

# Bristol Heart Institute

Newsletter December 2023

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## World class research at the BHI

### *Dr Giovanni Biglino reflects on our achievements in 2023 so far*

We are delighted that groundbreaking research continues at the Heart Institute and in particular, congratulations to Massimo Caputo on his BHF Heart Hero Award for his revolutionary type of 'heart plaster' to treat children with congenital heart disease and to Tom Johnson on his award for work involving a 2000 patient prospective registry investigating the real-world impact of optical coherence tomography (OCT) on percutaneous coronary intervention (PCI). Congratulation to Elisa Avolio and Lydia Simpson for their BHF Intermediate fellowship awards.

This year we had our 7<sup>th</sup> cohort of BHF-funded 4-Year Integrative Cardiovascular Sciences Programme students.

Congratulations to all our graduands on 31 July 2023.

We have exciting plans for next year and are pleased to announce that on Thursday 22<sup>nd</sup> February 2024 we will be holding a Heart Festival at the Watershed, Bristol. This event will be open to the public and will showcase our research as a civic university. There will be talks, activities, film screening and more.

A big thank you to everyone for your continued contribution to heart research. We wish you all continued success, a Merry Christmas and a prosperous New Year.

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# The BHF pays tribute to researchers

## *BHF Impact Review on Cardiac Surgery*



The BHF has funded research into cardiac surgery since 1961 and awarded over 500 grants worth more than £80m.

Research funded by the BHF into cardiac surgery has led to innovations which help the lives of patients.

The BHF funded research has played a key role in generating new knowledge. It has helped to understand why some patient's bodies reject their heart transplants and how we can stop this happening. Researchers have developed new methods to improve surgical outcomes. BHF funded research has made a huge impact on the way surgery is practiced. All of this research has led to innovations which help the lives of patients.

The BHF have released their impact review on cardiac surgery and acknowledge grateful thanks to Professor Gianni Angelini for his time and contributions.

[Read the full story and impact report](#)

# Professor Massimo Caputo wins BHF Research Story of the Year



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

We are delighted to congratulate [Professor Massimo Caputo](#), on this outstanding achievement. He received his award at a ceremony in London last night, Wednesday 6 December. The BHF's [Heart Hero Awards](#) recognise people who have gone the extra mile to help those with a heart and circulatory disease. [Read the full story](#)



Professor Caputo said: “My team and I are delighted to win the BHF Research Story of the Year. It’s an amazing recognition of all the work we have done to get to this point, and I want to thank BHF for their continued support.”

Calum Morris, pictured above was born with Truncus Arteriosus. Calum received lifesaving open heart surgery from Professor Caputo when he was just ten days old. Since then, Calum has had a further four major heart surgeries – all performed by Professor Caputo and his team.

Now 17, Calum and his family wanted to say thank-you to ‘their hero’. The family say thanks to Professor Caputo and his incredible team Calum has been able to achieve dreams that other boys take for granted like playing football.

Celebrity guest Pippa Middleton presented the award and helped to recognise the inspirational contributions of the BHF’s supporters. Photo credit: Danny Fitzpatrick / DFphotography.co.uk | Picture date: 06/12/23

**WATCH "[MENDING LITTLE HEARTS](#)"** Professor Caputo talks about the development of the heart plasters.

# Announcing the Bristol Heart Festival

*Thursday 22 February 2024*

## SAVE THE DATE

We are pleased to announce the Bristol Heart Institute will host a Heart Festival at the Watershed on Thursday 22 February 2024.

It will be a full day event with talks, film screenings and lots of events and activities for the general public to showcase the work of the BHI.

During the evening we will also be hosting film screenings and talks.

# €1M+ award for the AERO-Illumien V Study

## *Investigating the real-world impact of optical coherence tomography (OCT) on percutaneous coronary intervention (PCI).*

Tom Johnson, Associate Professor in Cardiology, Bristol Medical School (THS) has been awarded €1M+ as co-chief investigator for a 2000 patient prospective registry investigating the real-world impact of optical coherence tomography (OCT) on percutaneous coronary intervention (PCI).

