Igniting Tumorigenesis: Gamma-Glutamyl-Glutamine Induced Transformation of NIH 3T3 Cells

Jones, Sabrina (School: Arkansas School for Mathematics, Sciences and the Arts)

Studying metabolic functions of cancer cells can reveal novel treatment options. For example, increased glutamine uptake drives cancer cell proliferation. The first step in glutamine utilization is its conversion to glutamate by glutaminase (GLS). Glutamate is a precursor for glutathione (GSH) synthesis which is produced by a pathway that is activated in tumor cells. The gamma-glutamyl group from GSH is transferred to a free amino acid by gamma-glutamyl-transferase (GGT). In this study, transformation rates of the NIH 3T3 cell lines increased when cells were treated with greater concentrations (0.1, 1, 5, 10 mM) of gamma-glutamyl-glutamine (GGG). Thus, this study supported the hypothesis that GGG would have a dose response effect on transformation rates in NIH 3T3 cells. However, NIH 3T3 cells treated with GSH did not exhibit a dose response effect on transformation rates because NIH 3T3 cells are GGT negative. All experiments were performed in triplicate and transformants were counted at days 7, 14, and 21. The results of this study suggest that the neoplastic transformation of NIH 3T3 cells is influenced by the gamma-glutamyl cycle and therefore offers a potential for intervention in the process of carcinogenesis by varying amounts of intermediates that are part of this cycle, such as gamma-glutamyl-glutamine, glutaminase, or glutamine.

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