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Glutamine regulates amino acid transport and glutathione levels in a human neuroblastoma cell line

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Background: Both amino acid transport across the plasma membrane and glutathione play a key role in regulating cancer cell growth with the mechanism of supplying cells with amino acids for cellular metabolism and a major store of cellular reducing equivalents, respectively. Glutamine can serve as an important ATP source for cancer cells, and it can supply glutamate, a precursor for the synthesis of glutathione, by the hydrolysis of glutamine.

Methods: We examined the effects of glutamine concentrations [2 mM (control), 400 μM, 200 μM, and 0 μM] on cell growth, amino acid transport, and glutathione levels in a human neuroblastoma cell line, SK-N-SH, by using cell culture technique.

Results: Cell growth rates were dependent on glutamine concentrations in culture media. Glutamine deprivation resulted in the decrease of glutamine transport by decreasing the mRNA expression of its transporter, system ASC subtype ASCT2. However, glutamate transport significantly increased in glutamine-deprived groups, and this increase was remarkable in lower glutamine groups (200 μM and 0 μM). Intracellular glutathione decreased by 20% compared with control in glutamine-deprived groups, but the level in 0 μM glutamine was maintained with the same levels found in 400 μM and 200 μM glutamine. DNA and protein biosynthesis correlated directly with the glutamine concentration in culture media.

Conclusions: Our results suggest that glutamine mediates neuroblastoma cell proliferation by regulating amino acid transport and glutathione synthesis, both when sufficient nutrients are present and when key nutrients such as glutamine are in limited supply.