The AERO-Illumien V study recently received UK ethical approval and recruitment has commenced in Germany. Tom Johnson, is leading the imaging Corelab, recently set-up at the Bristol Heart Institute.

Researchers will recruit 2000 patients across 25 sites assessing the real-world impact of OCT on PCI outcomes.

The findings will build upon data from the landmark Illumien-IV RCT, for which Bristol was 1 of 4 recruiting UK sites, presented at the ESC congress in Amsterdam this summer.

### *December update*

The study is now enrolling in Germany & due to open in the UK in the next few weeks. The Bristol OCT Corelab is up and running and images are being analysed by Tom's fully funded fellow, Dr Nitin Chandra Mohan. The study is fully funded by Abbott Vascular.

# Congratulations to our students

## *Graduation 31 July 2023*

The ceremony took place at the Wills Memorial Building on 31st July 2023 at 10:30am. The Deputy Vice-Chancellor and Provost, Professor Judith Squires opened the ceremony.



## Why are women of Black African-Caribbean heritage at elevated risk of hypertensive disorders and hypertensive related stroke

### *BHF Research Grant*

Emma Hart's group have been awarded a BHF Research Grant for the above proposal. An intermediate BHF Fellowship has been awarded to Lydia Simpson who is currently at the University of Innsbruck.



The funding will cover 2 x projects over 4 years. We look forward to welcoming Lydia when she starts work in March 2024

## BHF awards £330,000 to investigate Agrin

### *Maria Giulia Bigotti on the potential benefits of Agrin on the heart*

Award title: "Investigating the extracellular matrix protein Agrin and its potential of inducing cardiac repair", (term 3 years) Pi: Maria Giulia Bigotti, Co-PIs: Danielle Paul, Katie Skeffington and Massimo Caputo.

The inability of the adult mammalian heart to regenerate lost cardiac muscle leads to extensive morbidity (heart failure) and mortality. The extracellular matrix proteoglycan Agrin has been shown to promote cardiac regeneration by binding its alpha-dystroglycan (α-DG) receptor at the cell surface. This interaction is still poorly described, mainly due to the size and complexity of the proteins involved, thus we have produced a miniaturized form of Agrin consisting only of the region specifically implicated in α-DG binding. Within the three years of the grant, we will employ this mini-Agrin to understand the molecular details of the interaction with its receptor and the regenerative mechanism it triggers. Our objective is to then use such fundamental information to strategically produce mini-Agrin variants with optimized regenerative potential, with the definite aim of developing Agrin-based therapies for cardiac repair.

The potential of the C-terminal portion of Agrin for cardiac regeneration has been known for a few years and shown in animal model systems such as the rodent and porcine ones. The idea to further shorten the C-terminal part of the protein and produce a miniaturized form that only contains the region of Agrin believed to be directly responsible for the cardioprotective effect, to my knowledge, is original to our work. Moreover, based on the literature available to date, the work as we propose it in the grant has never been attempted before, as we are the first who will be looking at high-resolution structural details of this protein, alone and in complex with its receptor at the cell membrane. The rationale behind our proposal is that the collection of this structural information will not only further our knowledge on this fundamental protein and interaction but will allow to plan variants of this miniaturized Agrin with augmented regenerative potential. Ideally, local administration of such protein(s) to patients with a damaged heart (after MI, open heart surgery or other kind of traumatic events) would help 1) more potently regenerate heart muscle and contrast heart fibrosis, 2) enhance other cardioprotective effects, such as suppression of the inflammatory response and improved angiogenesis, already shown in mice and pigs for the full-length Agrin C-term (see Baher et al., 2020, DOI: [10.1161/CIRCULATIONAHA.119.045116](https://doi.org/10.1161/CIRCULATIONAHA.119.045116)).



