

Bristol Heart Institute

Newsletter December 2022

.....

“The future is still there for you to grab: it has not been cancelled”.



BHI Director Gianni Angelini reflects

In March 2021 at the height of the COVID-19 pandemic, I titled the introduction of our newsletter “The future may be on hold, but it has not been cancelled” and I concluded my remarks with a good dose of optimism to cheer up the troops “The future is still there for you to grab: it has not been cancelled”.

The COVID-19 pandemic is not over yet, but we are almost back to normal life, and I am very pleased to see laboratories and lecture rooms getting busier, people talking to each other and slowly returning to socialising.

Zoom, Team etc... have changed our lives sometimes for the better and are here to stay. However, they cannot replace the face-to-face interaction over a cup of coffee so important to exchange views and develop new research ideas.

COVID-19, the Ukrainian war, cost of living, several prime ministers in the space of a flash have not changed:

- Our determination to continue to stand out as the leading academic cardiovascular centre in the UK, and amongst the foremost worldwide.
- Our ability to turn innovations into benefit for adult and paediatric patients, and the health system.
- Our creation of an environment where clinicians, basic scientists and clinical research methodologists can thrive, attract the most talented individuals and produce world-leading research.
- Our resolve to facilitate a smooth and timely transition to the next generation of cardiovascular clinicians and researchers.

The future is here for you to grab with both hands.
Happy Holidays and warm wishes for 2023!

In this issue

- BHF grant to fight age related cardiomyopathy
- Vascular endothelial glycocalyx dysfunction as a therapeutic target in sepsis-associated acute kidney injury
- Dr Sarah Smith awarded first BHF Research Grant
- Joseph Hawkins successfully defended his PhD thesis during his viva examination
- Congratulations to all the recipients of ARTERY22 awards and grants
- Diabetes breakthrough: gel-like sieve in blood vessels a new target for repairing damaged hearts
- COVID-19 Spike protein binds to heart’s vascular cells potentially contributing to severe microvascular damage
- Research aims to reduce strokes caused by tiny air bubbles entering the blood stream during heart surgery
- Multidisciplinary study could help doctors to predict heart failure
- BHI Charity Appeal
- Cardiovascular research in Bristol – event 2nd February 2023
- BHI SRI Steering Group

BHF Grant to fight age related cardiomyopathy using a longevity protein

Professor Paolo Madeddu explains heart failure



Heart failure is a serious condition requiring medical attention and frequent hospitalization. It can occur at any age but is most common in older people. In addition, many - apparently healthy - older people have awakened hearts without being aware of it. This is because with age the reserve capacity of the heart progressively decreases. It is believed this decline starts during early adulthood.

This project will investigate if the age-related weakening of the heart can be delayed or even rescued. We want to test this possibility by studying a gene that has acquired some changes during human evolution, allowing the carriers to live much longer than average people and to remain healthy until the very end of their life. In a recent project awarded by the BHF, we succeeded in demonstrating that the transfer of the gene rejuvenates the heart of old mice.

In this new study, we propose to repeat the experiment by giving the gene-encoded protein, which is a more practical method than injecting the gene. If successful, this will be an easier way to maintain the heart young despite aging.



[Image by vectorjuice](#) on Freepik

Applicant:
Paolo Madeddu
Organisation:
University of Bristol

**Funding sought
and awarded:**
£172,004.47

Massimo Caputo awarded nearly £750,000

Professor Massimo Caputo has been awarded nearly £750,000 by the BHF to further develop his stem cell patches for testing in patients so clinical trials can start in the next two years.

Read more about this revolutionary development in our next newsletter.

Vascular endothelial glycocalyx dysfunction as a therapeutic target in sepsis-associated acute kidney injury

Raina Ramnath, a Research Fellow at Bristol Renal has recently been awarded a 3-year British Heart Foundation (BHF) funding.

Raina will be principal investigator, starting January 2023, to understand the causal relationship between vascular endothelial glycocalyx damage and acute kidney injury in sepsis. Sepsis remains the leading cause of acute kidney injury (AKI), found in 40-50% of patients with AKI in intensive care units. Sepsis-AKI is associated with a high mortality rate of 41%. The renal microcirculation is profoundly disturbed in sepsis-AKI, leading to kidney damage. The glycocalyx is a protective layer found on the inner lining of all the blood vessels in the body, including the kidney (Fig 1). Loss of the glycocalyx has been associated with vascular and kidney injury.

