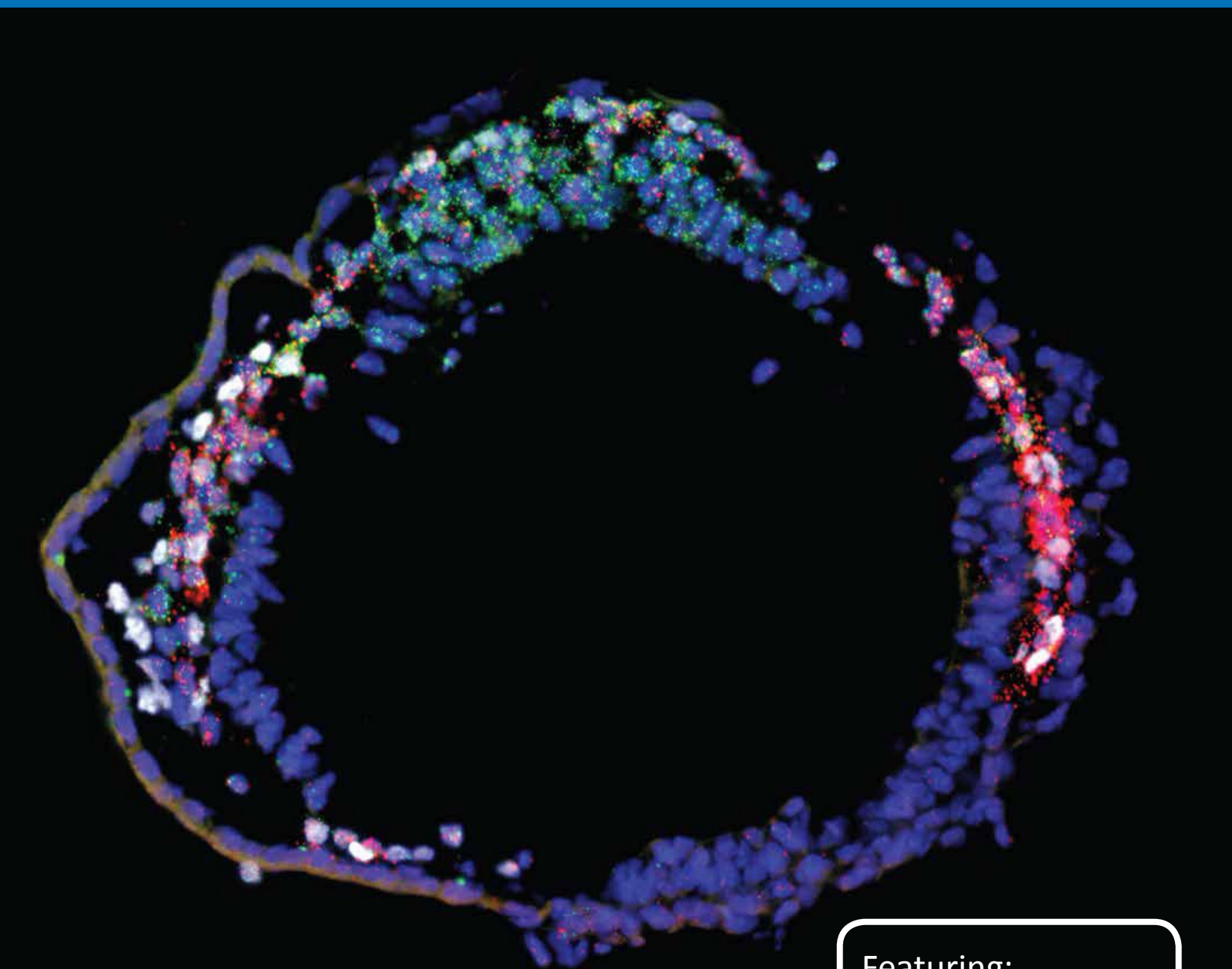
# CAMBRIDGE STEM CELL NEWS

Cambridge Stem Cell News can be downloaded at:
www.stemcells.cam.ac.uk

Issue 14 - Spring/Summer 2018

## Transforming Lives through Stem Cell Research



Featuring:

Institute news

Recent events

Research highlights

# In this issue:



# Prof Tony Green Institute Director

Life at the Cambridge Stem Cell Institute continues apace in 2018, with many events, awards and research highlights. The beginning of March saw Institute members and affiliate researchers meeting for our Annual Retreat, in unseasonally snowy and cold conditions! Despite the challenging weather, over 300 of us came together for a very enjoyable two days.

The last few months have seen a host of notable achievements within the Cambridge stem cell community. Azim Surani received the 2018 Canada Gairdner International Award; Ben Simons was awarded the inaugural Royal Society EP Abraham Professorship; and David Rowitch was elected to the Fellowship of the Academy of Medical Sciences. Kevin Chalut, Thóra Káradóttir and Kristian Franze were successful in their European Research Council consolidator awards. Sanjay Sinha had his British Heart Foundation Senior Fellowship renewed and Simon Buczacki was awarded a Cancer Research UK Clinician Scientist Fellowship. Robin Franklin was awarded the prestigious Barancik Prize for innovation in Multiple Sclerosis research and the Cheryll Tickle Medal was awarded to Jenny Nichols by the British Society of Developmental Biology.

The Institute continues to serve as a hub for the wider stem cell research community in Cambridge, organising and supporting regular cross-disciplinary events. Recent highlights include the popular Stem Cell Club together with the Theory of Living Matter seminars and pub tutorials, all specifically designed to bring researchers together to share insight and expertise from different scientific perspectives. We have also appointed five new affiliate researchers: Thorsten Boroviak, Walid Khaled, Mark Kotter, András Lakatos and Martin Turner – a warm welcome to you all.

Looking to the end of the year, we are excited by the move to our new home on the Cambridge Biomedical Campus, and are looking forward to celebrating the opening of the new building at the Cambridge International Stem Cell Symposium in September. Exciting times ahead.

**The Wellcome - MRC Cambridge Stem Cell Institute is a world-leading centre for stem cell research with a mission to transform human health through a deep understanding of stem cell biology. Bringing together biological, clinical and physical scientists, the Institute explores and defines the properties of stem cells to establish their true medical potential.**

**www.stemcells.cam.ac.uk** **@SCICambridge**

# Institute Updates

With the move to our new home on the Cambridge Biomedical Campus approaching, the opportunity was taken to revisit the Cambridge Stem Cell Institute's logo and branding. An internal competition was launched for scientists to channel their inner designer and create a contemporary logo for the Institute.

