

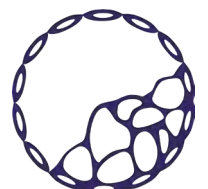
# The LokeCentre

for trophoblast research

Annual Report 2023/24



UNIVERSITY OF  
CAMBRIDGE



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# Welcome

Welcome to the Loke Centre for Trophoblast Research Annual Report for 2023-2024. We are incredibly grateful to Professor Charlie Loke, Amanda Loke, and the Loke family for their continued support of the Loke Centre for Trophoblast Research (Loke CTR), which will ensure the long-term sustainability of the Loke CTR. We are also very grateful to Amanda and Troy Daniel who coordinated redesigning of the beautiful modern new logo. We look forward to rolling out new branding in the coming year and will organise a public announcement of the renaming of the Loke Centre for Trophoblast Research in the next few months.

We are indebted to Professor Hilary Critchley who has steadfastly supported the Loke CTR as an Scientific Advisory Board (SAB) member and Chair of the SAB. We thank Hilary for her guidance and support and for being a terrific advisor to our Next Generation Fellows (NGFs) and PhD students. I am especially grateful for Hilary's kindness and support when starting my role during the pandemic. As a future Honorary Member of the Loke CTR, we very much hope Hilary will continue to keep in touch and remain connected to our network. I am thrilled that Professor Hubert Schorle and Professor Theresa Powell will be Honorary Members of the Loke CTR. We very much appreciate their generous contributions to the SAB and for all of their advice and support. We are delighted that Professor Gordon Smith has accepted the role of future Chair of the SAB. Gordon's advice on the Board of Managers has been absolutely vital in recruitment, steering priorities and ensuring financial sustainability. I believe Gordon will make an outstanding Chair and support the contributions of our world class SAB.

Over the past year, Loke CTR research groups continued to make hugely impressive progress in securing over £19 million in competitive grant funding and leading truly outstanding research

outputs and I hope you will enjoy reading about the highlights. We are absolutely delighted that one of these grants was a University Research Fellowship from the Royal Society awarded to Dr Claire Senner to launch her independent research group in the Physiology, Development and Neuroscience Department in Cambridge. We are also delighted that Dr Naomi McGovern was appointed as an Assistant Professor in the Pathology Department in Cambridge and secured an ERC Starting Grant to continue to lead Loke CTR research from the same lab where Charlie and Ashley were based! Also, huge congratulations to Dr Teresa Rayon for securing an ERC Starting Grant to lead her research group at the Babraham Institute. We also congratulate Loke CTR investigators Dr Thorsten Boroviak for his appointment as Assistant Professor in the Department of Physiology, Development and Neuroscience, and Professor Miguel Constância and Dr Catherine Aiken on well-deserved promotions to Professorship and Clinical Professorship!

We very much welcome Professor Paul Lehner, Professor of Immunology and Medicine at the Cambridge Institute of Therapeutic Immunology and Infectious Disease, Dr Emma Poole, Associate Professor in the Department of Pathology, and Dr Alberto Roselló-Díez, Associate Professor in Developmental Genetics in the Departments of Genetics and Physiology, Development and Neuroscience, and Dr Teresa Rayon, Tenure Track Group Leader at the Babraham Institute. We look forward to collaborating more with Paul, Emma Alberto, and Teresa over the coming years.

Loke CTR investigators have also impressively led several policy and public engagement projects and contributed to a UK Parliamentary POSTNote and submitted evidence to a call from the House of Lords on Food, Diet and Obesity. This leadership is vital in maintaining public and government support for Loke CTR-led research.



Loke CTR investigators have been pioneering in developing stem cell-based models of human development, including models of the embryo and placenta. To ensure governance keeps pace with the science, Loke CTR groups have contributed to the development of national self-governance of sophisticated stem cell models of human embryos and have recently completed a code of practice. In addition, Loke CTR groups have spearheaded public engagement projects on exploring extending the culture of human embryos for research, which will undoubtedly benefit our understanding of the human trophoblast.

Over the past year we have again prioritised matched funding and supporting core activities through grant funding where possible. We are delighted that Professor Martin Johnson and Dr Frank Woodman generously matched Loke CTR funding to support Julie Tang through a Johnson-Woodman fund at Christ's College. Julie will be working across the laboratories of Dr Courtney Hannah and Professor Anne Ferguson-Smith. We are also incredibly grateful for the support of Newnham College and the Cambridge Trust who are matching Loke CTR funding to support Isabel Marchand-Casas in the laboratories of Dr Naomi McGovern and Dr Emma Poole. The students are integral in fostering collaborative links between Loke CTR research groups. We are always looking for new partners to support Loke CTR studentships and would welcome all suggestions.

We are also thrilled by the appointment of Dr Tom Rawlings who will be sponsored by my laboratory. We envisage a number of exciting collaborative opportunities for Tom across Loke CTR laboratories. We look forward to welcoming Dr Noa Hasky who has secured a Rothschild Physician-Research Fellowship in Professor Steve Charnock-Jones' laboratory. We are also committed to supporting Dr Qian Li as we explore grant opportunities to bring together the vast and informative -omics datasets generated across Loke CTR research groups.



This year we were thrilled to welcome back Dr Tereza Cindrova-Davies who was appointed the Loke CTR Licensing Manager. Tereza has a wealth of experience in placental and endometrial biology and long-lasting connections with internationally leading research groups. She has already significantly expanded access to consented and donated samples and helped to coordinate compliance with HTA and HFEA regulations. We were also very fortunate to recruit Busma Butt, the Loke CTR Chief Technician, and Alice Truszczynska, Trainee Technician, who are absolutely outstanding at managing the Loke CTR lab space and supporting Tereza in licensing.

We are looking forward in this next year to prioritising long-term financial sustainability and ramping up support for collaborative research and grant applications. We plan to follow up on the collaborative grant brainstorming session at the Away Day with a grant writing workshop in the autumn, please watch this space. Thank you very much for all of your incredible support. I look forward to seeing you all at the Annual Meeting with a brilliant line-up of speakers, flash-talks and poster presenters!

**Professor Kathy Niakan**

Mary Marshall and Arthur Walton Professor of the Physiology of Reproduction  
 Director, Centre for Trophoblast Research  
 Chair, Cambridge Reproduction Strategic Research Initiative  
 Honorary Group Leader, Babraham Institute  
 Affiliated Member, Cambridge Stem Cell Institute

# Governance Updates

## Updates to the Scientific Advisory Board

*We thank Professor Hilary Critchley for her service as Chair of the Scientific Advisory Board (SAB), and welcome Professor Gordon Smith as incoming Chair.*



**Professor Hilary Critchley**

**University of Edinburgh**  
*SAB Chair, 2021-24*  
*SAB Member, 2014-21*

The Loke Centre for Trophoblast Research expresses its gratitude and appreciation of Professor Hilary Critchley as she steps down from the SAB at the end of her three-year term as Chair. Her support for mentorship, training, and the advancement of women's health research has been deeply appreciated by all. Professor Hilary Critchley has held a Personal Chair in Reproductive Medicine at the University of Edinburgh since 1999. She is Head of Deanery of Clinical Sciences at the University of Edinburgh, Co-Director, MRC Centre for Reproductive Health and Consultant Gynaecologist at the Royal Infirmary, Edinburgh, and an internationally recognised expert in the basic science of the uterine endometrium.



**Professor Gordon Smith**

**University of Cambridge**  
*Incoming SAB Chair, 2024*  
*Board of Managers, 2011-23*

We welcome Professor Gordon Smith as incoming Chair of the Scientific Advisory Board. He is a world-leading physician scientist with expertise in developing novel methods of screening for placentally-related complications of pregnancy and managing prospective clinical studies of pregnancy, including the Pregnancy Outcome Prediction Study. He is the Head of Department of Obstetrics & Gynaecology, and an Honorary Consultant in Maternal-Fetal Medicine, Cambridge University Hospitals NHS Foundation. Professor Gordon Smith has served on the Loke Centre for Trophoblast Research Board of Managers since 2011 and thus brings a deep knowledge of the Loke CTR to this role.

*We welcome two new members to the Scientific Advisory Board in 2023, Dr Miguel Branco and Professor Hongmei Wang.*



**Dr Miguel Branco**

**Blizard Institute,  
Queen Mary University of  
London**  
*SAB Member, 2023-present*

Dr Miguel Branco was awarded a Loke Centre for Trophoblast Research Next Generation Fellowship in 2011 and joined the Blizard Institute (QMUL) in October 2013 after securing a Sir Henry Dale Fellowship from the Wellcome Trust and Royal Society. He has expertise in epigenetics and placental evolution, and brings valuable perspectives as a previous Next Generation Fellow.



**Professor Hongmei Wang**

**Chinese Academy of  
Sciences**  
*SAB Member, 2023-present*

Professor Hongmei Wang is the Director of the State Key Laboratory of Stem Cell and Reproductive Biology at the Institute of Stem Cell and Regeneration, Chinese Academy of Sciences (CAS). She is internationally recognized for scientific expertise in nonhuman primate development, human early placentation, and pioneering stem cell-based embryo models.

## Updates to the Board of Managers

We welcome three new Managers to the Board of Managers in 2024, Dr Naomi McGovern, Professor Susan Ozanne, and Professor Steve Charnock-Jones, who collectively bring a wealth of expertise to the Board.



**Dr Naomi McGovern** is an early career Principal Investigator and Sir Henry Dale Fellow in the Department of Pathology, and a recent recipient of an NGF (2016). Her laboratory aims to understand the role of macrophages and dendritic cells within fetal membranes, such as the placenta, and within reproductive organs, such as the decidua.



**Professor Susan Ozanne** is a Professor of Developmental Endocrinology and Deputy Head of the Department of Clinical Biochemistry at the Institute of Metabolic Sciences (IMS). Her group studies the developmental programming of cardiovascular and metabolic disease during pregnancy.



