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Insulin suppresses the expression and function of breast cancer resistance protein in primary cultures of rat brain microvessel endothelial cells

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Abstract:
The aim of this study was to investigate the role of insulin in the regulation of breast cancer resistance protein (BCRP) function and expression using primary cultured rat brain microvessel endothelial cells (rBMECs) as an *in vitro* model of the blood brain barrier (BBB). The prazosin uptake assay and western blot analysis were used to assess the function and expression of BCRP, respectively. It was noted that the uptake of prazosin by rBMECs was time-, concentration- and temperature-dependent. The BCRP inhibitors novobiocin and imatinib mesylate significantly increased the uptake of prazosin by the cells in a concentration-dependent manner. The cells were also incubated with sera from diabetic rats for 72 h, serving as a diabetic *in vitro* model. We found that the uptake of prazosin by rBMECs incubated in the diabetic rat sera was 39.8% of that in normal rat sera, and insulin treatment reversed this decrease. Further results showed that insulin down-regulated the function and expression of BCRP in rBMECs in a concentration-dependent manner. Treatment with an antibody against the insulin receptor abolished the down-regulation of BCRP function and expression that was induced by insulin. These results indicate that insulin suppressed the function and expression of BCRPs in rBMEC primary cultures.

Key words:
breast cancer resistance protein, diabetes, insulin, rat brain microvessel endothelial cells