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Nitric Oxide and Cyclic GMP Signaling in Cancer Therapy

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ABSTRACT

The nitric oxide-3',5'-cyclic guanosine monophosphate signaling pathway (NO-cGMP signaling pathway) is a well-known signal transduction pathway which elicits several physiological processes including: cell proliferation, vasodilation, cardiac protection, etc. In this pathway, NO binds to the ferrous heme of histidine-105 on the prosthetic heme of the β_1 subunit of soluble guanylyl cyclase, resulting in the production of cGMP. This pathway, however, is inhibited in certain cancer cells—as observed in glioma cell lines. As a result, the production of cGMP is reduced. This mechanism may facilitate uncontrolled tumor cell growth.

The cancers under research—lung carcinoma, glioma, and pancreatic carcinoma—are all highly malignant cancers with low survival rates and few effective treatments. To save the lives of 213,920+ U.S. patients expected to die from these diseases, new therapies must be developed. We hypothesize that regulating the expression of sGC via pharmacology and/or genetic manipulation in the aforementioned cancers—which possess lower expression levels of subunits $sGC\alpha_1$ and $sGC\beta_1$—will increase cGMP synthesis.

As experimental approach, the H460 human large lung cell carcinoma cell line, the PA-TU-8988 human pancreatic adenocarcinoma cell line, and the U87 human glioma cell line were cultured in 2D and 3D culture. MTT assay, qRT-PCR, Western Blot, and ImageJ analysis were utilized to assess cell proliferation, detection and quantification of genes and proteins expression, and size of colonies in 3D culture, respectively.

Research is still continuing; results are not final. The expected results after treatment are: reduced cancer cell viability, enhanced sGC expression, presence of cGMP, and inhibited tumor growth

Key words: cGMP, lung carcinoma, pancreatic adenocarcinoma, glioma, cancer therapy

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