**Professor Stephen Charnock-Jones** is a Professor of Reproductive Biology, Department of Obstetrics and Gynaecology. His group investigates placental development and the aetiology of pre-eclampsia and mechanisms of angiogenesis under normal and pathological conditions.

## New Honorary Members

We warmly welcome two new honorary CTR members in 2023-24, Professor Hubert Schorle and Professor Theresa Powell.



**Professor Hubert Schorle**

**University Clinics Bonn, Germany**  
CTR SAB Member 2016-23

Professor Hubert Schorle is the Head of the Department of Developmental Pathology at the University Clinics Bonn, Germany. He is also head of the Molecular Diagnostics and the Core Gene Editing Facility. Professor Schorle is an internationally recognised molecular biologist who has made pioneering discoveries in understanding molecular mechanisms of lineage specification, germ cell biology, tumour biology and embryogenesis. He also has expertise in the translation of basic trophoblast stem cell biology, aiming to bridge the gap between basic molecular biology and clinical applications.



**Professor Theresa Powell**

**University of Colorado Anschutz Medical Campus**  
CTR SAB Member 2016-23

Dr Powell is Professor of Pediatrics and Obstetrics and Gynecology at the University of Colorado and internationally recognized for her work in determining the molecular mechanisms regulating nutrient transport in the human placenta. She has characterised changes in placental function associated with important pregnancy complications such as growth restriction and maternal metabolic diseases. Dr Powell's primary research focus is to better understand how the abnormal maternal metabolic environment of obesity and gestational diabetes affects placental function and long-term infant health.



# Loke Centre for Trophoblast Research

We are delighted to announce the renaming of the Loke Centre for Trophoblast Research, in honour of Professor Charlie Y. W. Loke's lifelong contribution to the field and the Loke family's invaluable support of the Centre.

A generous donation made by the Loke family in 2024 will support all core research and training activities of the Centre, ensuring its operation in perpetuity. In recognition of this gift and the enduring partnership between Professor Loke and the University of Cambridge, the Centre will be renamed the Loke Centre for Trophoblast Research. This new identity will be celebrated with a modern logo (page opposite), honouring Professor Loke's vision and lasting support for placental biology at the University.

Thanks to the founding support of Professor Charlie Y.W. Loke in 2007, the Loke Centre for Trophoblast Research has emerged as an international leader in the study of the placenta and maternal-fetal interactions during pregnancy. Spanning the School of Biological Sciences and School of Clinical Medicine, the Centre has embedded a collaborative and multidisciplinary approach that has led to several distinguished contributions to the field of trophoblast biology, detailed on page 14 of this report.

At the heart of the Centre's success is a focus on nurturing early career researchers in placental sciences. To date, the Centre has supported 17 Next Generation Fellows, 85% of whom have progressed to independent group leader

positions. It has developed into an international training hub through the establishment of a competitive PhD studentship programme, which has supported 25 PhD students to pursue graduate training at Cambridge, and the development of an international Placental Biology Course, which has attracted over 500 students from over 40 countries. These training initiatives have cultivated a global network of highly trained and eager early-career trophoblast scientists all over the world.

As you will see in this report, placental research at Cambridge continues to thrive. Our research groups continue to publish innovative, impactful work, securing competitive research grant funding and fostering a stimulating environment for training and research.

The Loke Centre for Trophoblast Research extends our sincere gratitude to Professor Charlie Y.W. Loke and his family for their tremendous generosity, which ensures that placental sciences will continue to flourish at Cambridge. We are thrilled that the new name will serve as a testament to his legacy and dedication to the field.



Professor Charlie Y.W. Loke, Amanda Loke and Troy Daniel visit to Cambridge, October 2022





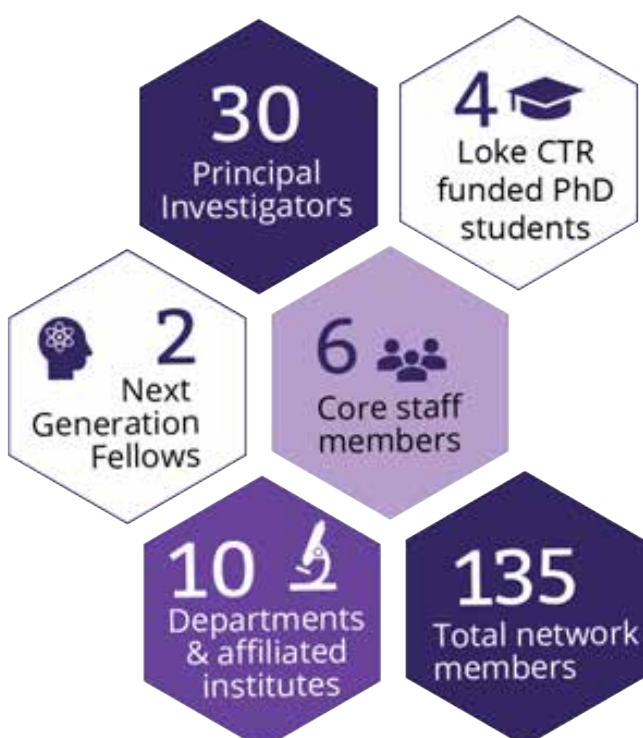
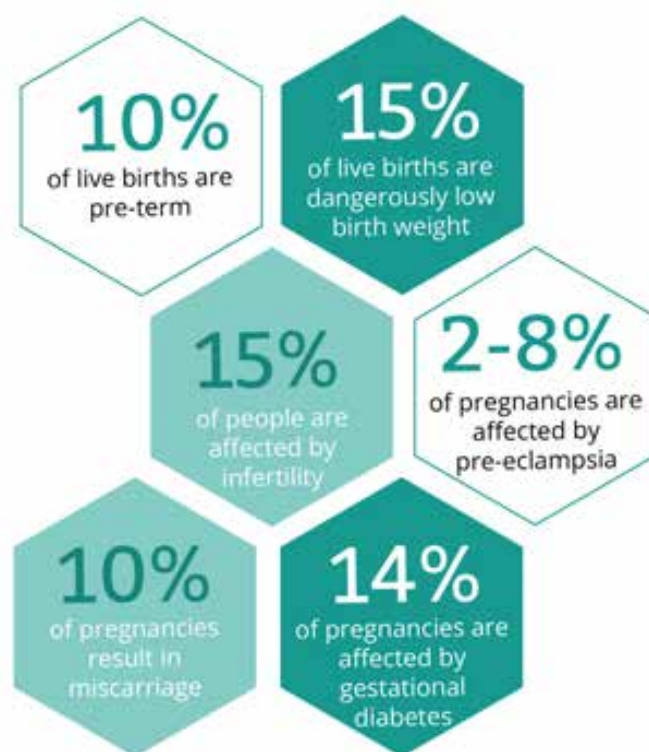
# The LokeCentre

for trophoblast research

# About

## The Challenge

Each year, pregnancy and childbirth lead to millions of maternal, fetal, and neonatal deaths and countless suffering. A significant proportion of these devastating consequences are caused by a spectrum of common placenta-related disorders. These range from miscarriage (affecting 10-12% of all pregnancies, with 90-95% occurring within the first 12 weeks), growth restriction (affecting 15% of live births), pre-eclampsia (occurring in 2-8% of pregnancies), pre-term birth (making up 10% of all live births) to stillbirth, which causes over 2 million perinatal deaths worldwide annually ([Horton & Samarasekera, 2016](#); [Magnus et al., 2019](#); [Stock & Aiken, 2023](#)). Despite these alarming statistics, our understanding of placental development and function remains inadequate. Until we understand the pathophysiology underlying these common disorders, we will not be able to offer effective interventions.



## Our Network of Expertise

Recognising the urgency and complexity of this challenge, the Loke Centre for Trophoblast Research (Loke CTR) was established in 2007 as the University of Cambridge's flagship cross-school initiative. The Centre serves as a nexus for interactions between basic and clinical sciences to unite the study of pregnancy complications that emerge at a late stage with the study of their developmental origins.

