I S—25 GTPase-activating protein regulates growth of chorionic villi in first trimester of pregnancy

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PURPOSE: GTPase-activating proteins (GAPs) stimulate GTP hydrolysis on small G-proteins such as p21-Ras and regulate the signal transduction for cellular growth and differentiation. To clarify the function of Ras-GAP on growth of chorionic villi in the first trimester, we examined the expression and activity of Ras-GAP on normal chorionic villi and hydatidiform mole, and effects of growth factors on Ras-GAP in choriocarcinoma cell line. MATERIALS AND METHODS: The expression of Ras-GAP at the protein level was examined by immunoblotting and immunostaining in freshly obtained tissues of human chorionic villi and hydatidiform mole. We also determined Ras-GTP hydrolytic activity of these tissues. Moreover, we studied the changes of Ras-GAP by adding several growth factors to cultured BeWo cells. RESULTS: The expression of Ras-GAP is more abundant in normal chorionic villi than molar villi. Immunostaining showed that cytoplasm of chorionic villi stained more intensely than that of mole. The GAP activity of chorionic villi was significantly higher than that of mole. The Ras-GAP of BeWo cells showed no reaction against growth factors. CONCLUSION: Ras-GAP may control the normal growth and development of human chorionic villi in the first trimester.

I S—26 Effect of insulin-like growth factor bindingprotein-1phosphoisomers on IGF-I-induced amino acid uptake by trophoblast cells.

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[Objective] Insulin-like growth factor (IGF) binding protein-1 (IGFBP-1) has been found to be phosphorylated and four to five phosphorylated forms (pIGFBP-1) and one nonphosphorylated form (npIGFBP-1) have been identified in various biological fluids. We have reported that levels of IGFBP-1 and the proportion of pIGFBP-1 against total IGFBP-1 were higher in mothers with intrauterine growth retardation than those in mothers with normal growth. To elucidate the biological effects of these phosphoisomers, we studied effects of npIGFBP-1 and pIGFBP-1 on amino acid uptake induced by IGF-I using cultured trophoblast cells. [Methods]IGFBP-1 was purified from mid term amniotic fluid using ammonium sulphate precipitation followed by phenyl Sepharose. Purified IGFBP-1 was further purified by DEAE Sepharose in which npIGFBP-1 and pIGFBP-1 were separated. Trophoblast cells obtained from term pregnancy were cultured in the presence or absence of 10 nmol/L IGF-I for 3 hr and further incubated with ^{3}H-a amino isobutyric acid (^{3}H-AIB) for 30 min. Cells were solubilized and the radioactivity in cells was counted by a scintillation counter. In another set of experiments, trophoblast cells were incubated with IGF-I in the presence or absence of 10 nmol/L npIGFBP-1 or pIGFBP-1 and uptake of ^{3}H-AIB was evaluated. [Results] IGF-I stimulated ^{3}H-AIB uptake by trophoblast cells by 730 % of control. Both npIGFBP-1 and pIGFBP-1alone had no effect on ^{3}H-AIB uptake, however, npIGFBP-1 enhanced IGF-I-stimulated ^{3}H-AIB uptake by 200% of IGF-I alone while pIGFBP-1 inhibited ^{3}H-AIB uptake by 33% of IGF-I alone. [Conclusions] Maternal IGF-I promotes fetal growth by stimulating nutrients transport in the placenta. It is elucidated that npIGFBP-1 stimulates this IGF-I action on the placenta while pIGFBP-1 inhibits IGF-I action. Thus, it is suggested that not only maternal IGF-I but also phosphoisomers of IGFBP-1 are tightly involved in fetal growth.