## BHF Intermediate Fellowship to explore MEK inhibition as a means to reprogram cardiac pericytes

### *Dr Elisa Avolio awarded £771k for a five-year study*

BHF Fellowship awarded to explore a new pharmacological treatment of heart ischemia through repurposing an anti-cancer drug.

Dr Elisa Avolio, a Senior Research Associate of the Bristol Medical School and Bristol Heart Institute, has recently been awarded a 5-year British Heart Foundation Intermediate Basic Science Research Fellowship (£ 771K) to explore MEK inhibition as a means to reprogram cardiac pericytes. The original idea is to repurpose an anti-cancer drug to rescue pericyte function and promote reparative vascularisation after myocardial infarction (MI).

Coronary artery disease is a leading cause of death worldwide and a major cause of disability in the growing elderly population. In the UK only, it is responsible for around 66,000 deaths each year. The ideal treatment is represented by the restoration of the perfusion using angioplasty or coronary bypass surgery. The proposed pharmacological solution aims to potentiate endogenous mechanisms of vascular repair through pericyte reprogramming.

Pericytes are the second most abundant cell type in the heart after cardiomyocytes and are specialised in guiding angiogenesis and stabilising blood vessels. Pericyte function is indispensable for myocardial health but progressively declines with ageing and ischemia, thereby restraining the heart's angiogenic response after injury. In her recent research performed together with Professor Paolo Madeddu, Elisa proposed a novel therapeutic approach that repurposes an anti-cancer drug - PD0325901, a specific MEK1/2 kinase inhibitor (MEKi) - to rescue the function of cardiac pericytes instrumental to therapeutic angiogenesis. Inhibition of MEK-ERK signalling using PD0325901 increased the angiogenic activity and pro-arteriogenic phenotype of human cardiac pericytes in vitro. Moreover, a 2-week treatment with PD0325901 promoted the revascularisation of murine hearts, improved left ventricular function, and mice survival after acute MI.

With her fellowship, Elisa will further investigate this promising pharmacotherapeutic approach to support its clinical translation. To understand the mechanisms of MEK inhibition therapy in vivo, she will use a clinically relevant model of reperfused MI in both young and old mice.



## BHF Fellowship to explore MEK inhibition to reprogram cardiac pericytes ... continued

### *Dr Elisa Avolio awarded £771k for a five-year study*

She will adopt pericyte genetic lineage tracing to demonstrate that cardiac pericyte differentiation feeds the formation of new arterioles; 3D light-sheet microscopy and PET/CT imaging to assess coronary microvasculature remodeling and perfusion; and a long-term follow-up to observe if the therapeutic benefits last over time. She will also perform sn-RNA-Seq of mice hearts to explore the mechanisms of MEKi therapy at the single-cell level, followed by the validation of relevant protein targets in situ. These in vivo studies will be complemented by in vitro studies in pericytes isolated from ventricular biopsies of elderly patients with coronary artery disease, and histological analyses of explanted post-ischemic failing hearts. Finally, Elisa will explore the interaction between the MEKi and a library of 700 anti-cardiovascular disease compounds in patients' cardiac pericytes. This screening may also allow the discovery of new drugs able to correct pericyte dysfunction.

This award will enable Dr Avolio to perform the first steps towards establishing herself as an independent research leader. The fellowship also includes a post for a research technician for 2 years.

Elisa is very grateful to the British Heart Foundation; Professor Paolo Madeddu, co-applicant and fellowship sponsor; Professor Gianni Angelini and Dr Svetlana Mastitskaya, internal collaborators; and Professor Sarah George, academic mentor.

Moreover, the fellowship counts on the support from external collaborations with Professor Costanza Emanuelli and Dr Prashant Srivastava (Imperial College London), Professor Chris Denning (Nottingham Biodiscovery Institute), Dr Stephen Paisey (Cardiff PETIC), and Professor Antonio P. Beltrami (University of Udine).

