Focus on ART

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The focus of society and science is now on assisted reproduction technology (ART) as never before. The cloning of Dolly in 1997 (Wilmot *et al.* 1997) and the first derivation of human embryonic stem (hES) cells in 1998 (Thomson *et al.* 1998) has led to an explosion of interest in the pre-implantation embryo and in techniques for manipulating early development. In the last few months alone there have been reports challenging the orthodoxies of mammalian reproductive biology including evidence for the presence of germline stem cells in the ovary (Johnson *et al.* 2004) and the demonstration that parthenogenesis can give rise to an adult mammal (Kono *et al.* 2004). Both of these papers have featured in recent Highlights in *Reproduction* (Albertini 2004, Moore & Ball 2004). Much interest of course has centred on hES cells, with a recent report of lines derived from embryos created by nuclear transfer cloning (Hwang *et al.* 2004) paving the way for so-called therapeutic cloning and the creation of isogenic cell lines for use in clinical treatment. Just to keep reproductive biologists happy, it is now possible to derive new germ cells from ES cell lines (mouse oocytes (Hubner *et al.* 2003) and sperm (Geijsen *et al.* 2004)). We include in this issue a review of the current state of the hES cell field from one of the first groups in the UK to derive a line, at the Newcastle Centre for Life (Stojkovic *et al.* 2004).

At the same time, there has never been a more pressing need to understand the basics of human embryology. ART successes attract front page headlines (e.g. the recent birth of a baby to a cancer patient using sperm cryopreserved for 21 years (Horne *et al.* 2004)) and yet the underlying efficiency of IVF and related infertility treatments is poor. Current data from the UK (Human Fertilisation and Embryology Authority, 2002/3) and the US (Jain *et al.* 2004) show that only about one quarter of IVF cycles result in a live baby, and when expressed per embryo, the success rate is a mere 15%. Concerns linger over abnormalities introduced by ART techniques, such as imprinting errors during culture and the possible risks of Intra Cytoplasmic Sperm Injection (ICSI).

In this issue we focus on two fundamental aspects of early development which may be important to understanding normal development of human embryos: the role of mitochondria (Van Blerkom 2004) and the genetic regulation of apoptosis (Jurisicova & Acton 2004). In the former, Van Blerkom argues that mitochondria are the

engines of growth and metabolism in embryos as in other cells, and these and other non-respiratory functions may have a particular role in conferring early developmental competence. Incompetent cells or embryos can on the other hand be eliminated from development by apoptosis. This form of cell death is likely to be necessary in the human embryo which contains high levels of genetic abnormality, but clearly such a potentially destructive force must also be tightly regulated throughout development. Jurisicova & Acton provide a landmark consideration of the genetic regulation of apoptosis in human embryos. The progress reported in both of these reviews is impressive, especially considering the practical, ethical and regulatory constraints associated with research on human embryos. As a result, these authors have also made use of data from animal models, particularly the mouse. However, murine development is considered a relatively poor model for the human and the fourth and final review in this Focus draws our attention to the study of non-human primate embryos, arguably the most suitable model of human development. Hewitson (2004) focuses this review on the use of non-human primates to model one of the most invasive of all reproductive technologies, ICSI.

2004 is a fantastic time to be a reproductive biologist. I hope this Focus captures some of the excitement in the field of assisted reproduction and I look forward to the progress sure to be made over the next few years.

References

- Albertini DF 2004 Micromanagement of the ovarian follicle reserve – do stem cells play into the ledger? *Reproduction* **127** 513–514.
- Geijsen N, Horoschak M, Kim K, Gribnau J, Eggan K & Daley GQ 2004 Derivation of embryonic germ cells and male gametes from embryonic stem cells. *Nature* **427** 148–154.
- Hewitson L 2004 Primate models for assisted reproductive technologies. *Reproduction* **128**.
- Horne G, Atkinson AD, Pease EH, Logue JP, Brison DR & Lieberman BA 2004 Live birth with sperm cryopreserved for 21 years prior to cancer treatment: case report. *Human Reproduction* **19** 1448–1449.
- Hubner K, Fuhrmann G, Christenson LK, Kehler J, Reinhold R, De La Fuente R *et al.* 2003 Derivation of oocytes from mouse embryonic stem cells. *Science* **300** 1251–1256.
- Human Fertilisation and Embryology Authority Twelfth Annual Report and Accounts 2002/3. Ed. D Darrell-Lambert.

- Hwang WS, Ryu YJ, Park JH, Park ES, Lee EG, Koo JM *et al.* 2004 Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst. *Science* **303** 1669–1674.
- Jain T, Missmer SA & Hornstein MD 2004 Trends in embryo-transfer practice and in outcomes of the use of assisted reproductive technology in the United States. *New England Journal of Medicine* **350** 1639–1645.
- Johnson J, Canning J, Kaneko T, Pru JK & Tilly JL 2004 Germline stem cells and follicular renewal in the postnatal mammalian ovary. *Nature* **428** 145–150.
- Juriscova A & Acton BM 2004 Deadly decisions: the role of genes regulating programmed cell death in human preimplantation embryo development. *Reproduction* **128**.
- Kono T, Obata Y, Wu Q, Niwa K, Ono Y, Yamamoto Y *et al.* 2004 Birth of parthenogenetic mice that can develop to adulthood. *Nature* **428** 860–864.
- Moore T & Ball M 2004 Kaguya, the first parthenogenetic mammal – engineering triumph or lottery winner? *Reproduction* **128** 1–3.
- Stojkovic M, Lako M, Strachan T & Murdoch A 2004 Derivation, growth and applications of human embryonic stem cells. *Reproduction* **128**.
- Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS *et al.* 1998 Embryonic stem cell lines derived from human blastocysts. *Science* **282** 1145–1147.
- Van Blerkom J 2004 Mitochondria in human embryos. *Reproduction* **128**.
- Wilmut I, Schnieke AE, McWhir J, Kind AJ & Campbell KH 1997 Viable offspring derived from fetal and adult mammalian cells. *Nature* **385** 810–813.