Raina Ramnath et al., have previously identified matrix metalloproteinase (MMP) 9-mediated endothelial glycocalyx shedding as a novel mechanism in human glomerular endothelial cell damage and kidney injury in diabetes. This study which includes collaboration with national and international experts, will investigate fully MMP9-mediated endothelial glycocalyx loss in sepsis-AKI and determine whether blockade of this mechanism reduces the severity of sepsis-AKI. It will also confirm the relevance of endothelial glycocalyx loss and its correlation with MMP activity in sepsis-AKI patient samples.

The vascular endothelial glycocalyx damage offers a novel therapeutic target in the treatment of sepsis-AKI. This study supports repurposing clinically available drugs with MMP9 inhibition properties e.g. tetracyclines in vascular dysfunction in sepsis-AKI. This promises a rapid way to translate preclinical work on endothelial glycocalyx protection to clinical application. This will be of benefit, to sepsis-AKI, by decreasing mortality in patients, and providing a wider health impact, by ameliorating systemic vascular diseases.

The BHF funding represents a key step towards Raina Ramnath becoming an independent research leader and to building and developing her own research group. It also leverages support for further funding in the field of vascular damage in sepsis-AKI.

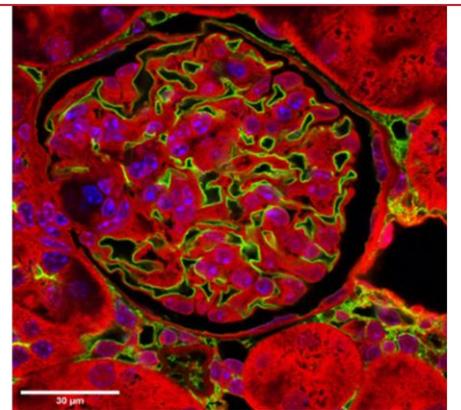


Fig 1. The glycocalyx stained green with lectin LEL can be seen lining the capillaries in the glomerulus. The membrane is stained red with R18.

Dr Sarah Smith awarded first BHF Research Grant

Congratulations to Dr Sarah Smith, Senior Research Associate in Translational Health Sciences

Dr Sarah Smith was recently awarded her first BHF research grant (£193k) for a project entitled 'Validation of novel LincRNAs with preventative roles in adverse cardiac fibrosis'.

Dr Smith has a special academic interest in molecular mechanisms influencing heart failure following myocardial infarction. The project aims to elucidate the specific roles of two LincRNAs that promote cardio-protective effects in the heart. Specifically, novel mechanisms influencing myocardial fibrosis, both common and distinct in major cardiac cell types, will be investigated. The functional impact of these LincRNAs will be further tested in fresh myocardial tissue to assess molecular changes overtime as well as changes in cellular architecture and contractibility.

Co-applicants supporting this project are Professors Raimondo Ascione, Sarah George and Jason Johnson. The ex-vivo component of this project utilises an advanced myocardial slice model in collaboration with Oxford University and Translational Biomedical Research Centre (TBRC) Facility.



Dr Sarah Smith was recently awarded her first BHF research grant (£193k)

Joseph Hawkins successfully defended his PhD thesis during his viva examination

Congratulations to Joseph Hawkins

Mark Bond's student Joseph Hawkins successfully defended his PhD thesis during his viva examination on Tuesday 8 November. He has written a summary of his project: My PhD project looked at the role of nuclear actin dynamics in the regulation of vascular smooth muscle cell (VSMC) inflammation. The project built upon previous work by our group which had shown that cyclic-AMP signalling could increase the levels of monomeric actin in the nucleus of VSMCs, leading to reduced activity of pro-mitotic transcription factors. Preliminary data indicated that this mechanism may also affect VSMC inflammation through the inhibition of the pro-inflammatory transcription factor, NF- κ B.



