

Bristol Heart Institute

Newsletter June 2023

World class research at the BHI

Giovanni Biglino reflects on our achievements in 2023 so far

Our heartfelt congratulations to all our teams at the BHI for their hard work over the past six months.

The ground-breaking research at the BHI helps change patient lives. The world class work is being recognised in the level of funding that has been secured for ongoing research and trials. For example, the BHF Award of £750,000 for 'heart plaster' that could improve the way surgeons treat children living with congenital heart disease, so they don't need as many open-heart operations. We also have the UK's first platform trial in cardiac surgery which will be run through the Bristol Trials Centre with collaborators from cardiac surgery centres across the country. It is supported by the Society of Cardiothoracic Surgeons.

In February, we held the joint meeting of the BHI and the BHF Bristol Accelerator Award. We were delighted that our Vice Chancellor, Evelyn Welch was able to attend our research showcase event. We welcomed a great crowd in person at Engineers' House. A series of presentations from our PhD students were particularly impressive, while colleagues in the BHI discussed important aspects of our research, including considerations around making trials more inclusive.

Following from the successful BHI meeting this year, we are considering the possibility of organising a broader public engagement event in 2024 to showcase our research as a civic university. We will be looking for contributions so stay tuned!

We wish you all continued success over the coming year.

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UK's first platform trial in cardiac surgery

Maria Pufulete and Ben Gibbison set up UK's first platform trial in cardiac surgery

Proposal for Strategic Research Investment Funding Bristol University
Professor Gianni D Angelini and Dr Maria Pufulete to develop a BHI research priority – the set-up of a platform clinical trial in cardiac surgery. Platform studies are “open ended”, meaning that multiple interventions can be added, assessed and removed as time goes on, without having to set-up a new study for each intervention. Award £100K. This follows the recent funding of the NIHR HTA Acceleration award to develop the platform study in cardiac surgery. The study is currently underway and has been advertised in the Bristol Heart Institute BHI Digest (see BHI Digest NIHR Accelerator Award to set up a platform trial in cardiac surgery).

Aims:

Develop networks / collaborations (nationally and internationally), research capacity and infrastructure to support the delivery of the platform, including patient and public involvement and engagement (PPIE). This will include engaging with both cardiac surgery centres and leading methodologists in platform trials so that we can integrate knowledge from existing studies
Write the “master protocol” for the platform, which includes defining: PICO (Population, Interventions, Comparator and Outcome) and estimands of interest and the statistical design to inform the master protocol
Develop and submit a high-quality funding application to the National Institute for Health Research (NIHR) or the British Heart Foundation to start the study .

Alongside i) to iii), work with theme leads in the BHI to develop research priorities and funding applications that will feed directly into the cardiovascular theme of the next NIHR BRC (2027) see write up on BHI site under news

A £60k Wellcome Trust Partnership Award Fellowship



Glomerular endothelium-specific gene transfer: the future of kidney disease treatments?

Dr Aldara Martin Alonso, a Postdoctoral Research Associate at Bristol Renal has recently been awarded funding to explore glomerular endothelium-specific gene transfer. Aldara has recently been awarded with a BBSRC Pathfinder Impact Acceleration Account (£ 18K) award followed by a Wellcome Trust Partnership Award Fellowship (£ 60K) to explore glomerular endothelium-specific gene transfer.

One of the main cell types of the glomerular filtration barrier in the kidney are the glomerular endothelial cells. In addition, covering the glomerular endothelium, the endothelial glycocalyx is important in vascular homeostasis and in barrier function. The dysfunction in the glomerular endothelium is pivotal to many glomerular diseases, including diabetic kidney disease (DKD). There is no cure for DKD and none of the current strategies, which aim to delay further kidney damage, target the glomerulus. Importantly, DKD still advances with these treatments. Bristol Renal has already developed gene therapy targeting the podocyte, the other key cell in the filtration barrier. However, glomerular endothelium-directed gene therapy has been hampered until now. In a project funded by an Institutional Translational Partnership, awarded to Dr Rebecca Foster and Prof Simon Satchell, Aldara developed a tool that can be used as a new platform for gene transfer to the glomerular endothelium. With this new funding, Aldara aims now to demonstrate function of this gene transfer tool to induce the expression of genes relevant in glomerular physiology and in endothelial glycocalyx. This will support the downstream application of this tool in basic research. In addition, this funding will allow to investigate if the glomerular endothelium-directed gene therapy prevents DKD in mouse models of diabetes. The data from these projects will also be used to protect this work via patents and to strengthen the potential for future partnerships.

Crucial advantages of this gene therapy are direct targeting of the glomerular endothelium and that it would consist of a single dose initially (the expression of the transgene should be continuous). Crucially, this tool has potential for treating numerous glomerular diseases, not only DKD.

