

ANNE MCLAREN RESEARCH FUND MEETING 2021

Synthetic gametes and germline development for science and society

23 March 2021, online

Germline: the enduring link between generations
Azim Surani (Cambridge)

Anne McLaren's legacy to the mammalian germline biology
Robin Lovell-Badge (Francis Crick Institute)

Ethics of germline research: gene editing and synthetic gametes
Sarah Chan (Edinburgh)

Human germline *in vitro* models for development and the epigenetic programme
Naoko Irie (Cambridge)

How to build a primate: modelling embryogenesis in a dish
Thorsten Boroviak (Cambridge)

Mitochondrial inheritance, germline purification and disease: can we fix it?
Mary Herbert (Newcastle)

Principles of embryogenesis - from polarisation to symmetry breaking
Magdalena Zernicka-Goetz (Cambridge)

The legal situation with regard to the generation of synthetic gametes from somatic stem cells
Emily Jackson (LSE)

A sociology of artificial gametogenesis
Noémie Merleau-Ponty (CNRS)

Panel discussion

Robert Bud (Science Museum), Amarpreet Kaur (Cambridge), Sarah Chan (Edinburgh), Robin Lovell-Badge (Francis Crick Institute), Thorsten Boroviak (Cambridge), Kathy Niakan (Cambridge)

More information: www.repro.cam.ac.uk/anne-mclaren-2021

Welcome

The Fund Managers of the Anne McLaren Trust, the Reproductive Sociology Research Group and the Chairs of the Strategic Research Initiative in Reproduction are pleased to welcome you to this Symposium, our second major conference dedicated to the interdisciplinary exploration of specific issues arising in the context of translational biomedicine. The first conference of this kind was held at the Wellcome Trust in December 2017, and we plan to hold future events of this kind every two or three years.

Anne would be very pleased this Symposium is being hosted at Cambridge, where she did so much of her own research, and where she worked with many of the people attending our event today. Anne was a passionate advocate of interdisciplinary collaborations in the name of better science, and she also worked energetically and enthusiastically to promote the study of reproduction in its broadest sense across the world. She would be both thrilled and satisfied to know that 'Reproduction' is the latest research area to be formally recognised as an 'SRI' -- or Strategic Research Initiative -- at Cambridge, meaning it is now a stand-alone, funded, cross-School and multi-disciplinary network uniting hundreds of researchers. Anne was one of the people who made this possible, as a keen early supporter of the Cambridge Interdisciplinary Research Forum (CIRF), which was the real start of the pathbreaking Reproduction SRI at Cambridge.

The Reproductive Sociology Research Group (ReproSoc) is the third co-sponsor of this event, and we are grateful to all of the funders who support the work of this research initiative, which will soon be entering its second decade here at Cambridge. In particular we are grateful for the support of the long-term support British Academy and the Wellcome Trust for the work of ReproSoc at Cambridge and elsewhere. Without such support we could not deliver events of this kind -- which are free, livestreamed, and made available in edited form as online Open Access resources afterwards.

We are especially grateful to our speakers and chairs for their contributions and we hope you have a wonderful day. We would welcome any feedback you'd like to offer on this event or the work of the Anne McLaren Fund more widely. Just speak to one of the organisers or drop us an email as we are keen to ensure Anne's legacy of distinctive curiosity combined with scientific rigour in the name of public service and social improvement continues to thrive in our community and beyond. I want in closing to thank especially our outstanding administrative team members -- Christina Roziek, Lois Gibbs and Yvonne Frankfurth -- for their hard work and eye for detail!

With best wishes,

Sarah Franklin

Chair, Anne McLaren Memorial Fund

About the Anne McLaren Fund

The Anne McLaren Memorial Fund was established in 2007 to support work related to her field. Since its inception the endowment has been used to support a wide variety of projects and events ranging from public lectures and scholarly grants to conferences and outreach activities. Hosted by Christ's College, the AMMF is a Registered Charity overseen by a Management Committee. You can find out more about the fund and its activities, contact us, or make a donation to the fund, on our website:

<https://www.gurdon.cam.ac.uk/anne-mclaren/about>

Anne McLaren Fund Managers:

- Professor Andrea Brand (Gurdon Institute)
- Professor Sarah Franklin (Chair, Christ's College)
- Professor Martin Johnson (Secretary, Christ's College)
- Professor Elizabeth Robertson (Oxford University)
- Professor Susan Michie (nominated family member)
- Miss Elizabeth Norris (Christ's College)
- Dr Thorsten Boroviak (Christ's College)
- Professor Sir Jim Smith (Christ's College)
- Professor Azim Surani (King's College)

Co-opted member:

- Professor Jonathan Michie (Kellogg College, Oxford)