Over the course of my PhD project, we have shown that cyclic-AMP-induced elevation of nuclear actin monomer levels leads to the repression of pro-inflammatory gene expression in VSMCs. Furthermore, we demonstrated that this effect is mediated by a reduction in the protein levels of the NF- κ B transcription factor. Our data indicated that elevated nuclear actin monomer levels triggered an acceleration of NF- κ B protein degradation, culminating in a loss of total NF- κ B protein. These findings formed the basis of a manuscript published this year in the peer-reviewed journal, *Cells*. Our data may have implications for the treatment of atherosclerosis, as well as other inflammatory diseases associated with excessive NF- κ B activity.

Following the recent completion of my PhD I have embarked upon a career in medical communications, utilising many of the skills I gained during the last three years

[Joseph has also recently had some of his PhD work published in *Cells*.](#)

Congratulations to all the recipients of ARTERY22 awards and grants

170 delegates from across Europe and beyond!

This year's ARTERY 22 conference held in Nancy, France, attracted over 170 delegates attending from across Europe and beyond and we are pleased to congratulate Dr Froso Sophocleous who won second place for her work on: Shape biomarkers of growth and remodelling in congenital heart disease patients with aortopathy.



**Dr Froso Sophocleous
won second place**

Diabetes breakthrough: gel-like sieve in blood vessels a new target for repairing damaged hearts

Professor Simon Satchell, Dr Yan Qiu

Drugs that repair damage to a gel-like layer in the tiny blood vessels of the heart could present a much-needed treatment for heart failure in people with diabetes, according to research carried out by Professor Simon Satchell, Dr Yan Qiu and their team from the Bristol Heart Institute.



These findings have far-reaching implications in protecting against other types of organ failure, since the glycocalyx is present in all blood vessels.

[Professor James Leiper](#), the British Heart Foundation Associate Medical Director, said:

“This is the first evidence that damage to the glycocalyx in the small vessels of the heart might be involved in diabetic heart failure. The results of this research increase our understanding of the biology underpinning this condition. If these exciting findings from animals can be reproduced in humans, they may identify potential new treatments for patients with diabetic heart failure.”

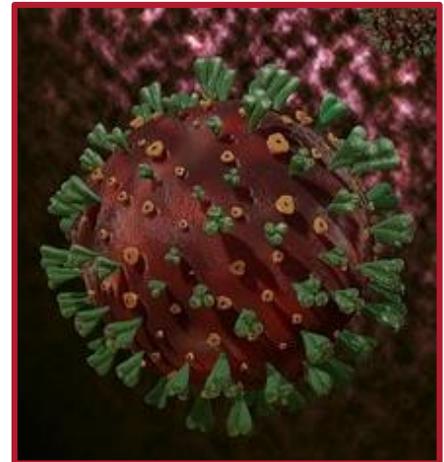
[Read more](#)

COVID-19 Spike protein binds to heart's vascular cells potentially contributing to severe microvascular damage

Multidisciplinary research on Covid-19

A multidisciplinary research team from the Bristol Heart Institute found that SARS-CoV-2 may contribute to severe microvascular damage seen in severely-ill COVID-19 patients by transforming human heart vascular cells into inflammatory cells, without infecting them.

The research has been supported by a pump-priming grant from the [Wellcome Trust](#), the [Elizabeth Blackwell Institute](#) (EBI) Rapid Response COVID-19 and a [British Heart Foundation](#) grant (number PG/20/10285). The authors are members of the [University of Bristol COVID-19 Emergency Research Group \(UNCOVER\)](#).



[Read more](#)

Research aims to reduce strokes caused by tiny air bubbles entering the blood stream during heart surgery

Dr Ben Gibbison, his team and the CO² study

Dr Ben Gibbison and his team from the Bristol Heart Institute and the Bristol Trials Centre are investigating how to reduce strokes and other brain problems following heart surgery, which can be caused by tiny air bubbles left in the bloodstream after opening the heart. These tiny air bubbles stop blood getting to part of the brain. The study, which started in October 2021, is called the CO₂ Study. It is funded by the National Institute for Health Research (NIHR) and sponsored by University Hospitals Bristol and Weston NHS Foundation Trust (UHBW).



