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Integrin Signaling Regulates Blastocyst Adhesion to Fibronectin at Implantation: Intracellular Calcium Transients and Vesicle Trafficking in Primary Trophoblast Cells

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Abstract

Accumulating evidence indicates that the endometrial extracellular matrix (ECM) modulates trophoblast adhesion during mouse blastocyst implantation. In previous studies of adhesion-competent mouse blastocysts, we have demonstrated that integrin-mediated fibronectin (FN)-binding activity on the apical surface of trophoblast cells is initially low, but becomes strengthened after embryos are exposed to FN. In the present study, we have examined whether the ligand-induced upregulation of trophoblast adhesion to FN is mediated by integrin signaling. The strengthening of adhesion to FN required integrin ligation, which rapidly elevated cytoplasmic-free Ca^{2+}. Chelation of intracellular Ca^{2+} using BAPTA-AM, or inhibition of the Ca^{2+}-dependent proteins, protein kinase C or calmodulin, significantly attenuated the effect of FN on binding activity. Furthermore, direct elevation of cytoplasmic Ca^{2+} levels with ionomycin upregulated FN-binding activity, demonstrating that Ca^{2+} signaling is required and sufficient for strong adhesion to FN. Ca^{2+} signaling may induce protein trafficking, a known requirement for ligand-induced upregulation of FN-binding activity. Indeed, intracellular vesicles accumulated in adhesion-competent blastocysts, but were absent after exposure to either FN or ionomycin. These findings suggest that, during implantation, contact between peri-implantation blastocysts and FN elevates intracellular Ca^{2+}, which strengthens trophoblast adhesion to ECM through protein redistribution.

Keywords

ovum implantation; blastocyst; trophoblast; fibronectin; integrins; extracellular matrix; trafficking; cell adhesion; Ca^{2+} signaling; signal transduction

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