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Transcriptome profile of early mammalian embryos in response to culture environment☆

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ABSTRACT

Early embryonic development, the period from maturation until blastocyst formation, is one of the most critical periods of mammalian development involves various morphological, cellular, and biochemical changes related to genomic activity. During the post-fertilization period, several major developmental events occur in the embryo which are regulating by a harmonized expression of genes and strongly influenced by culture conditions. The products of these genes are involved in various biological processes including metabolism, growth factor/cytokine signaling, stress adaptation, transcription and translation, epigenetic regulation of transcription, apoptosis, compaction and blastocyst formation. Post-fertilization culture environment is known to be the most important factor determining the quality of the resulting embryos as indicated in terms of cryo-tolerance and relative abundance of transcripts. However, the exact effect of culture conditions on gene expression and subsequent influences on molecular pathways controlling early development is still unknown. A number of culture environmental factors can influence the gene expression of produced embryos such as media composition, serum supplementation, number of embryos present in the culture drop and gas atmosphere. During the last ten years several studies were concerned with differences in the transcriptome profile of embryos produced under different environmental conditions and its subsequent influence on embryo developmental competence. From these studies, several genes have been determined as candidate genes controlling preimplantation embryo development and affecting its quality. Here we will discuss results of different experiments investigated the effect of different culture conditions on the transcriptome profile of bovine blastocyst. These experiments identified molecular mechanisms and pathways that influenced by culture conditions and this will enable to launch strategies to modify culture conditions to enhance the development of competent blastocyst.

1. Introduction

Gene expression has a fundamental role in the coordination of homeostatic and metabolic mechanisms during the preimplantation period of development. This period involves various morphological and biochemical changes related to genomic activity and comprise a complex set of physiological processes, many of which are still unknown. These processes are controlled by a harmonized expression of about 10,000 sequential and temporal genes and are strongly influenced by culture conditions (Niemann and Wrenzycki, 2000). During the last ten years several studies have provided evidence that suggest that the pattern of mRNA abundance in the blastocyst, and the quality of the blastocyst in terms of cryo-tolerance, relative abundance

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of transcripts and establishing a pregnancy, is dictated by the post-fertilization culture conditions (Rizos et al., 2002b; Tesfaye et al., 2004; Lonergan et al., 2006). Thus, understanding the expression patterns of genes involved in preimplantation embryonic development process in response to different environmental factors will aid in selecting candidate genes as markers for embryo quality, improve our knowledge on regulation of embryonic development and improve success of embryo culture.

Over the past three decades, applications of assisted reproductive technology (ART) include multiple ovulation and embryo transfer (MOET) and in vitro production (IVP) of embryos has been widely increased. These technologies offer several advantages over natural breeding, have a great potential for speeding up genetic improvement in farm animals and greatly advanced our basic understanding of embryo development. Despite ongoing advances in ARTs, pregnancy rates remain low and embryos produced in this way still differ from 'golden standard' embryos. The differences involve morphological and molecular aspects that impair embryo quality and developmental efficiency. Different ARTs commonly rely on the in vitro maturation (IVM) of oocytes, in vitro fertilization (IVF) and in vitro culture (IVC) of the resulting preimplantation embryos.

These essential three steps of IVP have been associated with several deviations from the normal in vivo development that resulted in development rate limited to 30–40% (Niemann and Wrenzycki, 2000; Gutierrez-Adan et al., 2001; Rizos et al., 2002c), higher incidence of chromosomal abnormalities (Viuff et al., 1999, 2002; Lonergan et al., 2004), gross morphological abnormalities (Pollard and Leibo, 1994; Abd El Razek et al., 2000) and a dramatic effect on gene expression pattern in embryos, which in turn has serious implications for the quality of blastocyst, lowering cryo-tolerance and decreasing pregnancy rates (Rizos et al., 2002a, 2003; Lonergan et al., 2003; Tesfaye et al., 2004). Several major developmental events occur in the embryo during the preimplantation period, including the first cleavage division, activation of the embryonic genome, compaction of the morula, and formation of the blastocyst. However, the exact influence of culture conditions during each of these critical events is still unknown.

