity of liver lesions in MASLD, and more specifically on interactions between exposure to each disrupter, sex, genotype, diet, socio-economic factors and lifestyle using data and biological samples available from the single European NAFLD cohort from the LITMUS project.

ARTEMIS
which will merge computer mechanism models and machine learning models to provide clinicians with "virtual twins" through a computer-assisted clinical decision-making system.

These virtual counterparts pave the way for personalised care, from the latent stages to critical complications such as liver cirrhosis and cancer, by predicting disease progression and associated cardiovascular risks and assessing various treatment strategies.

LIVERAIM
which will use AI to develop a screening platform enabling the early detection of liver diseases based on a combined set of biomarkers for early and personalised diagnosis of fibrosis. This platform will be validated by a clinical trial including 100,000 subjects from 6 representative EU countries.
A large number of existing biomarkers will first be tested to determine their accuracy in predicting fibrosis using plasma samples taken from 40,000 subjects from previous cohorts including LITMUS.

GRIPonMASH
which will develop a long-term, scalable platform enabling early detection of patients who are at risk of developing MASLD or have already been diagnosed with the condition by private physicians. This platform, implemented at 12 European centres of excellence, will facilitate improvements in patient stratification through AI-assisted decision-making tools that use both existing and novel biomarkers. It will also provide personalised advice on lifestyle by examining evidence-based lifestyle factors and the impact of nutrition recommendations.



In 2023, a **Bpifrance "Data challenges in healthcare" grant was also awarded under the France 2030 programme.** The **ANNITIA project** led by Prof. Vlad Ratziu seeks to stratify NAFLD progression risk by modelling the simultaneous longitudinal evolution of non-invasive tests using a digital twin.

To that end, the research team will assess trends in longitudinal changes for 3 non-invasive tests (liver stiffness by VCTE-Fibroscan, FibroTest/FibroSure and FIB4) through long-term follow-up of over 2,500 patients with non-alcoholic fatty liver disease (NAFLD) and deduce change thresholds linked to disease progression or regression. The principal hypothesis is that changes in values for these tests are indicative of liver fibrosis progression and can therefore be used to describe the natural history of the disease and monitor developments in fibrosis in treated and untreated patients.

These findings will considerably improve our understanding of how fibrotic liver diseases can be monitored using non-invasive tests during clinical follow-up and the limits of using current non-invasive tests in clinical practice. This will make it easier to treat patients in clinical practice and conduct future therapeutic trials.

"IHU ICAN plays a key role in research projects on metabolic steatosis and metabolic steatohepatitis, combining different cohorts to bring about innovative projects such as ANNITIA. The ANNITIA Data Challenge will use AI-assisted analysis of data from over 2,000 patients to investigate whether it is possible to predict liver disease progression and the onset of severe forms in a given individual based on consecutive measurements taken in non-invasive tests."

Leila KARA
Scientific Operations Manager - Hepatology

FINDINGS OF THE LITMUS PROJECT

Over the past seven years, LITMUS has successfully fulfilled its remit of developing and validating non-invasive biomarkers suitable for use as Diagnostic Biomarkers and for Diagnostic Enhancement, and robustly progressing them to regulatory qualification. This has led to the acceptance of two letters of intent by drug agencies in the United States and Europe and the submission of a detailed qualification plan for diagnostic enhancement to the Food and Drug Administration (FDA).

Other key achievements of the LITMUS consortium, to which ICAN has made a significant contribution, include:

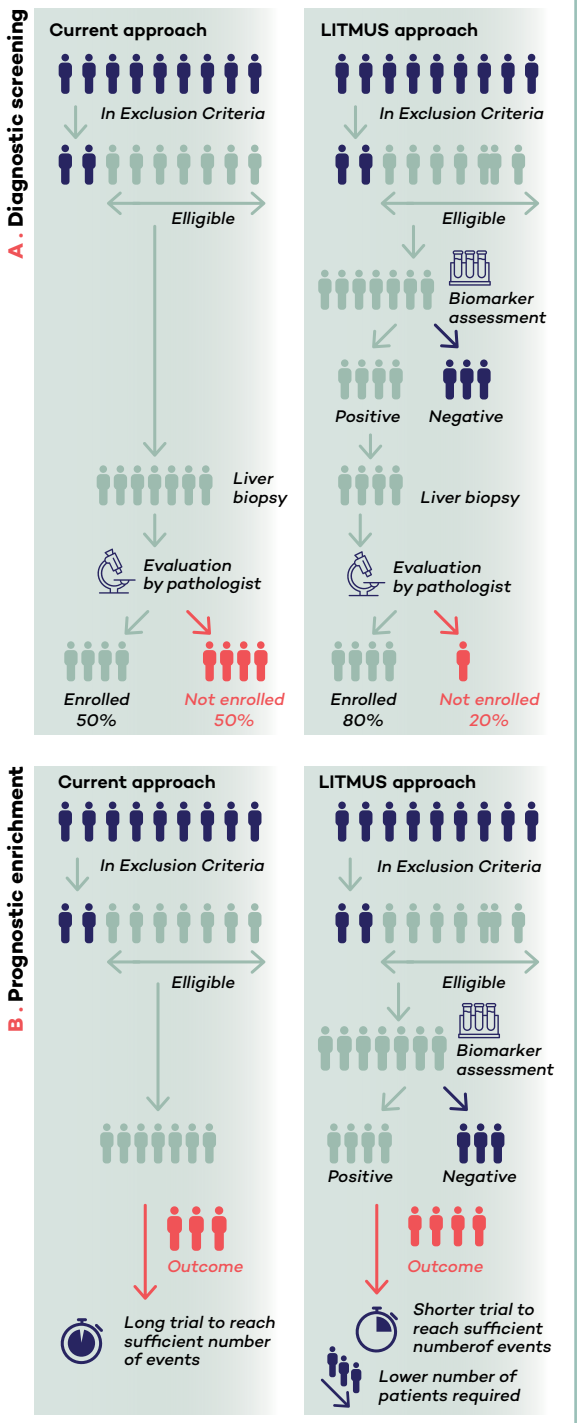
1. **An extension of the "European SLD Registry"** (formally the "European NAFLD Registry") making it the world's biggest histologically characterised cohort of MASLD patients with longitudinal follow-up, including clinical data for over 10,000 cases and a centralised collection of serum/plasma samples.

2. **The generation of large "multi-omics" data sets concerning these patients** (genetic, transcriptomic, proteomic, metagenomic and metabolomic data) characterising the entire pathophysiological spectrum of MASLD, with a view to discovering new circulating biomarkers. Combined with a wealth of cross-sectional and longitudinal clinical phenotype data generated within the cohort, these constitute a unique resource supporting innovation in the field of biomarkers.

3. **An evaluation of the diagnostic performance of several biomarker candidates** in over 2,500 histologically characterised MASLD cases to determine which diagnostic biomarkers are most accurate and easiest to use.

4. **A prospective imaging study** assessing the performance of a range of ultrasound-based biomarkers (Fibroscan VCTE, CAP) or MRI (MRI-PDFF, MRE, cT1, etc.) which was conducted at centres across Europe.

NOVEL USES OF NON-INVASIVE BIOMARKERS IN PHARMACEUTICAL CLINICAL TRIALS ON METABOLIC LIVER DISEASE



Daniel Guldager Kring Rasmussen, Quentin M. Anstee, Richard Torstenson, Bruno Golding, Scott D. Patterson, Clifford Brass, Paresh thakkern Stephen Harrison, Andrew N. Bilin, Detlef Schuppan, Jean-François dufour, Annel Anderson, Ioan Wigley, Elizabeth Shumbayawonda, Andrea Dennis, Corinna Schœlch, Vlad Ratziu, Carla Yunis, Patrick Bossuyt, Morten Asser Karsdal

FOCUS
Rare and genomic diseases

The term "cardiomyopathy" covers all diseases of the heart muscle. These diseases progress incrementally towards similar clinical complications, including heart failure and cardiac rhythm disorders. However, their causes at molecular, cellular and tissue level are extremely diverse and knowledge of them remains limited.

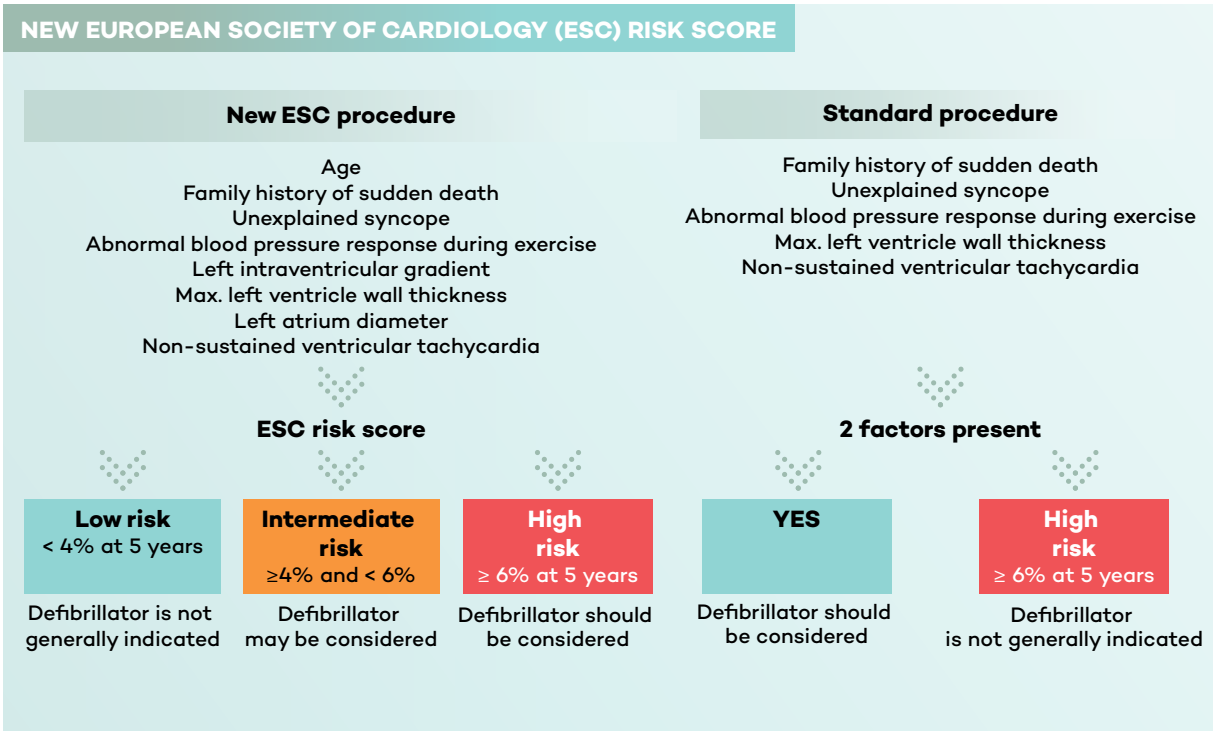
The subclass of "hereditary" cardiomyopathies covers severe diseases that are considered "rare", as they affect less than one in 2,000 individuals[1]. It notably includes dilated cardiomyopathies (DCMs), hypertrophic cardiomyopathies (HCMs), restrictive cardiomyopathies, so-called "right ventricular cardiomyopathies" (ARVCs/ARVDs), etc. Some forms remain unclassified.

Due to the rarity of these diseases, the various clinical and genetic data collected for them are heterogeneous and often relate to separate patient cohorts. Currently, cardiogeneticists at rare disease centres are all too often at a loss when faced with the results of genetic and cardiological tests prescribed as part of their disease assessment. In reality, the course of the disease is highly variable and difficult to predict. This is particularly true of patients' relatives who, despite having a similar genetic mutation, sometimes present with a completely different clinical picture and/or disease course.

CardI-HACK

To mark the **award of France 2030 "Data challenges in healthcare" funding** from Bpifrance, IHU ICAN will develop a research project focusing on **hypertrophic cardiomyopathy (HCM), a rare hereditary disease**.

1 European Union definition



The aim of the **CardI-HACK project led by Prof. Philippe Charron is to determine a polygenic risk score (PRS) for individual patients** based on a combination of common and high-risk genetic variants and incorporate it into cardiological data in order to better identify patients who would benefit from pro-active therapeutic treatment, particularly with an implanted medical device (e.g. an intracavitary or subcutaneous automatic defibrillator).

The general objective pursued by the project is to combine detailed genetic and clinical data from over 500 patients with hypertrophic cardiomyopathies (HCMs) and **apply artificial intelligence (AI) to prompt a transition to precision medicine** by identifying new bioclinical scores that more accurately predict the prognosis of these diseases.

AI will enable a new type of risk stratification with a direct translational application in terms of guiding therapeutic decision-making. We hope that it will allow clinicians to identify the level of risk to which their patients are exposed, helping them adapt their decision-making and follow-up frequency.