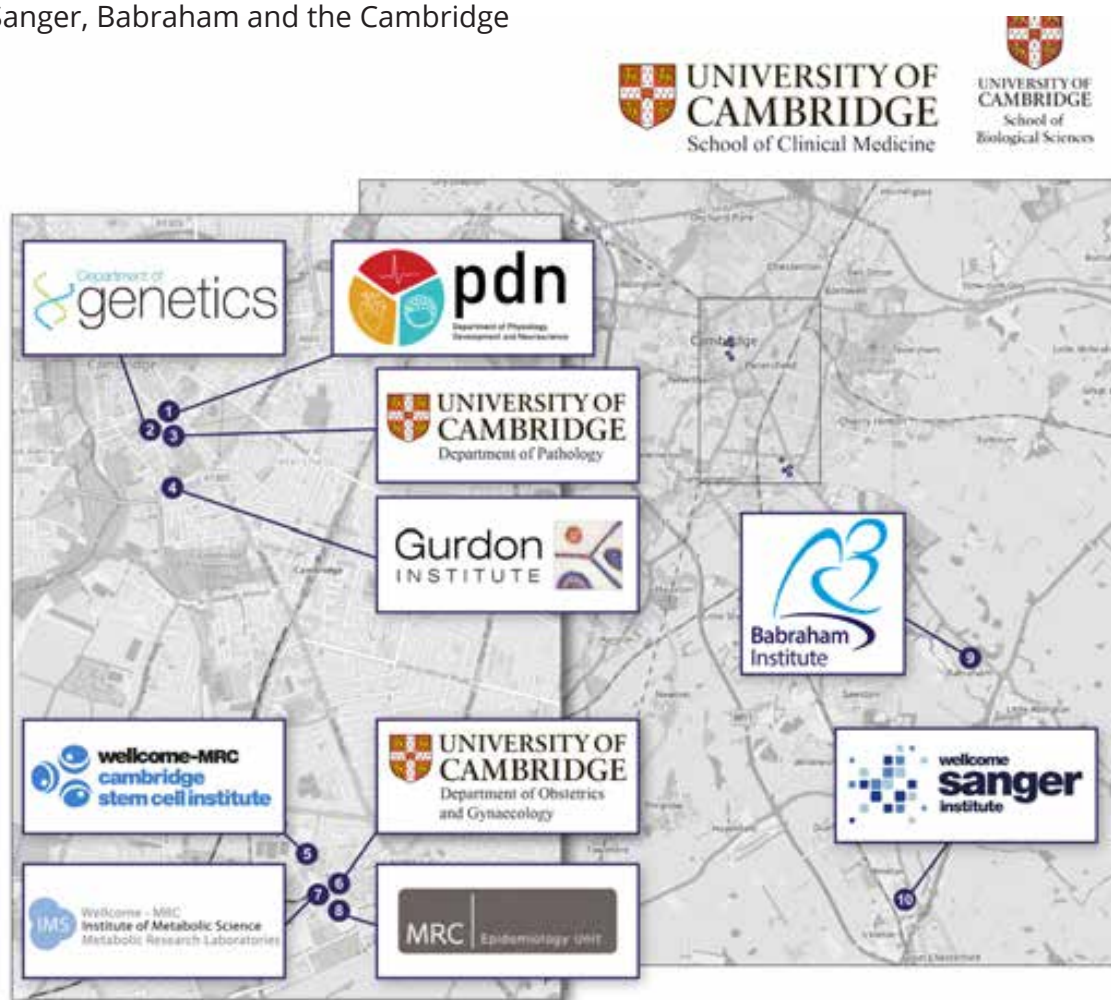
Over 17 years, the Loke CTR has evolved into a world-leading centre of excellence in placental research and training. Today, it unites 30 group leaders across 10 departments and affiliated institutes and provides diverse opportunities for scientific interaction through events and shared state-of-the-art facilities. All together, the Centre brings together over 100 researchers across these groups, including students, postdoctoral fellows, and technicians who are included as affiliate members of our network.

To support the next generation of trophoblast researchers, the Loke CTR directly funds PhD students and NGFs who benefit from close interactions in a vibrant, creative and diverse community of scientists.

The Loke CTR connects world leading trophoblast-related research across Cambridge in the School of Biological Sciences (Departments of Pathology, Genetics, and Physiology, Development and Neuroscience), School of Clinical Medicine (Institute of Metabolic Science, Medical Research Council Epidemiology Unit and Department of Obstetrics & Gynaecology) and affiliated institutes (Gurdon, Sanger, Babraham and the Cambridge

Stem Cell Institutes). Our administrative base and shared laboratory facilities are housed in the Department of Physiology, Development and Neuroscience.

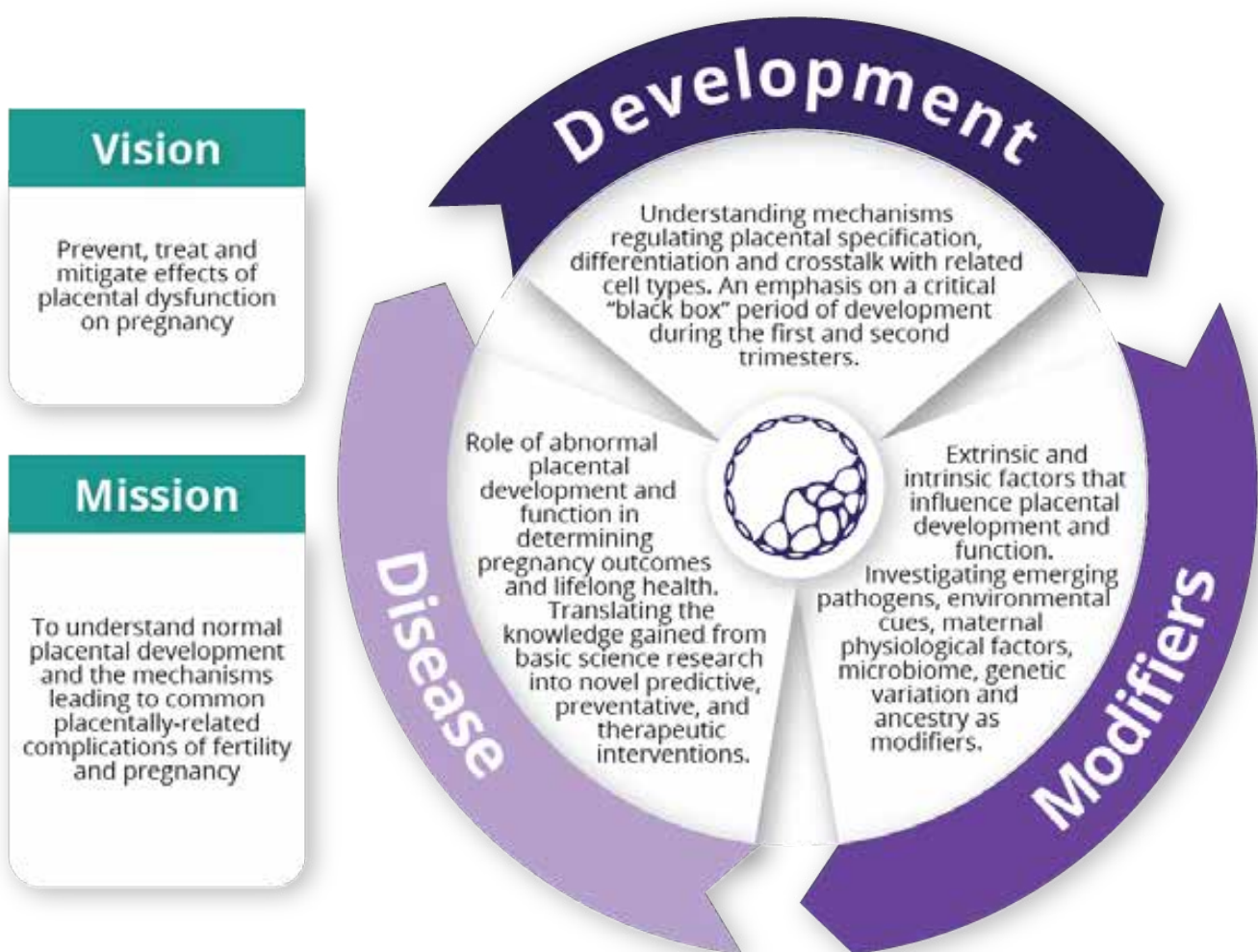
We have particular expertise in reproductive immunology, clinical research, epigenetics and genomic imprinting, single-cell and spatial multi-omics analysis, developmental and stem cell biology, metabolism, organoid models, trophoblast stem cell biology, and placental and fetal physiology.





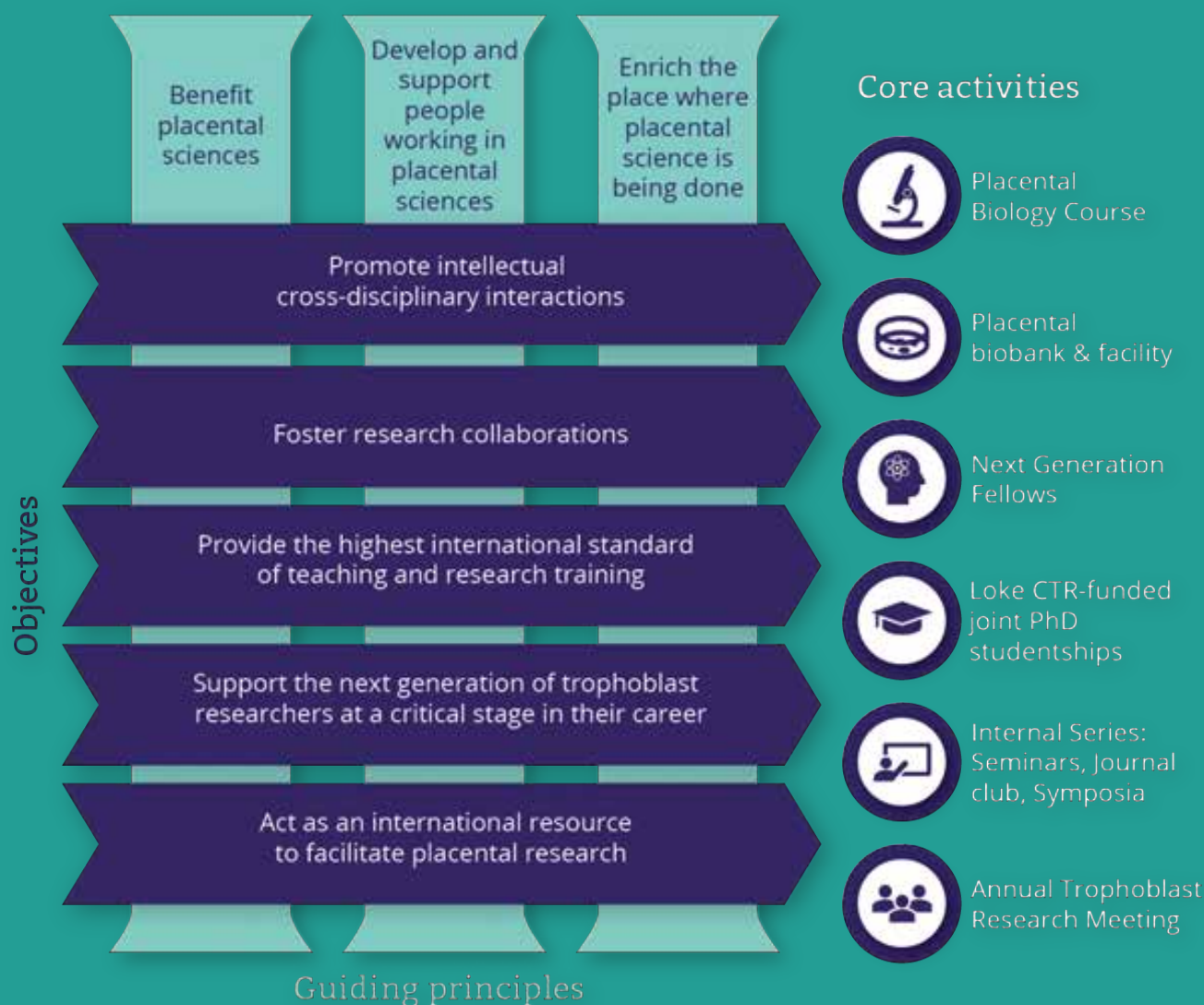
# Research Vision

Loke CTR members are brought together around a research mission to understand normal placental development and the mechanisms leading to common placentally-related complications of fertility and pregnancy. Interdisciplinary research aligned to our mission is split into three cross-cutting themes: Development, Modifiers, and Disease. Specific challenges within these themes will guide priority setting for funding over the next 5 years.