**Anne McLaren
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ABOUT ANNE MCLAREN

Anne McLaren (1927-2007) was one of the most eminent and highly respected reproductive biologists of the twentieth century. Her most enduring interest as a scientist was in germ cells and early mammalian development. Her work helped further recognition of the importance of stem cells in the treatment of human disease and her research in the basic science



underlying the treatment of infertility helped develop several human-assisted reproduction techniques. McLaren received an impressive array of awards for her contributions to the field, including the March of Dimes and the Japan Prizes (2002 and



2007). She moreover held positions of highest office across a wide range of fields during her career, as Founding Director of the Medical Research Council (MRC) Mammalian Development Unit in London (UCL 1974-1992), Fellow of the Royal Society (FRS 1975), fellow of the Royal College of Obstetricians and Gynecologists (1986), Fullerian professor of Physiology at the Royal Institution (1990-1995), President of the British Association for the Advancement of Science (1993-1994), and Fellow of the Academy of Medical Sciences (1998). McLaren's influence also extended

beyond science. She was, for example, famously the first woman to hold office in the 330-year-old history of the Royal Society, becoming its Foreign Secretary in 1991 (to 1996), and a year later its Vice President (1992-1996) and did much to promote the advancement of women in science. She also played a public role in ethical discussions on science as a member of the Warnock Committee tasked with making recommendations to government concerning the regulation of human fertilization and embryology in the wake of the 'legal vacuum' created by the birth of Louise Brown in 1978.

SPEAKER BIOGRAPHIES

(IN ALPHABETICAL ORDER)



Thorsten Boroviak originates from Austria, where he read molecular biology at the University of Vienna. After completion of his master's thesis in 2007, he was awarded a PhD-fellowship from the Department of Biomedical Science at the University of Sheffield to work on neuronal differentiation of mouse embryonic stem cells. Following his passion for pluripotency and embryonic development, he subsequently joined the laboratories of Prof. Austin Smith and Prof. Jennifer Nichols in 2010. His early postdoctoral research addressed the relationship of pluripotent embryonic stem cells to the early embryo. Thorsten pioneered genome-wide comparison of mouse to non-human primate development by lineage-specific RNA-seq, which identified a primate specific role for WNT signalling during early lineage specification. In 2017, he was awarded the Sir Henry Dale Fellowship to start his laboratory at the Department of Physiology, Development and Neuroscience at the University of Cambridge. The goal of his group is to bioengineer synthetic primate embryos and transform our understanding of implantation, germ cell specification and pluripotency in primate embryogenesis.



Robert Bud is Emeritus Keeper at the Science Museum. With a doctorate in the History and Sociology of Science from the University of Pennsylvania, he has been reflecting on public discourse about biotechnology for forty years. In 1986, he curated the Museum's 'permanent' chemical industry gallery which incorporated genetically modified tomato plants. Subsequently, as curator he acquired many of the iconic artefacts of recent biotechnology including Tracy the first transgenic sheep, and two of the first oncomice. In 1994 he published *The Uses of Life: A History of Biotechnology* (Cambridge University Press) and in 2007 *Penicillin: Triumph and Tragedy* (Oxford University Press). Both books deal with the ways in which lay discourse has been part of the definition of a field. He is currently completing a monograph history of the idea of applied science, which explores the role of discourse with the public. This culminates with ideas of translational research to which Anne McLaren contributed.



Sarah Chan is a Reader in Bioethics at the Usher Institute, University of Edinburgh; she is currently a Deputy Director of the Mason Institute for Medicine, Life Sciences and Law, and an Associate Director of the Centre for Biomedicine, Self and Society. Previously, from 2005 to 2015, she was a Research Fellow in Bioethics at the University of Manchester, first at the Centre for Social Ethics and Policy and from 2008 the Institute for Science Ethics and Innovation. Sarah's research focuses on the ethics of new biomedical technologies, including gene therapy and genetic modification; stem cell and embryo research; reproductive medicine; synthetic biology; and human and animal enhancement. Her current work draws on these interests to explore the ethics of emerging modes of biomedicine at the interface of health care research, medical treatment and consumer medicine, including population-level health and genetic data research; the use of human biomaterials in both research and treatment; and access to experimental treatments and medical innovation.



Sarah Franklin took up the Chair of Sociology at Cambridge in October 2011. In 2012 she received awards from the Wellcome Trust, ESRC, and British Academy to establish the Reproductive Sociology Research Group (ReproSoc) which has since gone on to become one of the leading research centres in the rapidly expanding field of reproductive studies.

Franklin was among the first researchers to begin to analyse the forms of social change associated with the introduction of new reproductive technologies in the 1980s. Since completing her PhD research on IVF in 1989, she has published extensively on the social aspects of new reproductive technologies. In addition to assisted conception technologies, Franklin has conducted fieldwork on cloning, preimplantation genetic diagnosis (PGD), and human embryonic stem cell derivation. Her research combines ethnographic methods with science studies, gender theory, and the study of kinship and she has contributed to a number of emergent fields in social theory including the 'new kinship studies', the feminist analysis of science, the anthropology of biomedicine, and reproductive studies.

