

Abilities of Brain-derived Neurotrophic Factor (BDNF) to Enhance the Developmental Competence of Bovine Oocytes during *In Vitro* Maturation Period are Promoted by Metformin

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Brain-derived neurotrophic factor (BDNF) signaling via TrkB receptors may play an important role in the maturation of mammalian oocytes. But, no data has been reported on the effect of supplementing with BDNF during the *in vitro* maturation (IVM) of bovine oocytes or culture (IVC) of embryos. It was also reported that metformin elevates the activity of Trk receptors, and may amplify BDNF signaling. This study was performed 1) to investigate which stage is susceptible to BDNF signaling in between IVM and IVC to enhance developmental competence of bovine *in vitro* fertilization (IVF) embryos, and 2) to investigate the collaborative effect of BDNF and metformin treatment during IVM on the developmental competence of IVC embryos. In Exp. 1, cumulus-oocyte complexes (COCs) were matured in tissue culture medium (TCM)-199 supplemented with 10% FBS, 0.005 IU/mL FSH, 1ug/mL 17 β -oestradiol. At 22 hr of IVM, oocytes were inseminated for 18hr and then cultured in mSOF for 7 days. 10 ng/mL BDNF was added during IVM and/or IVC. Cleavage and blastocyst formation were examined at 2 and 7 days of culture, respectively. When BDNF were supplemented during IVM, the rates of blastocyst formation increased significantly compared with control group in followed IVC (32% vs. 26%). However, supplementation of BDNF during both IVM and IVC did not have an effect. Moreover, the rates of blastocyst formation decreased when added during IVC alone (21% vs. 26%). To observe the clear effect of factors, in Exp. 2, TCM-199 containing no serum and hormone was used as control maturation medium, and then supplemented with BDNF (10

ng/mL), metformin (10⁻⁵M), or BDNF plus metformin for 22h. As a result, BDNF significantly enhanced the rates of the development to 8~16 cell embryos compared to control group (38% vs. 20%). In addition to this, BDNF plus metformin increased the rates more than the BDNF group (48% vs. 38%), whereas metformin alone had no effect. In Conclusion, BDNF enhanced the developmental competence of bovine oocytes when supplemented during IVM but not IVC, and the action of BDNF was promoted by collaboration for metformin. These results could further contribute to establishing chemically defined bovine IVM system.

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