These awards represent a key step towards Aldara Martin Alonso becoming an independent research leader and continuing her interest in gene therapies and translational research. It will also allow to further develop new approaches to glomerular disease treatment. Aldara is very grateful to her supervisors Dr Rebecca Foster and Prof Simon Satchell, to Bristol Renal, to Andrew Wilson, to the Impact Development team and the funders.

3 year grant of over £200k from Kidney Research UK awarded

Adiponectin receptor agonists prevent the development of kidney disease

Rebecca Foster, Emma Vincent, Simon Satchell and Matthew Bulter were recently awarded a 3 year grant from Kidney Research UK: Adiponectin receptor agonists prevent the development of kidney disease through protection of the glomerular endothelial glycocalyx for £211,026.30.

Adiponectin, secreted primarily by adipocytes, is an anti-diabetic adipokine and a protective cardiovascular agent, also protecting against diabetic kidney disease (DKD). Population studies have shown that circulating adiponectin levels are inversely associated with albuminuria and have a causal effect on reduced glomerular filtration rate (GFR), equating to loss of kidney function. Vascular endothelial cells have a protective gel-like layer, the endothelial glycocalyx (eGlx), including within glomerular microvessels. eGlx damage is an early event in endothelial dysfunction and causes albuminuria. We have shown that adiponectin protects from diabetes-related albuminuria and glomerular eGlx damage, through a matrix metalloproteinase (MMP)2-dependent mechanism. In an early model of aldosterone/high salt (AHS), we have shown glomerular eGlx disruption via the same mechanism. We suggest adiponectin prevents eGlx damage, and subsequent kidney disease, through a common mechanism. Adiponectin receptor (AdipoR) agonists, such as AdipoRon, are orally active and mimic the protective effects of adiponectin. Pre-clinical data for AdipoR agonists is strong in other diseases. We aim to prevent eGlx disruption and subsequent kidney damage in experimental AHS and DKD, using AdipoR agonists, and to demonstrate a role of adiponectin levels on eGlx integrity and kidney disease, using population studies. This will highlight the therapeutic potential of an AdipoR agonist in kidney disease.

Humanitarian charity missions to Romania and Palestine

Massimo Caputo describes his passion for paediatric cardiac surgery

Romania:

<https://youtu.be/-fp4Wx53YUQ>



Palestine:

<https://drive.google.com/file/d/1IAA2BzhaBYBSaHoTNayNSJwEzOVd79a1/view>



EXOMES - Exciting news from ALSPAC - Children of the 90s

Nicholas Timpson explains work with Wellcome Sanger will continue

“EXOMES - Exciting news from ALSPAC/Children of the 90s. With a substantial contribution from UKRI/MRC, it is now confirmed that our work with Wellcome Sanger Institute will continue generating whole exome sequences in ALSPAC and a series of sister collections (including Born in Bradford, The Millennium Cohort and the Fenland Study). This will bring the complete collection of whole exomes together in the study – numbering ~24,000 across index participants, mums, dads and new children – and enable a scaling up of rare and structural variant analyses.



Don't hesitate to get in touch if this is of interest
@Nicholas Timpson or @Alspac Exec Mailbox”

BHF Award of £750,000 for ‘heart plaster’

BHF Professor Massimo Caputo’s ‘heart plaster’

The BHF awarded £750,000 to BHF Professor Massimo Caputo at the University of Bristol to develop a new innovative type of ‘heart plaster’ that could improve the way surgeons treat children living with congenital heart disease, so they don’t need as many open-heart operations.



Professor Caputo and his team has developed the first type of mesenchymal cell patch to repair abnormalities to large blood vessel that controls blood flow from the heart to the lungs, and to mend holes between the two main pumping chambers of the heart. Mesenchymal cells are a type of cell that have the ability to change into a range of cell types including muscle and cartilage. These patches have the potential to adapt and grow with the child’s heart as they get older, removing the need for repetitive high risk heart surgeries and avoid complications such as arrhythmias.

As a result of this research, Professor Caputo has been nominated for a British Heart Foundation Heart Hero Awards 2023 - Research Story of the Year. There is no panel of judges to determine an overall winner of the category, so the three shortlisted projects will be put to a public vote in June to win this year's award. The BHF heart story team would like to showcase this research in the form of a 60 to 90 second video that will be used on the BHF website, social channels and in media outlets during the BHF voting process to encourage the public to cast their votes.

Massimo appeared on BBC 4 radio program last week called Best Medicine to talk about this subject.