In addition to directing the Reproductive Sociology Research Group, Franklin is a Wellcome Trust Senior Investigator, co-Editor of the journal *Reproductive Biomedicine and Society*, and Chair of the Anne McLaren Trust.



Mary Herbert is Professor of Reproductive Biology at Newcastle University and Honorary Consultant Embryologist/Scientific Director at Newcastle Fertility Centre. She was awarded a PhD from Newcastle University in 1998 and was appointed Consultant Embryologist at Newcastle NHS Hospitals Trust. In 2006 she moved to an academic position at Newcastle University and now leads a closely integrated team of research and clinical scientists. Her work in the field of mammalian reproductive cell biology is focused on understanding the basic mechanisms of chromosome segregation in oocytes and on developing clinically relevant methods to prevent disease transmission through the female germline. She was elected Fellow of the Academy of Medical Sciences in 2019.



Naoko Irie is Senior Research Fellow in the laboratory of Professor Azim Surani at the Wellcome Trust Gurdon Institute, Cambridge UK. Irie's research focusses on studying how human germline cells develop while maintaining their immortality to pass on genetic and epigenetic information to the next generation. Since joining Prof. Surani's group, Irie has established a robust human germ cell induction culture system and identified critical factors for human germ cell fate.



Emily Jackson is a Professor of Law at the London School of Economics and Political Science, where she teaches Medical Law. She is a Fellow of the British Academy, and was previously a Member and then Deputy Chair of the HFEA, and a Judicial Appointments Commissioner.



Amarpreet Kaur is a PhD student in the Department of Sociology at the University of Cambridge. Her research focusses on human germline genome editing as a reproductive choice in the UK. Her research is funded by the Cambridge ESRC DTP and she can be followed via Twitter (@lioness1992). Amarpreet completed a fellowship at the Parliamentary Office of Science and Technology in January 2020 where she researched and co-authored a four-page briefing document for MPs and Peers on Human Germline Genome Editing.

To read the POSTnote please visit:

<https://researchbriefings.parliament.uk/ResearchBriefing/Summary/POST-PN-0611>



Robin Lovell-Badge is a senior group leader and head of the Laboratory of Stem Cell Biology and Developmental Genetics at the Francis Crick Institute. He obtained his BSc in zoology at University College, London in 1975. He obtained his PhD in embryology at University College London in 1978, carrying out mouse stem cell and embryo research with Martin Evans.

After postdoctoral research in Cambridge, also with Martin Evans, and then in Paris, he established his independent laboratory in 1982 at the Medical Research Council (MRC) Mammalian Development Unit, University College, London, directed by Anne McLaren. In 1988 he moved to the MRC National Institute for Medical Research (now part of the Francis Crick Institute), becoming Head of Division in 1993. His lab relocated to the new Francis Crick Institute in October 2016.

He is very active in both public engagement and policy work, notably around stem cells, genetics, human embryo and animal research, and in the ways science is regulated and disseminated.



Noémie Merleau-Ponty is a permanent researcher at the French National Centre for Scientific Research. Her research is concerned with biotechnologies of human reproduction and regeneration. In France, India and the United Kingdom, she looks at the making of social relations through the making of science as well as at the intertwining of national contexts and global dynamics. Trained as a social anthropologist, Noémie is also inspired by feminist and postcolonial science and technology studies. While she primarily works ethnographically, Noémie also develops interdisciplinary collaborations between the social and life sciences.



Liz Robertson received her BA in Zoology at Oxford (1978), then pursued a PhD, followed by post-doctoral training with Martin Evans in the Department of Genetics at Cambridge. In 1988 she joined the faculty of the Department of Genetics and Development at Columbia University Medical School, New York where her lab was one of the first to report successful gene targeting experiments to reveal functional roles under physiological conditions *in vivo*. Liz was recruited to Harvard University in 1992 where over the next decade she studied the Nodal signalling pathway, discovering its critical role in both anterior-posterior and left-right axis patterning of the early mammalian embryo. Her lab also identified requirements for the zinc finger transcriptional repressor Blimp1 during specification of the mammalian germ line. Liz is currently a Wellcome Trust Principal Research Fellow and Professor of Developmental Biology in the Dunn School of Pathology, University of Oxford where her lab has focused on transcriptional networks governing cell fate decisions in the embryo and controlling adult tissue homeostasis. Liz is a Fellow of the Royal Society and the Academy of Medical Sciences, and a member of EMBO. She is a former Chair of the British Society for Developmental Biology.



Kathy Niakan is the Mary Marshall and Arthur Walton Professor of Reproductive Physiology, Director of the Centre for Trophoblast Research and Chair of the Strategic Research Initiative on Reproduction at the University of Cambridge and Group Leader at the Francis Crick Institute. Her laboratory investigates the mechanisms that direct cell fate in human embryos and stem cells.

