## Decoy Oligonucleotides Corresponding to NF-KappaB Binding Site in MGMT Promoter for Cancer Treatment and Drug Resistance. (Hadasit)

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**Need:**

There is a substantial unmet need for novel anti-drug-resistant cancer treatment. Alkylating agents (A certain type of chemotherapy) are the most widely used anti-cancer drugs. Drug resistance is a common obstacle for their use in cancer patients. Specifically, patients diagnosed with Glioblastoma Multiforme whose tumors are resistant to alkylating agents are in need for an effective way to overcome resistance.

**Innovation:**

The DNA repair protein O6-methylguanine-DNA methyltransferase (MGMT) has been implicated in resistance of human tumors to alkylating agents. The expression level of MGMT is regulated by NF-kappaB. Interference with the binding of NF-kappaB to MGMT promoter could reverse MGMT-induced chemoresistance. The present invention provides modified decoy oligonucleotides corresponding to NF-KappaB binding site within MGMT promoter as a novel approach for sensitizing tumor cells to alkylating agents. The decoy oligonucleotides can effectively reverse chemoresistance in several cancer cell lines.

**Findings:**

- The decoy oligonucleotides effectively reverse chemoresistance in several cancer cell lines.
- An In vivo model demonstrated the efficacy of the decoy oligonucelotides against human melanoma tumors transplanted in mice.

**Indications / Applications:**

The drug could be used widely to overcome the resistance to chemotherapy in most cancer patients including, brain tumors, melanoma, lymphoma, myeloma, leukemia and sarcoma.

**Competitive Advantages:**

Specific target: the drug specifically target MGMT, the main cause for resistance to alkylating agents. Specific NF-kappaB oligonucleotide decoy: we are using a unique oligonucleotide that binds to a specific NF-KappaB site within MGMT promoter. We anticipate that the proposed decoy would exhibit less toxicity in comparison to other methods which target a general NF-kappaB binding site.

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