# Strategy

A set of three principles guides the five primary objectives of the Loke CTR. Each of the core activities underlying our virtual network are informed by these objectives.



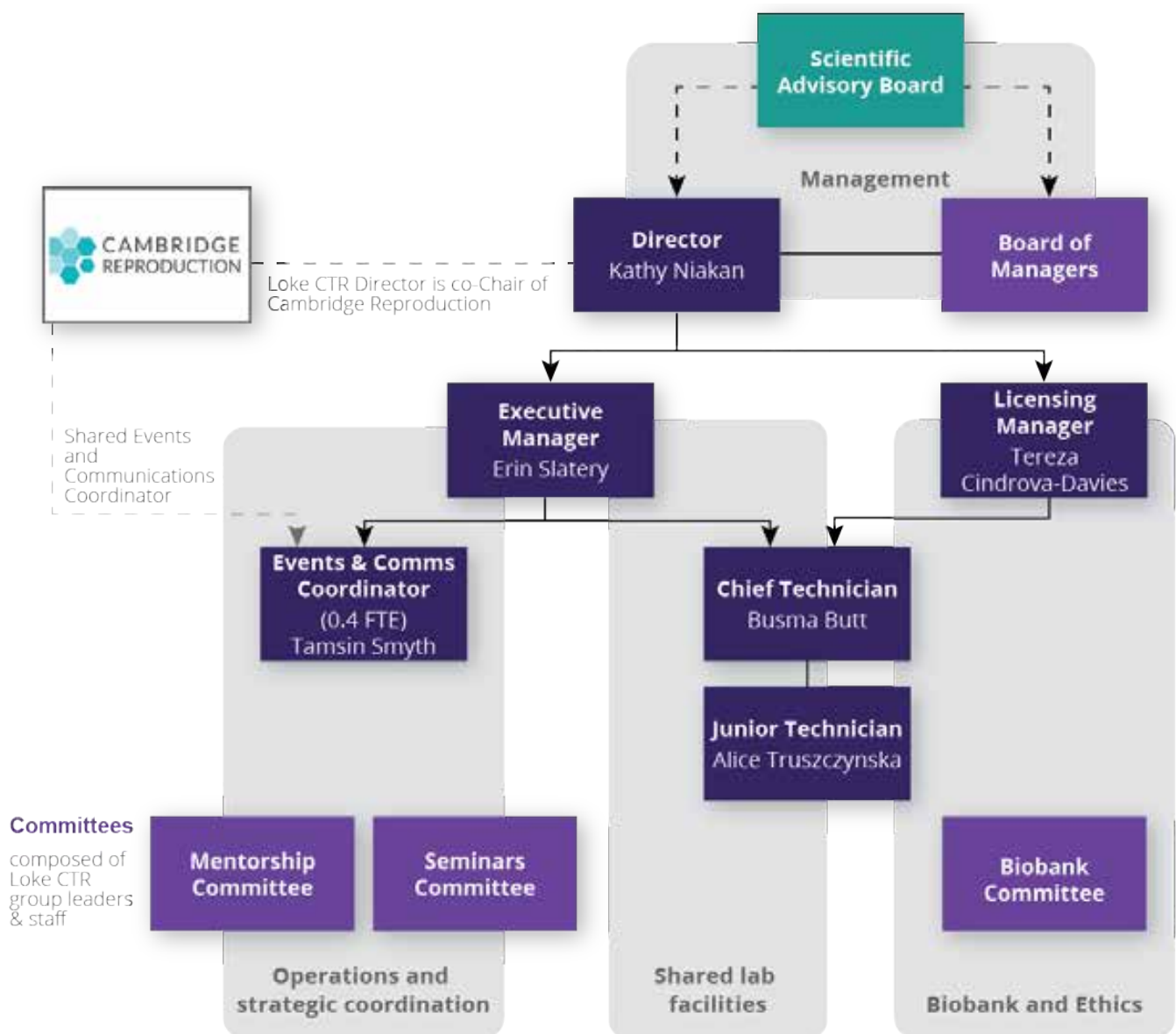
# History of Scientific Achievements







# Structure



The **Operations and Strategic Coordination Arm** develops funding opportunities in line with Loke CTR research strategy, while building and supporting research networks. This arm coordinates events, networking, and communications across the Loke CTR. Additionally, the team provides financial management, HR and visitor administration, and support for fellows and trainees.

The **Biobank and Ethics** and **Shared Lab Facilities** arms manage Loke CTR research licensing activities and associated laboratory facilities. This includes managing shared equipment, implementing communal lab policies, and providing technical support. This arm also coordinates training and teaching across the Centre, including provision of the Placental Biology Course.

# Core Facilities

## Biology of the Human Uterus in Pregnancy and Disease Tissue Bank

The Tissue Bank is a core priority for the Loke CTR, accessed by approximately half of Loke CTR research groups within the Department of Physiology, Development, and Neuroscience (PDN), Department of Pathology, and Department of Obstetrics and Gynaecology. These groups collect, store, and import placental and endometrial tissues relevant to the Centre's remit.

In January 2024, **Dr Tereza Cindrova-Davies** took over management of the Loke CTR Tissue Bank as our Licensing Manager, supported by **Busma Butt** and **Alice Truszczynska**. Over the past 6 months, Tereza has overseen a number of key improvements to the Tissue Bank:

- Patient Information Sheets (PIS) and consent forms were updated following feedback from patients, coordinated by the Patient Public Involvement (PPI) panel.
- A substantial Research Ethics Committee (REC) amendment was approved in May 2024 to expand the list of sources/hospitals from whom we collect and approve new patient forms.
- The bank has been successfully registered with Addenbrooke's NHS Trust, enabling sample collection from clinics at Addenbrooke's Hospital. Conversations are ongoing to facilitate endometrial biopsy collections from both control and cancer patients.



**Dr Tereza Cindrova-Davies**  
Loke CTR Licensing Manager



**Busma Butt**  
Loke CTR Chief Technician

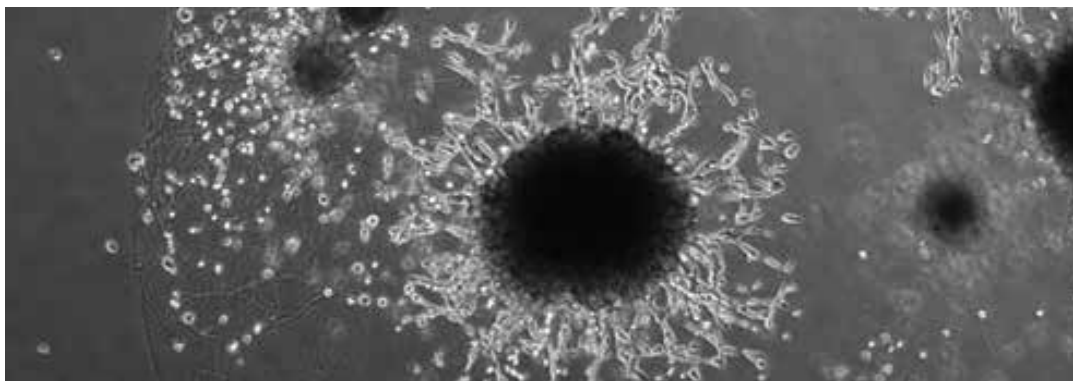
- Continuous updates to standard operating procedures (SOPs) and risk assessments (RAs) are underway. Tereza and Busma have conducted informal visits to relevant departments to discuss tissue collection, consent, documentation, and storage. Plans are in place to consolidate SOPs and RAs into an overarching protocol.
- A full audit was conducted of existing HTA tissue samples of our existing tissue bank of well-characterised collections of frozen and paraffin-embedded placental tissues. Plans are in place to list and share these resources with Loke CTR members. Additionally, the Boyd collection of 1950s pregnant hysterectomies will be audited and catalogued for accessibility to Loke CTR members.
- Regular biobank committee meetings are held to discuss research project approval and coordinate REC substantial amendments.