Wellcome Trust - Medical Research Council
Cambridge Stem Cell Institute

→

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stem cell institute

The winning entry came from Rodrigo Grandy, a Post-doc researcher in Prof Ludovic Vallier's lab. Working with design teams at the Wellcome and Medical Research Council, the design was polished off and revealed at the Annual Retreat in March. The new logo reflects stem cells in their niches, and also the 3 core research themes at the Institute: stem cell states, stem cells in disease and stem cell therapeutics.

We are now in the phase of rolling this new design out across the Institute.

## NEW AFFILIATE GROUP LEADERS

In the last few months we welcomed five new Affiliates to the Institute. Dr Thorsten Boroviak joins from the Department of Physiology, Development and Neuroscience, Dr Walid Khaled is based in the Department of Pharmacology, Dr Mark Kotter and Dr András Lakatos are both in the Department of Clinical Neurosciences and Dr Martin Turner is at the Babraham Institute.

Cambridge Stem Cell Institute affiliates are individuals invited by the Scientific Advisory Board to engage with the Institute. They are independent group leaders whose research intersects with stem cell biology and medicine.

We now have an outstanding group of 33 affiliate researchers and look forward to working closely with them to advance the excellent stem cell research ongoing in Cambridge.

Read more:
www.stemcells.cam.ac.uk/research/affiliates

## MOVING TO THE CAMBRIDGE BIOMEDICAL CAMPUS

Significant progress continues to be made towards the relocation of the Cambridge Stem Cell Institute into the new Capella building on the Cambridge Biomedical Campus later this year. With the external building being completed in 2017, the focus is now on the internal structures. The design and installation of state of the art lab spaces and equipment will provide the ideal space for the pioneering work of the Institute, and there will also be a lecture theatre, public art/engagement space and onsite cafe.

Outside the building there will be a large scale public art installation entitled 'CORPUS' (pictured below) commissioned by Scottish artists Dalziel and Scullion. The vertebrae inspired art effectively act as individual seats and benches, allowing patients, public and staff to rest and relax against their cool stony surface.

## AWARDS, APPOINTMENTS & PRIZES

### Prof. Azim Surani selected to receive the 2018 Canada Gairdner International Award

Affiliate group leader Azim Surani (based at the Gurdon Institute) was selected to receive the 2018 Canada Gairdner International Award for the discovery of mammalian genomic imprinting that causes parent-of-origin specific gene expression and its consequences for development and disease. This prestigious award recognises outstanding biomedical scientists who have made original contributions to medicine with the goal of contributing to increased understanding of human biology and disease.

### Prof. Ben Simons awarded the inaugural Royal Society Sir Edward Penley Abraham Professorship

Ben Simons was awarded the inaugural Royal Society EP Abraham Professorship. Ben does cross-disciplinary research using statistical methods from physics to describe the behaviour of stem cells. He studies how principles of self-organisation and emergence provide predictive insights into the process of tissue development, and how these programmes become subverted during the transition to diseased states. Following a multidisciplinary research approach, his lab applies concepts and methods from statistical theory to uncover conserved patterns of cell fate.

### Prof. David Rowitch elected to the Fellowship of the Academy of Medical Sciences

The fellowship recognises outstanding contributions to biomedical and health science, leading research discoveries, and translating developments into benefits for patients and the wider society. David is Professor and Head of the Department of Paediatrics here in Cambridge. He is a neonatologist and neuroscientist whose laboratory investigates genetic factors that determine development and diversity of glial cells of the brain and the response to injury.

### Prof. Robin Franklin wins the 2017 Barancik Prize for Innovation in Multiple Sclerosis Research

Robin is a senior scientist at the Cambridge Stem Cell Institute and Director of the Cambridge MS Society Centre for Myelin Repair. He is a world leader in the biology of oligodendrocytes, which are the myelinating cells in the brain that are damaged in Multiple Sclerosis. His team pinpointed a key factor that stimulates myelin repair (Retinoid X Receptors), which was the genesis of a clinical trial of a drug (bexarotene) already available for other conditions.

### Prof. Jenny Nichols awarded the Cheryll Tickle Medal

The British Society for Developmental Biology recognised Jenny Nichols' outstanding achievements in Developmental Biology by awarding her the Cheryll Tickle Medal. She was also recently promoted to Professor of Embryonic Pluripotency. Jenny's research focuses on understanding how the pluripotent lineage is specified, maintained and relinquished during embryonic development.
You can watch Jenny's Cheryll Tickle Lecture at:
http://bsdb.org/awards/the-cheryll-tickle-medal/#Movies.

## NEW FELLOWSHIPS

**Dr Simon Buczacki** (Affiliate group leader) was awarded a Cancer Research UK Clinician Scientist Fellowship to further develop his work using primary human colorectal cancer tissue to quantify the interaction between cellular identity, behaviour and mutational background, with a particular focus on understanding reserve cancer stem cell populations.

Simon will join the team of Principal Investigators at the Cambridge Stem Cell Institute once we move to the Cambirdge Biomedical Campus later in the year.

**Dr Sanjay Sinha** had his British Heart Foundation Senior Fellowship renewed to continue his research in vascular disease modelling using human pluripotent stem cell-derived smooth muscle cells. Sanjay's work has important implications for cardiovascular diseases, including heart attacks, strokes and aortic aneurisms. Alongside his research, Sanjay is also a Consultant in Cardiology at Addenbrooke's Hospital.

## EUROPEAN AWARDS FOR CAMBRIDGE STEM CELL SCIENTISTS

Cambridge stem cell researchers were awarded prestigious European Research Council (ERC) funding to undertake pioneering research that can drive paradigm shifts in their designated fields. The sole criterion for selection is scientific excellence and the aim of the funding is to recognise the best ideas coming from the top scientists across Europe.

**Dr Thóra Káradóttir** (Cambridge Stem Cell Institute & Department of Veterinary Medicine) will be using the funds to elucidate how neuronal activity regulates myelin plasticity in the central nervous system.

**Dr Kevin Chalut** (Cambridge Stem Cell Institute & Department of Physics) will research the use of biotechnology for investigating cell fate choices.

**Dr Kristian Franze** (Cambridge Stem Cell Institute Affiliate & Department of Physiology, Development & Neuroscience) will investigate the integration of mechanical and chemical signals in neuronal guidance.

## SCIENTISTS ELECTED AS EMBO MEMBERS

**Prof Ben Simons**, **Dr Michaela Frye** and **Dr Peter Campbell** were elected as members of the European Molecular Biology Organisation (EMBO), joining a group of more than 1800 of the best researchers in Europe and around the world.