The longevity-associated BPIFB4 gene supports cardiac function and vascularization in aging cardiomyopathy

Professor Paolo Madeddu explains how the BPIFB4 gene works

Professor Paolo Madeddu and his team are working to delay the ageing of the heart. He tells Dr Leanne Grech how this research could allow older people to live a healthier life for longer.

Each day, your heart beats around 100,000 times, pumping about eight pints of blood around your body. By the time you are 20, the heart's function can begin to decline as part of normal ageing. As you get older, activities like running or playing tennis become more difficult. However, some 100-year-olds, like those living in Okinawa, a cluster of islands in southern Japan, appear to have unlocked the secret to a long and healthy life, with some of them seemingly having a heart younger than their age. "It's a combination of a good lifestyle and good genes," explains Professor Paolo Madeddu at the University of Bristol. "And we have discovered that one of these good genes can stop ageing."



[Read the full story](#)

Mesenchymal cell plasters to stop children needing repeated heart surgeries

Professor Massimo Caputo has developed the first type of stem cell patch to repair abnormalities

Researchers at the University of Bristol, funded by the British Heart Foundation (BHF), have developed 'mesenchymal cell plasters' to revolutionise the way surgeons treat children living with congenital heart disease, so they don't need as many open-heart operations.

Heart defects are the most common type of anomaly that develop before a baby is born, with around 13 babies diagnosed with a congenital heart condition every day in the UK. These include defects to the baby's heart valves, the major blood vessels in and around the heart, and the development of holes in the heart.

[Read more here](#)



Joint meeting of the BHI and the BHF Bristol Accelerator Award

Cardiovascular Research Bristol - Meeting highlights from 2nd February 2023

We were delighted that our Vice Chancellor, Evelyn Welch was able to attend our research showcase event.

Professor Deborah Lawlor was our plenary speaker. Deborah Lawlor is the [BHF Professor of Cardiovascular Science and Clinical Epidemiology](#) at the University of Bristol.

Professors Angelini and Lawlor opened the event by providing updates on the BHI and BHF Accelerator Award. During the morning there were two sessions on 'Showcasing Research' and during the afternoon 18 PhD students gave 'Flash Presentations' to highlight aspects of their research. A thought provoking animation was shown reflecting on public engagement and finally Professor Lawlor gave the plenary talk and the student awards were announced.

[Photos from the event](#)



Tissue resilience in health and disease – Royal Society Conference

Working together towards a more resilient future

The first International Meeting on “Tissue Resilience in Health and Disease” took place in April, in the vibrant First Street quarter of Manchester. The meeting was organised jointly by [Dr Helen Weavers](#) (Bristol) and Prof [Anna Jazwinska](#) (Freiburg) and made possible by generous support from The Royal Society.

In this inter-disciplinary meeting, speakers from across Europe and the US shared their latest cutting-edge research exploring how animal and plant tissues can be conditioned, i.e. made more resilient, by non-lethal insult. A key focus was how these hormetic-like responses might best be harnessed for improved resilience in the field or clinic. Many talks highlighted the emerging impact of host age, diet and co-morbidities on a tissue’s resilience and its ability to be conditioned - overcoming these complications is a major ongoing challenge to successful clinical implementation.

Much discussion centred around how we can improve cardiac resilience to damage, with stimulating talks from leaders in the cardiac conditioning field including [Prof Gerd Heusch](#), [Prof Karin Przyklenk](#) and Bristol Medical School’s [Prof Saadeh Suleiman](#). In vivo experimental models were well-represented too, with [Prof Anna Jazwinska](#) presenting her group’s work using the tractable zebrafish model to interrogate the molecular mechanisms underlying cardiac remote conditioning.

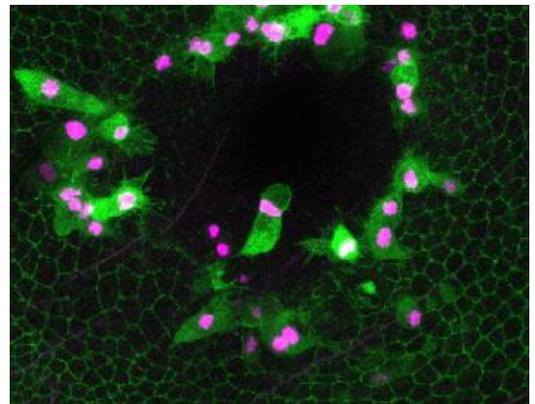


Image: Inflammatory response to tissue damage (Helen Weavers)



Image: Zebrafish heart (Anna Jazwinska Lab)

Tissue resilience in health and disease – Royal Society Conference ... cont'd

Working together towards a more resilient future, cont'd ...

