

## Effect of Heparin-binding Epidermal Growth Factor (HB-EGF) on Integrin $\alpha \nu \beta_3$ Expression in Preimplantation Mouse Embryos

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Heparin-binding epidermal growth factor (HB-EGF) is one of the EGF family to be expressed at the time of implantation in the mouse uterus. Although HB-EGF has been shown to stimulate the development of embryo and uterus in the mouse, its correlation between cell adhesion molecules remains undefined. Integrin  $\alpha \nu \beta_3$ , one of the cell adhesion molecules, is an important mediator of cell-substratum and cell-cell adhesion in implantation. In the present studies, we investigated the effects of HB-EGF on the embryonic development, initiation of implantation and expression of integrin  $\alpha \nu \beta_3$  in *in vitro* culture, blocking of HB-EGF, RT-PCR and immunofluorescence analysis.

The results showed that HB-EGF significantly improved the developmental rate of hatched embryos (24.1%,  $P < 0.01$ ) and outgrowth embryos (42.5%,  $P < 0.01$ ). On the other hand, this growth factor showed no effect before the hatching embryonic stage. Analysis of RT-PCR showed that HB-EGF upregulated the expression level of integrin  $\alpha \nu \beta_3$  subunit genes on the preimplantation embryo and outgrowth of blastocyst (120hr and 144hr after hCG injection). Immunofluorescence analysis showed that the integrin  $\alpha \nu \beta_3$  subunits localized at the pericellular borders and cell-cell contact areas. Increase in fluorescence intensity was observed in the HB-EGF treated embryos. Intrauterine injection of an anti-HB-EGF antiserum at day 3 significantly decreased the number of implantation sites (14.4,  $P < 0.01$ ) and significantly increased the number of recovered embryos (6.4,  $P < 0.05$ ) at day 5. From these results, it implies that HB-EGF improves the embryo development and accelerates the expression of integrin  $\alpha \nu \beta_3$  in the preimplantation mouse embryos.

Key words) *HB-EGF, Integrin  $\alpha \nu \beta_3$ , Mouse embryo, Preimplantation*