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Embryo transcriptome response to environmental factors: Implication for its survival under suboptimal conditions☆

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ABSTRACT

After its formation, the mammalian zygote undergoes a series of morphological, physiological and biochemical alterations prior to undergoing cell differentiation. The zygote is then transformed into a complex multicellular organism in a defined time window which may differ between species. These orderly embryonic developmental events are tightly regulated by temporal and spatial activation and/or deactivation of genes and gene products. This phenomenon may in turn be dependent on the intrinsic characteristics of the embryo itself, the physiological and biochemical composition of the maternal environment or by in vitro culture condition. In fact, when embryos are subjected to suboptimal culture condition, some of the embryos may escape the environmental stress by activating certain transcripts and some others which are unable to activate anti-stress agents may die or exhibit abnormal development. This phenomenon may partly depend on transcripts and proteins stored during oogenesis. Indeed after embryonic genome activation, the embryo destiny is governed by its own transcripts and protein synthesized over time. Therefore, this review begins by highlighting the type and quality of transcripts accumulated or degraded during oogenesis and its impact on the embryo survival. Thereafter, emphasis is given to the transcriptome response of preimplantation embryos to suboptimal culture conditions. In addition, the long term effect of preimplantation culture environment on the transcriptome response embryos/fetus during peri and post implantation has been addressed. Finally, a brief summary of the epigenetic control of culture induced genetic variation of the embryos has been highlighted.

1. Introduction

In mammals, upon its formation from the union of the two gametes, the zygotes undergo a series of morphological, physiological and biochemical alterations leading to cellular development and differentiation. The one cell embryo then gradually transforms into a complex multicellular organism in a defined time window. Basically, decision on the cell fate occurs during blastocyst formation when blastomeres segregate into inner cell mass and the trophectoderm (Zernicka-Goetz, 2006; Chen et al., 2010). These series of events occurring during the early embryonic development are controlled by temporally and spatially regulated array of genes and gene networks (Chen et al., 2010; Nien et al., 2011). Indeed, the early developmental stages of the embryo are an essential step to craft and load all the resources necessary for further embryonic survival and development. However, the type and quality of the biochemical composition of the embryo and

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the rate of development could be highly regulated by the physiological and biochemical composition of the maternal environment (in vivo condition). But when the embryos are cultured in vitro, the culture condition could result in alteration of developmentally related genes and could compromise embryonic development.

Several attempts have been performed to increase the quality and rate of embryonic development in vitro. For instance, addition of 5% bovine oviduct epithelial cell in during bovine embryo in vitro culture was found to improve rate of early development and this was accompanied by activation of glucose transporter 1(Glut-1) and heat shock protein (*HSP70*) genes (Zernicka-Goetz, 2006). Similarly, alteration in *BAX*, *SOD*, *SOX*, *LIF*, *LRβ*, *CX31* and *CX43* gene expression in blastocyst derived from zygotes cultured in the presence of synthetic oviduct fluid or in TCM-199 medium supplemented with granulosa cells has been also evidenced (Rizos et al., 2002). Moreover, addition of serum in culture media was found to induce the expression of *MnSOD*, *SOX*, *BAX* and LIF but reduced the level of *C43* and *IFN*-taugene expression (Rizos et al., 2003). In addition, Cagnone and Sirard (2013) described altered gene expression in blastocysts derived from embryos cultured in the presence of bovine serum albumin (BSA) and serum lipid fraction compared to those culture conditions supplemented with BSA alone. However, supplementation of culture media with serum may result in incomplete compaction, darker cytoplasm and inner cell mass disorganization of the developing embryos (Farin et al., 2004).