"EMBO Members are leading scientists working across all of the life sciences. They also strengthen the research community in Europe and beyond through their international collaborations and connections," says EMBO Director Maria Leptin.

# Recent Events & Activities

## ANNUAL RETREAT

On 1st and 2nd March 2018 the Cambridge Stem Cell Institute held its Annual Retreat at Tattersalls in Newmarket. This event focusses on fostering an integrated, collaborative culture between all levels of the Cambridge Stem Cell Institute and Affiliated Researchers. We heard talks from PIs across the Institute, as well as flash presentations from Postdocs and PhD students. Poster prizes were awarded to Suruchi Pacharne (Vassiliou Lab) and David Jorg (Simons Lab) for their work in acute myeloid leukaemia and diffusion mechanisms in proneural wave progression, respectively.

This year the event hosted representatives from Cambridge Enterprise and the Cambridge Academy of Therapeutics to discuss ideas and opportunities for Institute members to develop their research in novel directions.

The event also incorporated networking and social time for Institute members to interact in an informal setting, with the Institute Ale 'Regenerator' on tap at the Moonshine Brewery bar and music supplied by upbeat country band AcesHigh! A great time was had by all and plans are underway for next year's event!

## THEORY OF LIVING MATTER

The Theory of Living Matter, led by Institute junior researchers and affiliates, is a non-profit researcher network that brings together biologists, physicists, mathematicians and computer scientists interested in theoretical analysis and modelling of biological phenomena.

In April 2018 the Institute supported the group to coordinate their 11th General Meeting on "Developmental Dynamics: from stem cells to organisms" with talks from Olivier Pourquié (Harvard University) and Michael Stumpf (Imperial College London).

The group also run regular pub tutorials to bring members of the Cambridge scientific community up to speed on a rage of interdisciplinary topics, from machine learning to drosophila development segment patterning.
More here: www.tcm.phy.cam.ac.uk/tlm/

## STEM CELL CLUB

Stem Cell Club is a multi-disciplinary event organised by the Cambridge Stem Cell Institute open to researchers in and around Cambridge with an interest in stem cells. The aim is to spark new conversations on stem cell research between individuals from a range of backgrounds, including biology, physics and sociology. Each event comprises two talks from invited speakers followed by open discussions accompanied by food and drinks.

In February, we hosted Selina Wray (University College London) and Sanjay Sinha (Cambridge Stem Cell Institute), discussing stem cell models of Alzheimer's disease and complex human induced pluripotent stem cell models of disease to guide patient-specific therapies.

In May, Sara-Jane Dunn (Microsoft Research) and Austin Smith (Cambridge Stem Cell Institute), discussed mathematical models to understand stem cells and principles of pluripotency.

## LABORATORY-GROWN BLOOD CELLS: TRANSFUSION OF THE FUTURE

Dr Cédric Ghevaert's group are exploring new ways to produce red blood cells and platelets from stem cells in the laboratory. These cells have the potential to revolutionise transfusion medicine, so we asked the public and blood donors what questions they had for the scientists behind this pioneering work. Questions included:

- What are blood cells and what do they do?
- Why do we need laboratory grown blood cells?
- What are they and how are they produced?
- How will laboratory grown blood cells be used and what other potential benefits do they have?

These questions were put to Cédric and his team and the answers were recorded for the public to see. You can watch the video here: www.stemcells.cam.ac.uk/public/films

## CAMBRIDGE SCIENCE FESTIVAL 2018


In March, the Cambridge Stem Cell Institute hosted a range of events for the Cambridge Science Festival.

- **UniStem Day**: Elisa Laurenti, Justyna Rak (Méndez-Ferrer lab) and Nicole Mende (Laurenti lab) led activities with our stem cell robots for over 100 primary school children to mark this annual Europe-wide stem cell outreach day.
- **Brewing a Taste for Stem Cells**: Dan Bode (Kent Lab) and Tim Lohoff (Nichols Lab) organised a sell-out event for 75 beer and science fans at the University Social Club. This event follows up our highly successful collaboration with Moonshine Brewery which delivered 'Regenerator'- a scientific session ale.
- **The Big Stem Cell Knit**: Over 180 members of the public joined us to craft their own neurons, hear researchers talk about their work, and tour our labs, in partnership with Neural Knitworks.
- **Life in a Dish**: This event, organised with the Sociology department, explored the relationship between researchers and the living materials they study. Elisa Laurenti joined in conversations with her partnering artist from the Stem Cell Exchanges project to shed new perspectives on this often interesting topic.
- **Story Collider:** In March, the Institute hosted hit international story-telling show The Story Collider at the Cambridge Junction. A trail-blazer in science communication, Story Collider brings personal stories about science to life. The production team travelled from the USA to deliver the first ever Cambridge show on the theme of 'regeneration' as part of Cambridge Science Festival. Samantha Tilson (Vallier Lab) was one of five scientists who told their stories to a packed audience of over 100.
- **Magic Myelin**: As part of the final day of the Festival we were at the Cambridge Academy for Science and Technology with a hands-on exhibit developed with the Káradóttir and Franklin labs to talk about stem cells and myelin.

