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论文

谷氨酰胺:6-磷酸-果糖酰基转移酶抑制剂细胞筛选模型的建立

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摘要:

目的建立己糖胺途径的关键酶谷氨酰胺:6-磷酸-果糖酰基转移酶(glutamine:fructose-6-phosphate amidotransferase,GFAT)抑制剂的细胞筛选模型。方法用改进的GDH法测定GFAT的活性。以速效胰岛素依赖的葡萄糖摄取观察细胞对胰岛素的反应性;用长效胰岛素诱导HIRc细胞,形成己糖胺途径过度活跃和胰岛素抵抗的细胞模型,并应用该细胞模型和GDH法筛选GFAT抑制剂。结果用25 nmol·L^{-1}长效胰岛素刺激HIRc细胞36 h,可明显激活己糖胺途径,使GFAT活性上升47%;同时产生胰岛素抵抗,使速效胰岛素依赖的葡萄糖摄取能力降低21%。Azaserine可明显抑制该模型中GFAT的活性。结论长效胰岛素既可过度激活HIRc细胞己糖胺途径,又可使其产生胰岛素抵抗。该模型可用于筛选GFAT抑制剂。

关键词: 己糖胺途径 谷氨酰胺:6-磷酸-果糖酰基转移酶抑制剂 胰岛素抵抗 筛选

Establishment of an IR-HIRc cell model for screening GFAT inhibitor

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Abstract:

AimTo set up an IR-HIRc cell model for screening the inhibitor of GFAT (glutamine :fructose-6-phosphate amidotransferase), the key enzyme in the hexosamine biosynthesis pathway (HBP).MethodsFor GFAT activity assay, the GDH method was improved by adjusting the value of pH in the reaction system and the concentrations of the reactants.The sensitivity to insulin in the cells was estimated by the measurement of insulin-induced glucose-uptake.The IR-HIRc model was set up by the stimulation of long-action insulin for 36 h.The IR-HIRc model and GDH method was used for screening GFAT inhibitor.ResultsWith the administration of 25 nmol·L^{-1} long-action insulin in HIRc cells for 36 hours, the GFAT activity increased by 47% and the insulin-induced glucose-uptake decreased by 21%.Azaserine, a GFAT inhibitor, inhibited GFAT activity significantly in a dose-dependent manner in IR-HIRc model.ConclusionWith the stimulation of 25 nmol·L^{-1} long-action insulin for 36 h, excess hexosamine flux and insulin resistant in IR-HIRc cell model was set up, which can be used for screening GFAT inhibitors.

Keywords: glutamine:fructose-6-phosphate amidotransferase inhibitor insulin resistance screening hexosamine biosynthesis pathway

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