

Focus on mammalian embryogenomics

Isabelle Hue and Jean-Paul Renard

UMR 1198, ENVA, CNRS, FRE 2857, *Biologie du Développement et de la Reproduction*, Institut National de la Recherche Agronomique, 78350 Jouy en Josas, France

Correspondence should be addressed to I Hue; Email: isabelle.hue@jouy.inra.fr

The term 'embryogenomics' was coined by Minoru Ko (2001) in his pioneering studies on the profiling of gene expression during mouse embryonic development. It refers to the area of research that combines embryological approaches and large-scale genomics analysis to provide an integrated examination of the morphogenetic processes that lead to the first patterning events at the onset of embryonic development. The term was rapidly adopted by those of us contributing to the development of embryo biotechnologies in domestic mammalian species and therefore interested in studying the extensive regulative properties of early mammalian embryos grown *in vitro* prior to their transfer to surrogate females. This was because the global analysis of the expressed genome (RNA, proteins) proposed by Minoru Ko appeared to be a valuable means of deriving key information from those expensive embryos. At that time dedicated molecular resources formed by cDNA or SAGE libraries and arrays, already accessible in both the mouse and human, were still under construction in domestic species (reviewed in Ko 2004). Since then, the tiny amount of biological material accessible from relatively few preimplantation embryos has become amenable to molecular analysis with the first techniques of RNA amplification (Brady *et al.* 1995, Kacharina *et al.* 1999). However, the fidelity of the amplification procedures was still disputed when used in academic embryonic models (see for instance Baugh *et al.* 2001) or with samples of human tissues (Wang *et al.* 2000, Iscove *et al.* 2002).

It was to discuss these issues in the context of research conducted with embryos from domestic species that Marc-André Sirard (University of Laval) together with Andrew Watson (University Western Ontario) and Allan King (University of Guelph) launched the first 'Embryogenomics' meeting that took place in Quebec City in July 2002. This Canadian initiative was a marked success. It addressed recent progress and questions on cDNA library subtraction, SAGE analysis, use of heterospecific arrays, or RNA amplification procedures on oocytes or embryos from domestic species (see OECD proceedings, 2003). In the five intervening years, however, the landscape has

dramatically changed. The power of the molecular resources and arrays in domestic species has been markedly improved with the availability of increasing Unigene entries and the near completion of genome assembly in *Bos taurus* and *Sus scrofa* (<http://www.ncbi.nlm.nih.gov>), as well as other marked achievements in the use of proteomic tools (2D-DIGE for example). This led us to follow up on the Canadian initiative and to organize a second Embryogenomics meeting, which was held in Paris during October 2007.

This Focus Issue of *Reproduction* summarizes the main data provided in the 20 talks that were presented and discussed during this meeting. These presentations were organized into six sessions. In this issue of the journal the contributing authors within each session of the meeting collectively provide an innovative review of their session. Altogether, these reviews cover the fields of oocyte and follicle development (Bonnet *et al.* 2008), embryonic cleavage and blastocyst formation (Duranthon *et al.* 2008), blastocyst elongation and differentiation (Blomberg *et al.* 2008), and epigenetic reprogramming (Niemann *et al.* 2008). The emerging fields of bioinformatics and RNA inhibition were also presented in two interactive sessions, one of which was on the interpretation of transcriptomic profiles and is presented here (Rodriguez-Zas *et al.* 2008a). These articles are complemented by three original papers provided by three of the participating groups (Mitko *et al.* 2008, Rodriguez-Zas *et al.* 2008b, Torner *et al.* 2008).

From discussions with colleagues who work with mice and who attended the meeting, it became evident that the embryos of domesticated artiodactyls, where implantation takes place several days after the onset of gastrulation, are invaluable models to study the respective contribution of embryonic and extra-embryonic tissues to embryo growth and differentiation. These embryos are increasingly being used to dissect the long-term developmental consequences of early perturbations to *in vivo*-derived or *in vitro*-produced embryos. Such studies do not prioritize the genetics of development but rather integrate developmental biology, physiology, and reproduction by considering the embryo together with its *in utero*

(Spencer *et al.* 2008) or *in vitro* (Duranthon *et al.* 2008) environment. They provide further insights into the emerging related fields among which statistical network construction and functional genomics based on gain or loss of specific gene expression (using RNA inhibition or the sophisticated genetic constructs already largely used today in the mouse) will play an increasingly important role.

At the frontier of Embryogenomics, we foresaw the importance of large-scale epigenomics analysis, gene network modeling, and *in vivo* imaging for a comprehensive integration of molecular information to the study of basic biological processes at the cellular level of early embryo development. The conclusion of the meeting was that we should next meet probably within 2 years.

Finally, we would like to gratefully acknowledge the sponsors of the second Embryogenomics meeting held in Paris, as detailed in the acknowledgements and in the footnotes of the following review articles and research papers, as well as the Editorial Board of Reproduction who helped construct this Focus Issue.