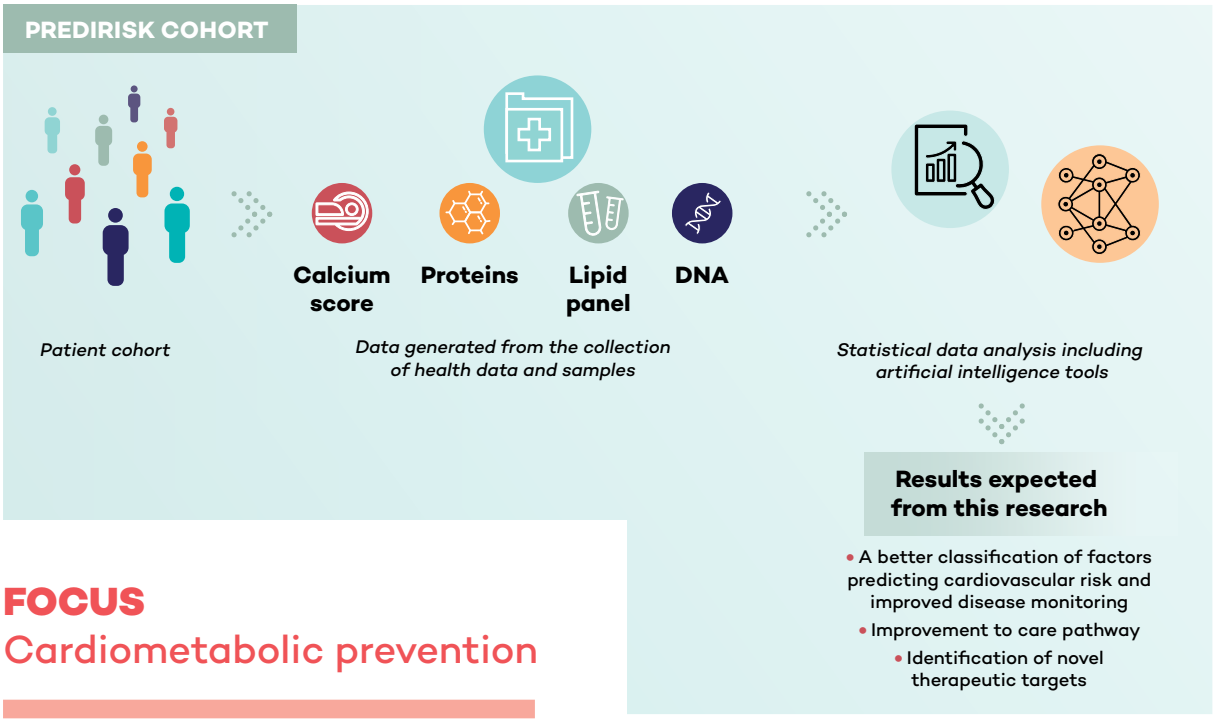
DCM-NEXT

Dilated cardiomyopathy (DCM) is one of the main causes of systolic heart failure and a major cause of sudden cardiac death. It often affects young adults with a prevalence of up to 1 in 2,500 individuals. While medical treatment currently plays an important role, it does not tackle the cause of the disease and the only curative option is a heart transplant at the terminal stage of DCM. The EU-funded project run by the European DCM-NEXT consortium will fill gaps in our knowledge of the genetic architecture of DCM through a detailed and integrative analysis of rare and common genetic variants. This project is supported by world-renowned experts in various fields, including phenotyping, cardiogenomics, artificial intelligence, and cell and animal models. The project's main goals are to:

- **identify and validate** new targets involved in DCM pathophysiology
- **revolutionise** diagnostic tests for this disease
- **better predict** cardiovascular risks related to the disease
- **develop new therapies for DCM**

Rare and hereditary cardiomyopathies are puzzling, as they can affect patients in various different ways, even within the same family. The emergence of genetic sequencing and its falling cost have considerably increased the quantity of data available to explain these varied phenotypes, thus adding a new source of complexity. Artificial intelligence will be of great help in interpreting these data, and ultimately enabling personalised treatment of patients suffering from these diseases. IHU ICAN created ICAN I/O – data sciences, a cutting-edge technological platform whose chief purpose is to accurately process data generated by new omics techniques."

Aurélie FOUCHER
Scientific Operations Manager - Cardiology



FOCUS
Cardiometabolic prevention

Cardiovascular diseases currently still account for over 30% of all deaths in developed countries, even though risk factors and major lipid metabolism mechanisms involved in the onset of these diseases have been identified, enabling the development of new drugs such as statins and PCSK9 inhibitors and improvements in treatment methods.
Although primary prevention has become a major focus of efforts to tackle this health crisis, it is mainly limited to an assessment of coronary risk based on identifying traditional risk factors. While the link between certain standard biological markers (standard lipid profile, LDL cholesterol) and the risk of cardiovascular disease is beyond dispute, it is not currently possible to precisely stratify this population based solely on the use of these markers in medical practice.

Due to breakthroughs in imaging techniques, such as chest CT scans of the large and small arteries, it is now possible to precisely and non-invasively assess vascular disorders in patients who do not have established cardiovascular disease. However, these techniques are not yet integrated in decision-making algorithms or used systematically in clinical practice. These techniques will enable the detection of individuals at low and/or medium risk, who are probably the most suitable candidates for preventive medical therapy, as well as subjects with an elevated risk of cardiovascular disease, who could benefit from more aggressive preventive treatment. Moreover, **other discoveries have been made on the link between cardiovascular health and the microbiota.** For instance, by eating high-fibre foods such as a Mediterranean diet, patients can reduce their risk of developing atherosclerosis, since fibre is converted by bacteria into short-chain fatty acids.

We therefore need to address multi-factor risks and take account of all risk factors that have an impact on our metabolism. These environmental factors are particularly linked to diet (excess fat, sugar, salt, calories or insufficient fibre, etc.), and exposure to xenobiotics (drugs, pesticides, food additives, etc.)

PREDIRISK

The aim of the PREDIRISK study led by Dr Antonio Gallo is to analyse data and samples collected in the course of routine care for approximately 10,000 patients followed up over several years in the Lipidology and Cardiovascular Prevention Unit at Pitié-Salpêtrière Hospital by Dr Philippe Giral, with a view to investigating predictive factors for cardiovascular diseases (CVDs), their long-term effects, and the onset of complications associated with these diseases.

The research objective is to create a retrospective and prospective cohort of patients who exhibit one or more cardiovascular risk factors in order to investigate predictive factors for CVD progression. By integrating genetic, clinical, biological, imaging, metabolic and lipid data sets using artificial intelligence, it will be possible to develop new, more specific algorithms to predict patients' risk trajectories and more precisely tailor their treatment, particularly in subjects who are most likely to develop CVD.

The endpoint is the correlation between identified predictive factors and the development/ severity of cardiovascular risk and the onset of cardiometabolic events: non-fatal coronary heart disease, defined as acute coronary syndrome, coronary revascularisation (angioplasty, bypass, stent, etc.), non-fatal ischaemic stroke, lower extremity arterial disease and diabetes.

The predictive factors under investigation are mainly focused on blood biomarkers (lipidomic, metabolomic and proteomic biomarkers) or imaging biomarkers (carotid-femoral Doppler ultrasound, MRI, coronary CT angiography and chest CT scans), and the gut microbiota.

and pollutants. In order to assess the effects of these multiple factors on our bodies, we therefore need to develop our tools for evaluating environmental risks and the traces they leave on our bodies. **Significant progress has been made with scientific and biomedical research in this field, enabling the incorporation of these risk factors based on omics data encompassing metagenomics, metabolomics, lipidomics and proteomics** that represent an imprint of the individual genome-exposome[1] relationship.

The effects of patients' medical treatments must be carefully considered and constitute a further barrier that needs to be overcome, since their side effects have not yet been fully elucidated and distort study markers. Without predictive tools, it is difficult to personalise patient follow-up and choose the most appropriate treatments and optimal doses, while also limiting side effects associated with treatments (statins).

1. Exposome: the impact on a body of all the environmental factors to which it has been exposed during a lifetime

Familial hypercholesterolaemia (FH) is a major cause of early-onset cardiovascular disease and represents an accelerated disease progression model. By monitoring the course of the disease in these patients, it is possible to access risk prediction indicators over a limited period of time.

Recent data have demonstrated that, even in cases of familial hypercholesterolaemia, non-invasive coronary imaging can be used to predict the incidence of cardiovascular events in asymptomatic subjects, with high predictive power over a follow-up period of less than 3 years.

However, these techniques are not fully integrated in decision-making algorithms or used systematically in clinical practice.

By liaising with Prof. Bertrand Cariou from Nantes University Hospital regarding this virtual twin use case and using the results of the SAFIR cohort from the RHU CHOPIN project and Dr Antonio Gallo's PREDIRISK cohort, the MEDITWIN consortium, comprising 7 Hospital-University Institutes (IHUs) including IHU ICAN, Nantes University Hospital, Inria, partner startups and Dassault Systèmes, is seeking to develop a service to diagnose individual predisposition to cardiovascular diseases and select the best treatment strategies, while also factoring in patients' environment by considering elements such as their gut microbiota and nutrition.

These twins' predictions on the course of disease and any improvements in this could be used to support practitioners with treatment and it may also help them give patients a clearer picture of possible outcomes if no action is taken in a bid to improve their compliance with treatment. It will be possible to measure the impact of solutions provided using data on reductions in the number of patients suffering from cardiovascular events (coronary, cerebrovascular, arterial, etc.).

These outcomes will benefit patients by tailoring their treatment to their individual risk profile, linked directly to disease progression, and also practitioners by offering them tools to identify and treat chronic diseases from their early stages.

ICAN plays a key role in research projects in which biological and clinical data are analysed to identify new biomarkers for cardiovascular diseases using AI-based methods. Innovative, large-scale projects such as Meditwin, in which ICAN's involvement covers cardiometabolic applications, will bring major developments for the scientific community and patients, since clinical, biological and imaging data on the cardiac vessels will be analysed and incorporated using AI-based methods. This ambitious project will culminate in the development of new algorithms that will allow physicians to diagnose patients more effectively and personalise their treatment.

Arturo Hernández-Cervantes
Scientific Operations Manager - Endocrinology

FOCUS
Cardiometabolic imaging

Due to progress on imaging techniques, it is now possible to explore highly innovative new avenues of research. **Imaging currently plays a key role in elucidating pathophysiological mechanisms *in vivo*. Diseases can thus be detected at an earlier stage, and individuals' risk of developing a disease and suffering from a severe form can be assessed. As a result, patient care can be improved by developing personalised medicine.**

However, there is a shortage of cardiovascular and liver imaging data for the general population and particularly the 20-40 age bracket. Individuals aged under 45 are very poorly represented in population studies.

ICONIC

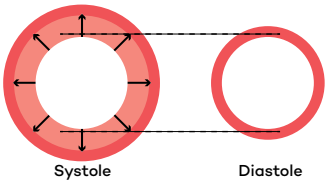
The ICONIC project led by Prof. Alban Redheuil will be conducted at the ICAN Imaging Platform in relation to the Inserm CONSTANCES cohort managed by Prof. Marie Zins from Université Paris Cité.

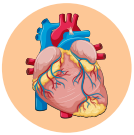
As well as providing important demographic information on health, these data will also shed fresh light on causes of diseases and ageing. Moreover, they will enable us to detect diseases at a very early stage, determine new individual cardiovascular and metabolic risk profiles, and form a benchmark multimodal imaging cohort for research on common and rare diseases.

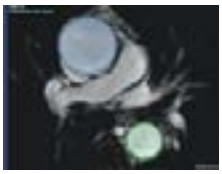
The primary objective of the ICONIC project will be to generate normative data by age bracket and sex based on an analysis of MRI and echocardiographic images within the French population. These normative data could provide a basis for validating novel biomarkers and serve as a control for basic or clinical studies involving human data.

New diagnostic and prognostic tools are being developed to encompass multiple parameters by incorporating clinical, biological and imaging data. This database will help break down barriers in medicine and will be available to physicians and researchers, enabling French teams to collaborate on current and future international population-based imaging projects.

ICONIC STUDY

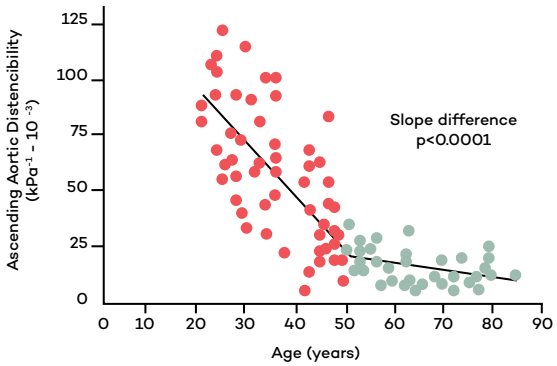


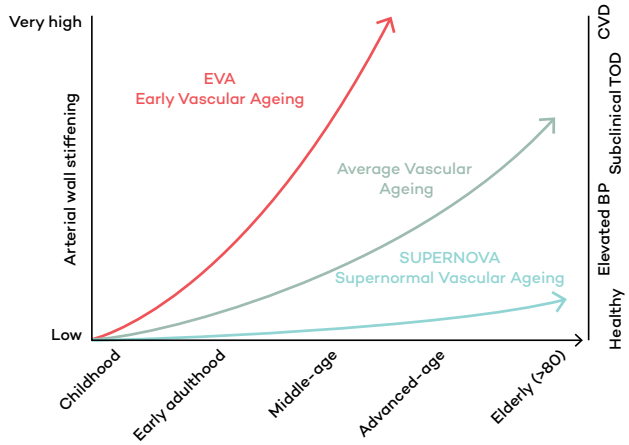




Wall cross-sectional area

Change in lumen area (AA) = maximal aortic area (Amax) - minimum aortic area (Amin)





N = 2400 participants
From 20 to 79 years old
200 men and 200 women by decade (25% devoid of risk factors)

Blood sample
Genome • Metabolome
Lipidome

Imaging
Liver, heart and aorta
Ultrasound and MRI

Medical examination
Body composition • Physical exercise • Central and peripheral blood pressure • Heart rate and ECG • Cardiometabolic risk factors • AGE reader

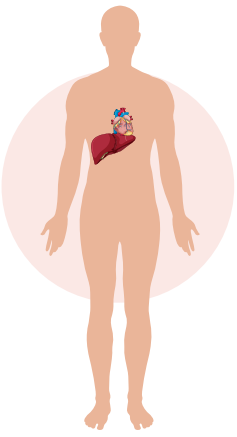
HEART
Volume • Mass • Fibrosis
Deformation • Pressure gradient

VESSELS
Arterial stiffness • Aortic stiffness
Advanced Glycation Endproducts

INFLAMMATION
Cytokines • Tissue inflammation

HORMONES
Androstenedione • 18-progesterone
18-hydroprogestérone

MÉTABOLOMIQUE LIPIDOMIQUE
Amino acids, SCFAs • Tryptophan & Choline metabolic pathways • Glycerophospho, sphingo- and neutral lipids • Sterols and biliary acids



LIVER
Fibrosis • Steatosis Elasticity
Liver enzymes

FAT
Subcutaneous • Visceral
Ectopic • Epicardial

KIDNEY
Serum uric acid • Creatinine
Blood urea nitrogen

PHYSICAL
Body composition • Physical exercise

GENOMICS
Whole genome sequencing

"ICONIC is a meeting of two major research infrastructures: the IHU ICAN imaging platform and CONSTANCES. Together, we'll be able to provide crucial new data to improve the prevention and treatment of numerous cardiometabolic diseases."