# Research Highlights

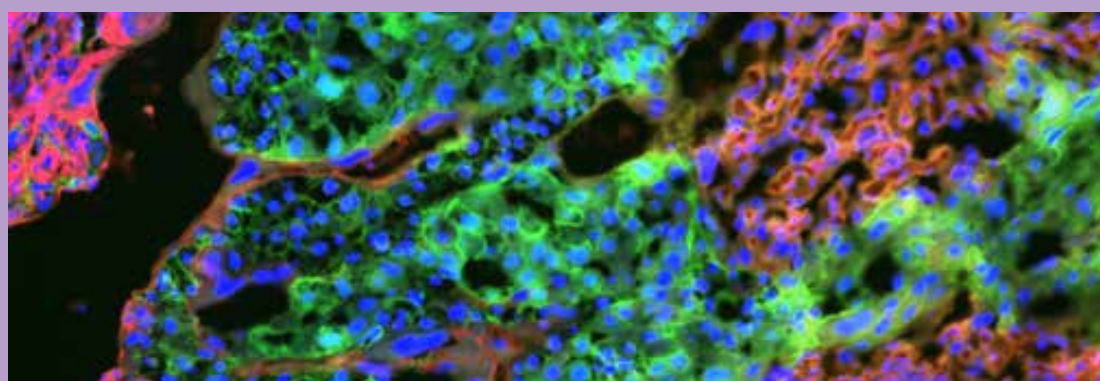




**Professor Ashley Moffett, Dr Roser Vento-Tormo, and CTR Honorary Member Dr Margherita Turco used trophoblast organoids to dissect the role of uterine natural killer (NK) cells in human implantation**

In previous work, Professor Moffett and colleagues identified genes that increase the risk of or protect against conditions such as pre-eclampsia. These highlighted the important role of immune cells uniquely found in the uterus, known as uterine NK cells. While it is known that NK cells mediate the interactions between the endometrium and the trophoblast, but due to the technical limitations of studying human implantation, their precise role has remained unclear. In their new study, led by Dr Qian Li, the team applied proteins secreted by the uterine NK cells to trophoblast organoids to mimic conditions where the placenta implants. Using single cell-RNA sequencing and in vitro modeling, they identified particular proteins that were crucial to helping the organoids develop extravillous trophoblast. These proteins will contribute to successful implantation, allowing the placenta to invade the uterus and transform the mother's arteries. The work, published in *Cell Stem Cell*, was covered on [ITV news](https://www.itvnews.com).

**Reference:** Li, Q *et al.* (2024). [doi.org/10.1016/j.stem.2023.12.013](https://doi.org/10.1016/j.stem.2023.12.013)

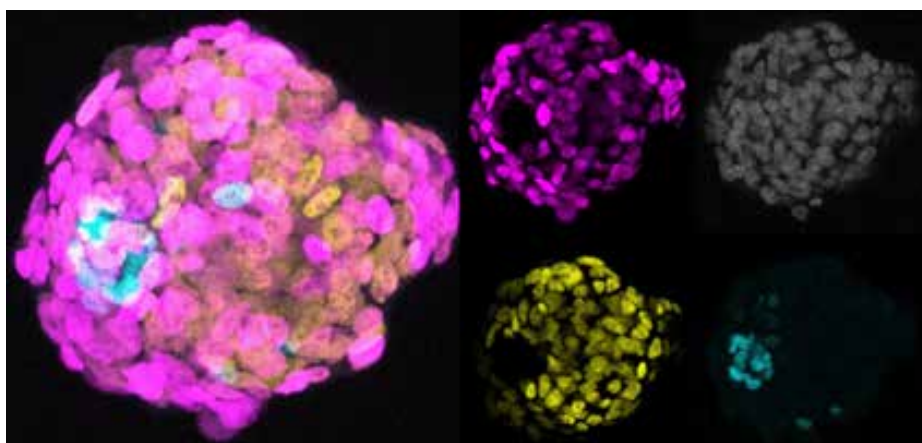


**A project led by Dr Jorge Lopez-Tello, Professor Amanda Sferruzzi-Perri and Professor Miguel Constância demonstrated the importance of placental endocrine function in driving maternal physiological changes during pregnancy**

The fetus has evolved ways to manipulate maternal physiology to enhance placental nutrient transfer, but the mechanisms involved remain unclear. Using a sophisticated genetic mouse model, the groups investigated the role of the paternally-expressed imprinted gene, *Igf2*, in placental endocrine function. *Igf2* encodes the 'Insulin Like Growth Factor 2' protein, a hormone similar to insulin with key roles in the development of the placenta, liver, and brain. They found that deletion of the *Igf2* gene in placental endocrine cells impaired maternal nutrient handling and lead to fetal growth restriction with long-lasting effects on offspring metabolism in adulthood. Importantly, the study provides the first direct evidence that a gene inherited from the father is signalling to the mother to divert nutrients to the fetus.

**Reference:** Lopez-Tello, J. *et al.* (2023). <https://doi.org/10.1016/j.cmet.2023.06.007>

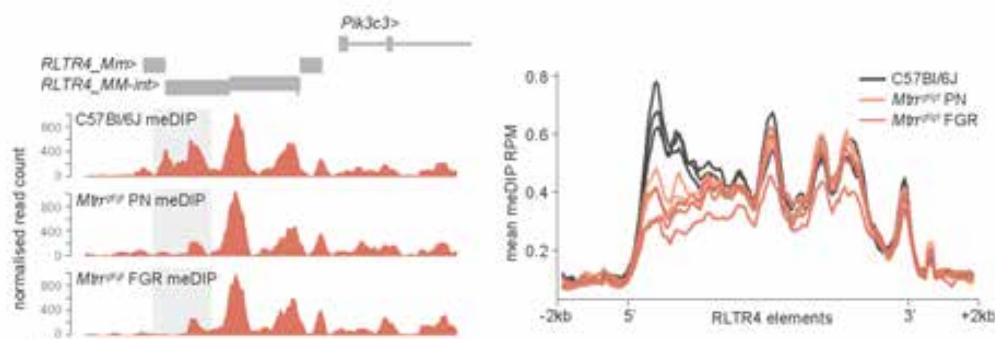




## Dr Teresa Rayon's laboratory led a collaborative study using human pluripotent stem cells to learn more about how amniotic ectoderm arises in human embryos

The work, led by Dr Shota Nakanoh in Dr Teresa Rayon's lab in collaboration with Professor Ludovic Vallier's lab at the Wellcome-MRC Cambridge Stem Cell Institute, uncovered the degree of cell crowding in the early human embryo influences whether cells develop as extraembryonic cells or become a part of the embryo and eventually give rise to skin, hair and nails. Combining a newly identified signalling cocktail for culturing human pluripotent stem cells (hPSC) with three-dimensional culture and single cell RNA sequencing analysis, they demonstrate a sequential differentiation trajectory for amniotic ectoderm from surface ectoderm and a key role of cell crowding. This study provides an integrative understanding of how embryonic and extra-embryonic human development is coordinated around gastrulation. It also offers a way to improve the methods to produce amniotic and surface ectoderms and could pave the way for integrated stem cell-based embryo models better representing the human embryo.

**Reference:** Nakanoh, S. *et al.* (2024). [doi.org/10.1126/sciadv.adh7748](https://doi.org/10.1126/sciadv.adh7748)



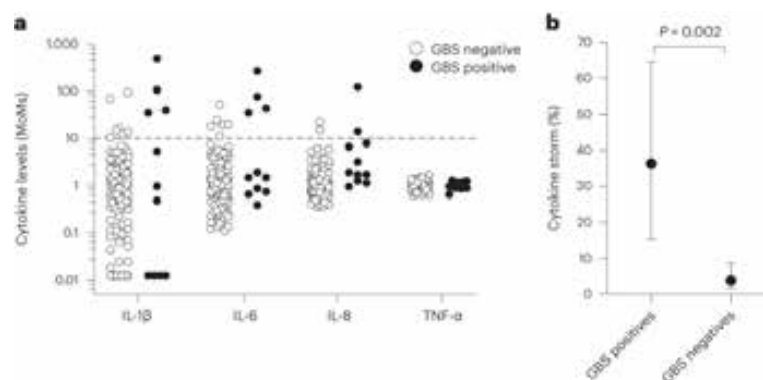
## Loke CTR NGF Dr Claire Senner and Dr Erica Watson collaborated with Honorary Member Dr Miguel Branco to investigate the role of one-carbon metabolism in epigenetic stability of the mouse placenta

Epigenetic inheritance, unlike genetic inheritance, is a mechanism by which environmental factors encountered by germ cells or during pregnancy influence health of the grandchildren. In this study, the team investigated molecular mechanisms of epigenetic inheritance by profiling genome-wide DNA methylation in a genetic mouse model, *Mtrrgt*. *Mtrrgt* mice have disrupted one-carbon metabolism (similar to folate deficiency) and exhibit pregnancy complications, including impaired implantation, placental insufficiency, and fetal growth restriction. They discovered that a subset of transposable elements – RLTR4 – showed low methylation and ectopic expression in *Mtrrgt/gt* mutant placentas. This mis-expression could have profound consequences for placental development; transposable elements must remain heavily methylated to ensure genome stability. Their analysis also revealed that the inheritance of other epimutations present in *Mtrrgt* mice were unlikely mediated directly through DNA methylation, but rather through disruption of histone modifications. Altogether, the work provides mechanistic understanding of epigenetic inheritance and highlights the importance of one-carbon metabolism in maintaining genome-wide epigenetic stability.

**Reference:** Senner, C. E. *et al.* (2023). [frontiersin.org/articles/10.3389/fcell.2023.1209928](https://frontiersin.org/articles/10.3389/fcell.2023.1209928)



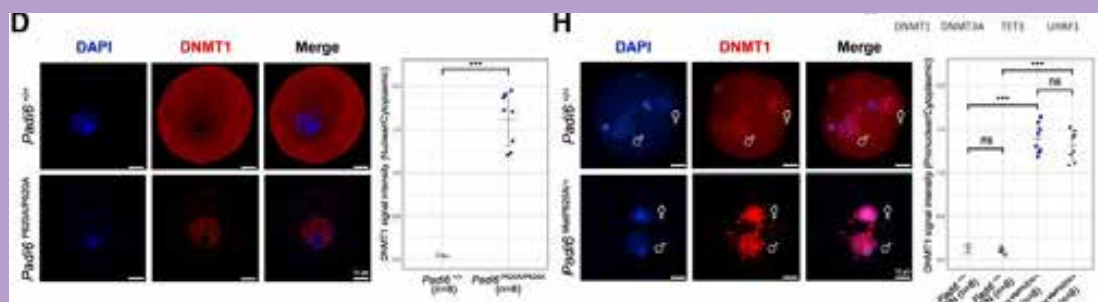




## Professor Gordon Smith, Professor Steve Charnock-Jones and Dr Francesca Gaccioli discover that placental group B Streptococcus is associated with increased risk of adverse fetal outcome

*Streptococcus agalactiae* (known as Group B Streptococcus, or GBS) infection is the leading cause of neonatal sepsis, causing 100,000 infant deaths globally each year. Previous research by led by Francesca Gaccioli across the groups of Professor Gordon Smith and Professor Steve Charnock-Jones, identified that GBS was the only bacterial species present in the placenta at term, affecting 5% of women before labour. In this study, they sought to determine whether the placenta was a potential route for infection of the fetus. The team analysed the link between the presence of GBS in the placenta and the risk of admission of the baby to a neonatal unit. They discovered that placental GBS was associated with a two- to three-fold increased risk of neonatal unit admission, with one in 200 babies admitted with sepsis associated with GBS – almost 10 times the previous estimate. To improve detection, the researchers have developed an ultrasensitive PCR test, which amplifies tiny amounts of DNA or RNA from a suspected sample to check for the presence of GBS. The findings from the study have significant public health implications for the UK, which currently lacks routine GBS screening for pregnant women, and was covered in the [Independent](#).

