Drug and Method for the Therapeutic Treatment of Primary Brain Tumors (Such As Intracranial Human Glioma, Astrocytomas, Medulloblastomas and Metastatic Tumors to the Central Nervous System)

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Technology description

Summary

Epidermal growth factor receptor ("EGFR") is amplified or over expressed in many malignant gliomas, other primary brain tumors, and carcinomas of epithelial origin (e.g., breast, lung, etc.) but is low or undetectable in normal brain tissue. TGF-alpha-PE38 represents a growing class of recombinant toxins designed for use in targeted cancer therapy. These genetically engineered chimeric proteins consist of a targeting moiety and a cytotoxic moiety. While TGF-alpha- PE38 is extremely toxic to tumor cells that have a relatively high expression of EGFR, it is also active against primary human brain tumor cells which are known to have moderate to high EGFR expression. Direct delivery of TGF-alpha-PE38 into brain tumors by intratumoral implanted catheters or controlled-release biodegradable polymers or intrathecal administration into the cerebrospinal fluid of patients with leptomeningeal carcinomatosis, may represent clinically useful applications of recombinant toxin therapy in tumors with high EGFR expression.

Anaplastic astrocytoma and glioblastoma, the most common primary brain tumors in adults, respond poorly to all current therapies: median survival for patients with these tumors ranges from 19 to 57 weeks. Local tumor recurrence also constitutes a significant problem in medulloblastoma, the most common childhood brain tumor. Despite 5-year survivals for medulloblastoma exceeding 80% in some studies, nearly half of these patients will eventually die from progressive tumor. Treatment failure in patients with brain tumors is a multifactorial process involving the intrinsic resistance of these tumors to radiation therapy and chemotherapy, the development of acquired treatment resistance, and limitations of drug delivery due to blood-brain barrier restrictions. Local recurrence of brain tumors represents the most common pattern of treatment failure. Accordingly, the identification of new therapeutic agents that have high intrinsic activity against brain tumors and are appropriate for local therapy remains a major goal of the NIH.

Institution

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