

Abstract

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Glutamine Deprivation Alters Intestinal Tight Junctions via a PI3-K/Akt Mediated Pathway in Caco-2 Cells.

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BACKGROUND: Glutamine (Gln) is important for intestinal barrier function and regulation of tight junction (TJ) proteins, but the intracellular mechanisms of action remain undefined.

OBJECTIVE: The purpose of this study was to test the hypothesis that Gln regulates intercellular junction integrity and TJ proteins through the phosphatidylinositol 3-kinase (PI3K)/Akt pathway in Caco-2 cells.

RESULTS: Deprivation of exogenous and endogenous glutamine decreased transepithelial electrical resistance (TER) ($P < 0.01$) and increased permeability ($P < 0.01$). Both wortmannin and LY294002, PI3K inhibitors, prevented the TER decrease and the permeability increase induced by Gln deprivation ($P < 0.001$). Gln deprivation also caused decreased TJ protein claudin-1 ($P < 0.001$). Both wortmannin and LY294002 treatment prevented this effect ($P < 0.001$). Deprivation of Gln increased phosphor-Akt protein. Gln supplementation reversed this effect. Decreased TER and increased permeability associated with Gln deprivation were not observed in small interfering RNA for p85 transfected Caco-2 cells.

CONCLUSION: In conclusion, Gln regulates intercellular junction integrity and TJ proteins through the PI3-Kinase/Akt pathway.

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