Prof. Marie Zins
Epidemiologist, Head of Inserm UMS 011 Population-Based Epidemiological Cohorts Unit, Scientific and Technical Coordinator of the CONSTANCES cohort

SHEDDING LIGHT ON OUR CARDIOVASCULAR AND HEPATIC CLOCKS: INSIGHTS ON AGEING THROUGH POPULATION-BASED IMAGING

Biological age is increasingly recognised over chronological age for its prognostic value, alongside the heterogeneity of ageing processes that can vary by organ and system. A study of very large samples of Chinese centenarians and middle-aged individuals using a multiomic, multi-organ approach recently indicated that organs age at different rates. The authors also demonstrated that organ-specific biological ages can predict associated diseases and highlighted the value of related genomic data.

However, crosstalk between organs was not assessed and only facial skin imaging was used in this study. We posit that direct assessment of organ structure and function using non-invasive imaging has now attained sufficient technical maturity and feasibility, and that precision *in vivo* phenotyping may offer higher diagnostic and prognostic value than indirect biological approaches.

SUPPORT FROM THE MSDAVENIR ENDOWMENT FUND

Through a sponsorship agreement worth €1.2 million, MSDAVENIR is providing major support for the pilot phase of this project, which will contribute to the creation of a cardiovascular and liver imaging repository in young adults aged 20 to 40 that is unique worldwide.

This combination of medical imaging and epidemiology will produce world-unique population-based data that includes young adults.

"Medical imaging now plays a key role in understanding, early detection, prognostic assessment and personalised patient care. (...) ICONIC will lead to the creation of the first French multimodal imaging cohort combining ultrasound and MRI scans of the heart, vessels, liver and adipose tissue, using the latest technologies and incorporating young subjects aged under 40 from the CONSTANCES cohort."

Prof. Alban Redheuil
Cardiac Radiographer (AP-HP), Head of ICT Cardiovascular and Thoracic Imaging (Pitié-Salpêtrière Hospital), Medical and Scientific Head of ICAN Imaging (IHU ICAN)

FOCUS
Cardiac surgery

Despite current organ shortages, some hearts are not being harvested from donors, as the duration of ischaemia needed to transport them is incompatible with transplantation. IHU ICAN has developed an innovative research programme on heart transplantation.

PHENIX: Programme to increase the pool of available human donor hearts by developing innovative biomarkers and using medical devices enabling *ex-vivo* hypothermic preservation

The PHENIX programme consists of 3 projects all aimed at improving heart transplantation conditions in France:

1. By increasing the number of available donor hearts
   - By extending the current maximum period of 6 hours between taking a heart from a donor's chest and transplanting it in a recipient's chest, based on a new organ preservation system: **PEGASE** project
   - By revealing a safe donor organ retrieval technique in Maastricht III stage patients: **MAC 3** project

2. By objectively assessing the organ preservation quality of new devices: **MANDRAGORE** project

PEGASE, conducted by the Paris Public Hospital Network (AP-HP) and IHU ICAN in collaboration with Martinique University Hospital and Guadaloupe University Hospital, seeks to assess the feasibility of preserving a heart using XVIVO's hypothermic oxygenated perfusion-based preservation device. In this study, the donor's heart is retrieved following the usual procedures, then installed in the hypothermic oxygenated preservation device to be transported by air from the Caribbean to Paris. On arrival at Pitié Salpêtrière Hospital AP-HP after over 12 hours' preservation, the heart is transplanted into a recipient following the usual procedures.

This unprecedented transatlantic transit on a commercial airline is designed to challenge geographic and time limits for heart transplantation. The first transplant was successfully completed in early January 2024, and was described in a paper published in the prestigious *The Lancet* journal. The study will be continued in order to corroborate this breakthrough and create new opportunities for performing transplant procedures, particularly at isolated or remote centres in locations such as the French West Indies, and to increase the number of available donor hearts. The target is to enrol around 20 patients in this study.

MAC 3

Patients receiving palliative or end-of-life care or those suffering from an acute condition with an unfavourable short-term prognosis may have their life-sustaining treatment withheld or withdrawn due to the need to avoid therapeutic obstinacy. In these cases, death occurs after cardiac arrest following the discontinuation of treatment by decision implemented in accordance with the provisions of the Leonetti and Clayes-Leonetti laws[1]. Currently, the liver and kidneys of organ donor patients who are in a sufficiently good condition can be retrieved and transplanted into patients who are waiting for an organ donation.
However, this is still not the case for donor hearts, due largely to the lack of an appropriate technique for retrieving them in optimal preservation conditions while also ensuring compliance with procedures in force allowing the family to be present until the end of the procedure. This study seeks to demonstrate the feasibility of such retrievals.

MANDRAGORE

The aim of the MANDRAGORE project on a Multimodal MRI and Metabolic Assessment Model for Donor Hearts in Transplantation is to take initial steps towards improving the preservation and therefore quality of donor hearts by limiting the consequences of ischaemia. The term ischaemia refers to acute circulatory failure that occurs when the blood supply is cut off from an organ, in this case the heart. This critical stage in heart transplants allows the heart to stop pumping and rest while it is transported to the recipient. This protects it for a period of 4 hours.

Within 24 hours of receiving a heart transplant, 42% of patients experience a deterioration in their cardiac contractile function, causing distress to all organs and potentially leading to rejection of the donor heart. By protecting hearts more effectively, it may be possible to limit cases of early dysfunction and complications for patients which are responsible for 40% of deaths in the months following a heart transplant. We have drawn up a protocol to compare new donor heart transport devices that are emerging on the market and claim to improve donor heart protection during transport.

1 The concept of withholding and withdrawing life-sustaining treatment should not be confused with the notions of euthanasia and assisted suicide.

Our objectives within this framework are to:
a **Identify initial magnetic resonance imaging (MRI) distress markers** validated by biochemical results (omics) by creating an objective donor heart quality assessment model.
b **Apply** a standardised protocol to assess **the performance of 3 devices that are under development or on the market** (Sherpa Pack by PARAGONYX, HEART BOX by XVIVO), alongside the routinely used method of hypothermic preservation without temperature control (icebox).

The ultimate aim of these two trials is to issue recommendations which will help optimise the management of resources used to transport donor hearts.

PSPC CALYPSO

The aim of the CALYPSO programme, in which IHU ICAN is involved, is to optimise and then clinically validate CorWave's Neptune device, a left ventricular assist device (LVAD) with physiological behaviour designed to reduce the risk of complications associated with existing LVADs and intended for patients with severe heart failure.

This project consists of 2 sub-projects:

- **ECPELLA aims to assess right ventricular function to improve eligibility selection for LVAD, thus increasing survival rates among these patients at high surgical risk (bridge to bridge).**
Haemodynamic (Swann-Ganz) and echographic data in particular were analysed to determine predictive criteria for ECMO weanability and therefore for preserved right ventricular function (a predictive factor for successful LVAD implantation).

- **IMPULSMACS, once post-operative follow-up has been completed on the last patients enrolled, it will be possible to perform omics analyses and analyses of LVAD data to determine algorithms predicting the risk of adverse effects subsequent to LVAD implantation, including severe infectious complications, right ventricular failure, pericardial effusion, major aortic valve fusion and insufficiency, haemorrhagic shock, occlusive syndromes and severe cardiac rhythm disorders.**

This collaboration showcases the ability of IHU ICAN teams to lead ambitious commercial research projects. The young French company CorWave is developing a new approach in the field of cardiac support based on a wave membrane that allows pulsatile blood flow similar to that of a native heart.

Prof. Guillaume Lebreton
Heart surgeon

The PHENIX programme offers great promise for the future of heart transplantation, as it explores several hypotheses to address the current shortage of donor hearts (with 1 heart per 2 recipients). IHU ICAN has provided me with the ideal environment in which to develop my research projects. Based on interactions with medical imaging and biotechnology experts, I was able to refine the design for the PHENIX project. Thanks to logistical and financial support from the IHU, I was also able to launch the first component of this programme with the PEGASE study in 2023. This large-scale clinical study is vital given the shortage of donor hearts currently affecting France. The IHU has been a catalyst for developing innovative and collaborative research focused on concrete outcomes for patients.

HORUS

This European project, led by Hannah Kaminski from the University of Bordeaux, seeks to improve the prediction of cytomegalovirus, which can occur as a result of anti-rejection treatment used during organ transplants, in order to improve the prevention and treatment of this infection. The ambitious objective of the HORUS project is to improve our understanding of CMV/host interactions in immunosuppressed patients, with particular emphasis on:

1. characterising signatures associated with control, or conversely CMV infection risk, post-transplant
2. characterising signatures associated with the risk of progression to refractory CMV disease
3. discovering new specific immunomodulatory molecules to help control CMV while continuing to prevent donor organ rejection

To achieve these objectives, HORUS has created the first European longitudinal cohort of solid organ (kidney, lung, heart, liver) transplant patients. The project began in June 2023.

HORUS EUROPEAN PROJECT

HORUS European project

Casting light on **HO**st-cytomegalovi**RU**s interaction in **S**olid organ transplantation

Coordination : Hannah Kaminski, MD, PhD
University of Bordeaux

Contribution UE : €7, 136, 104.42
Horizon Europe programme

Grant agreement no: 101057651
Project length: 2022-2027

What is cytomegalovirus (CMV)?

- Virus type (herpes family)
- Transmission: bodily fluids, transfusion, transplantation, etc.
- Infection in healthy people: few or no symptoms
- After infection, CMV lies dormant (inactive)

CMV effects in transplant patients

- Anti-rejection treatments -> weakens immune defences in transplant patients
- Risk of more serious opportunistic infections (viruses, bacteria, fungi)
- CMV = the most common opportunistic infection (reactivation or another infection via the donor)
- Increase in rejection risk

HORUS project aims

Establishment and monitoring of the **first European cohort** of 450 organ transplant patients

24 partners / 7 European countries

- Improve understanding of how CMV is transmitted or reactivated after transplantation
- Identify those patients more susceptible to developing CMV infection -> personalised medicine
- How immune defences are able to control CMV despite anti-rejection treatment

TRAINING
TOMORROW'S EXPERTS

International training and collaborations

Annual training camps for young researchers were launched in 2012, with the winter camp in Quebec set up by ICAN's long-standing Canadian partner, the Cardiometabolic Health, Diabetes and Obesity Research Network (CMDO). Every year, these camps provide PhD students and postdoctoral fellows with an opportunity to discover international research ecosystems, allowing them to gain experience and develop their expertise in their research disciplines. Based on the winter camp template, IHU ICAN has been holding a summer camp in Paris every year in June since 2022. This event seeks to bring together young researchers from several international research centres in order to promote collaborations outside mainland France.

In 2023, 3 nationalities took part, with 4 students from the CMDO in Quebec, 3 students from the UAE and 4 French students.

A new partnership between IHU ICAN and the United Arab Emirates University in Al Ain was forged in 2023, allowing 4 members of the ICAN community to undertake a trip to the UAE. This camp was organised within the scope of scientific collaborations between IHU ICAN and several entities in the UAE.

Report on the 2023 winter camp

The 2023 winter camp held by the CMDO network in Quebec between 2 and 11 February provided 4 PhD students and postdoctoral fellows from IHU ICAN's scientific community with the opportunity to take part in some intensive training involving interactive workshops with globally renowned lecturers. Every year, the 4-day winter camp includes 16 training modules based around the key topic of cardiometabolism. Participants were able to improve their knowledge of translational research and find out about the latest innovations for tackling cardiometabolic diseases, with a focus on diabetes and obesity treatment in Canada.

Moreover, the winter camp provided valuable opportunities to socialise and make use of this special networking space to explore new openings for basic, clinical and epidemiological postdoctoral research on cardiometabolic health across the Atlantic.

Report on the 2023 summer camp

Between 12 and 16 June, IHU ICAN was delighted to welcome young researchers from France, Quebec and the UAE to Paris for a week of training at the Sorbonne University and Pitié-Salpêtrière Hospital site.

The summer camp gave participants the opportunity to discover or learn more about scientific topics relating to cardiometabolic diseases including iPS, omics, use of health data and MASH. They also attended a course that offered guidance on careers in research, providing them with insights on potential careers in the public and private sector and equipping them to seize opportunities.

During the summer camp, I had the opportunity to visit various ICAN entities. I particularly enjoyed the tour of the MRI facility and discussions with our afternoon trainer, who introduced me to new career opportunities. The get-togethers and activities were also real highlights enabling us to make contacts with the other participants.

Anonymous feedback
from the post-camp satisfaction survey

Report on the 2023 autumn camp

Between 11 and 15 December 2023, PhD students and postdoctoral fellows from the IHU ICAN community took part in the first ever autumn camp held in Al Ain by the United Arab Emirates University. IHU ICAN was able to join this camp for young CMDO researchers in Quebec due to its partnership with CMDO.

This new autumn camp gave me a new outlook on the benefits of a healthy and sustainable diet and its impact on health and the environment. I also enjoyed learning about recommendations issued to people in the UAE to help them improve their lifestyles and communications used to convey key messages to the public. It was a real bonus to be able to share knowledge with our international counterparts!

Anonymous feedback
from the post-camp satisfaction survey

The young researchers took part in several presentation and discussion modules around the central scientific topic of "Sustainable Nutrition and Cardiometabolic Diseases". This enabled them to discover or learn more about culinary traditions in the United Arab Emirates, the concept of sustainable nutrition, and nutrition recommendations aimed at tackling cardiometabolic diseases. The camp was interspersed with nutrition-related activities and social events promoting cultural exchange.

Booklets helping patients better understand their disease

In 2023, IHU ICAN published two booklets for patients, one on heart failure and the other on MASH. These booklets are designed to help patients better understand their condition and access expert advice to improve the treatment of their chronic disease. They offer patients guidance when attending appointments with healthcare professionals and also when travelling. Patients can use the booklets to jot down their questions and any personalised recommendations made by their doctors to track the course of their cardiometabolic disease.

UMRS 1166/IHU ICAN seminar

In collaboration with UMRS 1166, IHU ICAN holds monthly face-to-face or remote scientific seminars training and briefing participants on the latest innovations and practices in the field of cardiometabolic diseases. Each expert invited by a member of the ICAN community gives a talk on a cutting-edge research topic.