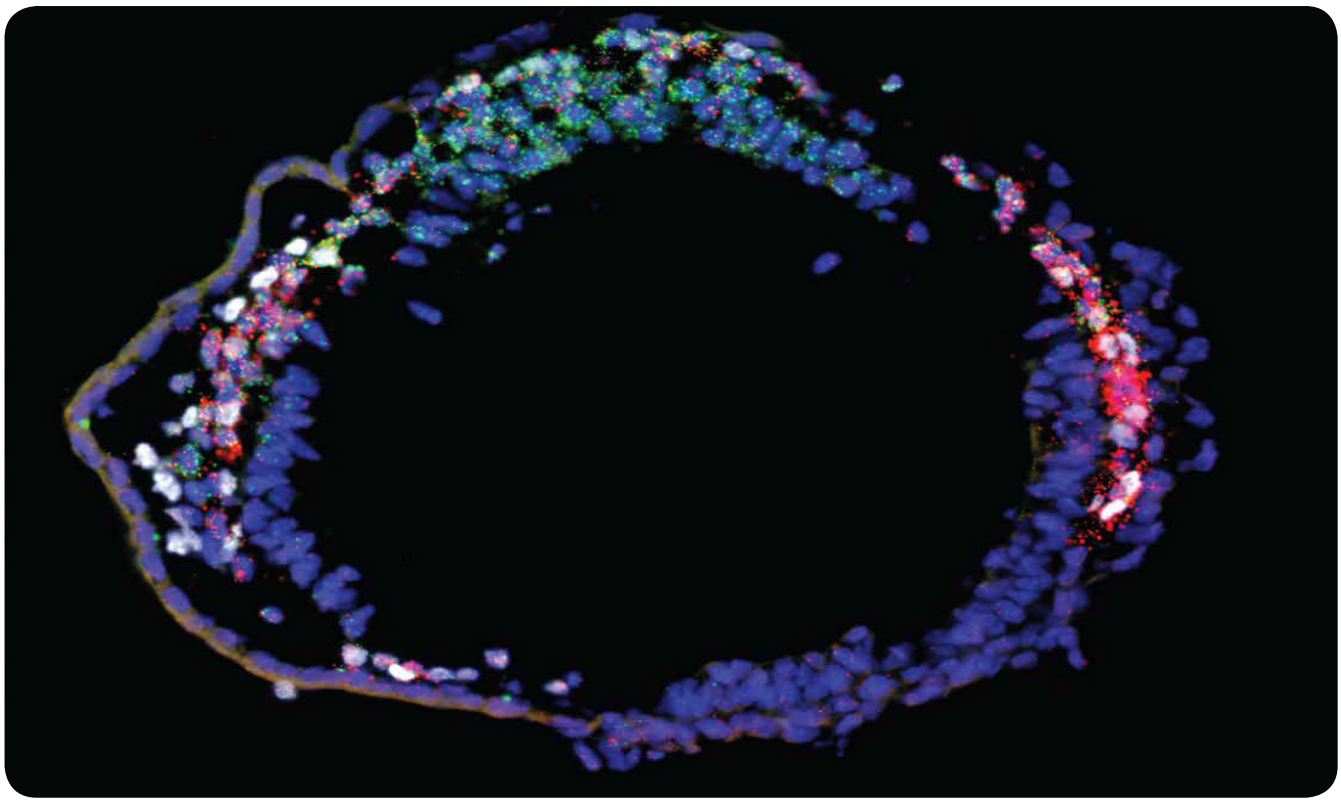
# Research highlights

## MATTERS OF THE HEART: SCIENTISTS REVEAL HOW STEM CELLS DRIVE CARDIAC DEVELOPMENT & GROWTH

**Prof Bertie Göttgens** and collaborators from the Université Libre de Bruxelles used cutting-edge technology to show for the first time how embryonic stem cells diversify to generate the progenitor cells required for the development of the heart. The researchers hope that this new understanding will pave the way for future therapeutic opportunities for infants born with heart defects and other heart diseases.

The study, published in the journal Science, used pioneering single-cell technology to study the genetic activity of the earliest heart progenitor cells present in the mouse embryo. The scientists took advantage of a cell labelling strategy based on a gene called Mesp1, which is critical for directing stem cells to become cardiac cells in the developing heart. Using powerful computer analysis, the researchers could pinpoint the distinct progenitor cell populations that would go on to develop into the specific cell types required for a fully functioning heart. The results also showed that development of the different cell populations begins at different time points, and that the cells migrate through specific locations in the early embryo.

Prof Göttgens said *"Our new discoveries critically depend on recent technological innovations that now allow us to determine the gene activity in individual single cells. Not only can we study tiny cell populations which wasn't possible before, but we can also use the computer to separate the individual single cells into subgroups or cell types, based on their gene activity profiles. From these newly discovered gene profiles, we can discover new candidate genes that may be exploited for developing new therapies to repair the heart".*



*Cell staining can be used to detect the newly defined heart progenitor populations in early mouse embryos*
*Image credit: Göttgens Lab*

**Reference:** Defining the earliest step of cardiovascular lineage segregation by single cell RNA-seq. F. Lescroart, X. Wang, X. Lin, B. Swedlund, S. Gargouri, A. Sànchez-Dànes, V. Moignard, C. Dubois, C. Paulissen, S. Kinston, B. Göttgens and C. Blanpain is published in Science.

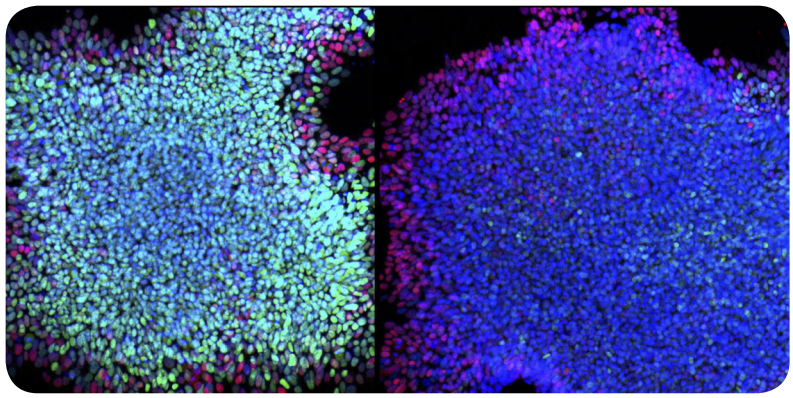
## MISSING LINK FOUND BETWEEN PATHWAYS INVOLVED IN CELL DEVELOPMENT

**Prof Ludovic Vallier** led a study revealing a new mechanism that coordinates human development in response to signals from outside the cell. Reported in Nature, the study describes how SMAD2 and SMAD3 proteins (SMAD2/3) link and coordinate many different pathways in the cell that were previously believed to be separate. In addition to switching on specific genes on command, researchers saw for the first time that SMAD2/3 precisely regulates the timing of their expression, fine-tuning the processes needed for embryo development and growth.

This new mechanism could be essential for other processes that need a rapid response - such as organ repair, immune response or cancer growth - and this finding could inspire novel methods of studying these processes.

Dr Alessandro Bertero, a first author on the paper and former PhD student at the Cambridge Stem Cell Institute, said: *"To our knowledge this is the first time that anyone has seen that SMAD2/3 can interact with so many multiple processes, unexpectedly coordinating different cell pathways. Our study shows that SMAD2/3 is like a multi-function Swiss army knife instead of the specialised tool it was previously thought to be, creating a link between various key pathways."* Prof Ludovic Vallier said: *"Our study reveals that cell signalling with SMAD2/3 coordinates cellular mechanisms and allows the cells to change state quickly. Understanding this could be important for studying diseases such as cancer where cellular processes are often investigated in isolation. These findings could also change the way mechanisms such as mRNA processing, DNA repair and transcriptional regulations are studied and open entire new fields of investigation."*

**Reference:** The SMAD2/3 interactome reveals that TGFβ controls m6A mRNA methylation in pluripotency. Alessandro Bertero & Stephanie Brown et al. is published in Nature.



