Composition and methods of multi-targeted siRNA cocktail for treatment of Glioblastoma Multiforme

Value Proposition
Glioblastoma is the most common primary malignant brain tumor in adults, and the prognosis of this disease is dismal, despite aggressive standard-of-care therapy with chemoradiation and gross tumor resection. Several molecular mechanisms are known to contribute to the tumorigenicity of glioblastoma. Major players include EGFR, VEGF, and MGMT, which are involved in cell survival, the development of new blood vessels, and resistance to chemotherapeutics, respectively. Studies have shown that monovalent therapeutics targeting these molecules elicit appreciable antitumor effects; nevertheless, acquired resistance to these therapies generally occurs. Thus, the current consensus on glioblastoma treatment is that multi-targeted approaches are likely required to treat this devastating tumor.

Technology
Dr. Hai Yan, renowned in the field of glioma research, has developed an RNA-interference-based modality using siRNA for suppressing multiple oncogenic genes within glioblastoma cells. Molecules of relevance include, but are not limited to, EGFR, VEGF, and MGMT. siRNAs targeting these genes, which have been shown to significantly suppress the expression of their targets, are administered with a pharmaceutically acceptable carrier and can be preferentially targeted to glioblastoma cells using an array of glioblastoma cell-focused ligands (e.g. EGFR receptor ligand). Such a modality has the potential to elicit direct tumoricidal effects and cause glioblastoma cells to become vulnerable to conventional treatments (e.g. temozolomide chemotherapy).

Other applications
The activity of the oncogenic proteins EGFR, VEGF, and/or MGMT has been detected in non-glioma tumors. Therefore, this invention may have application beyond gliomas for alternative tumor types.

Advantages
The current invention targets at least three distinct mechanisms that are known to contribute glioblastoma viability: proliferation, angiogenesis, and chemotherapeutic resistance. This is particularly advantageous given that the profound heterogeneity of glioblastoma tumors is thought to underlie its ability to acquire resistance to monovalent therapies. By targeting a broad array of oncogenic molecules that are involved in unique tumorigenic pathways, there is an a priori increased likelihood of therapeutic success.
success.

Patents

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