In this relaxed but focused setting, nearly all attendees had the opportunity to present their latest work and early career researchers could network and exchange ideas with leaders in the field. Although brimming with cutting-edge research, here the emphasis was on stimulating discussion, with almost equal time dedicated to this throughout the day and into the evening. The intimate environment and small-scale nature promoted engagement between participants in a way that is not possible at much larger scientific meetings. Undoubtedly this Meeting helped resilience researchers build new, inspiring collaborations and friendships, and above all, formulate exciting ideas to unravel and translate this remarkable phenomenon; we're looking forward to more Resilience-focused Meetings in the future.

For more info about the conference please see <https://royalsociety.org/science-events-and-lectures/2023/04/tissue-resilience/>



First Street Quarter, Manchester

Nomination in this year's Recognising Success Awards

Nomination for Innovation and Improvement Award in the Recognising Success Awards 2023

Radwa Bedair reports that her team have received a nomination for innovation and improvement in this year's recognising success awards. This is for their work in introducing the percutaneous therapy for superior sinus venosus defect. The winner has been announced and unfortunately we did not win but it is brilliant that we were nominated in the first place!

Many thanks for all your help dedication to this project

Well done!

SCTS 2023 John Parker Medal awarded at the Annual General Meeting

Amerikos Argyriou and Jeremy Chan recognised at the AGM

Two of our researchers were awarded the following prestigious prizes at the SCTS 2023 annual general meeting, held at the ICC Birmingham.

Amerikos Argyriou was awarded the John Parker Medal in May for Best Clinical Presentation entitled Incidence and outcomes of surgical pulmonary embolectomy in the UK, to be presented formally next March.

Jeremy Chan achieved the highest scoring poster in the SCTS poster competition entitled: Off Pump Coronary Artery Bypass Grafting in the United Kingdom: trend and early clinical outcomes

Congratulations to you both.



Our latest publications

Remember to send details of your latest publications to bcv-info@bristol.ac.uk and add keywords to Pure to ensure publications feed into the BHI feed <http://www.bristol.ac.uk/research/institutes/heart/>

Our latest publications

•Shubhra Sinha, MBBS, Tim Dong, MSc, Arnaldo Dimagli, MD, Hunaid A Vohra, PhD, Chris Holmes, PhD, Umberto Benedetto, PhD, Gianni D Angelini, MD Author Notes. Comparison of Machine Learning Techniques in Prediction of Mortality following Cardiac Surgery: Analysis of over 220,000 patients from a Large National Database. [European Journal of Cardio-Thoracic Surgery](#) 8 May 2023

•Pradeep Narayan FRCS(CTH) ¹ *, Arnaldo Dimagli MD ² *, Daniel P. Fudulu PhD ², Shubhra Sinha MD ², Tim Dong MSc ², Jeremy Chan MD ², Gianni D. Angelini MD ² Risk Factors and Outcomes of Reoperative Surgical Aortic Valve Replacement in the United Kingdom. *The Annals of Thoracic Surgery*. <https://doi.org/10.1016/j.athoracsur.2022.12.045> 27 January 2023

•Monica Cattaneo ¹, Antonio P Beltrami ², Anita C Thomas ³, Gaia Spinetti ¹, Valeria Alvino ³, Elisa Avolio ³, Claudia Veneziano ², Irene Giulia Rolle ², Sandro Sponga ², Elena Sangalli ¹, Anna Maciag ¹, Fabrizio Dal Piaz ⁴, Carmine Vecchione ^{4,5}, Aishah Alenezi ⁶, Stephen Paisey ⁶, Annibale A Puca ¹ ⁴, Paolo Madeddu ³ [The longevity-associated BPIFB4 gene supports cardiac function and vascularization in aging cardiomyopathy](#). *Cardiovasc Res.* 2023 Jan 13;cvad008. PMID: 36635236 DOI: 10.1093/cvr/cvad008. Online ahead of print.

•Jeremy Chan¹, Arnaldo Dimagli¹, Daniel P. Fudulu¹, Shubhra Sinha¹, Pradeep Narayan^{1,2}, Tim Dong¹ and Gianni D. Angelini¹. ¹Bristol Heart Institute, University of Bristol, Bristol, United Kingdom ²NH Rabindranath Tagore International Institute of Cardiac Sciences, Kolkata, India. [Trend and early outcomes in isolated surgical aortic valve replacement in the United Kingdom](#). 9 January 2023 *Frontiers in Cardiovascular Medicine*

•Daniel J. P. Burns MD, MPhil, Gianni D. Angelini MD, Umberto Benedetto MD, PhD, Massimo Caputo MD, Franco Ciulli MD, Hunaid A. Vohra MD. [Early mortality and neurologic outcomes following mitral valve surgery in the very elderly](#). 6 November 2022. <https://onlinelibrary.wiley.com/>