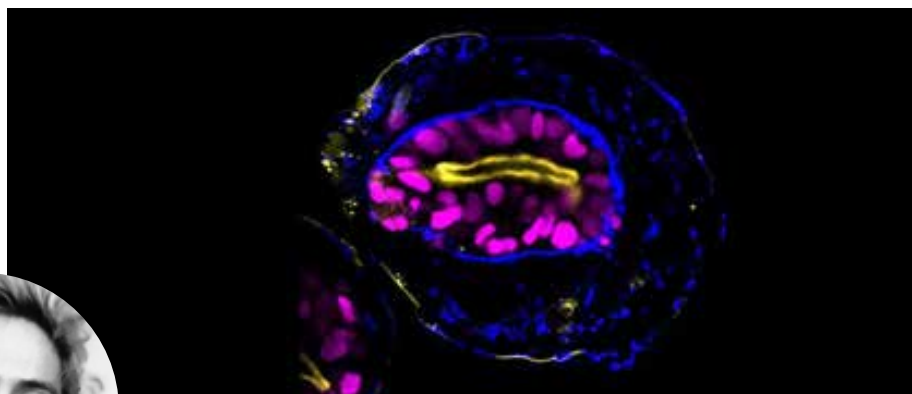
**Reference:** Gaccioli, F. *et al.* (2023). [doi.org/10.1038/s41564-023-01528-2](https://doi.org/10.1038/s41564-023-01528-2)



## Professor Gavin Kelsey led a collaborative study investigating the role of the subcortical maternal complex in the origin of imprinting disorders

The subcortical maternal complex (SCMC) and cytoplasmic lattices (CPL) are abundant structures in the egg cytoplasm that, in some way, are involved in controlling epigenetic processes in the egg and preimplantation embryo. Mutations in components of the SCMC/CPL in humans are a cause of gestational trophoblast disease (hydatidiform mole) or imprinting disorders, such as Beckwith-Wiedemann syndrome (BWS), but the mechanistic linkages have been obscure. Gavin Kelsey worked with Andrea Riccio's group in Naples, who recreated a mutation in mouse Padi6, a component of cytoplasmic lattices that they had found to cause BWS in humans. The Padi6 mutation causes relocalisation of DNMT1 to the nucleus from where it is normally located in the egg cytoplasm. Consistent with this aberrant localisation, using single-cell multiomic sequencing, they found excessive maintenance of DNA methylation in the 2-cell embryo, at the time when the genome should be undergoing extensive demethylation. This confirms that the SCMC/CPL is required to control normal epigenetic reprogramming events in the embryo.

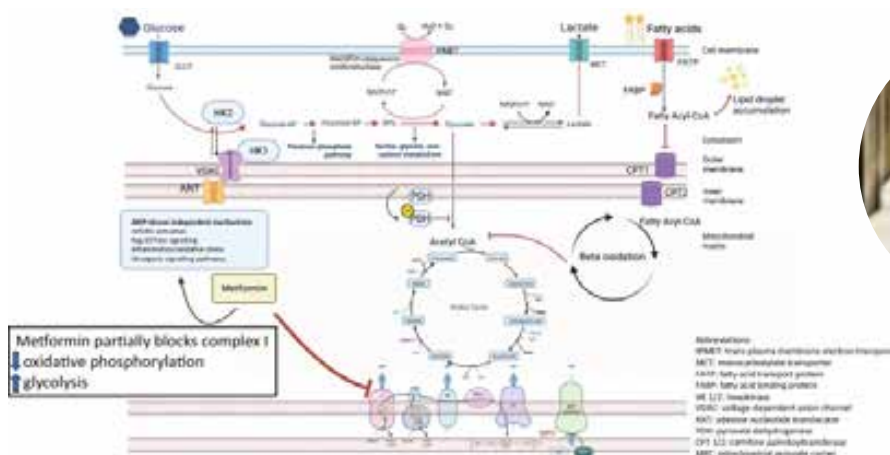
**Reference:** Giaccari C. *et al.* (2024). [doi.org/10.1101/gad.351238.123](https://doi.org/10.1101/gad.351238.123)



## Professor Magdalena Zernicka-Goetz's group established a stem cell-derived model of the postimplantation human embryo

A huge proportion of pregnancies fail during the first two weeks of development, just after the embryo implants into the lining of the uterus. Researching this stage of pregnancy is extremely challenging. In this study, the team sought to use stem cells to generate a 3D embryo model that recapitulated aspects of the second week of development, inspired by the Zernicka-Goetz lab's previous work with mouse embryo models. They assembled aggregates of wild-type embryonic stem cells and two extraembryonic cell types generated by transcription factor overexpression: hypoblast-like cells resulting from GATA6 and SOX17 overexpression and trophoblast-like cells from GATA3 and TFAP2C overexpression. The study, reported in tandem with a similar stem cell-derived model developed at the Weizmann Institute, received considerable press attention, including coverage in the *New York Times*, *BBC*, *CNN*, the *Guardian*, *Smithsonian Magazine*, and *Scientific American*. Collectively, these models provide powerful tools to study early human development in vitro, and an important complement to research using donated human embryos surplus to IVF treatment.

**Reference:** Weatherbee, B. A. T., Gantner, C. W., *et al.* (2023). [doi.org/10.1038/s41586-023-06368-y](https://doi.org/10.1038/s41586-023-06368-y)

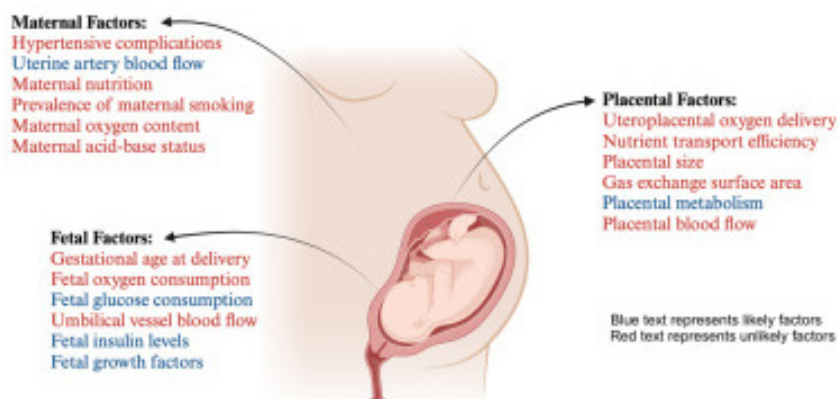


## Dr Catherine Aiken, together with CTR colleagues Professor Susan Ozanne and Professor Andrew Murray, defines the metabolic response of trophoblast to metformin treatment

Metformin is commonly used as a treatment for gestational diabetes, yet few studies have investigated how metformin impacts the placenta. Due to the known association of metformin use in pregnancy and decreased birthweight, it is essential to understand how metformin modulates placental metabolism. In this study, the team used an established model of primary human trophoblast cultured from term placenta treated with metformin at clinically relevant concentrations, and analysed metabolic function using high-resolution respirometry, radioisotope-labelled assays, glycolytic stress assays and lipidomics. Metformin treatment caused a reduction in oxidative phosphorylation through partial inactivation of complex I and accumulation of lipids. These results conclude that a careful analysis of risk versus benefit should be considered when using metformin in pregnancy.

**Reference:** Tarry-Adkins, J. L. *et al.* (2023). [doi.org/10.1007/s00125-023-05996-3](https://doi.org/10.1007/s00125-023-05996-3)

## Spotlight: Pregnancy at High Altitude



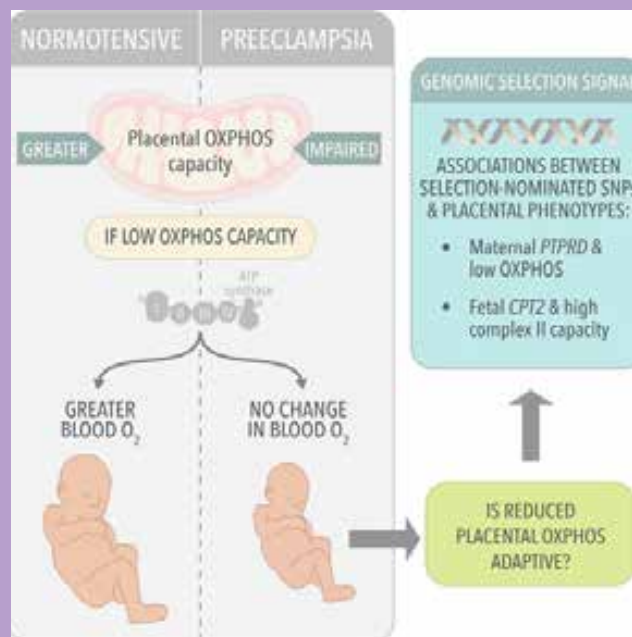
### Professor Dino Giussani worked with Emily Brown, a Biological and Biomedical Sciences (BBS) Part II student, to analyse evidence that high-altitude pregnancy increases the incidence of fetal growth restriction and reduces birth weight

The publication is the result of a Part II student undergraduate project by Emily supervised by Professor Dino Giussani. Their meta-analysis of 70 studies conducted across the globe, including studies from Bolivia, Peru, and the United States, reports that birth weight decreases by 90 grams for every 1000 meter increase in altitude. Furthermore, there is a clear consensus across studies that highland ancestry protects against this reduction in birth weight, decreasing birth weight reduction at altitude by half. Investigating the mechanisms behind this phenomenon, the team highlight that fetal hypoglycaemia and hypoinsulinaemia are important in fetal growth restriction at high altitude. Further, evidence in the literature supports that uterine artery and placental metabolic adaptations protect against fetal growth restriction at altitude. Understanding the mechanisms underlying fetal growth restriction at high altitude will aid in its prevention and treatment, thereby contributing to a reduction in infant mortality and in cardiovascular disease for future generations of individuals living at high altitude.