Kathy Niakan obtained a B.Sc. in Cell and Molecular Biology and a B.A. in English Literature from University of Washington. She was inspired to pursue molecular biology and genetics following undergraduate research in Wendy Raskind's laboratory, with the support of a Mary Gates Research Scholarship. She obtained her PhD at University of California, Los Angeles with Edward McCabe and was supported by a National Institutes of Health Pre-doctoral Training Grant, Paul D. Boyer Fellowship and a Chancellor's Dissertation Year Fellowship. She undertook postdoctoral training with Kevin Eggan at Harvard University. She was a Centre for Trophoblast Research Next Generation Research Fellow at University of Cambridge.



Azim Surani was born in Kenya and obtained his PhD in 1975 at Cambridge University under Professor Sir Robert Edwards FRS (Nobel Laureate, 2010). He discovered the phenomenon of Genomic Imprinting in 1984, a pivotal discovery that established the field of epigenetics. He showed that chromosomes retain a memory of their parental origin in the form of DNA methylation tags, which are erased and then re-established in the germline. He went onto identify several imprinted genes and their functions in development, growth and behavior, which are known to contribute to human diseases. He was appointed the Marshall-Walton Professor jointly at the Dept of Physiology, Development and Neuroscience, and the Gurdon Institute in 1992, where he is currently Director of Germline and Epigenetics Research. His recent work has focused on the genetic basis for mouse and human germ cell specification and the initiation of the unique epigenetic program towards generating the totipotent state. He is a Fellow of the Royal Society. He has multiple other awards, including Rosenstiel Award, a Royal Medal from the Royal Society, the ISSCR McEwen Award for Innovation, and the Gairdner International Award for genomic imprinting and epigenetics.



Magdalena Zernicka-Goetz is Professor in Developmental and Stem Cell Biology at the University of Cambridge, Bren Professor of Biology and Biological Engineering at the California Institute of Technology (Caltech), a Wellcome Trust Investigator, and fellow of Sidney Sussex College. She studies both mouse and human embryo development and has used the knowledge she gained to pioneer approaches for building mouse and human embryo models from stem cells in vitro. She also established the first culture system that allows human embryo development outside the body of the mother until day 14. She has recently written a biographical book *The Dance of Life*, which is devoted to human reproduction, developmental and stem cell biology, but also describes her scientific and personal journey.

PROGRAMME

SESSION 1 **CHAIR: SARAH FRANKLIN, CAMBRIDGE**

- 10:00 - 10:10 Opening remarks (Sarah Franklin, Cambridge)
- 10:10 - 10:25 Germline: the enduring link between generations
(Azim Surani, Cambridge)
- 10:25 - 10:35 Discussion
- 10:35 - 10:50 Anne McLaren's legacy to the mammalian germline biology
(Robin Lovell-Badge, Francis Crick Institute)
- 10:50 - 11:00 Discussion
- 11:00 - 11:15 Ethics of germline research: gene editing and synthetic gametes
(Sarah Chan, Edinburgh)
- 11:15 - 11:25 Discussion
- 11:25 - 11:45 Coffee Break

SESSION 2 **CHAIR: ROBERT BUD, SCIENCE MUSEUM**

- 11:45 - 12:00 Human germline in vitro models for development and the
epigenetic programme (Naoko Irie, Cambridge)
- 12:00 - 12:10 Discussion
- 12:10 - 12:25 How to build a primate: modelling embryogenesis in a dish
(Thorsten Boroviak, Cambridge)
- 12:25 - 12:35 Discussion
- 12:35 - 12:50 Mitochondrial inheritance, germline purification and disease:
can we fix it? (Mary Herbert, Newcastle)
- 12:50 - 13:00 Discussion
- 13:00 - 14:00 Lunch Break

SESSION 3 **CHAIR: LIZ ROBERTSON, OXFORD**

- 14:00 - 14:15 Principles of embryogenesis - from polarisation to symmetry breaking
(Magdalena Zernicka-Goetz, Cambridge)
- 14:15 - 14:25 Discussion
- 14:25 - 14:40 The legal situation with regard to the generation of synthetic gametes
from somatic stem cells (Emily Jackson, LSE)
- 14:40 - 14:50 Discussion
- 14:50 - 15:05 A sociology of artificial gametogenesis (Noémie Merleau-Ponty, CNRS)
- 15:05 - 15:15 Discussion
- 15:15 - 15:50 Tea Break

SESSION 4 **CHAIR: KATHY NIAKAN, CAMBRIDGE**

- 15:50 - 16:30 Panel discussion: Robert Bud (Science Museum), Amarpreet Kaur
(Cambridge), Sarah Chan (Edinburgh), Robin Lovell-Badge (Francis Crick
Institute), Thorsten Boroviak (Cambridge)
- 16:30 - 16:45 Thanks and closing comments
- 16:45 Optional virtual & sociable drinks and nibbles

TALK ABSTRACTS

(IN CHRONOLOGICAL ORDER)

Germline: the enduring link between generations

(Azim Surani, Cambridge)

Germ cells transmit heritable information for the development of an organism, and potentially, for endless generations. Accordingly, the germline is uniquely 'immortal' while the soma perishes with each generation. Darwin, Weismann and others contributed to the development of concepts that distinguish germ cells from the soma. The origin of germ cells in mammals was also keenly sought by many, including Kirstie Lawson and Anne McLaren, which lead to the conclusion that ~ 30-40 primordial germ cells (PGC; precursors of sperm and eggs) originate in early mouse postimplantation embryos at around the time of gastrulation.

