

1. Institution

Chair of Reproductive Biology, Clinical Sciences Research Institute, Warwick Medical School, CSB – University Hospital, Clifford Bridge Road, Coventry, CV2 2DX, United Kingdom

<http://www2.warwick.ac.uk/fac/med/research/csri>

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2. Principle investigator and contact person

Professor Justin St. John (j.c.st-john@warwick.ac.uk)

3. Key personnel

Dr Yan Jiang	Yan.jiang@warwick.ac.uk	Nuclear transfer & mtDNA
Dr Helena Fulka	h.fulkova@warwick.ac.uk	NT, ESC & Epigenetics
Dr Manu Vatish	M.Vatish@warwick.ac.uk	Maternal/fetal interactions, growth restriction, pre-eclampsia, placental function
Dr Ben Rollo	b.n.rollo@warwick.ac.uk	mtDNA replication & Cell fusion
Peter Rae	Peter.rae@hotmail.com	ESC & angiogenesis
Catherine Butcher	c.r.butcher@warwick.ac.uk	Genetic analysis

4. Research Profile

Our research primarily focuses on the transmission and replication of mitochondrial DNA (mtDNA) pre- and post-fertilisation. We use a comparative approach by analysing: i) *in vitro* fertilisation (IVF) models to understand how transmission and replication normally take place; and ii) nuclear transfer (NT; cloning) as a model where these mechanisms are violated. This provides a basis for determining which factors are vital for the regulation of mtDNA replication and transmission. We use embryonic stem cells, fetal tissue and live offspring to determine how the events in the oocyte and embryo need to be regulated for subsequent mitochondrial proliferation to coincide with cellular differentiation. We are funded by the Medical Research Council to generate cross species embryonic stem cells and by the British Heart Foundation to understand mitochondrial DNA replication during cellular differentiation.

We are also interested in maternal/fetal interactions and the effects of growth restriction, pre-eclampsia and placental function.

5. Key technologies and tools

Nuclear transfer – embryonic stem cells – mitochondrial transplantation – mitochondrial supplementation – embryonic stem cell derivation – embryonic stem cell characterisation – embryonic stem cell differentiation – implantation – placentation – angiogenesis – PCR – RT-PCR – confocal microscopy – immunocytochemistry – western blotting – cell fusion – DNA methylation analysis – ChIP – allele specific PCR – tissue culture – cell culture.

6. Selected publications

Bowles EJ, Tecirlioglu RT, French AJ, Holland MK, St John JC. Mitochondrial DNA transmission and transcription after somatic cell fusion to one or more cytoplasts. *Stem Cells* 2008; **26**: 775-82.

Facucho-Oliveira JM, Alderson J, Spikings E, Egginton S, St. John J. Mitochondrial DNA replication during differentiation of murine embryonic stem cells. *Journal of Cell Science* 2007; **120**: 4025-4034.

Bowles EJ, Lee J-H, Alberio R, Lloyd RE, Campbell KHS, St. John JC. Failure of nuclear reprogramming leads to premature mtDNA replication in nuclear transfer embryos with preferential replication of donor mtDNA. *Genetics* 2007; **176**: 1511-26.

Spikings EC, Alderson J, St. John JC. Regulated mtDNA replication during oocyte maturation is essential for successful porcine embryonic development. *Biology of Reproduction* 2007; **76**: 327-35.

Lloyd RE, Lee J-H, Alberio R, Bowles EJ, Ramalho-Santos J, Campbell KHS, St. John JC. Aberrant nucleo-cytoplasmic cross-talk results in donor cell mtDNA persistence in cloned embryos. *Genetics* 2006; **172**: 2515-27.