**Reference:** Brown ER, Giussani DA (2024). [doi.org/10.1016/j.isci.2024.109702](https://doi.org/10.1016/j.isci.2024.109702)

### Andrew Murray's group reveals that genetic adaptations that evolved to cope with high-altitude hypoxia can become maladaptive under the stress of preeclampsia

High-altitude pregnancy increases the incidence of placental pathologies and leads to fetal growth restriction. While native highland Andeans are relatively protected from altitude-associated fetal growth restriction, they remain vulnerable to severe pregnancy complications like preeclampsia. The study, led by postdoctoral fellow Katie O'Brien, examined 79 preeclamptic and normotensive Andean mother-infant pairs residing in La Paz, Bolivia. By integrating genetic selection scans and molecular studies, they found that the relationship between low placental oxygen consumption and high oxygen delivery to the fetus is lost in preeclampsia. This occurs alongside suppressed placental mitochondrial respiratory capacity at term. The study suggests a role for mitochondrial metabolism in regulating fetal oxygen delivery, which may lead to therapeutic strategies to improve hypoxia tolerance or address uteroplacental hypoxia.



**Reference:** O'Brien, K. A. et al. (2024). [doi.org/10.1161/HYPERTENSIONAHA.123.21748](https://doi.org/10.1161/HYPERTENSIONAHA.123.21748)



# Awards



**Professor Anne Ferguson-Smith** was appointed **Executive Chair of Biotechnology and Biological Sciences Research Council (BBSRC)**, and will take up the post from 1st July 2024. This follows her 2023 appointment as **Commander of the Order of the British Empire (CBE)**, awarded for services to medical research in recognition of her discovery research in the field of genomic imprinting and epigenetic inheritance. A current Loke Centre PI, Professor Ferguson-Smith is an internationally recognised developmental geneticist and epigeneticist and served on the Loke Centre Board of Managers from 2018-2020. She is the Arthur Balfour Professor of Genetics and current Pro-Vice-Chancellor for Research and International Partnerships.



**Professor Azim Surani's** seminal 1984 discovery of genomic imprinting was celebrated at the **40th anniversary Festschrift** held at King's College, Cambridge and in a *Nature News and Views* article "The Phenomenon of Genomic Imprinting Was Discovered 40 Years Ago." Professor Surani has received several awards recognising his contribution to the field of epigenetics, including the Gabor Medal (2001), the Royal Medal (2010), the Mendel Lectures (2010), Commander of the British Empire (2007), the Lewis S Rosenstiel Award (2006) and co-award of the prestigious Canada Gairdner International Award (2018) with Dr Davor Solter. A Fellow of King's College, he is currently the Director of Germline and Epigenetics Research and a Loke Centre PI. Professor Azim Surani served as the inaugural Chair of the Scientific Advisory Board from 2008 - 2013.

**Reference:** Ferguson-Smith, Anne C. & Marisa S. Bartolomei. (2024). <https://doi.org/10.1038/d41586-024-01338-4>.



**Emeritus Professor Ashley Moffett** was awarded **Karolinska Institutet's Honorary Doctorate** for a lifetime of research that has made groundbreaking discoveries concerning the biological mechanisms behind serious conditions associated with pregnancy - including preeclampsia, intrauterine growth restriction (IUGR) and unexplained fetal death, which together affect up to 10% of all pregnancies. Professor Moffett was also elected an **Honorary Member of the Society for Reproductive Investigation (SRI)**, along with Professor Graham Burton. Professor Ashley Moffett retired in 2023 following a long career advocating for the importance of maternal health research. She is actively involved in revoking the erroneous belief that the immune cells can be responsible for rejection of the fetus during pregnancy, as well as promoting research in African obstetrics. Professor Moffett served on the Board of Managers from 2008 - 2017.



I am delighted to receive this award from the Karolinska Institutet, where Natural Killer cells [...] were first discovered. The award of an Honorary Doctorate is a great honour but it is also a tribute to the Centre for Trophoblast Research founded by Charlie Loke where so much progress has been made in understanding early pregnancy and the interaction between the mother and her developing fetus.





Attendees at Professor Azim Surani's 40th anniversary Festschrift held at King's College. Photo credit: Walfred Tang



**Professor Magdalena Zernicka-Goetz** was awarded the prestigious **2023 Ogawa-Yamanaka Stem Cell Prize** by Gladstone Institutes. Magdalena Zernicka-Goetz was selected for her work revealing fundamental principles of early mammalian development and pluripotent stem cell self-assembly, which has enabled the creation of stem cell-based embryo models and provides a foundation for regenerative medicine strategies, and appeared in *Nature's* list of "Seven technologies to watch in 2023".

**Professor Dino Giussani** received the International Society for **Reproductive Investigation (SRI) 2024 President's Achievement Award** at this year's annual meeting in Vancouver, and was elected SRI President Nominee. This award recognises a member of the Society whose record in scientific investigation is outstanding and assures a continued productive career in research.



**Dr Marta Shahbazi**, Loke CTR Group Leader in the MRC Laboratory of Molecular Biology (LMB)'s Cell Biology Division, has been announced as one of the 2024 recipients of the **Suffrage Science award** in the Life Sciences category. The Suffrage Science scheme, supported by the MRC Laboratory of Medical Sciences (LMS), celebrates the scientific achievements of women in science and aims to encourage more women to pursue science.



**Dr Claire Senner**, Loke CTR NGF (2019-2024), was awarded a **Royal Society University Research Fellowship** to establish her independent research group in the Department of Physiology, Development as a Loke CTR Group Leader. Claire's research programme will commence in October 2024 and is entitled "Sense and Nonsense: RNA decay Pathways in Mammalian Reproduction."



**Dr Jorge Lopez-Tello**, Loke CTR Member, has been awarded a **Cesar Nombela Research Fellowship** to become a Principal Investigator at the Faculty of Medicine, Autonomous University of Madrid, where he will continue his work on placental metabolic function in maternal health.



**Teruhito Ishihara**, incoming Loke CTR Member, was awarded a **Marie Skłodowska-Curie Actions (MSCA) post-doctoral fellowship** (funded by conversion to an EPSRC Horizon Europe Guarantee MSCA Postdoctoral Fellowship) to join Professor Gavin Kelsey's research group.



**Katarina Harasimov**, Loke CTR Member, was awarded a **European Molecular Biology Organisation (EMBO) Fellowship** to join Professor Kathy Niakan's research group.

# Grants

Value of grants awarded in 2023-2024: £19.1 million



## UKRI - Medical Research Council

- “The impact of metformin on early placental development and metabolism” - **Dr Catherine Aiken, Professor Sue Ozanne, Professor Andrew Murray**, MRC Project Grant
- “Vitamin C regulation of human placental stem cell function” - **Dr Irving Aye, Professor Stephen Charnock-Jones, Professor Gordon Smith**, MRC Project Grant
- “Feto-maternal communication and the developmental programming of metabolic disease” - **Professor Sue Ozanne, Professor Miguel Constancia**, MRC Metabolic Disease Unit Programme support
- “The molecular and immunological mechanisms regulating human cytomegalovirus latency, reactivation and pathogenesis” - **Dr Emma Poole** (Co-Investigator), MRC Programme Grant



## UKRI - Biotechnology and Biological Research Council

- “Mechanisms underlying Epigenetic Resilience in Development and Ageing (MERIDA)” - **Professor Gavin Kelsey, Dr Peter Rugg-Gunn, Dr Teresa Rayon**, BBSRC Institute Strategic Programme Grant
- “Public engagement to inform policy changes related to stem cell-based embryo models” - **Professor Kathy Niakan**, BBSRC Impact Acceleration Awards
- “Exploring mechanisms of placental toxicity following xenobiotic exposure” - **Dr Amanda Sferruzzi-Perri**, BBSRC iCASE Collaborative Training Partnership in collaboration with Unilever



## ERC (European Research Council)

- “Placental macrophages: Their development and role in the placenta” - **Dr Naomi McGovern**, ERC Starting Grant
- “TempoReg: Molecular and metabolic pathways controlling developmental timing” - **Dr Teresa Rayon**, ERC Starting Grant



## The Royal Society

- “Placental ATP-citrate lyase (AclY) regulates trophoblast stemness and feto-placental growth in mice” - **Dr Irving Aye**
- “Sense and Nonsense: RNA decay Pathways in Mammalian Reproduction” - **Dr Claire Senner**, Royal Society Award

## Other research funders in 2023-2024



# New Partnerships & Appointments



**Dr Tom Rawlings** was appointed to a 2024 Next Generation Fellowship, commencing in December. Tom will be sponsored by Professor Kathy Niakan and based in the shared Loke Centre for Trophoblast Research lab space in the Department of Physiology, Development and Neuroscience.