We decided to investigate the molecular logic of the establishment of PGCs, and found three critical genes for the founding of the mouse germ cell lineage, which was pivotal for advances in mammalian germline biology by us and others, leading to the derivation of PGCs and viable gametes from pluripotent stem cells and 'reprogrammed' somatic cells. Similar research has also led to advances in human germline biology, with a potential for in vitro gametogenesis (IVG) and 'synthetic' gametes from reprogrammed human somatic cells.

There are compelling reasons to pursue research on in vitro models of the 'immortal' germline and gametogenesis; to address the causes of human infertility, and more widely for regenerative medicine and age-related diseases. In vitro models of the human germline could also be used for testing the precision of human germline gene editing of heritable genetic diseases, as well as for breeding farm animals, and most importantly, for the rescue of many currently endangered wild mammals.

Anne McLaren's legacy to the mammalian germline biology

(Robin Lovell-Badge, Francis Crick Institute, London)

Anne McLaren was fascinated by all things concerning germ cells and the germ line, particularly in the mouse, her favoured subject for study. She published close to a hundred research papers and reviews dealing with everything from the origins of primordial germ cells in the early embryo, how their biology differs from somatic cells, how they colonise the gonads, become different in males and females, and how they relate to ovary and testis differentiation, their unique epigenetic status and how they can be reprogrammed back to early embryo like cells, and so on. It is an impossible task to review all of her contributions in a short talk; I will therefore skim the surface, highlighting some of Anne's main findings that have helped to shape how we think about the mammalian germline and which form the basis of current studies by others.

Ethics of germline research: gene editing and synthetic gametes

(Sarah Chan, Edinburgh)

The decades since the establishment of the UK regulatory framework for human embryo research have seen the emergence of numerous technological possibilities: from early approaches to IVF, through pre-implantation genetic testing, the derivation of embryonic and induced pluripotent stem cells, in vitro gametogenesis, nuclear transfer, and most recently, genome editing. Alongside this, our social as well as scientific understandings of the embryo have evolved to encompass the ethical dimensions opened up by these technologies. No longer fixed entities with the sole origin of fertilisation and the sole destination of reproduction, human embryos move through multiple potential positions in our reproductive and scientific narratives. As the fixed categories of regulation increasingly struggle with the hybridity and multiplicity of embryonic natures produced by novel technologies, this paper seeks to explore the question: what next for the regulation of reproductive research?

Human germline in vitro models for development and the epigenetic programme

(Naoko Irie, Cambridge)

How can germline be immortal over the generations by resetting the ability to create whole new organisms? The human germ cell fate initiates with the specification of primordial germ cells (PGCs), the precursors of egg and sperm, week 2-3 after fertilization. This is followed by PGC migration and colonization in the developing gonads, future ovary and testis where germ cells undergo unique events including epigenetic programming. The human germline is largely inaccessible which makes the research challenging. Consequentially, our knowledge of human germ cell development is still limited.

To achieve a breakthrough, our research established efficient in vitro PGC induction using human pluripotent stem cells (hPSCs), ES cells and iPS cells. It is essential to recapitulate in vivo stepwise development by inducing germline precursors from hPSCs for a successful in vitro PGC specification. In vitro induced PGCs exhibit the characteristics of nascent PGCs prior to migration into gonads. Using the model, we revealed that the transcription factor SOX17, which was known as a regulator for somatic cell lineage, is essential for PGC specification. Subsequent studies showed SOX17 expression in the nascent PGCs of monkey and porcine unlike mouse, a primary model for mammalian development. This suggests an important evolutionary diversity and appropriate animal models for studying human germline development.

Taken together, our research has shown the significance of in vitro experimental platforms which will provide a basis for further understanding human reproduction, germ cell disorders, as well as the transmission of genetic and epigenetic information that impacts on human health.

How to build a primate: modelling embryogenesis in a dish

(Thorsten Boroviak, Cambridge)

Implantation is a landmark event where the embryo undergoes major reorganisation. In rodents, the pluripotent epiblast gives rise to a cup-shaped epithelium, the egg-cylinder. However, primate development diverges from the rodent paradigm: The primate epiblast forms a flat disc and segregates an extraembryonic lineage after implantation, the amnion. The very recent discovery that primates may specify germ cells from nascent amnion highlights the fundamental importance of this enigmatic lineage decision. Human embryos of these early development stages are difficult to access, thus the underlying mechanisms of embryo implantation in our own species have remained elusive.