WHEN	TOPIC	SPEAKER
January	Characterising RNA splicing factors involved in metabolic regulation of the liver	**Santiago Vernia** Head of the Metabolism and Gene Regulation Group - MRC London Institute of Medical Sciences Imperial College London
February	Atrial fibrillation and the pulmonary veins	**Lisa Gottlieb** Medical Doctor, PhD, Postdoctoral Researcher - Department of Biomedical Sciences, University of Copenhagen
March	Regulation of the cardiac sodium channel Nav1.5 by 14-3-3	**Isabelle Deschênes** PhD Physiology and Cell Biology - Ohio State University
April	Lp(a) and aortic stenosis	**Franck Boccara** Professor of Cardiology and Vascular Diseases - UMRS 938 - Saint-Antoine Research Centre
April	Role of Iron in Cardiovascular Diseases	**Professor Hossein Ardehali** MD, PhD - Director of the Feinberg Cardiovascular and Renal Research Institute, Center for Molecular Cardiology, Northwestern University, Chicago, USA
May	Progress and limits of designing an *in vitro* liver sinusoid on a chip: steps towards developing biomimetic multi-cell culture systems	**Mathieu Hautefeuille** Researcher - Developmental Biology Laboratory, Paris-Seine Institute of Biology, Sorbonne University
June	Importance of mitochondrial inner membrane integrity in cardiac homeostasis	**Erminia Donnarumma** Postdoctoral Research Associate - Institut Pasteur
Sept.	Adipocyte extracellular vesicles: small but powerful	**Soazig Le Lay** Institut du Thorax

SPONSORSHIP & **FUNDRAISING**

Sponsorship – an important tool driving progress with research

The **MSDAVENIR** endowment fund for health research set up by the pharmaceutical company MSD France is supporting IHU ICAN with the **ICONIC** project to create a heart/liver imaging atlas for the general population aged 20 to 80. MSDAVENIR's contribution of **€1.2 million** in the pilot phase of this project will enable the creation of **a cardiovascular and liver imaging repository in young adults aged 20 to 40 that is unique worldwide.**

The ICONIC project led by Prof. Alban Redheuil will be conducted at IHU ICAN's ICAN Imaging Platform in relation to the Inserm CONSTANCES cohort managed by Prof. Marie Zins.

As well as providing important demographic information on health, these data will also shed fresh light on causes of diseases and ageing. Moreover, they will enable us to detect diseases at a very early stage, determine new individual cardiovascular and metabolic risk profiles, and form a benchmark multimodal imaging cohort for research on common and rare diseases.

See page 49 for further information on the ICONIC project

> *ICONIC will lead to the creation of the first French multimodal imaging cohort combining ultrasound and MRI scans of the heart, vessels, liver and adipose tissue, using the latest technologies and incorporating young subjects aged under 40 from the CONSTANCES cohort. Support from MSDAVENIR is absolutely critical for completing the pilot phase of the project.*

Prof. Alban Redheuil
Cardiac Radiographer (AP-HP), Head of ICT Cardiovascular and Thoracic Imaging (Pitié-Salpêtrière Hospital), Medical and Scientific Head of ICAN Imaging (IHU ICAN)

Keen to make a major contribution, MSDAVENIR – France's leading fund supporting research in life sciences – has allocated €1.2 million to the ICONIC project led by IHU ICAN in partnership with Inserm. This combination of cardiac and hepatic imaging and epidemiology will produce unique population-based data that includes young adults: a worldwide first! Since 2015, MSD has been eager to create synergies between the public and private sectors and support researchers to encourage the emergence of innovations benefiting patients. ICONIC perfectly illustrates MSD's desire to support the most innovative research projects with a view to developing tomorrow's medicine and showcasing the excellence of French research.

Dr Golriz Pahlavan Chair of the MSDAVENIR Scientific Advisory Board

IHU ICAN steps up for the 2023 Heroes' Race!

For the second consecutive year, IHU ICAN took part in the Heroes' Race, calling on its community to raise funds for the PEGASE project that offers huge potential in the field of heart transplantation.

In this study, **donor hearts are retrieved and then transported for long periods** using an *ex-vivo* perfusion device that preserves the heart until transplantation. All the participants were up for the challenge, collecting a minimum of €250 from their networks to join the starting line of the race or walk depending on their preference. Everyone then met up afterwards to recharge their batteries with a picnic where a good time was had by all. Our small team raised nearly €5,000, which helped fund the world's first transatlantic heart transplant! This was a great achievement for all the fundraisers and donors involved in the IHU ICAN Heroes' Race.

A big thank you to everyone!

SPONSORSHIP SAVES LIVES!

In 2023, the Bouygues Group became an IHU ICAN sponsor to support research on heart transplantation. Metabolic diseases are often complicated by heart conditions such as heart failure. The final stage of heart failure is life-threatening for patients if they are unable to obtain a heart transplant. However, France is currently facing a donor heart shortage. It is therefore vital to speed up research on heart transplantation, so that potential donor hearts currently excluded from the system can be used. Sponsorship is essential for funding this cutting-edge research. The entire IHU ICAN team would like to sincerely thank Bouygues for agreeing to support the PEGASE pilot study.

"As a sponsor, Bouygues is delighted to be supporting the PEGASE project launched by IHU ICAN and led by the heart surgeon Guillaume Lebreton to increase heart transplant numbers by using an ex-vivo perfusion device that preserves the heart until transplantation. Bouygues' donation in 2023 enabled the launch of this project with a first heart transplant carried out in January of this year at Pitié-Salpêtrière Hospital. This proved successful, paving the way for other opportunities relating to the extended preservation of vital organs."

Pierre Auberger,
Corporate Communications
Director of the Bouygues Group

© Sophie Loubaton

In 2023, IHU ICAN

raised over

€1 million

thanks to the generosity of committed sponsors.

Many thanks to our sponsors:

ADICARE

BIOTRONIK

BOSTON SCIENTIFIC

BOUYGUES

CRÉDIT AGRICOLE MÉCÉNAT IDF

ENTREPRENEURS AND GO

FRENCH FEDERATION OF CARDIOLOGY

CARREFOUR FOUNDATION

CONSTANCE AND ANDREI RHOE FOUNDATION

TRIOMPHE DU CŒUR FOUNDATION

SICAME GROUP ENDOWMENT FUND

MEDTRONIC

MSDAVENIR

NELLI MEDICAL

Mrs FOTIADI

YOUR DONATIONS ARE VITAL
Thank you

HR & FINANCIAL **REPORT**

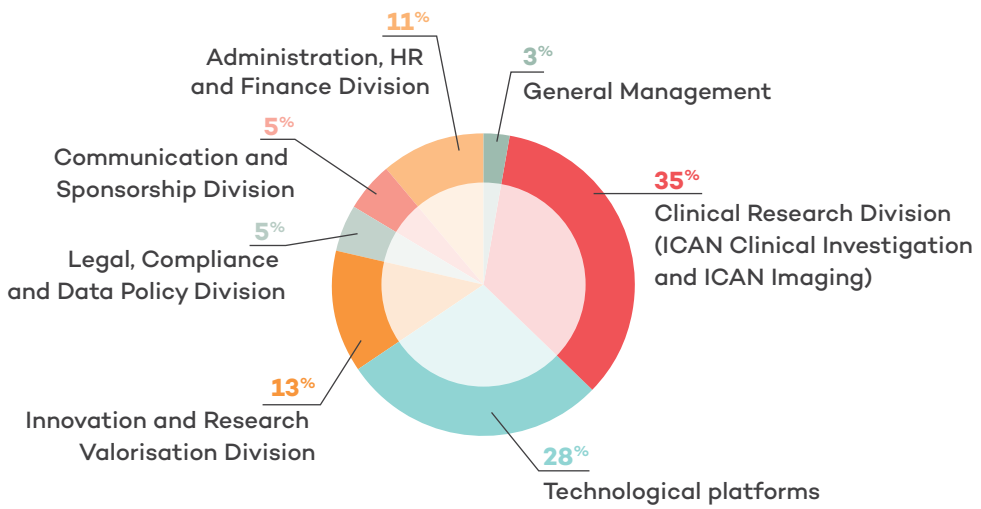
HR

74% WOMEN

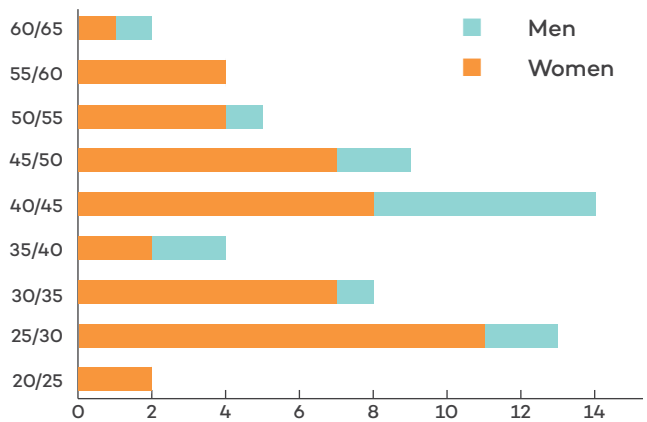
26% MEN

915 HRS OF TRAINING

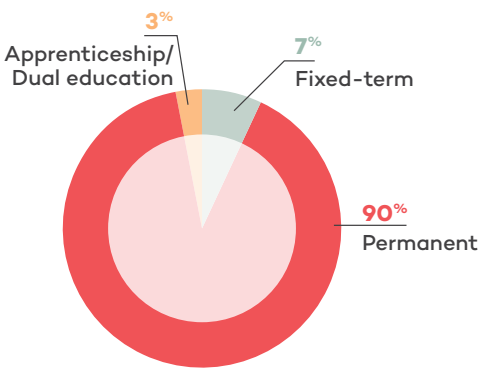
STAFF BREAKDOWN



BREAKDOWN BY AGE BRACKET



BREAKDOWN BY CONTRACT TYPE



Report on the Foundation's position and development over the 2023 financial year

In 2023, the IHU continued its policy of prudent and careful financial management.

Over the course of 2023, the Foundation saw a sharp increase in its operating income, reflecting increased activity in terms of project management and research collaboration and services, as well as a continued rise in revenue derived from public fundraising. Income for this financial year was up 50% from the previous financial year, rising from €4.978 M in 2022 to €7.454 M in 2023. However, project-dedicated funds carried forward accounted for a significant proportion of operating income due to funding allocated to multiannual projects.

Over the course of the financial year, the Foundation continued to implement its fundraising (sponsorship) strategy set out in the 2020-2024 financial trajectory. Financial support from sponsors rose significantly, up 60% from 2022 (€1.09 M vs. €591,000). 2023 notably saw the signing of the MSDAVENIR agreement concerning a contribution to the ICONIC project (€1.2 million over 3 years of which €560,000 was paid in 2023).

FOCUS on sponsorship activity

Income from sponsorship activity collected over the 2023 financial year

Private donors	35,320
Companies	183,135
Foundations/Associations	872,699
	1,091,154

The research and clinical investigation platforms continued their high level of activity with 60 studies in progress in 2023 (34 commercial studies and 26 academic studies) of which 23 were new and 20 were completed. Income for services (sales of output) was up €1.228 M compared to the previous financial year at a sum of €2.267 M for 2023.

Operating expenses were up 44% from the previous financial year (€5.787 M in 2022 vs. €8.335 M in 2023) due mainly to a €2.261 M increase in expenses relating to project-dedicated funds carried forward between the two financial years.

Balance sheet

The balance sheet total as at 31 December 2023 was €12,914,756.

As at 31 December 2023, the Institute's assets and liabilities broke down as follows:

ASSETS	LIABILITIES
1. Fixed assets: €1,583,526	**3. Association funds: €3,232,842** (Foundation endowment, profit/loss for the financial year, carry-forward and investment subsidy)
2. Current assets: €11,331,231 (Accounts receivable, available funds, deferred expenditure)	**4. Provisions and dedicated funds: €4,166,539** (Provisions for contingencies, dedicated funds related to other resources)
	5. Accounts payable: €5,515,375 (Trade payable, tax and social contributions payable, other amounts payable, deferred revenue)

As at 31 December 2023, there were provisions of €164,400 and dedicated funds of €4,002,139, relating to operating income that was accounted for as ICAN income in the year that it was paid, but for which the corresponding expenditure had not been incurred as at 2023 year-end.

This essentially relates to projects funded by private foundations, the French National Research Agency (ANR) and the EU.

2023 restated income statement

	2023
Service and sales revenues	2,266,960
Grants, subsidies and awards	1,675,968
PIA IHU grant (ANR)	1,572,017
Sponsorship (including financial contributions)	1,091,154
Consumption of project-dedicated funds	834,708
Other revenues	13,219
TOTAL OPERATING INCOME	**7,454,026**
Operating expenses	(1,850,087)
Depreciation and provision expenses	(464,459)
Employees	(3,259,380)
Project-dedicated funds carried forward	(2,761,096)
TOTAL OPERATING EXPENSES	**(8,335,022)**
Financial profit/loss	144,897
PRE-TAX PROFIT/LOSS	**(736,098)**
Exceptional profit/loss	(1,923)
TOTAL INCOME	**7,732,560**
TOTAL EXPENSES	**(8,470,581)**
NET PROFIT/LOSS	**(738,021)**

Financial statement by income source and expense type

A - INCOME AND EXPENSES BY SOURCE AND TYPE	FINANCIAL YEAR N	
	TOTAL	Portion raised from the public*
INCOME BY SOURCE		
1 - INCOME FROM PUBLIC FUNDRAISING		
1.1 Subscriptions without consideration		
1.2 Donations, legacies and sponsorship		
- Donations by hand	47,500	47,500
- Legacies, gifts and life insurance policies		
- Sponsorship	170,955	170,955
1.3 Other income from public fundraising		
2 - INCOME FROM SOURCES OTHER THAN PUBLIC FUNDRAISING		
2.1 Subscriptions with consideration		
2.2 Corporate sponsorship		
2.3 Financial contributions without consideration	872,699	
2.4 Other income from sources other than public fundraising	4,126,867	
3 - GRANTS AND OTHER PUBLIC COMPETITIONS	1,675,968	
4 - WRITE-BACK OF PROVISIONS AND DEPRECIATION	3,863	
5 - USE OF PREVIOUS DEDICATED FUNDS	834,708	32,439
TOTAL	**7,732,560**	**250,894**
EXPENSES BY TYPE		
1 - SOCIAL MISSIONS		
1.1 Carried out in France		
- Initiatives implemented by the organisation	4,194,682	171,135
- Payments to a central organisation or other organisations operating in France		
1.2 Implemented abroad		
- Initiatives implemented by the organisation		
- Payments to a central organisation or other organisations operating in France		
2 - FUNDRAISING EXPENSES		
2.1 Public fundraising expenses	23,724	23,724
2.2 Expenses for raising income from other sources	94,776	
3 - OPERATING EXPENSES	1,322,554	
4 - DEPRECIATION AND PROVISION EXPENSES	73,750	
5 - PROFITS TAX		
6 - PROJECT-DEDICATED FUNDS CARRIED FORWARD	2,761,096	56,035
TOTAL	**8,470,581**	**250,894**
SURPLUS OR DEFICIT	-738,021	-

Financial contributions are not included in the financial statement by income source and expense type.