*Human embryonic stem cells differentiated into the neuroectoderm germ layer. Normal cells on the right have differentiated, whereas many cells on the left with impaired SMAD2/3 mechanism have not. Image credit: Vallier Lab*

## NEW STEM CELL RESEARCH FUNDAMENTALLY CHANGES OUR UNDERSTANDING OF MALE AND FEMALE EARLY DEVELOPMENT

**Dr José Silva**'s lab revealed new insight into sex chromosome changes in embryos that fundamentally alters the way we think about male and female early development. The lab's latest research, published in the journal Cell Stem Cell, shows for the first time that a process called 'X Chromosome Inactivation' occurs transiently on male X chromosome, rather than just in females as previously thought. X Chromosome Inactivation is an essential developmental process that ensures individuals receive the correct amount of genetic information for normal cell functions to occur. In males, who carry one X and one Y chromosome (XY), this genetic dosage is naturally delivered. In females, who carry two X chromosomes (XX), the correct genetic dosage is obtained through silencing of one of their X chromosomes via X Chromosome Inactivation.

*"Our study shows that initiation of X chromosome inactivation occurs before the cell realizes whether it is male or female"* explained Elsa Sousa, who led the current research. *"We previously thought that cells realised their sex by counting their X chromosomes prior to the initiation of X Chromosome Inactivation if female. Our research changes this paradigm. We now know we need to look earlier in the process to better understand the mechanisms driving sex-specific development."*

*"This finding fundamentally changes how we think about embryonic development"* added Dr José Silva. *"The new understanding that male cells undergo X chromosome inactivation allows us to study the process from a new perspective which we hope will serve as a springboard for future discoveries in the field".*

**Reference:** Exit from Naive Pluripotency Induces a Transient X Chromosome Inactivation-like State in Males, Elsa J. Sousa, Hannah T. Stuart, Lawrence E. Bates, Mohammadmersad Ghorbani, Jennifer Nichols, Sabine Dietmann, José C.R. Silva is published in Cell Stem Cell.

## PROTECTIVE ROLE OF Y CHROMOSOME GENETICS DISCOVERED

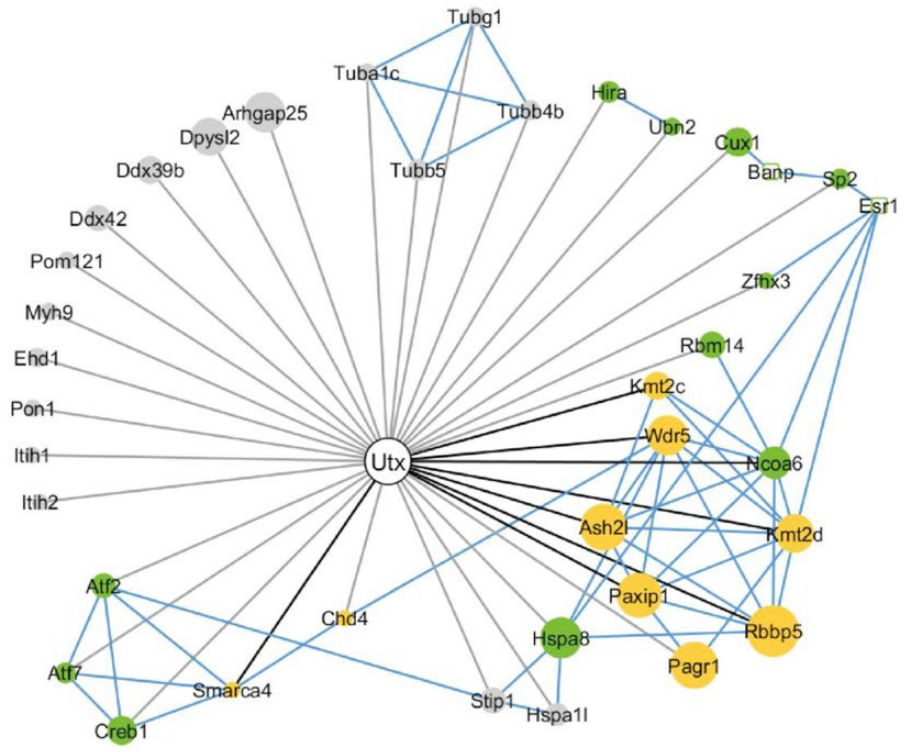
Acute myeloid leukaemia is an aggressive blood cancer that affects people of all ages. It develops in cells in the bone marrow and leads to life-threatening infections and bleeding. Mainstream acute myeloid leukaemia treatments have remained unchanged for decades.

**Prof Brian Huntly** and **Dr George Vassiliou** recently discovered the first leukaemia protective gene that is specific to the male-only Y chromosome. The researchers found that this Y-chromosome gene protects against the development of acute myeloid leukaemia and other cancers.

The study, published in Nature Genetics, investigated how loss of the X-chromosome gene UTX, which is known to be mutated in many tumours, hastens the development of acute myeloid leukaemia. However, they found that UTY, a related gene on the Y chromosome, protected male mice lacking UTX from developing the leukaemia. The authors then show that in acute myeloid leukaemia, and in several other human cancer types, loss of UTX is accompanied by loss of UTY, confirming that the cancer-suppressing role of UTY extends beyond acute myeloid leukaemia.

Prof Brian Huntly said*: "It is known that men often lose the Y chromosome from their cells as they age, however the significance of this was unclear. Our study strengthens the argument that loss of the Y chromosome can increase the risk of cancer and describes a mechanism for how this may happen."*

Dr George Vassiliou said*: "Treatments for AML have not changed in decades and there is a large unmet need for new therapies. This study helps us understand the development of AML and gives us clues for developing new drug targets to disrupt leukaemia-causing processes. We hope this study will enable new lines of research for the development of previously unforeseen treatments and improve the lives of patients with AML."*




*The network shows protein-protein interactions centred around UTX. Circle size represents abundance of the protein. Grey lines represent novel interactions identified in the study, light blue lines represent interactions reported in the literature, and black edges represent previously reported interactions.*
*Credit: Vassiliou and Huntly labs*

**Reference**: UTX-mediated enhancer and chromatin remodeling suppresses myeloid leukemogenesis through noncatalytic inverse regulation of ETS and GATA programs, Malgorzata Gozdecka et al. is published in Nature Genetics.