Acknowledgements

The articles in the special 'Focus on Mammalian Embryogenomics' section of this issue were presented at the 2nd International Meeting on Mammalian Embryogenomics, 17–20 October 2007. The conference was supported by the OECD Co-operative Research Programme on Biological Resource Management for Sustainable Agricultural Systems, whose financial support made it possible for most of the invited speakers to participate in the conference. The meeting was also sponsored by Le conseil Regional Ile-de-France, the Institut National de la Recherche Agronomique (INRA), Cogenics-Genome Express, Eurogentec, Proteigene, Sigma-Aldrich France and Diagenode sa.

Funding

The authors purchase products from Cogenics-Genome Express, Eurogentec, Proteigene, Sigma-Aldrich France and Diagenode sa but receive no funding from these organizations and therefore have no financial relationship with them. As organizers of the meeting, the authors did not receive any financial support from OECD. The authors received no funding from Le conseil Regional Ile-de-France. The authors belong to an INRA-funded research institute and thus receive funding from the INRA.

OECD Disclaimer

The opinions expressed and arguments employed in this publication are the sole responsibility of the authors and do not necessarily reflect those of the OECD or of the governments of its Member countries.

References

- Baugh LR, Hill AA, Brown EL & Hunter CP 2001 Quantitative analysis of mRNA amplification by *in vitro* transcription. *Nucleic Acids Research* **29** E29.
- Blomberg LA, Hashizume K & Viebahn C 2008 Blastocyst elongation, trophoblastic differentiation, and embryonic pattern formation. *Reproduction* **135** 181–195.
- Bonnet A, Dalbiès-Tran R & Sirard MA 2008 Opportunities and challenges in applying genomics to the study of oogenesis and folliculogenesis in farm animals. *Reproduction* **135** 119–127.
- Brady G, Billia F, Knox J, Hoang T, Kirsch IR, Voura EB, Hawley RG, Cumming R, Buchwald M & Siminovitch K 1995 Analysis of gene expression in a complex differentiation hierarchy by global amplification of cDNA from single cells. *Current Biology* **5** 909–922. Erratum in: *Current Biology* 1995 **5** 1201.
- Duranthon V, Watson AJ & Lonergan P 2008 Preimplantation embryo programming: transcription, epigenetics, and culture environment. *Reproduction* **135** 141–150.
- Iscove NN, Barbara M, Gu M, Gibson M, Modi C & Winegarden N 2002 Representation is faithfully preserved in global cDNA amplified exponentially from sub-picogram quantities of mRNA. *Nature Biotechnology* **20** 940–943.
- Kacharina JE, Crino PB & Eberwine J 1999 Preparation of cDNA from single cells and subcellular regions. *Methods in Enzymology* **303** 3–18.
- Ko MS 2001 Embryogenomics: developmental biology meets genomics. *Trends in Biotechnology* **19** 511–518.
- Ko MS 2004 Embryogenomics of pre-implantation mammalian development: current status. *Reproduction, Fertility, and Development* **16** 79–85.
- Mitko K, Ulbrich SE, Wenigerkind H, Sinowatz F, Blum H, Wolf E & Bauersachs S 2008 Dynamic changes in messenger RNA profiles of bovine endometrium during the oestrous cycle. *Reproduction* **135** 225–240.
- Niemann H, Tian XC, King WA & Lee RSF 2008 Epigenetic reprogramming in embryonic and foetal development upon somatic cell nuclear transfer cloning. *Reproduction* **135** 151–163.
- OECD Organisation for Economic Co-operation and Development 2003. *Biological Resource Management in Agriculture Mammalian Embryo Genomics (Complete Edition - ISBN 9264104267)*, pp 1–120, Paris, France: OECD Publishing.
- Rodriguez-Zas SL, Schellander K & Lewin HA 2008a Biological interpretations of transcriptomic profiles in mammalian oocytes and embryos. *Reproduction* **135** 129–139.
- Rodriguez-Zas SL, Ko Y, Adams HA & Southey BR 2008b Advancing the understanding of the embryo transcriptome co-regulation using meta-, functional-, and gene network analysis tools. *Reproduction* **135** 213–224.
- Spencer TE, Sandra O & Wolf E 2008 Genes involved in conceptus–endometrial interactions in ruminants: insights from reductionism and thoughts on holistic approaches. *Reproduction* **135** 165–179.
- Torner H, Ghanem N, Ambros C, Hölker M, Tomek W, Phatsara C, Alm H, Sirard MA, Kanitz W, Schellander K *et al.* 2008 Molecular and subcellular characterisation of oocytes screened for their developmental competence based on glucose-6-phosphate dehydrogenase activity. *Reproduction* **135** 197–212.
- Wang E, Miller LD, Ohnmacht GA, Liu ET & Marincola FM 2000 High-fidelity mRNA amplification for gene profiling. *Nature Biotechnology* **18** 457–459.