PUBLICATIONS
2023

10 key articles

1. Schmidt M, Hajage D, Lebreton G, Dres M, Guervilly C, Richard JC, Sonneville R, Winiszewski H, Muller G, Beduneau G, Mercier E, Roze H, Lesouhaitier M, Terzi N, Thille AW, Laurent I, Kimmoun A, Combes A ; PRONECMO Investigators, the REVA Network, and the International ECMO Network (ECMONet). **Prone Positioning During Extracorporeal Membrane Oxygenation in Patients With Severe ARDS: The PRONECMO Randomized Clinical Trial**. JAMA. 2023 Dec 26;330(24):2343-2353. doi: 10.1001/jama.2023.24491. PMID: 38038395

2. Ratziu V, Harrison SA, Hajji Y, Magnanensi J, Petit S, Majd Z, Delecroix E, Rosenquist C, Hum D, Staels B, Anstee QM, Sanyal AJ. **NIS2+(TM) as a screening tool to optimize patient selection in metabolic dysfunction-associated steatohepatitis clinical trials**. J Hepatol. 2024 Feb;80(2):209-219. doi: 10.1016/j.jhep.2023.10.038. Epub 2023 Dec 5.PMID: 38061448

3. Danial P, Olivier ME, Bréchot N, Ponnaiah M, Schoell T, D'Alessandro C, Demondion P, Clément M, Juvin C, Carillion A, Bouglé A, Combes A, Leprince P, Lebreton G. **Association Between Shock Etiology and 5-Year Outcomes After Venoarterial Extracorporeal Membrane Oxygenation**.J Am Coll Cardiol. 2023 Mar 7;81(9):897-909. doi: 10.1016/j.jacc.2022.12.018.PMID: 36858709

4. Urbain F, Ponnaiah M, Ichou F, Lhomme M, Materne C, Galier S, Haroche J, Frisdal E, Mathian A, Durand H, Pha M, Hie M, Kontush A, Cluzel P, Lesnik P, Amoura Z, Guerin M, Cohen Aubart F, Le Goff W. **Impaired metabolism predicts coronary artery calcification in women with systemic lupus erythematosus**. EBioMedicine. 2023 Oct;96:104802. doi: 10.1016/j.ebiom.2023.104802. Epub 2023 Sep 17.PMID: 37725854

5. Andrikopoulos P, Aron-Wisnewsky J, Chakaroun R, Myridakis A, Forslund SK, Nielsen T, Adriouch S, Holmes B, Chilloux J, Vieira-Silva S, Falony G, Salem JE, Andreelli F, Belda E, Kieswich J, Chechi K, Puig-Castellvi F, Chevalier M, Le Chatelier E, Olanipekun MT, Hoyles L, Alves R, Helft G, Isnard R, Køber L, Coelho LP, Rouault C, Gauguier D, Gøtze JP, Prifti E, Froguel P; MetaCardis Consortium; Zucker JD, Bäckhed F, Vestergaard H, Hansen T, Oppert JM, Blüher M, Nielsen J, Raes J, Bork P, Yaqoob MM, Stumvoll M, Pedersen O, Ehrlich SD, Clément K, Dumas ME. **Evidence of a causal and modifiable relationship between kidney function and circulating trimethylamine N-oxide**. Nat Commun. 2023 Sep 20;14(1):5843. doi: 10.1038/s41467-023-39824-4.PMID: 37730687

6. Guillas I, Lhomme M, Pionneau C, Matheron L, Ponnaiah M, Galier S, Lebreton S, Delbos M, Ma F, Darabi M, Khoury PE, Abifadel M, Couvert P, Giral P, Lesnik P, Guerin M, Le Goff W, Kontush A.. **Identification of the specific molecular and functional signatures of pre-beta-HDL: relevance to cardiovascular disease**.Basic Res Cardiol. 2023 Aug 28;118(1):33. doi: 10.1007/s00395-023-01004-2. PMID: 37639039

7. Ha Van G, Schuldiner S, Sultan A, Bouillet B, Martini J, Vouillarmet J, Menai M, Foucher A, Bourron O, Hartemann A, Perrier A. **Use of the SINBAD score as a predicting tool for major adverse foot events in patients with diabetic foot ulcer: A French multicentre study**. Diabetes Metab Res Rev. 2023 Nov;39(8):e3705. doi: 10.1002/dmrr.3705. Epub 2023 Jul 31.PMID: 37525456

8. Hermida A, Ader F, Millat G, Jedraszak G, Maury P, Cador R, Catalan PA, Clerici G, Combes N, De Groote P, Dupin-Deguine D, Eschalier R, Faivre L, Garcia P, Guillon B, Janin A, Kugener B, Lackmy M, Laredo M, Le Guillou X, Lesaffre F, Lucron H, Milhem A, Nadeau G, Nguyen K, Palmyre A, Perdreau E, Picard F, Rebotier N, Richard P, Rooryck C, Seitz J, Verloes A, Vernier A, Winum P, Yabeta GA, Bouchot O, Chevalier P, Charron P, Gandjbakhch E. **NEXN Gene in Cardiomyopathies and Sudden Cardiac Deaths: Prevalence, Phenotypic Expression, and Prognosis** Circ Genom Precis Med. 2024 Feb;17(1):e004285. doi: 10.1161/CIRCGEN.123.004285. Epub 2023 Dec 7.PMID: 38059363

9. Gosseaume C, Fournier T, Jéru I, Vignaud ML, Missotte I, Archambeaud F, Debussche X, Droumaguet C, Fève B, Grillot S, Guerci B, Hieronimus S, Horsmans Y, Nobécourt E, Pienkowski C, Poitou C, Thissen JP, Lascols O, Degrelle S, Tsatsaris V, Vigouroux C, Vatier C. **Perinatal, metabolic, and reproductive features in PPARG-related lipodystrophy.** Eur J Endocrinol. 2023 Mar 2;188(3):lvad023. doi: 10.1093/ejendo/lvad023. PMID: 36806620

10. Winters J, Isaacs A, Zeemering S, Kawczynski M, Maesen B, Maessen J, Bidar E, Boukens B, Hermans B, van Hunnik A, Casadei B, Fabritz L, Chua W, Sommerfeld L, Guasch E, Mont L, Batlle M, Hatem S, Kirchhof P, Wakili R, Sinner M, Stoll M, Goette A, Verheule S, Schotten U. **Heart Failure, Female Sex, and Atrial Fibrillation Are the Main Drivers of Human Atrial Cardiomyopathy: Results From the CATCH ME Consortium**. J Am Heart Assoc. 2023 Nov 20;12(22):e031220. doi: 10.1161/JAHA.123.031220. Online ahead of print. PMID: 37982389

2023 articles with a SIGAPS score greater than or equal to 18

1. Schmidt M, Hajage D, Lebreton G, Dres M, Guervilly C, Richard JC, Sonneville R, Winiszewski H, Muller G, Beduneau G, Mercier E, Roze H, Lesouhaitier M, Terzi N, Thille AW, Laurent I, Kimmoun A, Combes A Prone Positioning During Extracorporeal Membrane Oxygenation in Patients With Severe ARDS: The PRONECMO Randomized Clinical Trial. JAMA 2023 PMID: 38038395

2. Freund Y, Viglino D, Cachanado M, Cassard C, Montassier E, Douay B, Guenezan J, Le Borgne P, Yordanov Y, Severin A, Roussel M, Daniel M, Marteau A, Peschanski N, Teissandier D, Macrez R, Morere J, Chouihed T, Roux D, Adnet F, Bloom B, Chauvin A, Simon T Effect of Noninvasive Airway Management of Comatose Patients With Acute Poisoning: A Randomized Clinical Trial. JAMA 2023 PMID: 38019968

3. Freund Y, Cohen-Aubart F, Bloom B Review of Pulmonary Embolism-Reply. JAMA 2023 PMID: 36809325

4. Fenioux C, Abbar B, Boussouar S, Bretagne M, Power JR, Moslehi JJ, Gougis P, Amelin D, Dechartres A, Lehmann LH, Courand PY, Cautela J, Alexandre J, Procureur A, Rozes A, Leonard-Louis S, Qin J, Cheynier R, Charmeteau-De Muylder B, Redheuil A, Tubach F, Cadranel J, Milon A, Ederhy S, Similoswki T, Johnson DB, Pizzo I, Catalan T, Benveniste O, Hayek SS, Allenbach Y, Rosenzwajg M, Dolladille C, Salem JE Thymus alterations and susceptibility to immune checkpoint inhibitor myocarditis. Nat Med 2023 PMID: 37884625

5. Schmidt M, Hajage D, Landoll M, Pequignot B, Langouet E, Amalric M, Mekontso-Dessap A, Chiscano-Camon L, Surman K, Finnerty D, Santa-Teresa P, Arcadipane A, Millán P, Roncon-Albuquerque R, Blandino-Ortiz A, Blanco-Schweizer P, Ricart P, Gimeno-Costa R, Albacete CL, Fortuna P, Schellongowski P, Dauwe D, Winiszewski H, Kimmoun A, Levy B, Hermans G, Grasselli G, Lebreton G, Guervilly C, Martucci G, Karagiannidis C, Riera J, Combes A Comparative outcomes of extracorporeal membrane oxygenation for COVID-19 delivered in experienced European centres during successive SARS-CoV-2 variant outbreaks (ECMO-SURGES): an international, multicentre, retrospective cohort study. Lancet Respir Med 2023 PMID: 36640786

6. Dubern B, Clément K Unravelling leptin variants: advancing precision medicine in obesity. Nat Rev Endocrinol 2023 PMID: 37525005

7. Huang F, Ammirati E, Ponnaiah M, Montero S, Raimbault V, Abrams D, Lebreton G, Pellegrino V, Ihle J, Bottiroli M, Persichini R, Barrionuevo-Sánchez MI, Ariza-Solé A, Ng PY, Sin SWC, Ayer R, Buscher H, Belaid S, Delmas C, Ferreira R, Albuquerque RR, L?pez-Sobrino T, Bunge JJH, Fisser C, Franchineau G, McCanny J, Ohshimo S, Sionis A, Hernández-Pérez FJ, Barge-Caballero E, Balik M, Muglia H, Park S, Donker DW, Porral B, Aïssaoui N, Mekontso Dessap A, Burgos V, Lesouhaitier M, Fried J, Jung JS, Rosillo S, Scherrer V, Nseir S, Winszewski H, Jorge-Pérez P, Kimmoun A, Diaz R, Combes A, Schmidt M Fulminant myocarditis proven by early biopsy and outcomes. Eur Heart J 2023 PMID: 37941449

8. Roussel M, Bloom B, Taalba M, Choquet C, Douillet D, Fémy F, Marouk A, Gorlicki J, Gerlier C, Macrez R, Arnaud E, Bompard R, Montassier E, Hugli O, Czopik C, Eyer X, Benhamed A, Peyrony O, Chouihed T, Penaloza A, Marra A, Laribi S, Reuter PG, Behringer W, Douplat M, Guenezan J, Javaud N, Lucidarme O, Cachanado M, Aparicio-Monforte A, Freund Y Temporal Trends in the Use of Computed Tomographic Pulmonary Angiography for Suspected Pulmonary Embolism in the Emergency Department : A Retrospective Analysis. Ann Intern Med 2023 PMID: 37216659

9. Roussel M, Teissandier D, Yordanov Y, Balen F, Noizet M, Tazarourte K, Bloom B, Catoire P, Berard L, Cachanado M, Simon T, Laribi S, Freund Y Overnight Stay in the Emergency Department and Mortality in Older Patients. JAMA Intern Med 2023 PMID: 37930696

10. Ammirati E, Vorovich E, Combes A Myocarditis: a primer for intensivists. Intensive Care Med 2023 PMID: 37430155

11. Lehmann LH, Heckmann MB, Bailly G, Finke D, Procureur A, Power JR, Stein F, Bretagne M, Ederhy S, Fenioux C, Hamwy O, Funck-Brentano E, Romano E, Pieroni L, Münster J, Allenbach Y, Anquetil C, Leonard-Louis S, Palaskas NL, Hayek SS, Katus HA, Giannitsis E, Frey N, Kaya Z, Moslehi J, Prifti E, Salem JE Cardiomuscular Biomarkers in the Diagnosis and Prognostication of Immune Checkpoint Inhibitor Myocarditis. Circulation 2023 PMID: 37317858

12. Salem JE, Bretagne M, Abbar B, Leonard-Louis S, Ederhy S, Redheuil A, Boussouar S, Nguyen LS, Procureur A, Stein F, Fenioux C, Devos P, Gougis P, Dres M, Demoule A, Psimaras D, Lenglet T, Maisonobe T, Pineton DE Chambrun M, Hekimian G, Straus C, Gonzalez-Bermejo J, Klatzmann D, Rigolet A, Guillaume-Jugnot P, Champtiaux N, Benveniste O, Weiss N, Saheb S, Rouvier P, Plu I, Gandjbakhch E, Kerneis M, Hammoudi N, Zahr N, Llontop C, Morelot-Panzini C, Lehmann L, Qin J, Moslehi JJ, Rosenzwajg M, Similowski T, Allenbach Y Abatacept/Ruxolitinib and Screening for Concomitant Respiratory Muscle Failure to Mitigate Fatality of Immune-Checkpoint Inhibitor Myocarditis. Cancer Discov 2023 PMID: 36815259

13. Ratziu V, Harrison SA, Hajji Y, Magnanensi J, Petit S, Majd Z, Delecroix E, Rosenquist C, Hum D, Staels B, Anstee QM, Sanyal AJ NIS2+™ as a screening tool to optimize patient selection in metabolic dysfunction-associated steatohepatitis clinical trials. J Hepatol 2023 PMID: 38061448