To illuminate the black box of postimplantation development in primates, we established a new platform for spatial profiling of marmoset embryos. Our laser capture microdissection approach includes recording of the original location of each sample within a structurally intact embryo and permits digital 3D reconstruction of primate embryogenesis. We delineate genome-wide expression gradients in the embryonic disc and show that primitive streak formation is hallmarked by conserved signalling cascades, while the pluripotent compartment is confined towards the anterior domain, in contrast to mouse. Amnion specification occurs at the boundaries of the embryonic disc in response to BMP-signalling, providing a developmental rationale for amnion specification from human and non-human primate pluripotent stem cells (PSCs). Spatial identity mapping demonstrates that primed marmoset PSCs exhibit highest similarity to the anterior embryonic disc, while naïve PSCs resemble the preimplantation epiblast. Our 3D-transcriptome models reveal the molecular code of lineage specification in the primate embryo and provide an *in vivo* reference to decipher human development.

Mitochondrial inheritance, germline purification and disease: can we fix it?

([Mary Herbert](#), Yuko Takeda, Jordan Marley & Linlin Wang, Newcastle)

Mitochondrial replacement (MR) techniques were developed with the aim of preventing transmission of mtDNA disease from mother to child. In the context of clinical treatment, MR involves transplanting the nuclear genome from an affected woman's egg to an enucleated egg from an unaffected donor. The nuclear DNA is transplanted in a karyoplast, which is fused with the enucleated donor egg. Because the karyoplast contains a small amount of cytoplasm, a small fraction of mtDNA is inevitably co-transferred with the nuclear genome. Under optimal conditions, this accounts for <2% of the mtDNA content of MR embryos. Despite this, ~20% of embryonic stem (ES) cell lines derived from MR embryos exhibit complete reversion to the nuclear genome's native mtDNA. While the relevance of this to embryonic development *in vivo* is currently unclear, the finding raises the possibility that MR might not prevent transmission of mtDNA disease in all cases. For this reason, currently available MR treatments are regarded as risk reduction, rather than prevention strategies. A major focus of our ongoing research is to bridge this gap by developing techniques to minimise the contribution of maternal mtDNA to the mitochondrial genome of the developing embryo.

Principles of embryogenesis - from polarisation to symmetry breaking

(Magdalena Zernicka-Goetz, Cambridge)

I plan to talk about early mouse and human development and how we can now study its underlying principles using different types of stem cells from which we can make chimeras and generate embryo-like structures. Anne would have loved this approach as she was very fond of chimeras. These experiments have given us insight into how the embryo's different stem cell types are able to interact and self-organise into complex patterns.

The legal situation with regard to the generation of synthetic gametes from somatic stem cells

(Emily Jackson, LSE)

The law which applies to the creation and use of synthetic gametes in the UK is clear and straightforward. It is possible to apply for a research licence from the Human Fertilisation and Embryology Authority in order to carry out research, but the use of synthetic gametes in treatment would be a criminal offence. In this presentation, I will set out how the current regulatory system works, and I will explain why the law takes the form that it does.

Of course, in the future there may be calls to revisit the current legal regime. I will consider what reasons there might be to change the law in the future, as well as exploring both how that could be achieved, and what obstacles there might be to law reform.

A sociology of artificial gametogenesis

(Noémie Merleau-Ponty, CNRS)

Artificial gametogenesis is the attempt to make gametes in the laboratory using embryonic or somatic cells. To this day, basic scientists across the world have published important papers on the molecular mechanisms involved in gamete's differentiation during the early development of embryos. This said, functional human stem cell-derived gametes do not exist. Nonetheless, their futuristic reproductive potential fuels heated bioethical debates around the end of infertility or genome editing of the germline. This framework of technological making is a classical sociocultural understanding of biotechnology as a force for social change based on emergent biological findings.

At the Gurdon Institute, I worked with Dr. Naoko Irie in Prof. Azim Surani's laboratory, a leading academic space where basic science of artificial gametogenesis is being made. The empirical knowledge I have documented shows that the sociality of artificial gametogenesis is not only already quite vivid, but, more importantly, is one of its key components. Changing the focus, from the future social impact of artificial gametogenesis to the present of its social dynamics, unravels questions that are currently significantly undebated. By presenting them, I will advocate for an understanding of sociology as a technology.

DISH LIFE: THE GAME

Part-Sims, part-Tamagotchi game puts players in the shoes of a budding stem cell researcher as they progress from undergraduate student to professor

"Dish Life" is a new free-to-play game developed by researchers from ReproSoc (Reproductive Sociology Research Group) and the Cambridge Stem Cell Institute, and produced by software and games company Pocket Sized Hands. The game allows players an insight into the life of a stem cell scientist and the various challenges of living and working in a lab: growing cells, completing research projects, and building their scientific reputation. The game is free to download on App Store (Apple), Google Play (Android) and Steam (PC).