Apart from the embryonic culture media, the oocyte maturation condition could be one of the factors responsible for compromising the embryonic development. For instance, supplementation of 75 μM stearic acid or a combination non esterified fatty acids (75 μm steric acid, 150 μM palmatic acid and 200 μM oleic acid) during oocyte maturation increased the lactate consumption of the embryos and the level of *DNMT3A*, *IGF2R* and *SLC2A1* mRNA expression in the resulting blastocysts (Van Hoeck et al., 2011). This would suggest that the culture condition of the oocyte also in part can affect the embryo metabolic activity, development and gene expression. In addition to all these, in vitro culture condition may result in lower number of gap junction like structures in the inner cell mass of the resulting blastocysts and these structure are completely missing in the trophectoderm (Boni et al., 1999). Thus, the embryo development could be affected by the intrinsic quality of the oocytes and the post fertilization environmental conditions. Abnormalities in one of these could induce aberrant embryo development and alteration in embryonic biochemical composition. However, it can also be suggested that when preimplantation embryos are challenged by certain culture induced stress factors, the competent ones could escape the stress environment by activating certain transcripts and those embryos which are unable to activate anti-stress agents would perish at any stages of embryonic development. Indeed, the rate limiting step in the embryo competency in most cases is predesigned during the time of oocyte development and maturation. Therefore, this review firstly highlights about the type of transcripts accumulated or degraded during oogenesis and its impact on the embryo survival. Secondly the review focuses on the transcriptome profile changes of the preimplantation embryos due to suboptimal culture conditions. In addition, the consequence of preimplantation embryo culture conditions on the transcriptome response of embryos during the peri-implantation and post implantation period has been also outlined. Finally, this review will be concluded after compiling a brief summary regarding the transcriptional control mechanism of embryos cultured under suboptimal culture condition.

2. Oocytes transcripts are fundamental for preimplantation embryo development

Most often while considering the female gamete, an immediate thought that could flash to our imagination would be the haploid chromosomal contribution of the oocyte during zygote formation. What else beyond that the oocytes can contribute for the developing embryo? What is happening in the oocyte during its journey from primordial germ cell until it attains the stage of fully fertilizable gamete? Though these questions seem trivial, they have a wider broader sense when it comes to creation of an organism by union of the two gametes. Basically, the oocyte plays the key role by contributing the bigger portion of the structural and cytoplasmic composition of embryo (Macaulay et al., 2011) which later on differentiated into epiblast, trophectoderm and the primitive endoderm (Chazaud et al., 2006). In turn, the epiblast cells of those surviving embryos eventually become the precursors of primordial germ cells where oogonia are originating after a series of cell divisions and DNA synthesis (Bilodeau-Goeseels and Magyara, 2012). Therefore, the oocytes are the powerhouses in crafting and designing the fate of the developing embryo and the resources stored during oogenesis may direct the embryos to cope even under stress conditions.

Indeed, in addition to nuclear DNA transcription, the mammalian oocytes accumulate mitochondrial DNAs during development. For instance, the developing bovine oocyte is reported to contain between 260,000 and 370,000 copies mtDNA (Michaels et al., 1982; Tamassia et al., 2004). Similarly, the mouse oocyte can accumulate about 175,000 copies mtDNA and the expression of transcripts which are associated with encoding proteins required for mtDNA replication were increased during oocyte growth, although, the expression of these genes were reduced after the oocytes were fully grown (Mahrous et al., 2012). Thus, during the time of its growth and development, the oocyte acquires several mRNAs species including oocyte-specific transcripts (Eichenlaub-Ritter and Peschke, 2002). In fact the amount of cytoplasmic RNA stored by the growing oocytes varies depending on its developmental capacity and the size of the cytoplasm (Bachvarova, 1992; Fair et al., 1996). For instance mature oocyte with the diameter of 100–120 μm may store as much as 2.4 ng total RNA or 40–60 pg mRNA (Bilodeau-Goeseels and Schultz, 1997).

In addition to knowing the total RNA storage of the oocytes, it would be a greater relevance, to understand the annotation of those stored RNAs to uncover the type and cluster of gene transcripts that are accumulated or degraded during the time of oogenesis. In line to this, Mahrous et al. (2012) analyzed the transcriptome analyzed