Animal Reproduction

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Metaboloepigenetic modulation the during early development promotes alterations in chromatin accessibility and transcription in bovine embryos.

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Resumo

Embryos are interesting models to study metaboloepigenetics, since they undergo broad metabolic changes and widespread epigenetic remodeling. The modulation of α-Ketoglutarate (AKG) and Succinate (SUC) ratio was capable to alter the levels of 5-methylcytosine (5mC) in embryos (Ispada, 2020). In the present work, the transcription profile on inner cell mass (ICM) of these embryos was accessed. After that, gene accessibility of the most affected transcripts was checked. For this, Bovine embryos were in vitro produced using standard protocols and cultured as control (CO) or treated from day 0 of cleavage until day 4 with analogs for AKG or SUC. Embryos were collected at day 7 and the ICMs were removed by microimmunosurgery and polled (3 ICMs per treatment for RNAseq and 15 ICMs per treatment for ATACseq) for later analysis. The RNAseq resulted in a total of 174 differently expressed genes (DEGs) between CO and AKG, with 119 being downregulated and 55 upregulated in embryos from the AKG. The comparison between CO and SUC reveled 356 DEGs in total, with 241 downregulated and 115 upregulated in embryos from the SUC group. SUC and AKG groups had the greatest differences in DEGs number, with 274 being upregulated in AKG and 263 upregulated in SUC embryos. The 10 DEGs with lowest adjusted p-values between comparisons were selected, with NEB and TNRC18 upregulated and MAP3K4, EIF2B5, FER, CLPB, RPF2, PTK2, KIAA1217 and KMT2B downregulated in AKG, when compared to CO. For SUC, FAT1 and ACAT2 upregulated and AHNAK, ATXN2L, RESTB, SSR2, PEG3, FLNA, CEP68 and MED16 downregulated in relation to the CO. The comparison between AKG and SUC resulted in TBL1XR1, SCHIP1, MELK, RNF112, WIPI1, PLD2 and CDC40 upregulated in SUC, while SOCS7, SMARCC2 and SPRED2 were upregulated in AKG. The chromatin accessibility revealed that 277 peaks were obtained for the CO, with CASK, SORCS3, NAA35, METTL25, LRRFIP1, ALCAM, C2H2orf76, CSMD3, ASCC1, CFAP4, CACNA2D3 as the 10 most significative ones. For AKG, the genes CSMD3, SORCS3, CASK, ALCAM, IMMT, NAA35, PKIA, METTL25, CFAP43 and CACNA2D3 were most accessible, from the total of 1564 peaks. On SUC, the total of 168 peaks were identified, with SIMC1, NAA35, METTL25, CASK, C2H2orf76, CSMD3, SORCS3, RYR2, IMMT and CACNA2D3 as the 10 most significative genes. So far, the preliminary analysis of ICM from embryos treated with AKG or SUC resulted in chromatin and transcription alterations. Considering the changes promoted by the metaboloepigenetic modulators, it is possible to assume that the perturbation/stimulation of DNA demethylation in bovine embryos promote strong effects and physiological and molecular alterations up to blastocyst stage.