Players must balance competing demands: growing a range of ever-hungry cells while adding to their lab's wellbeing and reputation – all as they negotiate the scientific career ladder through publication and promotion. Dish Life is littered with dilemmas that occur while players are racking up research and cell cultures. From workplace issues such as bullying and maternity cover, through to societal dramas – e.g. media controversies and government committees – and ethical quandaries encompassing animal testing and CRISPR. As players rise from student to principal investigator and eventually professor, they acquire extra dishes for cells and rooms in the lab, as well as broader perspectives.

Dish Life has won the award for Best Educational Game by Pocket Gamers 2021.

The Dish Life project was funded by the Wellcome Trust and the Economic and Social Research Council.

THE PAPERS OF PROFESSOR SIR ROBERT EDWARDS, AT CHURCHILL ARCHIVES CENTRE

The archive comprises 141 boxes of personal and scientific papers including correspondence, research and laboratory notebooks, draft publications and journal articles, newspaper clippings, photographs, videos and film. The archive was deposited at Churchill Archives Centre by the family of Robert Edwards and by Bourn Hall Clinic (which Edwards founded with Patrick Steptoe and Jean Purdy).

The Edwards papers will be valuable for researchers in the history of science and medicine, but also in the history of ethics,



Archive reference: EDWS 18/9/1/4

social implications of medical developments, political history, history of the media, and the history of scientific publishing. The archive is strong on the political, legal, religious and social reaction to IVF and other assisted reproductive technologies.

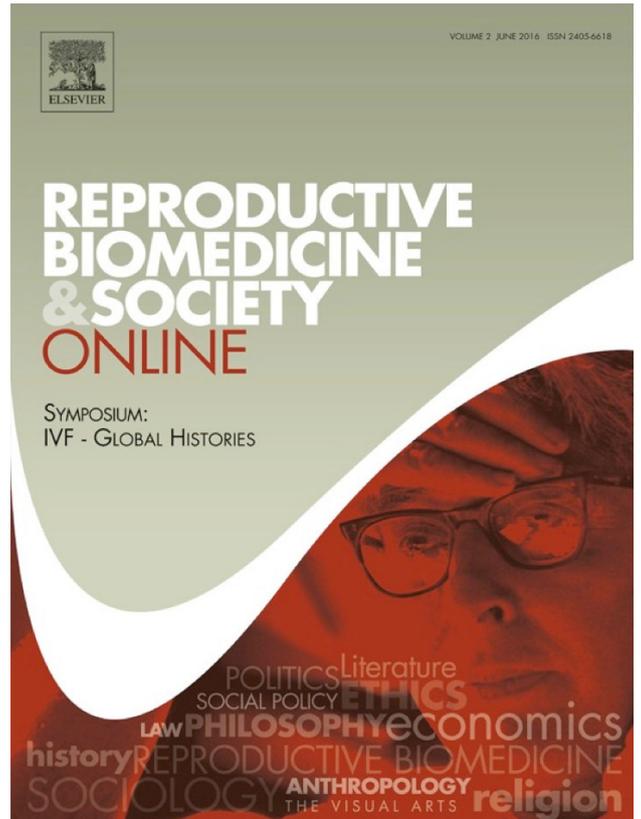
The archive was opened to researchers in June 2019 following an 18-month Wellcome Trust funded project to catalogue and conserve the collection.



Anyone wishing to see the collection can make an appointment at the Archives Centre by calling 01223 336087, or emailing archives@chu.cam.ac.uk

REPRODUCTIVE BIOMEDICINE & SOCIETY

Reproductive BioMedicine & Society (RBMS) is a new journal dedicated to interdisciplinary discussion and debate of the rapidly expanding field of reproductive biomedicine, particularly all of its many societal and cultural implications. It brings to attention new research in the social sciences, arts and humanities on human reproduction, new reproductive technologies, and related areas such as human embryonic stem cell derivation. Its audience comprises researchers, clinicians, practitioners, policy makers, academics and patients. This is an open access journal: all articles will be immediately and permanently free for everyone to read and download. To provide open access, this journal has an open access fee (also known as an article publishing charge APC) which needs to be paid by the authors or on their behalf e.g. by their research funder or institution.



Relevant topics

RBMS will accept high-quality original articles, reviews and commentaries on topics in the Social Sciences, Arts and Humanities concerning Reproductive Bioscience and Medicine. The subject areas of interest will include Politics, Sociology and Social Policy, Philosophy, Psychology, Anthropology, the Visual and Written Arts, Economics, History, Religion, Ethics and Law related to Reproductive Biomedicine. Below we summarise the main features of each submission category.

Types of manuscript

Original articles: Manuscripts presenting the outcomes of original research or analysis concerning reproductive medicine and society from any field of the arts and sciences will be considered. Article drafts submitted for consideration will not generally exceed 7000 words. An unstructured abstract in a single paragraph, 250 words maximum is required. RBMS gives priority to reports of original research that are likely to change practice or thinking about human reproduction.

Short communications: must not exceed 1,500 words with no more than one table or illustration and ten references. An unstructured abstract of no more than 200 words is required.