# Recent Publications

**Exit from Naive Pluripotency Induces a Transient X Chromosome Inactivation-like State in Males. S**ousa EJ, Stuart HT, Bates LE, Ghorbani M, Nichols J, Dietmann S, Silva JCR. **Cell Stem Cell.** 2018 Jun 1;22(6):919-928.e6.

**UTX-mediated enhancer and chromatin remodeling suppresses myeloid leukemogenesis through noncatalytic inverse regulation of ETS and GATA programs.** Gozdecka M, Meduri E, Mazan M, Tzelepis K, Dudek M, Knights AJ, Pardo M, Yu L, Choudhary JS, Metzakopian E, Iyer V, Yun H, Park N, Varela I, Bautista R, Collord G, Dovey O, Garyfallos DA, De Braekeleer E, Kondo S, Cooper J, Göttgens B, Bullinger L, Northcott PA, Adams D, Vassiliou GS, Huntly BJP. **Nature Genetics.** 2018 May 7. doi: 10.1038/s41588-018-0114-z.

**Defining the earliest step of cardiovascular lineage segregation by single-cell RNA-seq.** Lescroart F, Wang X, Lin X, Swedlund B, Gargouri S, Sànchez-Dànes A, Moignard V, Dubois C, Paulissen C, Kinston S, Göttgens B, Blanpain C. **Science.** 2018 Mar 9;359(6380):1177-1181

**The SMAD2/3 interactome reveals that TGFβ controls m6A mRNA methylation in pluripotency.** Bertero A, Brown S, Madrigal P, Osnato A, Ortmann D, Yiangou L, Kadiwala J, Hubner NC, de Los Mozos IR, Sadée C, Lenaerts AS, Nakanoh S, Grandy R, Farnell E, Ule J, Stunnenberg HG, Mendjan S, Vallier L. **Nature.** 2018 Mar 8;555(7695):256-259.

**Defining murine organogenesis at single-cell resolution reveals a role for the leukotriene pathway in regulating blood progenitor formation**. Ibarra-Soria X, Jawaid W, Pijuan-Sala B, Ladopoulos V, Scialdone A, Jörg DJ, Tyser RCV, Calero-Nieto FJ, Mulas C, Nichols J, Vallier L, Srinivas S, Simons BD, Göttgens B, Marioni JC. **Nature Cell Biology.** 2018 Feb;20(2):127-134

**Mutant calreticulin knockin mice develop thrombocytosis and myelofibrosis without a stem cell self-renewal advantage**. Li J, Prins D, Park HJ, Grinfeld J, Gonzalez-Arias C, Loughran S, Dovey OM, Klampfl T, Bennett C, Hamilton TL, Pask DC, Sneade R, Williams M, Aungier J, Ghevaert C, Vassiliou GS, Kent DG, Green AR. **Blood**. 2018 Feb 8;131(6):649-661.

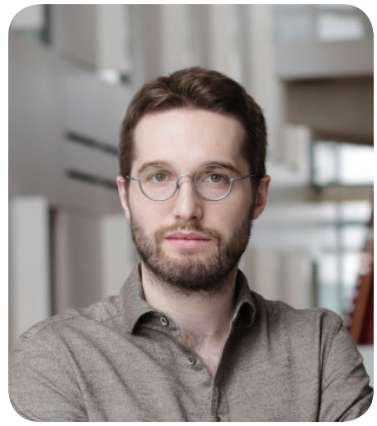
**From haematopoietic stem cells to complex differentiation landscapes.** Laurenti E, Göttgens B. **Nature.** 2018 Jan 24;553(7689):418-426.

**Single-cell RNA-sequencing uncovers transcriptional states and fate decisions in haematopoiesis**. Athanasiadis EI, Botthof JG, Andres H, Ferreira L, Lio P, Cvejic A. **Nature Communications**. 2017 Dec 11;8(1):2045.

**Promoter-bound METTL3 maintains myeloid leukaemia by m6A-dependent translation control.** Barbieri I, Tzelepis K, Pandolfini L, Shi J, Millán-Zambrano G, Robson SC, Aspris D, Migliori V, Bannister AJ, Han N, De Braekeleer E, Ponstingl H, Hendrick A, Vakoc CR, Vassiliou G, Kouzarides T. **Nature**. 2017 Dec 7;552(7683):126-131

# Interview

## 15 MINS WITH...DR HARRY LEITCH



Dr Harry Leitch started studying medicine in Cambridge and later became a PhD student at the Cambridge Stem Cell Institute, co-supervised by Profs Austin Smith and Azim Surani. He worked as a junior doctor for a year and then moved on to London as part of the clinician-scientist programme - the Chain-Florey Scheme. He is now an independent Group Leader at the MRC London Institute of Medical Sciences. We asked him about his time at the Institute and how it prepared him for his future career.

### Q1: Why did you choose to do your PhD at the Cambridge Stem Cell Institute?

I did my PhD as part of the MB/PhD programme at the School of Clinical Medicine. I was lucky in that we were given the freedom to talk to Group Heads from any Department or Institute. My choices were greatly influenced by the time I spent working in Bill Colledge's lab. I became interested in pluripotency through learning about his background and the seminal work he did with Martin Evans (who got the Nobel prize for deriving embryonic stem cells). It was this new found fascination that led me into a joint project between Austin Smith at the Cambridge Stem Cell Institute and Azim Surani at the Gurdon Institute. I was very lucky that two such fantastic supervisors accepted me into their labs, and also lucky to combine their respective expertise in pluripotent stem cell biology and primordial germ cell development. So I jumped at the opportunity to work with Austin – and probably didn't realise quite how lucky I was to get that opportunity.

### Q2: What is your favourite memory from your time at the Institute?

Wow. That's a really tricky question. I loved pretty much every minute. My experience prior to my PhD had given me a taste for research, and the thought that I might be suited to it. However, the PhD gave me that grounding, creative focus and extended period of time to develop as an independent scientist – and I think I quite quickly realised that research was the path I wanted to follow. In that way, I guess my time at the Cambridge Stem Cell Institute was a really important and formative period that changed the direction of my life. I was surrounded by incredible scientists and soaked up all the knowledge and skills I could from them. I totally immersed myself in the environment and met some great people, lifelong friends, along the way. From that time forward, I've been inspired to do as much research as possible alongside my clinical training.