14. Pais R, Cariou B, Noureddin M, Francque S, Schattenberg JM, Abdelmalek MF, Lalazar G, Varma S, Dietrich J, Miller V, Sanyal A, Ratziu V A proposal from the Liver Forum for the management of comorbidities in nonalcoholic steatohepatitis therapeutic trials. J Hepatol 2023 PMID: 37001695

15. Ratziu V, Harrison SA, Loustaud-Ratti V, Bureau C, Lawitz E, Abdelmalek M, Alkhouri N, Francque S, Girma H, Darteil R, Couchoux H, Wolf M, Sanyal A, Vonderscher J, Scalfaro P Hepatic and renal improvements with FXR agonist vonafexor in individuals with suspected fibrotic NASH. J Hepatol 2023 PMID: 36334688

16. Franchineau G, Jonkman AH, Piquilloud L, Yoshida T, Costa E, Rozé H, Camporota L, Piraino T, Spinelli E, Combes A, Alcala GC, Amato M, Mauri T, Frerichs I, Brochard LJ, Schmidt M Electrical Impedance Tomography to Monitor Hypoxemic Respiratory Failure. Am J Respir Crit Care Med 2023 PMID: 38127779

17. Chommeloux J, Valentin S, Winiszewski H, Adda M, de Chambrun MP, Moyon Q, Mathian A, Capellier G, Guervilly C, Levy B, Jaquet P, Sonneville R, Voiriot G, Demoule A, Boussouar S, Painvin B, Lebreton G, Combes A, Schmidt M One-Year Mental and Physical Health Assessment in Survivors after Extracorporeal Membrane Oxygenation for COVID-19-related Acute Respiratory Distress Syndrome Am. J. Respir. Crit. Care Med. 2023 PMID: 36150112

18. Danial P, Olivier ME, Bréchot N, Ponnaiah M, Schoell T, D'Alessandro C, Demondion P, Clément M, Juvin C, Carillion A, Bouglé A, Combes A, Leprince P, Lebreton G Association Between Shock Etiology and 5-Year Outcomes After Venoarterial Extracorporeal Membrane Oxygenation. J Am Coll Cardiol 2023 PMID: 36858709

19. Peyronel F, Haroche J, Campochiaro C, Pegoraro F, Amoura Z, Tomelleri A, Mazzariol M, Papo M, Cavalli G, Benigno GD, Fenaroli P, Grigoratos C, Mengoli MC, Bonometti A, Berti E, Savino G, Cives M, Neri I, Pacinella G, Tuttolomondo A, Marano M, Muratore F, Manfredi A, Broccoli A, Zinzani PL, Didona B, Massaccesi C, Buono A, Ammirati E, Di Lernia V, Dagna L, Vaglio A, Cohen Aubart F EPIDEMIOLOGY AND GEOGRAPHIC CLUSTERING OF ERDHEIM-CHESTER DISEASE IN ITALY AND FRANCE. Blood 2023 PMID: 37871575

20. Wai-Sun Wong V, Anstee QM, Nitze LM, Geerts A, George J, Nolasco V, Kjær MS, Ladelund S, Newsome PN, Ratziu V FibroScan-aspartate aminotransferase (FAST) score for monitoring histological improvement in non-alcoholic steatohepatitis activity during semaglutide treatment: post-hoc analysis of a randomised, double-blind, placebo-controlled, phase 2b trial. EClinicalMedicine 2023 PMID: 38058795

21. Guérin E, Belin L, Franchineau G, Le Guennec L, Hajage D, Diallo MH, Frapard T, Le Fèvre L, Luyt CE, Combes A, Germain S, Hayon J, Asfar P, Bréchot N FX06 to rescue SARS-CoV-2-induced acute respiratory distress syndrome: a randomized clinical trial. Crit Care 2023 PMID: 37641136

22. Velly L, Cancella de Abreu M, Boutolleau D, Cherubini I, Houas E, Aurousseau A, Hausfater P Point-of-care multiplex molecular diagnosis coupled with procalcitonin-guided algorithm for antibiotic stewardship in lower respiratory tract infection: a randomized controlled trial. Clin Microbiol Infect 2023 PMID: 37549731

23. Chasset F, Jaume L, Mathian A, Abisror N, Dutheil A, Barbaud A, Kottler D, Girard C, Jousse-Joulin S, Tauber M, Livideanu CB, Avettand-Fenoel V, Lhote R, Pha M, Amoura Z Rapid Efficacy of anifrolumab in refractory cutaneous lupus erythematosus: a prospective study of 11 patients with systemic lupus erythematosus. J Am Acad Dermatol 2023 PMID: 36878316

24. Corpechot C, Lemoinne S, Soret PA, Chazouillères O, de Lédinghen V Reply: Improving access to transient elastography data for Real-World Prognostic Applications in primary biliary cholangitis. Hepatology 2023 PMID: 38150175

25. Ratziu V, Francque S, Behling CA, Cejvanovic V, Cortez-Pinto H, Iyer JS, Krarup N, Le Q, Sejling AS, Tiniakos D, Harrison SA Artificial intelligence scoring of liver biopsies in a phase ii trial of semaglutide in non-alcoholic steatohepatitis. Hepatology 2023 PMID: 38112484

26. Corpechot C, Lemoinne S, Soret PA, Hansen B, Hirschfield G, Gulamhusein A, Montano-Loza AJ, Lytvyak E, Pares A, Olivas I, Eaton JE, Osman KT, Schramm C, Sebode M, Lohse AW, Dalekos G, Gatselis N, Nevens F, Cazzagon N, Zago A, Russo FP, Floreani A, Abbas N, Trivedi P, Thorburn D, Saffioti F, Barkai L, Roccarina D, Calvaruso V, Fichera A, Delamarre A, Sobenko N, Villamil AM, Medina-Morales E, Bonder A, Patwardhan V, Rigamonti C, Carbone M, Invernizzi P, Cristoferi L, van der Meer A, de Veer R, Zigmond E, Yehezkel E, Kremer AE, Deibel A, Bruns T, Große K, Wetten A, Dyson JK, Jones D, Dumortier J, Pageaux GP, de Lédinghen V, Chazouillères O, Carrat F Adequate vs. deep response to UDCA in PBC: To what extent and under what conditions is normal ALP level associated with complication-free survival gain? Hepatology 2023 PMID: 37399238

27. Ratziu V, Reau N Reply: more questions than answers: response to the POP-NEXT project. Hepatology 2023 PMID: 37329168

28. Mallet M, Silaghi CA, Sultanik P, Conti F, Rudler M, Ratziu V, Thabut D, Pais R Current challenges and future perspectives in treating patients with NAFLD-related cirrhosis. Hepatology 2023 PMID: 37183906

29. Allaire M, Thabut D Reply: portal hypertension and variceal bleeding in patients with liver cancer: evidence gaps for prevention and management. Hepatology 2023 PMID: 36896969

30. Allaire M, Thabut D Portal hypertension and variceal bleeding in patients with liver cancer: Evidence gaps for prevention and management. Hepatology 2023 PMID: 36631021

31. Urbain F, Ponnaiah M, Ichou F, Lhomme M, Materne C, Galier S, Haroche J, Frisdal E, Mathian A, Durand H, Pha M, Hie M, Kontush A, Cluzel P, Lesnik P, Amoura Z, Guerin M, Cohen Aubart F, Le Goff W Impaired metabolism predicts coronary artery calcification in women with systemic lupus erythematosus. EBioMedicine 2023 PMID: 37725854

32. Coppens A, Zahr N, Chommeloux J, Bleibtreu A, Hekimian G, de Chambrun MP, LeFevre L, Schmidt M, Robert J, Junot H, Combes A, Luyt CE Pharmacokinetic/pharmacodynamic of ceftobiprole in patients on ECMO. Int J Antimicrob Agents 2023 PMID: 36804372

33. Dubern B, Faccioli N, Poitou C, Clément K Novel therapeutics in rare genetic obesities: A narrative review. Pharmacol Res 2023 PMID: 37037398

34. Soubrane O, Scatton O The development of Transplant Oncology may worsen the liver gap and needs new technical options in liver transplantation. Ann Surg 2023 PMID: 37622319

35. Amarenco P, Lavallée PC, Kim JS, Labreuche J, Charles H, Giroud M, Lee BC, Mahagne MH, Meseguer E, Nighoghossian N, Steg PG, Vicaut É, Bruckert E "More Than 50 Percent Reduction in LDL Cholesterol in Patients With Target LDL <70 mg/dL After a Stroke." Stroke 2023 PMID: 37376989

36. Soret PA, Lemoinne S, Mallet M, Belkacem KB, Chazouillères O, Corpechot C Obeticholic acid as a second-line treatment for low phospholipid-associated cholelithiasis syndrome. Aliment Pharmacol Ther 2023 PMID: 37818704

37. Poynard T, Deckmyn O, Peta V, Paradis V, Gautier JF, Brzustowski A, Bedossa P, Castera L, Pol S, Valla D Prospective direct comparison of non-invasive liver tests in outpatients with type 2 diabetes using intention-to-diagnose analysis. Aliment Pharmacol Ther 2023 PMID: 37642160

38. Allaire M, Campion B, Demory A, Larrey E, Wagner M, Rudler M, Roux C, Blaise L, Carrie NG, Thabut D Baveno VI and VII criteria are not suitable for screening for large varices or clinically significant portal hypertension in patients with hepatocellular carcinoma. Aliment Pharmacol Ther 2023 PMID: 37300315

39. Bachelot G, Dhombres F, Sermondade N, Haj Hamid R, Berthaut I, Frydman V, Prades M, Kolanska K, Selleret L, Mathieu-D'Argent E, Rivet-Danon D, Levy R, Lamazière A, Dupont C A Machine Learning Approach for the Prediction of Testicular Sperm Extraction in Nonobstructive Azoospermia: Algorithm Development and Validation Study. J Med Internet Res 2023 PMID: 37342078

40. Silvain J, Lattuca B, Puymirat E, Ducrocq G, Dillinger JG, Lhermusier T, Procopi N, Cachanado M, Drouet E, Abergel H, Danchin N, Montalescot G, Simon T, Steg PG Impact of transfusion strategy on platelet aggregation and biomarkers in myocardial infarction patients with anemia. Eur Heart J Cardiovasc Pharmacother 2023 PMID: 37609995

41. Pasqua R, Davaine JM Paediatric Vascular Surgery with Total Visceral and Renal Vessel Replacement. Eur J Vasc Endovasc Surg 2023 PMID: 36273678

42. Levy JH, Frere C, Koster A Resistance to unfractionated heparin in the ICU: evaluation and management options. Intensive Care Med 2023 PMID: 37278759

43. Sanyal AJ, Ratziu V, Loomba R, Anstee QM, Kowdley KV, Rinella ME, Sheikh MY, Trotter JF, Knapple W, Lawitz EJ, Abdelmalek MF, Newsome PN, Boursier J, Mathurin P, Dufour JF, Berrey MM, Shiff SJ, Sawhney S, Capozza T, Leyva R, Harrison SA, Younossi ZM Results from a new efficacy and safety analysis of the REGENERATE trial of obeticholic acid for treatment of pre-cirrhotic fibrosis due to nonalcoholic steatohepatitis. J Hepatol 2023 PMID: 37517454

44. Harrison SA, Ratziu V, Magnanensi J, Hajji Y, Deledicque S, Majd Z, Rosenquist C, Hum D, Staels B, Anstee QM, Sanyal AJ NIS2+™, an optimization of the blood-based biomarker NIS4® technology for the detection of at-risk NASH: a prospective derivation and validation study. J Hepatol 2023 PMID: 37224923

45. Andrikopoulos P, Aron-Wisnewsky J, Chakaroun R, Myridakis A, Forslund SK, Nielsen T, Adriouch S, Holmes B, Chilloux J, Vieira-Silva S, Falony G, Salem JE, Andreelli F, Belda E, Kieswich J, Chechi K, Puig-Castellvi F, Chevalier M, Le Chatelier E, Olanipekun MT, Hoyles L, Alves R, Helft G, Isnard R, Køber L, Coelho LP, Rouault C, Gauguier D, Gøtze JP, Prifti E, Froguel P, Zucker JD, Bäckhed F, Vestergaard H, Hansen T, Oppert JM, Blüher M, Nielsen J, Raes J, Bork P, Yaqoob MM, Stumvoll M, Pedersen O, Ehrlich SD, Clément K, Dumas ME Evidence of a causal and modifiable relationship between kidney function and circulating trimethylamine N-oxide. Nat Commun 2023 PMID: 37730687

46. Roeser A, Bravetti M, Dong LD, Azoulay LD, Charlotte F, Miyara M, Ghillani-Dalbin P, Emile JF, El Kouari F, Ouni H, Lacorte JM, Brocheriou I, Amoura Z, Cohen-Aubart F, Haroche J Serum vascular endothelial growth factor is associated with cardiovascular involvement and response to therapy in Erdheim-Chester disease Haematologica 2023 PMID: 36005561

47. Guillas I, Lhomme M, Pionneau C, Matheron L, Ponnaiah M, Galier S, Lebreton S, Delbos M, Ma F, Darabi M, Khoury PE, Abifadel M, Couvert P, Giral P, Lesnik P, Guerin M, Le Goff W, Kontush A Identification of the specific molecular and functional signatures of pre-beta-HDL: relevance to cardiovascular disease. Basic Res Cardiol 2023 PMID: 37639039

48. Giani M, Rezoagli E, Guervilly C, Rilinger J, Duburcq T, Petit M, Textoris L, Garcia B, Wengenmayer T, Bellani G, Grasselli G, Pesenti A, Combes A, Foti G, Schmidt M Timing of Prone Positioning During Venovenous Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome Crit. Care Med. 2023 PMID: 36519981

49. Cazzagon N, Gonzalez-Sanchez E, El-Mourabit H, Wendum D, Rainteau D, Humbert L, Corpechot C, Chazouillères O, Arrivé L, Housset C, Lemoinne S Protective potential of the gallbladder in primary sclerosing cholangitis. JHEP Rep 2023 PMID: 36923239

50. Massart N, Camus C, Nesseler N, Fillâtre P, Flecher E, Mansour A, Verhoye JP, Le Fevre L, Luyt CE Multiple-site decontamination to prevent acquired infection in patients with veno-venous ECMO support. Ann Intensive Care 2023 PMID: 37024761