Review articles: comprehensive reviews of prior publications relating to an important subject. An unstructured abstract of no more than 250 words is required. The Introduction should indicate why the topic is important and should state the specific objective(s) of the review. The Discussion should include any practical implications and observations regarding the need for additional research. Systematic reviews should follow the QUOROM guidelines.

Commentaries: for topics that authors wish to 'air'. Ideally, these should not exceed 2,000 words with no more than one table or illustration and 10 references. An unstructured abstract of no more than 200 words is required. The text can be unstructured or structured under headings of author's choice.

Letters to the Editor: a question or challenge to an article published recently in RBMS, no longer than 300 words. Meetings reports, book reviews etc (by invitation only)

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THANKS & ACKNOWLEDGEMENTS

We are grateful to the 'Reproduction' SRI and to the Reproductive Sociology Research Group (ReproSoc) at Cambridge for co-sponsoring this event with the Anne McLaren Memorial Fund. In particular we want to thank Christina Roziek (SRI Coordinator), and the ReproSoc Administrative team -- Chantal Holland, Yvonne Frankfurth, and Lois Gibbs -- for their help in organising this event today. The entire team has worked tirelessly for the past two years to ensure the smooth running of all aspects of today's Symposium. Thank you also to Joe Cotton of the Cambridge Sociology Department for arranging the Livestreaming of our event today and to Avenue AV for providing technical support. Without our distinguished Programme of speakers, chairs, and panellists – and without all of you who are attending today – this event would not be possible. Lastly we wish to express our the Symposium funders: the British Academy, the Wellcome Trust, the Anne McLaren Memorial Fund and the University of Cambridge.

CAMBRIDGE REPRODUCTION STRATEGIC RESEARCH INITIATIVE

Cambridge Reproduction SRI was created in 2018 to explore the urgent challenges posed by reproduction today. Our vision is to pool resources to address the most urgent, challenging and complex questions about reproduction and the diverse ways that it has an impact on our lives. We facilitate close engagement between the arts, humanities and social sciences, biology and medicine to offer fresh perspectives on broad issues which range from global policies to those which affect individuals, families and populations.

The rapid advances we see in reproductive technologies are instigating new legal, biological, medical, ethical and sociological challenges regarding topics such as gene editing, artificial gametes, developmental programming, parenting and family structures. The Cambridge Reproduction SRI enables these issues to be approached holistically – from historical, ethical, legal, cultural, gender-based, sociological, psychological, demographic, public health, policy, biological and clinical perspectives – and through engagement with policy teams and funding bodies.

We have an exciting programme of activities planned for the current academic year, including the Anne McLaren research symposium on synthetic gametes, termly networking events, a monthly seminar series for early career researchers, and several public events at the Cambridge Festival. To find out more about these, please visit our website.

Membership of the SRI is open to all staff and graduate students in the University of Cambridge and its affiliated institutions who have an interest in any aspect of reproduction. To join our network, or to find out more about our activities, contact the SRI Coordinator, Christina Rozeik, at coordinator@repro.cam.ac.uk.

Visit our website: www.repro.cam.ac.uk

Follow us on social media:



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THE REPRODUCTIVE SOCIOLOGY RESEARCH GROUP (REPROSOC)

The Reproductive Sociology Research Group was established in October 2012 to develop and support funded research on the technological transformation of reproduction and related forms of social and cultural change.

Led by Sarah Franklin, ReproSoc is based in the Department of Sociology and has raised over £10m in funding since 2013 from the Wellcome Trust, British Academy, ESRC, ERC, Leverhulme Trust and other funding bodies. The group consists of 20-25 members who meet regularly throughout the year to share and develop research in progress. Post-docs, post grads, academic staff and affiliated researchers all participate in regular weekly events including readings groups, research workshops, films, skills training sessions, brown bag lunches, talks and small conferences.

ReproSoc hosts a Visiting Scholars programme and Affiliated Scholars from within and outside Cambridge. Our research covers a broad range of topics including the history of IVF, 'repronationalism', reproduction and the environment, reproductive justice, visual cultures of reproduction, non-heterosexual parenting aspirations, regenerative medicine, the IVF-stem cell interface, racialized reproduction, and reproductive inequality.

By developing new sociological approaches to the intersection of reproduction and technology, our aim is to develop more generalizable claims about, for example, changing definitions of nature and ethics, the biologization of technology, translational biomedicine, and the political economy of reproduction. Our work thus contributes to sociology and anthropology, science and technology studies, social and oral history, feminist and queer theory, and the social study of biomedicine, bioscience and biotechnology, as well as other fields.

We run a programme of visiting speakers, public lectures, workshops, conferences and other events that are open to the public and we welcome inquiries about our work via our webpage, which offers many resources related to the study of reproduction, technology and society. You can follow us on Twitter and Facebook, or join our mailing list for updates and announcements.

We are committed to making outreach not only part of what we do, but part of how we learn.

Read our blog: www.reprosoc.com

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