### Q3: How did your time at the Institute prepare you for your future career?

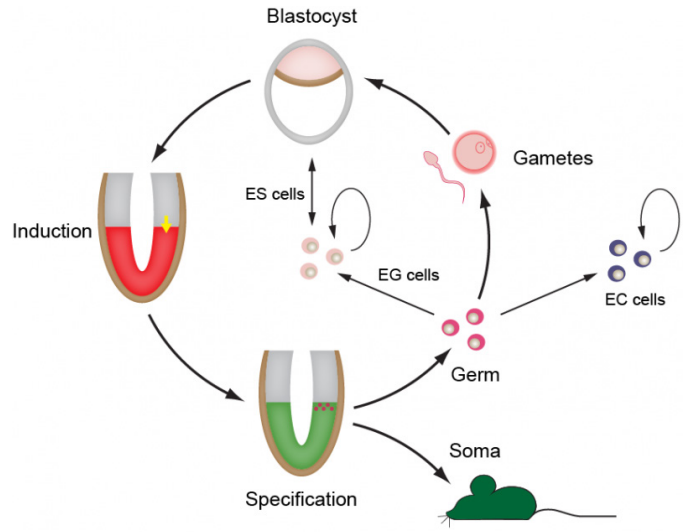
The single most important lesson was learning to think clearly and creatively. The environment in Austin's lab was paramount to that. The lab meetings and journal clubs were pretty awesome. I learnt so much from being surrounded by smart, talented colleagues – hearing them formulate questions or critique sloppy work. It was a really meritocratic environment which was important too. The best ideas were respected, regardless of who they came from. This also meant that you had to be on your game to escape the withering eye!

### Q4: What advice would you offer to current PhD students at the Institute?

I'm maybe still a bit too 'early career' to be offering too much advice. The obvious thing is to enjoy it – but that's a bit of a cop out. Doing a PhD isn't always easy and there may well be really crap times along the way. However, it's a unique time in terms of the freedom to learn and follow your interests (and make mistakes!). Learn your trade, become an expert in a difficult technique if possible and keep challenging yourself. Don't be too cynical too quickly. Make sure you're surrounding yourself with people who are cleverer than you, and that you learn from (this was always easy for me!).

## Q5: What most excites you about stem cell research?

My PhD was titled 'Pluripotency and the germline'. I've just started my own lab and eventually came up with the highly original lab name 'Germline and pluripotency' – so you can tell my interests have deviated massively since my time at the Institute! For me, this area of research allows to me to ask fundamental questions about germline development, stem cell biology, cell fate, epigenetics, cell signalling and reproduction. With my medical hat on I also think that by studying these basic questions we can provide the foundations required to build successful regenerative medicine approaches and in particular, inform attempts at in vitro gametogenesis.



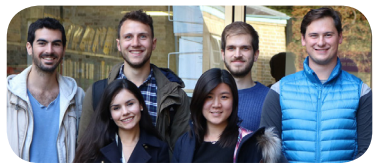

***The mammalian germline cycle as a pluripotent cycle:*** *schematic summary of the germline cycle showing primordial germ cell (PGC) induction, PGC specification and segregation of germ from soma. The origin of naive pluripotent embryonic stem (ES) and embryonic germ (EG) cells is also shown, alongside that of embryonal carcinoma (EC) cells - the stem cell compartment of teratocarcinomas.*

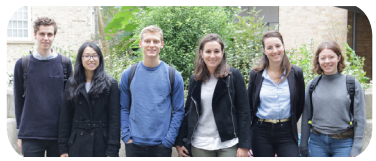
**We would like to extend our thanks to Harry for talking to us about his time at the Cambridge Stem Cell Institute and we wish him the very best of luck for the next stage of his career.**

If you are part of the alumni community from the Cambridge Stem Cell Institute, and would like to share your experiences, please contact Abi Herrmann sci-coordinator@stemcells.cam.ac.uk.

# FOUR YEAR PHD PROGRAMME IN STEM CELL BIOLOGY & MEDICINE

Stem cell research is one of the most exciting and rapidly developing areas in current biomedical science. The challenges involved in this area are complex and range across many different disciplines from basic science through disease modelling to clinical medicine. Consequently, students on this Programme come from a variety of different backgrounds with little or no specialist education in this field. This course provides students with a thorough introduction to the concepts and practices of stem cell research through a structured PhD Programme with a broad-ranging first year.





The first year of the programme is designed to give training in the conceptual foundations, experimental systems, practical techniques, and current state of knowledge in stem cell biology and medicine. In parallel with workshops and discussion sessions, three laboratory rotations give the students practical research training and the experience of working with different stem cell types and in different laboratories. This empowers the students to make an informed decision when choosing their research question and host laboratory for the PhD project (in years 2-4).

**Application for 2019 entry onto our Four Year PhD Programme in Stem Cell Biology & Medicine opens in October 2018. Please visit our website www.stemcells.cam.ac.uk/join-us/study for more details of the Programme, including instructions on how to apply.**

# 6th Cambridge International Stem Cell Symposium, 19-21 September

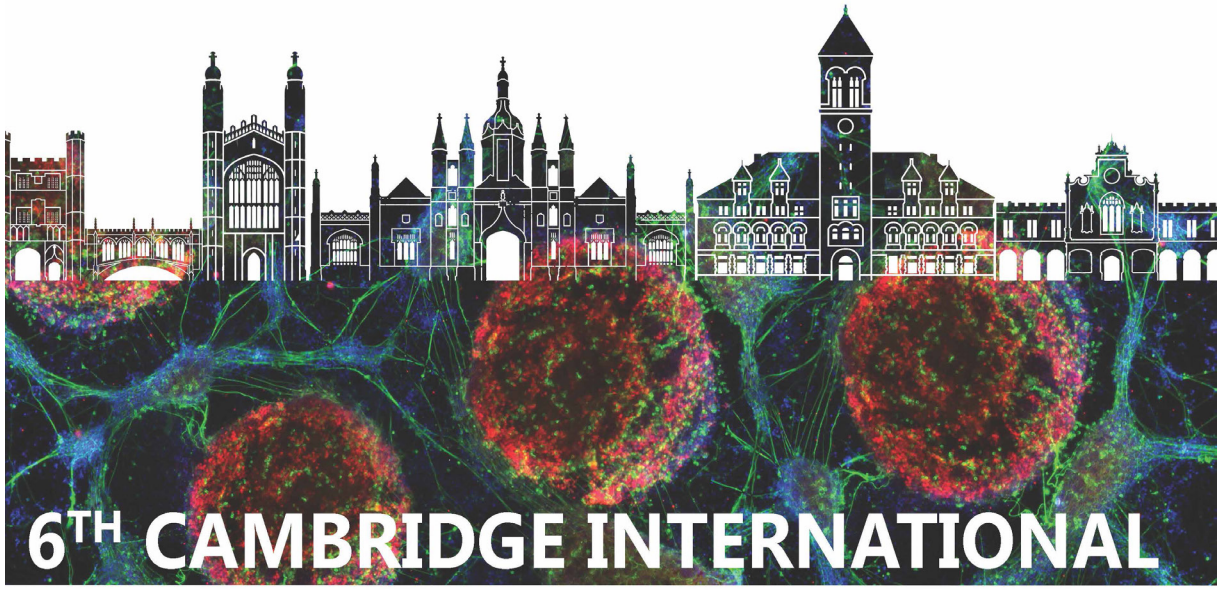
The 6th Cambridge International Stem Cell Symposium marks the Institute's move to our new building on the Cambridge Biomedical Campus and will celebrate the great advances being made in stem cell biology in Cambridge, the UK and around the world.