Elisa is also grateful to the Bristol Medical School and Bristol Heart Institute for supporting and hosting her fellowship.



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

## *Nicholas Timpson updates on EXOMES*

Nicholas Timpson is pleased to say the first data are in on the EXOMES study. It is being processed and is already feeding into existing rare variant analysis work.

We look forward to future updates on this exciting research.



# Nominations for outstanding achievements

## *Nomination for a Doctoral prize*

Stanley Buffonge, has recently completed his PhD from the prestigious 4-year BHF programme and has gained recognition for his outstanding thesis and research, earning a nomination for a Doctoral prize. He has recently worked with the British heart foundation on a compelling video offering a glimpse into the daily life of a cardiovascular scientist. You can watch the video on the BHF Heart Matters website [here](#).



During his PhD, he initiated the impactful 'Black in Cardio' initiative, dedicated to showcasing and educating individuals from the Black community on cardiovascular diseases and cutting-edge research worldwide. The initiative culminates annually in the Black in Cardio week, fostering discussions among scientists on pertinent topics. For a comprehensive overview of Black in Cardio, refer to the feature in Nature reviews Cardiology [here](#).

Stanley has presented at several meetings and conferences, including the Bristol Heart Institute meeting, earning him awards for best presentation. Additionally, he served as a Widening Participation Tutor at the University, passionately encouraging school students to pursue careers in science.

## Congratulations!

## Our latest publications

Remember to send details of your latest publications to [bcv-info@bristol.ac.uk](mailto: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/>

Jeremy Chan, Pradeep Narayan, Daniel P. Fudulu, Tim Dong, Gianni D. Angelini; November 25, 2023 [Trend in mitral valve prostheses of choice and early outcomes in the United Kingdom](#) *International Journal of Cardiology* [10.1016/j.ijcard.2023.131607](https://doi.org/10.1016/j.ijcard.2023.131607)

Arnaldo Dimagli, Mario Gaudino, Lamia Harik, Shubhra Sinha, Daniel Fudulu, Jeremy Chan, Roberto Perezgrovas Olaria, Giovanni Soletti Jr., Talal Alzghari, Gianmarco Cancelli, Kevin R., Umberto Benedetto, Gavin Murphy, Gianni Angelini, November 15, 2023 [A Comparative Analysis of CABG Outcomes in Women Using Different Conduits In The National UK Dataset](#) *The Annals of Thoracic Surgery* DOI: [10.1016/j.athoracsur.2023.11.012](https://doi.org/10.1016/j.athoracsur.2023.11.012)

McQueen L.W. 1,†ORCID, Ladak S.S. 1,†, Layton G.R.1 ORCID, Wadey K.2, George S.J. 2, Angelini G.D.2, Murphy G.J.1 and Zakkar M. 1,\* [Osteopontin Activation and Microcalcification in Venous Grafts Can Be Modulated by Dexamethasone](#), (15 November 2023) *Cells* 2023, *12*(22), 2627

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Cattaneo M, Aleksova A, Malovini A, Avolio E, Thomas A, Alvino VV, Kilcooley M, Pieronne-Deperrois M, Ouvrard-Pascaud A, Maciag A, Spinetti G, Kussauer S, Lemcke H, Skorska A, Vasudevan P, Castiglione S, Raucci A, David R, Richard V, Beltrami AP, Madeddu P, Puca AA. *BPIFB4 and its longevity-associated haplotype protect from cardiac ischemia in humans and mice. Cell Death Dis.* 2023 Aug 15;14(8):523. doi: [10.1038/s41419-023-06011-8](https://doi.org/10.1038/s41419-023-06011-8)

Shubhra Sinha, Tim Dong, Arnaldo Dimagli, Hunaid A Vohra, Chris Holmes, Umberto Benedetto, Gianni D Angelini. Comparison of machine learning techniques in prediction of mortality following cardiac surgery: analysis of over 220 000 patients from a large national database. *EJCTS*, Volume 63, Issue 6, June 2023, ezad183, <https://doi.org/10.1093/ejcts/ezad183>