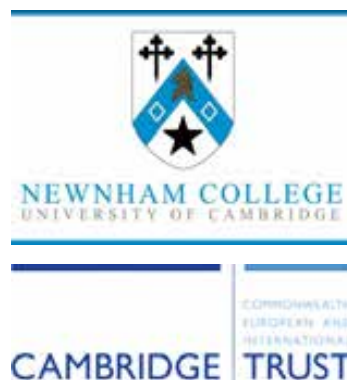
The title of Tom's research programme is **Modulating the proliferative phase endometrium to prevent recurrent miscarriage**.

“ Each miscarriage increases the risk of further loss, and with no effective therapeutics available. My research focuses on understanding how a proliferative phase imbalance in specific endometrial cells impacts embryo implantation and early placentation to ultimately identify potential drug treatments to prevent loss in early pregnancy.



**Isabel Marchand-Casas** was awarded a Loke Centre for Trophoblast Research-funded PhD Studentship in conjunction with a Cambridge International & Newnham College Scholarship. Isabel will be supervised by Dr Naomi McGovern and Dr Emma Poole in the Department of Pathology.

The title of Isabel's project is: **Determining the molecular mechanisms placental macrophages use to protect the placenta from cytomegalovirus infection**



**Julie Tang** was awarded a Johnson Woodman - Loke Centre for Trophoblast Research PhD Studentship in partnership with the Professor Martin Johnson and Dr Frank Woodman fund at Christ's College. Julie will be supervised by Dr Courtney Hanna and Prof Anne Ferguson-Smith in the Department of Physiology, Development and Neuroscience.

The title of Julie's project is: **The impact of DNA methylation on gene regulation in placental development**





# Policy and Outreach

## Human Stem Cell-Based Embryo Models

**Professor Kathy Niakan**, in partnership with Cambridge Reproduction and the Progress Education Trust (PET) oversight group, has led the Governance of Stem Cell-Based Embryo Models (G-SCBEM) project to develop the first Code of Practice for UK research involving embryo models. Newly established human stem cell-based embryo models, many of which were developed by Loke CTR groups, offer advanced new techniques to model and understand the earliest stages of human trophoblast development and implantation. Because the science is so new, there is currently no dedicated governance for their use in research – a “governance gap” that hinders research and risks damaging public confidence.

The G-SCBEM project began in March 2023, bringing together a working group composed of a wide range of researchers, legal and bioethics experts, regulators, and research funders to prepare a draft Code of Practice. The draft



*Professor Kathy Niakan and Dr Peter Rugg-Gunn present at the Cambridge Festival Event, “Reproductive Futures: Stem cell-based embryo models.” Photo courtesy of Christina Rozeik.*

guidelines were circulated widely for feedback from interested researchers, and in early 2024 input from the public was received through a commissioned Public Dialogue. Several Loke CTR group leaders have contributed to the Code of Practice, including Loke CTR members **Dr Peter Rugg-Gunn** and **Dr Marta Shahbazi**, and honorary member **Professor Jennifer Nichols**. The project has been funded by two BBSRC Impact Acceleration Awards. It has been covered by several major news outlets, including *the Guardian* and *the New York Times*, and resulted in a POSTNote a briefing to the UK Parliament. The Nuffield Council has taken on the governance of stem cell-based embryo models as a policy topic, with Professor Kathy Niakan as a member of the working group.

Read more about the [G-SCBEM project](#), [Public Dialogue](#), [POSTNote](#), ongoing [Nuffield Council policy project](#).

## UK Public Dialogue on Human Embryo Research

**Dr Peter Rugg-Gunn** led a foundational UK public dialogue on human embryo research to consider how early human embryo research can be used to its fullest, 14-day rule of research using human embryos and the fast-paced field of stem cell-based embryo models.

The dialogue, co-funded by the Human Developmental Biology Initiative (HDBI) and



*Panel Discussion at the Science Museum Lates event, “STEMBRYOS: The future of Reproduction.” Photo courtesy of Christina Rozeik.*



Human Developmental  
Biology Initiative







Dr Andrew Sharkey lecturing virtually at the Placental Research Capacity Building Workshop. Photo courtesy of Noguchi, University of Ghana

UKRI Sciencewise, engaged a group of 70 people broadly reflective of the UK population in over 15 hours of activities including a series of online and face-to-face workshops with scientists, ethicists, philosophers, policy makers and people with relevant lived experience (such as embryo donors from IVF procedures). The dialogue revealed a strong public appetite for a review of the 14-day rule, which would enable researchers to study key processes in trophoblast implantation. The public also expressed a high level of confidence in how human embryo research is regulated, and strong support for research that would improve fertility rates, for example raising the success rates of IVF procedures.

The findings are published in a full report available on the [HDBI website](#).

## Placental Research Capacity Building workshop, Accra, Ghana

**Dr Andrew Sharkey** and **Dr Irving Aye** were co-organisers, along with Dorotheah Obiri (Loke CTR visitor, 2022) and speakers at the inaugural Placental Research Capacity Building workshop in Accra, Ghana (photo, top right). This biannual event aims to promote and help facilitate placental research in Ghana. The workshop focused on basic and clinical considerations for placental research, advocacy considerations in placental research, translating placental research and cell isolation from placentas and explant cultures.



## Food, diet and obesity

**Professor Susan Ozanne** and **Dr Catherine Aiken** submitted evidence for the call from the House of Lord's on Food, diet and obesity. Read more about the call on the [UK Parliament website](#)



## Climate and sustainability

**Professor Amanda Sferruzzi-Perri** took part in a Cambridge Reproduction-led series of interdisciplinary discussion on highlighting the centrality of reproduction when studying climate change.



The Loke CTR was awarded a second consecutive Scientific Meeting and Sustainable Conferencing donation from the Company of Biologists to support the 2024 hybrid Annual Meeting. This funding supports the virtual element of our programme in order to make the conference accessible to a larger and more diverse audience and to promote inclusivity, accessibility and sustainability.



Cambridge Reproduction is a strategic research initiative (SRI) that spans the numerous internationally-recognised reproductive studies groups across the arts, humanities, social sciences, biology and medicine at the University, including the Loke CTR. The Cambridge Reproduction SRI network fosters integration across disciplines, and facilitates policy and outreach for many Loke CTR Members.

# Publications

## Catherine Aiken

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# Governance

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*Decides on the funding priorities for the Centre, and elects to Studentships and NGFs*

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- Dr Peter Rugg-Gunn (Babraham Institute)
- Dr Erica Watson (Department of Physiology, Development and Neuroscience)
- Professor Susan Ozanne (Institute of Metabolic Science)
- Professor Steve Charnock-Jones (Department of Obstetrics and Gynaecology)
- Dr Naomi McGovern (Department of Pathology)

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*Advises on all aspects of the scientific programme, policy, and future directions of the Centre.*

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- Professor Andrew Murray
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## Image Credits

### Cover page

Description: Image showing the signalling cells (in green) of the mouse placenta that are key for remote controlling the metabolism of the mother to support nutrient supply and growth of the fetus. Image credit: Sferruzzi-Perri lab

### Page 3, 5, 17, 18, 38

Image credit: Photography by ©Lucinda Price Photography.

### Page 8

Description: Professor Charlie Y.W. Loke, Amanda Loke and Troy Daniel visit to Cambridge, October 2022. Image Credit: Loke Centre for Trophoblast Research

### Page 19

Top, Description: Placental organoid (circle in the centre). Trophoblast cells are invading out of the organoid, mimicking placental cells invading the uterus in the early weeks of pregnancy. Image Credit: Friedrich Miescher Institute/University of Cambridge

Bottom, Description: Image showing the signalling cells (in green) of the mouse placenta that are key for remote controlling the metabolism of the mother to support nutrient supply and growth of the fetus. Image credit: Sferruzzi-Perri lab

### Page 20

Description: A cell aggregation of human pluripotent stem cells and amniotic ectoderm

cells generated by the published culture method and mimicking the gastrulation event in human embryos. Right: Images showing the individual cell features and markers identified using immunofluorescent staining and compiled in the image shown on the left. Gray: nuclei, Cyan: amniotic ectoderm marker, Yellow: pluripotency marker, Magenta: gastrulation marker. Image credit: Dr Shota Nakanoh, Babraham Institute / Wellcome-MRC Cambridge Stem Cell Institute.

#### Page 21

Image credit: Illustration produced by Antonio Garcia. All rights reserved.

#### Page 22

Description: Day 4 embryo model showing an inner epiblast like domain in magenta that has apico-basal polarity (yellow apical, blue basal), similar to the epiblast of the human embryo just after implantation. Image Credit: Zernicka-Goetz Laboratory, University of Cambridge

#### Page 24

Description: Attendees at Professor Azim Surani's 40th anniversary Festschrift held at King's College. Image credit: Walfred Tang

#### Page 25

Left, Description: Panel Discussion at the Science Museum Lates event, "STEMBRYOS: The future

of Reproduction." Image credit: Christina Rozeik, Cambridge Reproduction

Right, Description: Professor Kathy Niakan and Dr Peter Rugg-Gunn present at the Cambridge Festival Event, "Reproductive Futures: Stem cell-based embryo models." Image credit: Christina Rozeik, Cambridge Reproduction

#### Page 26

Top, Description: Dr Andrew Sharkey lecturing virtually at the Placental Research Capacity Building Workshop. Image credit: Photo courtesy of Noguchi, University of Ghana. All rights reserved.

Bottom, Description: Professor Amanda-Sferruzzi speaking on a panel at the Cambridge Reproduction-led series of interdisciplinary discussion on highlighting the centrality of reproduction when studying climate change. Image credit: Reetika Subramanian, University of Cambridge Centre for Gender Studies.

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Description: Loke Centre for Trophoblast Research Spring Half Away Day. Image credit: Busma Butt



Loke CTR Annual Away Day at the Postdoc Centre in Eddington, Cambridge on 17 May 2024



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