The 2018 Symposium will bring together biological, clinical and physical stem cell scientists, working across multiple tissues and at different scales, to share data, discuss ideas and address the biggest fundamental and translational questions in stem cell biology.

The research talks will span 3 days, including exceptional keynote presentations, cross-disciplinary panel debate, over 100 scientific posters and an engaging trade exhibition. Delegates will also have the opportunity to attend a gala dinner at Trinity College.

Registration is open until 3rd August 2018. We currently have more than 300 people registered for this exciting event with poster places and seats at the gala dinner still available.

Register here: https://sci-events.eventhq.co.uk/6th-cambridge-international-stem-cell-symposium



# 6TH CAMBRIDGE INTERNATIONAL STEM CELL SYMPOSIUM

## 19th-21st September 2018

### Confirmed speakers include:

Cédric Blanpain
Université Libre de Bruxelles

Elena Cattaneo
University of Milan

Frederic de Sauvage
Genentech Inc

Stuart Forbes
University of Edinburgh

Allon Klein
Harvard University

Cristina Lo Celso
Imperial College London

Hiromitsu Nakauchi
Stanford University

Malin Parmar
Lund University

Emmanuelle Passegué
Columbia Stem Cell Initiative

Duanqing Pei
Guangzhou Institute

Thomas Rando
Stanford University

Peter Reddien
Massachusetts Institute of Technology

Bill Richardson
Wolfson Institute

David Scadden
Harvard University

Dirk Schübeler
Friedrich Miescher Institute for Biomedical Research

Kate Storey
University of Dundee

Masayo Takahashi
RIKEN Center for Developmental Biology

Adrian Thrasher
University College London

Andreas Trumpp
HI-STEM

Fiona Watt
King's College London

Leonard Zon
Harvard University

Organised by: wellcome-MRC cambridge stem cell institute

Registration now open
www.stemcells.cam.ac.uk/symposium2018

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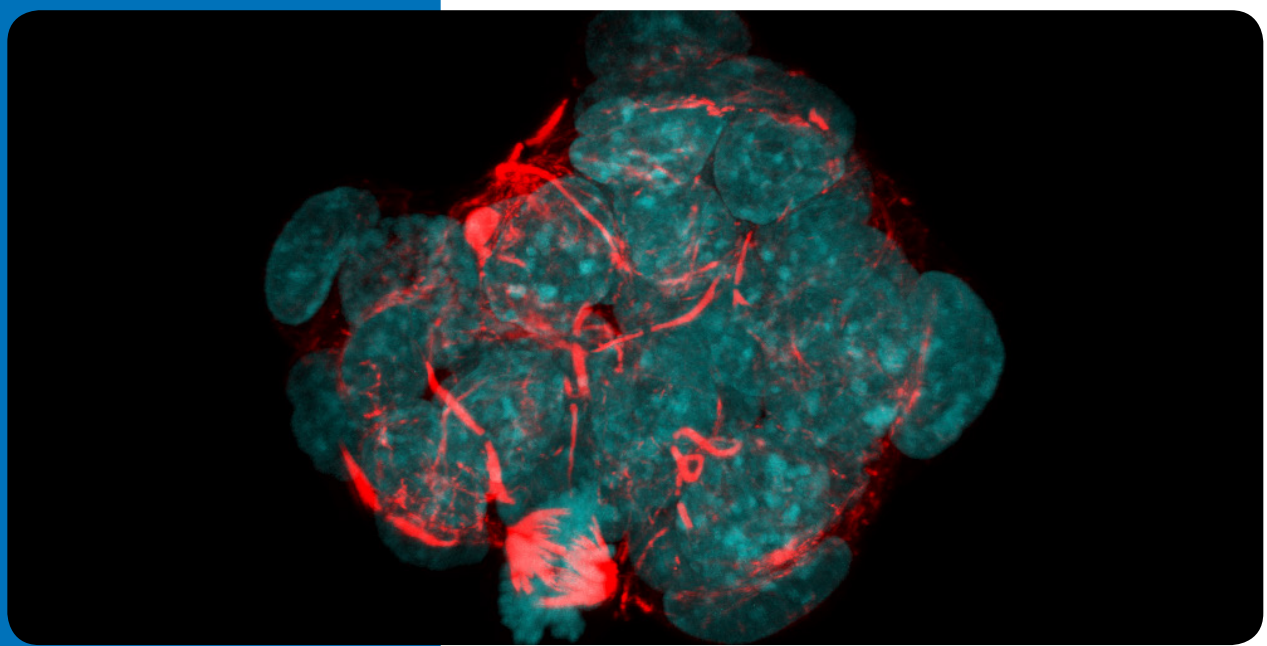
Cambridge Stem Cell News is produced by the Cambridge Stem Cell Institute to provide an accessible summary of recent Institute research, events and interdisciplinary activities.

We are keen to hear feedback on the publication and are also very open to suggestions for features and content for future editions.

To share your thoughts simply email sci-coordinator@stemcells.cam.ac.uk



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Email: reception@stemcells.cam.ac.uk
Phone: +44 (0) 1223 760 240

Our regular office hours are
Monday to Friday, 9 a.m. to 5 p.m.

Follow us on Twitter & Facebook
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**Front Cover Image:** Cell staining can be used to detect the newly defined heart progenitor populations in early mouse embryos.
Credit: Göttgens Lab

**Back Cover Image:** Mouse embryonic stem cells, expressing H2B-mTurquoise, immunostained with antibody to acetylated alpha-tubulin.
Credit: Nichols Lab

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