Avolio E, Srivastava PK, Ji J, Carrabba M, Tsang CWT, Gu Y, Thomas AC, Gupta K, Berger I, Emanuelli C, Madeddu P. *Murine studies and expressional analyses of human cardiac pericytes reveal novel trajectories of SARS-CoV-2 Spike protein-induced microvascular damage. Signal Transduct Target Ther.* 2023 Jun 2;8(1):232. doi: [10.1038/s41392-023-01489-2](https://doi.org/10.1038/s41392-023-01489-2)

McQueen L.W. 1,†ORCID, Ladak S.S. 1,†, Layton G.R.1 ORCID, Wadey K.2, George S.J. 2, Angelini G.D.2, Murphy G.J.1 and Zakkar M. 1,\* [Osteopontin Activation and Microcalcification in Venous Grafts Can Be Modulated by Dexamethasone](#), (15 November 2023) *Cells* 2023, *12*(22), [2627](https://doi.org/10.1016/j.cel.2023.11.012); (registering DOI)

# Our latest publications

*Continued ...*

Publications continued ...

Dong T. <sup>1</sup>,\*ORCID, Sunderland N. <sup>1</sup>, Nightingale A. <sup>1</sup> ORCID, Fudulu D.P.<sup>1</sup>, Chan J <sup>1</sup>, Zhai B. <sup>2</sup>, Freitas A. <sup>3</sup> ORCID, Caputo M.<sup>1</sup>, Dimagli A.<sup>1</sup>, Mires S.<sup>1</sup>, Wyatt M.<sup>4</sup>, Benedetto U. <sup>1</sup> and Angelini G D. Development and Evaluation of a Natural Language Processing System for Curating a Trans-Thoracic Echocardiogram (TTE) Database (10 November 2023) [2023, 10\(11\), 1307](#)

Avolio E, Campagnolo P, Katare R, Madeddu P. (2023) [The role of cardiac pericytes in health and disease: therapeutic targets for myocardial infarction](#). *Nature Rev Cardiol*. Epub ahead of print.

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Catsis, S., Champneys, A. R., Hoyle, R., Currie, C., Enright, J., Cheema, K., Woodall, M., Angelini, G., Nadarajah, R., Gale, C., Gibbison, B. (19 July 2023) [Process modelling of NHS cardiovascular waiting lists in response to the COVID-19 pandemic](#). *BMJ* [10.1136/bmjopen-2022-065622](https://doi.org/10.1136/bmjopen-2022-065622)

Tim Dong · Shubhra Sinha Shubhra Sinha · Ben Zhai, Gianni D Angelini (2023) [Cardiac surgery risk prediction using ensemble machine learning to incorporate legacy risk scores: A benchmarking study](#) <https://doi.org/10.1177/20552076231187605>

Katrina Hope<sup>1</sup>, Ben Chant<sup>1</sup>, Thomas Hinton<sup>1</sup>, Adrian H Kendrick<sup>1,2</sup>, Angus K Nightingale<sup>1,3</sup>, Julian F R Paton<sup>4</sup>, Emma C Hart<sup>1</sup> July 4, 2023 [Ventilatory Efficiency Is Reduced in People With Hypertension During Exercise](#) [10.1161/JAHA.121.024335](https://doi.org/10.1161/JAHA.121.024335)

Daniel P Fudulu, Georgia R Layton, Bao Nguyen, Shubhra Sinha, Arnaldo Dimagli, Gustavo Guida, Riccardo Abbasciano, Alessandro Viviano, Gianni D Angelini, Mustafa Zakkar. Trends and outcomes of concomitant aortic valve replacement and coronary artery bypass grafting in the UK and a survey of practices . *EJCTS*, Volume 64, Issue 4, October 2023, ezad259, <https://doi.org/10.1093/ejcts/ezad259>