[Dr Gibbison](#), Consultant Senior Lecturer in Cardiac Anaesthesia and Intensive Care at the University of Bristol, says:

“If you come for heart surgery currently, you have a 50% chance of getting CO₂ in the wound. This study will tell us whether it is effective and everyone should use CO₂ or whether it doesn’t work and we should stop using it.”

[Read more](#)

Multidisciplinary study could help doctors to predict heart failure

Professor Ascione and Dr Andrew Cookson

A multidisciplinary team of researchers, including computational scientists from the University of Bath and experts from the University of Bristol's Translational Biomedical Research Centre and the Bristol Heart Institute, have uncovered data from studying heart attacks in animal models which could help determine whether a patient will go on to develop heart failure.

Professor Ascione, co-senior author on the paper together with [Dr Andrew Cookson](#) from the University of Bath, said the research was important for two key reasons:

“Firstly, the identification of the early abnormal regional strain in the heart might enable doctors in the future to predict heart failure in advance and therefore start treatments much earlier to prevent the heart stretching and failing,”

“Secondly, the discovery of those few molecules accumulating in the failed heart could trigger the development of new drugs to prevent or treat heart failure.”

[Read the full story](#)

BHI Charity Appeal

£57,000 awarded to Bristol & Weston Hospitals Charity

[Bristol & Weston Hospitals Charity](#) (formerly Above and Beyond) has been awarded £57,000 from NHS Charities Together to support its appeal to provide at-home monitoring service for BHI patients with pacemakers.

Thousands of BHI patients have a cardiac implantable electronic device (CIED) or pacemaker to help control or monitor irregular heartbeats. Having a CIED requires them to attend hospital as often as every six weeks to be checked.

[Read more](#)

at-home
monitoring
service for BHI
patients with
pacemakers.

Cardiovascular research in Bristol

Joint meeting of the Bristol Heart Institute, Specialist Research Institute and the British Heart Foundation Bristol Accelerator Award

A warm welcome to join us at this joint meeting. The programme will include talks, student presentations, a plenary and award ceremony. Programme details will be sent to registered delegates in due course.

Thursday 2nd February 2023
9:00am to 5:00pm

Engineers' House, The Promenade,
Clifton Down, Clifton, Bristol BS8 3NB

Lunch and refreshments provided including tea, coffee and breakfast rolls on arrival.

[For more information, programme details and to register](#)



In-person for
better
networking
opportunities

BHI SRI Steering Group 2022

BHI Specialist Research Institute Steering Group

[Meet the members](#) of the BHI Specialist Research Institute Steering Group.

Director

[Professor Gianni Angelini](#): BHF Professor of Cardiac Surgery and Cardiovascular theme lead at the NIHR Bristol Biomedical Research Centre

Deputy Director

[Professor Alastair Poole](#): Professor of Pharmacology and Cell Biology

Members

[Dr Giovanni Biglino](#): Biostatistics

Zoe Holland: Research Development Manager, Faculty of Health Sciences

[Professor Massimo Caputo](#): Congenital heart surgery

[Dr Becky Foster](#): Renal, diabetic and hypertensive disease

[Professor Sarah George](#): Cardiovascular signalling

[Dr Emma Hart](#): Cardionomics

[Dr Andrew James](#): Cardiac biology

[Dr Jason Johnson](#): Pathology of cardiovascular diseases

[Professor Paolo Madeddu](#): Cardiovascular regenerative medicine

[Professor Stuart Mundell](#): Vascular biology and atherothrombosis

[Professor Ruth Newbury-Ecob](#): Clinical genetics

[Dr Angus Nightingale](#): Consultant cardiologist

[Dr Guido Pieles](#): Sports and exercise cardiology

[Professor Simon Satchell](#): Renal, diabetic and hypertensive disease

[Professor Saadeh Suleiman](#): Cardiac biology

[Professor Nic Timpson](#): Population health and epidemiology

Keep in touch:

[Subscribe to the Fortnightly BHI Digest](#)

Thank you to everyone who has contributed to this edition.

If you have BHI news, events, videos or publications to share, contact:

Clare Williams,
BHI Communications Officer
bcv-info@bristol.ac.uk