51. Bourcier S, Coutrot M, Ferré A, Van Grunderbeeck N, Charpentier J, Hraiech S, Azoulay E, Nseir S, Aissaoui N, Messika J, Fillatre P, Persichini R, Carreira S, Lautrette A, Delmas C, Terzi N, Mégarbane B, Lascarrou JB, Razazi K, Repessé X, Pichereau C, Contou D, Frérou A, Barbier F, Ehrmann S, de Montmollin E, Sztrymf B, Morawiec E, Bigé N, Reuter D, Schnell D, Ellrodt O, Dellamonica J, Combes A, Schmidt M Critically ill severe hypothyroidism: a retrospective multicenter cohort study. Ann Intensive Care 2023 PMID: 36892784

52. Ha Van G, Schuldiner S, Sultan A, Bouillet B, Martini J, Vouillarmet J, Menai M, Foucher A, Bourron O, Hartemann A, Perrier A "Use of the SINBAD score as a predicting tool for major adverse foot events in patients with diabetic foot ulcer: A French multicentre study." Diabetes Metab Res Rev 2023 PMID: 37525456

53. Ha Van G, Schuldiner S, Sultan A, Bouillet B, Martini J, Vouillarmet J, Menai M, Foucher A, Bourron O, Hartemann A, Perrier A Use of the SINBAD score as a predicting tool for major adverse foot events in patients with diabetic foot ulcer: A French multicentre study Diabetes-Metab. Res. Rev. 2023 PMID: 37525456

54. Vali A, Dalle H, Loubaresse A, Gilleron J, Havis E, Garcia M, Beaupère C, Denis C, Roblot N, Poussin K, Ledent T, Bouillet B, Cormont M, Tanti JF, Capeau J, Vatier C, Fève B, Grosfeld A, Moldes M Adipocyte glucocorticoid receptor activation with high glucocorticoid doses impairs healthy adipose tissue expansion by repressing angiogenesis. Diabetes 2023 PMID: 37963392

55. Drygalski K, Lecoutre S, Clément K, Dugail I Hyaluronan in Adipose Tissue, Metabolic Inflammation, and Diabetes: Innocent Bystander or Guilty Party? Diabetes 2023 PMID: 36668999

56. Harrison SA, Ratziu V, Anstee QM, Noureddin M, Sanyal AJ, Schattenberg JM, Bedossa P, Bashir MR, Schneider D, Taub R, Bansal M, Kowdley KV, Younossi ZM, Loomba R Design of the phase 3 MAESTRO clinical program to evaluate resmetirom for the treatment of nonalcoholic steatohepatitis. Aliment Pharmacol Ther 2023 PMID: 37786277

57. Emile JF, Hélias-Rodzewicz Z, Durham BH, Héritier S, da Silva M, Younas K, Cohen-Aubart F, Abdel-Wahab OI, Diamond EL, Donadieu J, Haroche J Histiocytic neoplasm subtypes differ in their MAP2K1 mutations. Blood Adv 2023 PMID: 37878806

58. Azoulay LD, Bravetti M, Cohen Aubart F, Emile JF, Charlotte F, Amoura Z, Cluzel P, Haroche J Cardiac involvement resolution is frequent and associated with improved outcome in Erdheim-Chester disease. Blood Adv 2023 PMID: 37611157

59. Hermida A, Ader F, Millat G, Jedraszak G, Maury P, Cador R, Antoine Catalan P, Clerici G, Combes N, De Groote P, Dupin-Deguine D, Eschalier R, Faivre L, Garcia P, Guillon B, Janin A, Kugener B, Lackmy M, Laredo M, Le Guillou X, Lesaffre F, Lucron H, Milhem A, Nadeau G, Nguyen K, Palmyre A, Perdreau E, Picard F, Rebotier N, Richard P, Rooryck C, Seitz J, Verloes A, Vernier A, Winum P, Yabeta GA, Bouchot O, Chevalier P, Charron P, Gandjbakhch E NEXN Gene in Cardiomyopathies and Sudden Cardiac Deaths: Prevalence, Phenotypic Expression, and Prognosis. Circ Genom Precis Med 2023 PMID: 38059363

60. Drouillard M, Trunet S, Hervochon R, Azoulay LD, Amoura Z, Cohen-Aubart F, Emile JF, Tankéré F, Haroche J Sinonasal and ear manifestations of Erdheim-Chester disease. Br J Haematol 2023 PMID: 37394840

61. Roule V, Beygui F, Cayla G, Range G, Motovska Z, Delarche N, Jourda F, Goube P, Guedeney P, Zeitouni M, El Kasty M, Laredo M, Dumaine R, Ducrocq G, Derimay F, Van Belle E, Manigold T, Cador R, Combaret N, Vicaut E, Montalescot G, Silvain J P2Y12 inhibitor loading time before elective PCI and the prevention of myocardial necrosis. Can J Cardiol 2023 PMID: 37660934

62. Rahoual G, Zeitouni M, Charpentier E, Ritvo PG, Rouanet S, Procopi N, Boukhelifa S, Charleux P, Guedeney P, Kerneis M, Barthélémy O, Silvain J, Montalescot G, Redheuil A, Collet JP Phenotyping Coronary Plaque by Computed Tomography in Premature Coronary Artery Disease. Eur Heart J Cardiovasc Imaging 2023 PMID: 37597177

63. Montalescot G, Ferrante A Clopidogrel: still king of the ring for elective percutaneous coronary intervention! EuroIntervention 2023 PMID: 36939107

64. Fourati S, Hamon A, Daclat R, Salem JE, Peoc'h K, Le Beyec J, Joly F, Lacorte JM Circulating Apolipoprotein B-48 as a Biomarker of Parenteral Nutrition Dependence in Adult Patients with Short Bowel Syndrome. Nutrients 2023 PMID: 37764766

65. Decourtye-Espiard L, Clemessy M, Leneuve P, Mire E, Ledent T, Le Bouc Y, Kappeler L Stimulation of GHRH Neuron Axon Growth by Leptin and Impact of Nutrition during Suckling in Mice. Nutrients 2023 PMID: 36904077

66. Bourcigaux N, Dubost E, Buzzi JC, Donadille B, Corpechot C, Poujol-Robert A, Christin-Maitre S Focus on liver function abnormalities in Turner syndrome patients: risk factors and evaluation of fibrosis risk. J Clin Endocrinol Metab 2023 PMID: 36896592

67. Gosseaume C, Fournier T, Jéru I, Vignaud ML, Missotte I, Archambeaud F, Debussche X, Droumaguet C, Fève B, Grillot S, Guerci B, Hieronimus S, Horsmans Y, Nobecourt E, Pienkowski C, Poitou C, Thissen JP, Lascols O, Degrelle S, Tsatsaris V, Vigouroux C, Vatier C Perinatal, Metabolic and Reproductive Features in PPARG-related Lipodystrophy. Eur J Endocrinol 2023 PMID: 36806620

68. Cambray S, Dubreuil S, Tejedor I, Dulon J, Touraine P Family building after diagnosis of premature ovarian insufficiency - a cross-sectional survey in 324 women. Eur J Endocrinol 2023 PMID: 36763040

69. Delaunay JL, Elbahnsi A, Bruneau A, Madry C, Durand-Schneider AM, Stary A, Housset C, Gautheron J, Callebaut I, Ait-Slimane T Ivacaftor-Mediated Potentiation of ABCB4 Missense Mutations Affecting Critical Motifs of the NBDs: Repositioning Perspectives for Hepatobiliary Diseases Int. J. Mol. Sci. 2023 PMID: 36674751

70. Dietenbeck T, Bouaou K, Houriez-Gombaud-Saintonge S, Guo J, Gencer U, Charpentier E, Giron A, De Cesare A, Nguyen V, Gallo A, Boussouar S, Pasi N, Soulat G, Redheuil A, Mousseaux E, Kachenoura N Value of aortic volumes assessed by automated segmentation of 3D MRI data in patients with thoracic aortic dilatation: A case-control study. Diagn Interv Imaging 2023 PMID: 37105782

71. Voland L, Yuan M, Lecoutre S, Debédat J, Pelloux V, Pradeau M, Coles E, Merabtene F, Zhang C, Mardinoglu A, Le Roy T, Soula H, Clément K Tissue pleiotropic effect of biotin and prebiotic supplementation in established obesity. Am J Physiol Endocrinol Metab 2023 PMID: 37646578

72. Backus B, Bloom B, Lazzeri C, Yordanov Y, Freund Y The evolution of academic publishing: mega journals and artificial intelligence-authored articles. Eur J Emerg Med 2023 PMID: 37103895

73. Goldman S, Aldana M, Cluzel P Resonant learning in scale-free networks. PLoS Comput Biol 2023 PMID: 36809235

74. Sermondade N, Hesters L, De Mouzon J, Devaux A, Epelboin S, Fauque P, Gervoise-Boyer MJ, Labrosse J, Viot G, Bergère M, Devienne C, Jonveaux P, Levy R, Pessione F Fetal growth disorders following medically assisted reproduction: due to maternal context or techniques? A national French cohort study. Reprod Biomed Online 2023 PMID: 36906455

75. Lim C, Turco C, Goumard C, Jeune F, Perdigao F, Savier E, Rousseau G, Soubrane O, Scatton O Perceptions of surgical difficulty in liver transplantation: A European survey and development of the Pitié-Salpêtrière classification. Surgery 2023 PMID: 37543467

76. Worku E, Schmidt M, Shekar K Is It Time to Put Low-Flow Extracorporeal Carbon Dioxide Removal to REST? Crit Care Med 2023 PMID: 37318293

77. Blandin A, Dugail I, Hilairet G, Ponnaiah M, Ghesquière V, Froger J, Ducheix S, Fizanne L, Boursier J, Cariou B, Lhomme M, Le Lay S Lipidomic analysis of adipose-derived extracellular vesicles reveals specific EV lipid sorting informative of the obesity metabolic state. Cell Rep 2023 PMID: 36862553

78. Martínez Martínez M, Schmidt M, Broman LM, Roncon-Albuquerque R, Langouet E, Campos I, Argudo E, Domènech Vila JM, Martín Sastre S, Gallart E, Ferrer R, Combes A, Riera J Survival and Long-Term Functional Status of COVID-19 Patients Requiring Prolonged ECMO Support. Ann Am Thorac Soc 2023 PMID: 38134435

79. Marquet Y, Hékimian G, Lebreton G, Kerneis M, Rouvier P, Bay P, Mathian A, Bréchot N, Chommeloux J, Petit M, Gautier M, Lefevre L, Saura O, Levy D, Quentric P, Moyon Q, Ortuno S, Schmidt M, Leprince P, Luyt CE, Combes A, Pineton de Chambrun M Diagnostic yield, safety and therapeutic consequences of myocardial biopsy in clinically suspected fulminant myocarditis unweanable from mechanical circulatory support. Ann Intensive Care 2023 PMID: 37653258

80. Chouik Y, Chazouillères O, Francoz C, De Martin E, Guillaud O, Abergel A, Altieri M, Barbier L, Besch C, Conti F, Corpechot C, Dharancy S, Durand F, Duvoux C, Gugenheim J, Hardwigsen J, Hilleret MN, Houssel-Debry P, Kamar N, Maucort-Boulch D, Minello A, Neau-Cransac M, Pageaux GP, Radenne S, Roux O, Saliba F, Serée O, Samuel D, Vanlemmens C, Woehl-Jaegle ML, Leroy V, Duclos-Vallée JC, Dumortier J Long-term outcome of liver transplantation for autoimmune hepatitis: a French nationwide study over 30?years. Liver Int 2023 PMID: 36825353

81. Ungureanu IA, Cohen-Aubart F, Héritier S, Haroche J, Donadieu J, Emile JF PU.1 is a useful nuclear marker to distinguish between histiocytosis and histiocyte-rich tumours. Histopathology 2023 PMID: 37012662

82. Mosbah H, Vatier C, Andriss B, Belalem I, Delemer B, Janmaat S, Jéru I, Le Collen L, Maiter D, Nobécourt E, Vantyghem MC, Vigouroux C, Dumas A Patients' perspective on the medical pathway from first symptoms to diagnosis in genetic lipodystrophy. Eur J Endocrinol 2023 PMID: 38128113

83. Bignard J, Atassi F, Claude O, Ghigna MR, Mougenot N, Soilih Abdoulkarim B, Deknuydt F, Gestin A, Monceau V, Montani D, Nadaud S, Soubrier F, Perros F T-cell dysregulation and inflammatory process in Gcn2 (Eif2ak4$^{-/-}$) deficient rats in basal and stress conditions. Am J Physiol Lung Cell Mol Physiol 2023 PMID: 36852942

84. Chouik Y, Corpechot C, Francoz C, De Martin E, Guillaud O, Abergel A, Altieri M, Barbier L, Besch C, Chazouillères O, Conti F, Dharancy S, Durand F, Duvoux C, Gugenheim J, Hardwigsen J, Hilleret MN, Houssel-Debry P, Kamar N, Minello A, Neau-Cransac M, Pageaux GP, Radenne S, Roux O, Saliba F, Samuel D, Vanlemmens C, Woehl-Jaegle ML, Leroy V, Duclos-Vallée JC, Dumortier J Autoimmune hepatitis recurrence after liver transplantation: "Les jeux sont faits." Liver Transpl 2023 PMID: 37788303

85. Dumortier J, Conti F, Hiriart JB, Dharancy S, Duvoux C, Besch C, Houssel-Debry P, Latournerie M, Chermak F, Meszaros M, Pageaux GP, Radenne S, Boillot O, Hardwigsen J, Kounis I, Kamar N, Saliba F, Erard D, Del Bello A Treatment of donor-specific anti-HLA antibodies-mediated rejection after liver transplantation: A French nationwide retrospective study. Liver Transpl 2023 PMID: 37367954

86. Lim C, Scatton O, Wu AGR, Zhang W, Hasegawa K, Cipriani F, Sijberden J, Aghayan DL, Siow TF, Dokmak S, Herman P, Marino MV, Mazzaferro V, Chiow AKH, Sucandy I, Ivanecz A, Choi SH, Lee JH, Prieto M, Vivarelli M, Giuliante F, Ruzzenente A, Yong CC, Yin M, Fondevila C, Efanov M, Morise Z, Di Benedetto F, Brustia R, Dalla Valle R, Boggi U, Geller D, Belli A, Memeo R, Gruttadauria S, Mejia A, Park JO, Rotellar F, Choi GH, Robles-Campos R, Wang X, Sutcliffe RP, Pratschke J, Lai ECH, Chong CCN, D'Hondt M, Monden K, Lopez-Ben S, Kingham TP, Ferrero A, Ettorre GM, Cherqui D, Liang X, Soubrane O, Wakabayashi G, Troisi RI, Cheung TT, Sugioka A, Han HS, Long TCD, Liu R, Edwin B, Fuks D, Chen KH, Abu Hilal M, Aldrighetti L, Goh BKP Impact of liver cirrhosis and portal hypertension on minimally invasive limited liver resection for primary liver malignancies in the posterosuperior segments: An international multicenter study. Eur J Surg Oncol 2023 PMID: 37591027

87. Diallo A, Andreelli F, Pattou F, Guillot C, Servy H, Josse C, Robert M, Galtier F Perceptions of bariatric surgery in patients with type 2 diabetes: data from a self-administered questionnaire. Surg Obes Relat Dis 2023 PMID: 37573156

Articles: profiles of early-career researchers

Profile of Nadine Suffee page 13

1. Takaoka M , Zhao X, Lim HY, Magnussen C, Suffee N, Schrank P, Ang O, Tsiantoulas A, Sommer F, Mohanta S, Harrison J, Meng Y, Laurans L, Wu F, Lu Y, Masters L, Newland S, Denti L, Hong M, Chajadine M, Juonala M, Koskinen J, Kähönen M, Kaisho T, Habenicht A, Tedgui A, Ait-Oufella H, Zhao T, Nus M, Ruhrberg C, Taleb S, Williams J, Raitakari O, Angeli V, Mallat Z. Childhood hyperlipidaemia alters resident arterial macrophages and accelerates atherosclerosis (revision Nature).