Transcriptomics have been employed successfully to contrast gene expression in mammalian oocytes and early embryos. Recent advances in bioinformatics and high-throughput technologies such as Next-generation sequencing and microarray analysis have revolutionized the way we can analyze the entire transcriptome within a population of cells which improve our understanding of the molecular mechanisms underlying normal and dysfunctional biological processes (Marioni et al., 2008; Wang et al., 2009; Marguerat and Bahler, 2010). The aim of this short review is to highlight the influences of different culture conditions, either in vivo or in vitro, on the transcriptome profile of preimplantation mammalian embryos. Different experiments have been conducted to investigate functions and pathways influenced by different culture conditions. Some of these experiments are summarized in Table 1.

Table 1
Impact of different culture conditions on functions and pathways in mammalian oocytes and embryos.

Function/pathway	Abundance of transcripts (up ↑ or down ↓ regulated)	Culture conditions	References
Oxidative phosphorylation pathway	ATP5B ↑, ATP5G3 ↑, ATP5H ↑, ATP5I ↑, ATP5L ↑, ATP5O ↑, ATP6VOD2 ↑, COX4I1 ↑, COX5A ↑, COX7B ↑, CYC1↑, NDUFA1 ↑, NDUFA5 ↑, NDUFA6 ↑, NDUFA12 ↑, NDUFA13 ↑, NDUFA9 ↑, NDUFB2 ↑, NDUFB8 ↑, NDUFB10 ↑, NDUFC2 ↑, NDUFS2 ↑, NDUFV1 ↑, UCRC ↑, UQCR ↑, UQCRB ↑	Bovine blastocysts developing in the reproductive tract of superovulated vs. unstimulated heifers	Gad et al. (2011)
Carbohydrate metabolism	AP2M1 ↑, FN1 ↑, KIT ↑, PSAP ↑, ANXA2 ↑, NANS ↑, CTNNB1 ↑, LGALS1 ↑		
Lipid metabolism	GSTP1 ↑, AP2M1 ↑, ACSL3 ↑, RAB4A ↑, FN1 ↑, ANXA2 ↑, ADH5 ↑, EBP ↑, INSIG2 ↑, PTGES3 ↑, SREBF1 ↑, KIT ↑, PSAP ↑, PTGS2 ↑, SFN ↑, PDHB ↑, LGALS1 ↑, PRDX2 ↑		
Metabolic pathways	CYP11A1 ↑, ALAS2 ↑, FH ↑, GAA ↓, PHGDH ↓, GLDC ↓, HSD3B1 ↑, PON1 ↑, MAN1C1 ↓, TAT ↑	Bovine blastocysts developed under high vs. normal circulating progesterone concentrations	Carter et al. (2010)
PPAR signaling pathway	APOA1 ↑, FADS2 ↑		
Oocyte competence and glucose metabolism	GAPDH ↑, IGFR2 ↑, CCNB1 ↑, GREM1 ↑	Bovine oocytes matured under low vs. high oxygen tension	Bermejo-Alvarez et al. (2010a,b)
Transcription and translation	HMG2 ↑, DOT1L ↑, FOXO3A ↑, CCR4-NOT ↑, PABPN1 ↑, GNBL2 ↑, EEF1G ↑, REA ↑, 3XC10R ↑, 9_G06 ↑	In vivo vs. in vitro produced bovine blastocyst	Corcoran et al. (2006)
Stress response genes	SOX ↓, Mn-SOD ↓, BAX ↓, IFt ↓, G6PD ↓	In vivo vs. in vitro produced bovine embryos	Gutierrez-Adan et al. (2004)
Pluripotency	OCT4 ↑, NANOG ↑, SOX2 ↑	In vivo vs. in vitro produced porcine embryos	Kumar et al. (2007), Magnani and Cabot (2008)
Apoptosis and oxidative stress	Bax ↓, SOD ↑, SOX ↓		
Gap junction communication	Cx31 ↓, Cx43 ↑	In vivo vs. in vitro bovine blastocyst	Rizos et al. (2002b)
Differentiation and implantation	LIF ↓, LR-b ↓		