2. Suffee N, Baptista E, Piquereau J, Ponnaiah M, Doisne N, Ichou F, Lhomme M, Pichard C, Galand V, Mougenot N, Dilanian G, Lucats L, Balse E, Mericskay M, Le Goff W, Hatem SN. Impacts of a high-fat diet on the metabolic profile and the phenotype of atrial myocardium in mice. Cardiovasc Res. 2022 PMID: 34971360.

3. Suffee N, Moore-Morris T, Jagla B, Mougenot N, Dilanian G, Berthet M, Proukhnitzky J, Le Prince P, Tregouet DA, Pucéat M, Hatem SN. Reactivation of the Epicardium at the Origin of Myocardial Fibro-Fatty Infiltration During the Atrial Cardiomyopathy. Circ Res. 2020 PMID: 32175811.

4. Suffee N, Moore-Morris T, Farahmand P, Rücker-Martin C, Dilanian G, Fradet M, Sawaki D, Derumeaux G, LePrince P, Clément K, Dugail I, Puceat M, Hatem SN. Atrial natriuretic peptide regulates adipose tissue accumulation in adult atria. Proc Natl Acad Sci U S A. 2017 PMID: 28096344

5. Haemers P, Hamdi H, Guedj K, Suffee N, Farahmand P, Popovic N, Claus P, LePrince P, Nicoletti A, Jalife J, Wolke C, Lendeckel U, Jaïs P, Willems R, Hatem SN. Atrial fibrillation is associated with the fibrotic remodelling of adipose tissue in the subepicardium of human and sheep atria. Eur Heart J. 2017 PMID: 26612579.

6. Suffee N, Hlawaty H, Meddahi-Pelle A, Maillard L, Louedec L, Haddad O, Martin L, Laguillier C, Richard B, Oudar O, Letourneur D, Charnaux N, Sutton A. RANTES/CCL5-induced pro-angiogenic effects depend on CCR1, CCR5 and glycosaminoglycans. Angiogenesis. 2012 PMID: 22752444

Profile of Louis Parker page 14

1. Hemodynamic and recirculation performance of dual lumen cannulas for venovenous extracorporeal membrane oxygenation, *Scientific Reports*, 2023. DOI: 10.1038/s41598-023-34655-1.

2. Cannulation configuration and recirculation in venovenous extracorporeal membrane oxygenation, *Scientific Reports*, 2022. DOI: 10.1038/s41598-022-20690-x.

3. Impact of altered vena cava flow rates on right atrium flow characteristics, *Journal of Applied Physiology*, 2022. DOI: 10.1152/japplphysiol.00649.

4. Proximal false lumen thrombosis is associated with low false lumen pressure and fewer complications in type b aortic dissection, *Journal of Vascular Surgery*, 2021. DOI: j.jvs.2021.10.035.

5. Morphology and hemodynamics in isolated common iliac artery aneurysms impacts proximal aortic remodeling, *Arteriosclerosis, Thrombosis and Vascular Biology*, 2019. DOI: ATVBAHA.119.312687.

Profile of Carine Beaupère page 15

1. Patnaik PK, Beaupere C, Barlit H, Romero AM, Tsuchiya M, Muir M, Martínez-Pastor MT, Puig S, Kaeberlein M, Labunskyy VM., Deficiency of the RNA-binding protein Cth2 extends yeast replicative lifespan by alleviating its repressive effects on mitochondrial function. (2022) Cell Reports, Jul 19;40(3):111113

2. Beaupere, C., Dinatto, L., Wasko, B.M., Chen, R.B., VanValkenburg, L., Kiflezghi, M.G., Lee, M.B., Promislow, D.E.L., Dang, W., Kaeberlein, M., Labunskyy, V.M. Genetic screen identifies adaptive aneuploidy as a key mediator of ER stress resistance in yeast (2018) Proceedings of the National Academy of Sciences of the United States of America, 115 (38), pp. 9586-9591

3. Beaupere, C., Wasko, B.M., Lorusso, J., Kennedy, B.K., Kaeberlein, M., Labunskyy, V.M. CAN1 Arginine Permease Deficiency Extends Yeast Replicative Lifespan via Translational Activation of Stress Response Genes (2017) Cell Reports, 18 (8), pp. 1884-1892.

Profile of Jérémie Gautheron page 16

1. Identification of a new NEMO/TRAF6 interface affected in incontinentia pigmenti pathology. Gautheron J, Pescatore A, Fusco F, Esposito E, Yamaoka S, Agou F, Ursini MV, Courtois G. Hum Mol Genet. 2010 Aug 15;19(16):3138-49. doi: 10.1093/hmg/ddq222. Epub 2010 Jun 7. (P)

2. A positive feedback loop between RIP3 and JNK controls non-alcoholic steatohepatitis. Gautheron J, Vucur

M, Reisinger F, Cardenas DV, Roderburg C, Koppe C, Kreggenwinkel K, Schneider AT, Bartneck M, Neumann UP, Canbay A, Reeves HL, Luedde M, Tacke F, Trautwein C, Heikenwalder M, Luedde T. EMBO Mol Med. 2014 Aug;6(8):1062-74. doi: 10.15252/emmm.201403856. (P)

3. The necroptosis-inducing kinase RIPK3 dampens adipose tissue inflammation and glucose intolerance. Gautheron J, Vucur M, Schneider AT, Severi I, Roderburg C, Roy S, Bartneck M, Schrammen P, Diaz MB, Ehling J, Gremse F, Heymann F, Koppe C, Lammers T, Kiessling F, Van Best N, Pabst O, Courtois G, Linkermann A, Krautwald S, Neumann UP, Tacke F, Trautwein C, Green DR, Longerich T, Frey N, Luedde M, Bluher M, Herzig S, Heikenwalder M, Luedde T. Nat Commun. 2016 Jun 21;7:11869. doi: 10.1038/ncomms11869. (P)

4. RIPK1 Suppresses a TRAF2-Dependent Pathway to Liver Cancer. Schneider AT*, Gautheron J*, Feoktistova M, Roderburg C, Loosen SH, Roy S, Benz F, Schemmer P, Büchler MW, Nachbur U, Neumann UP, Tolba R, Luedde M, Zucman-Rossi J, Panayotova-Dimitrova D, Leverkus M, Preisinger C, Tacke F, Trautwein C, Longerich T, Vucur M, Luedde T. *Shared co-first authorship. Cancer Cell. 2017 Jan 9;31(1):94-109. doi: 10.1016/j.ccell.2016.11.009. Epub 2016 Dec 22. (P)

5. Inhibition of receptor-interacting protein kinase 1 improves experimental non-alcoholic fatty liver disease. Majdi A, Aoudjehane L, Ratziu V, Islam T, Afonso MB, Conti F, Mestiri T, Lagouge M, Foufelle F, Ballenghien F, Ledent T, Moldes M, Cadoret A, Fouassier L, Delaunay JL, Aït-Slimane T, Courtois G, Fève B, Scatton O, Prip-Buus C, Rodrigues CMP, Housset C, Gautheron J. J Hepatol. 2020 Apr;72(4):627-635. doi: 10.1016/j.jhep.2019.11.008. Epub 2019 Nov 21. (DC)

6. EPHX1 mutations cause a lipoatrophic diabetes syndrome due to impaired epoxide hydrolysis and increased cellular senescence. Gautheron J, Morisseau C, Chung WK, Zammouri J, Auclair M, Baujat G, Capel E, Moulin C, Wang Y, Yang J, Hammock BD, Cerame B, Phan F, Fève B, Vigouroux C, Andreelli F, Jeru I. Elife. 2021 Aug 3;10:e68445. doi: 10.7554/eLife.68445. (PC)

7. Loss of phospholipase PLAAT3 causes a mixed lipodystrophic and neurological syndrome due to impaired PPARγ signaling. Schuermans N*, El Chehadeh S*, Hemelsoet D*, Gautheron J*, Vantyghem MC, Nouioua S, Tazir M, Vigouroux C, Auclair M, Bogaert E, Dufour S, Okawa F, Hilbert P, Van Doninck N, Taquet MC, Rosseel T, De Clercq G, Debackere E, Van Haverbeke C, Cherif FR, Urtizberea JA, Chanson JB, Funalot B, Authier FJ, Kaya S, Terryn W, Callens S, Depypere B, Van Dorpe J; Program for Undiagnosed Diseases (UD-PrOZA); Poppe B, Impens F, Mizushima N, Depienne C, Jéru I, Dermaut B. *Shared co-first authorship. Nat Genet. 2023 Nov;55(11):1929-1940. doi: 10.1038/s41588-023-01535-3. Epub 2023 Nov 2. (P). News & Views in Nat Rev Endocrinol 2024. doi: 10.1038/s41574-023-00950-0.

Profile of Eloïse Giabicani page 17

1. H1.Imprinting Disorders. Eggermann T, Monk D, Perez de Nanclares G, Kagami M, Giabicani E, Riccio A, Tümer Z, Kalish J, Tauber M, Duis J, Weksberg R, Maher E, Begemann M, Elbracht M. Nature Reviews Disease Primers 2023 Jun 29;9(1):33.

2. Maintenance of methylation profile in imprinting control regions in human induced pluripotent stem cells. Pham A, Selenou C, Giabicani E, Fontaine V, Marteau S, Brioude F, David L, Mitanchez D, Sobrier ML, Netchine I. Clin Epigenetics. 2022 Dec 28;14(1):190.

3. Dental pulp stem cells as a promising model to study imprinting diseases. Giabicani E, Pham A, Selenou C, Sobrier ML, Andrique C, Lesieur J, Linglart A, Poliard A, Chaussain C, Netchine I. International Journal of Oral Science, 2022 Apr;14(19).

4. Height and body mass index in molecularly-confirmed Silver-Russell syndrome and the long-term effects of growth hormone treatment. Sodipe OK, Giabicani E, Canton APM, Ferrand N, Child J, Wakeling EL, Binder G, Netchine I, Mackay DJG, Inskip HM, Byrne CD, Temple IK, Davies, JH. Clinical Endocrinology (Oxf), 2022 Mar 9.

5. Transcriptional profiling at the DLK1/MEG3 domain explains clinical overlap between imprinting disorders. Abi Habib W, Brioude F, Azzi S, Rossignol S, Linglart A, Sobrier ML, Giabicani E, Harbison MD, Le Bouc Y et Netchine I. Science advances. 2019 feb; 5 : eaau9425 22.

6. Increasing knowledge in IGF1R defects in fetal growth retardation: lessons from 35 new patients. Giabicani E, Willems M, Steunou V, Chantot-Bastaraud S, Thibaud N, Abi Habib W, et al. Journal of Medical Genetics. 2020 Mar;57(3):160-168.

7. Roles of Type 1 Insulin-Like Growth Factor (IGF) Receptor and IGF-II in Growth Regulation: Evidence From a Patient Carrying Both an 11p Paternal Duplication and 15q Deletion. Giabicani E, Chantot-Bastaraud S, Bonnard A, Rachid M, Whalen S, Netchine I, et al. Frontiers in Endocrinology. 2019;10:263.

8. Chromosome 14q32.2 imprinted region disruption as an alternative molecular diagnosis of Silver-Russell Syndrome. Geoffron S, Abi Habib W, Chantot-Bastaraud S, Dubern B, Steunou V, Canton A, Busa T, Dufourg MN, Esteva B, Fradrin M, Geneviève D, Isidor B, Linglart A, Oliver Petit I, Phillip, Picard, Pienkowski C, Rio M, Rossignol S, Sandreau C,Tauber M, Thevenon J, Vu-Hong TA, Harbison MH, Brioude F, Netchine I, Giabicani E. Journal of Clinical Endocrinology and Metabolism. 2018 Jul 1;103(7):2436-2446.

9. Diagnosis and management of Silver-Russell syndrome: first international consensus statement. Wakeling EL, Brioude F, Lokulo-Sodipe O, O'Connell SM, Salem J, Bliek J, Canton AP, Chrzanowska KH, Davies JH, Dias RP, Dubern B, Elbracht M, Giabicani E, Grimberg A, Grønskov K, Hokken-Koelega AC, Jorge AA, Kagami M, Linglart A, Maghnie M, Mohnike K, Monk D, Moore GE, Murray PG, Ogata T, Petit IO, Russo S, Said E, Toumba M, Tümer Z, Binder G, Eggermann T, Harbison MD, Temple IK, Mackay DJ, Netchine I. Nature Reviews Endocrinology. 2017 Feb;13(2):105-124.

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