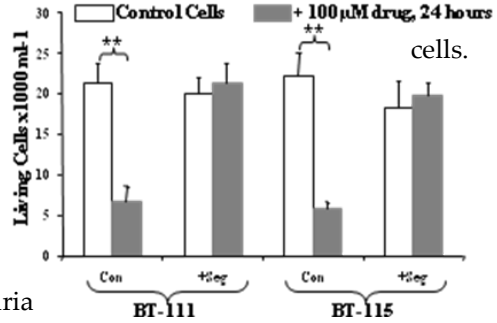
HOUSTON METHODIST INVENTION:

Novel Mitochondrial Targeted Glioblastoma Drugs

Invention

The invention is a blood/ brain barrier permeable prodrugs which are selectively activated by an enzyme that is highly upregulated in glioma cells. The activation selectively targets the drug "warhead" to the mitochondria of glioma cells at high concentration and damages or destroys the mitochondrial DNA. Cancer cells including glioma cells contain far fewer mitochondria than normal cells but cannot survive without a minimum number of mitochondria for pyrimidine synthesis. This requirement is the cancer cell's "Achilles Heel" since destruction of the mitochondria leads to rapid cancer cell death. In addition, mitochondria DNA damage does not upregulate DNA repair enzymes therefore targeting mitochondrial DNA avoids the development of drug resistance.



Background

There are 10,000 new glioma cases in the US alone every year and the survival rate is <3% at 5 years. The most aggressive form of glioma, Glioblastoma multiforme (GBM) is also the most frequent type and no GBM patients survive for >1 year. GBM is topographically diverse and frequently cannot be completely resected. Gliomas are currently treated with a combination of surgery, radiotherapy and chemotherapy with DNA acylating agents such as temozolomide or carmustine or rarely with the topoisomerase inhibitor irinotecan. Carmustine is sometimes supplied as wafers placed into the post surgical wound. No current treatments are effective at prolonging survival for more than a few months.

Advantages

- Prodrug is blood / brain barrier permeable.
- Prodrug is selectively activated in glioma cells by a specifically upregulated enzyme.
- Active drug is concentrated 500 fold in the mitochondria.
- Active drug damages mitochondrial DNA resulting in mitochondrial destruction and glioma cell death.
- Will not trigger drug resistance since DNA repair pathways are not upregulated.
- A variety of "warhead" drugs can be attached to the targeting moiety for glioma mitochondrial delivery.

For more information, contact the Office of Technology Transfer by e-mail at OTT@HoustonMethodist.org.

About Houston Methodist

Houston Methodist is comprised of a leading academic medical center in the Texas Medical Center® and four community hospitals serving the greater Houston area. Houston Methodist Hospital, the system's flagship, is consistently listed among U.S. News & World Report's best hospitals and we extend that same level of quality care across the system. Houston Methodist Research Institute is home to some of the world's brightest physician-scientists, working in a collaborative environment on more than 700 clinical trials. The Research Institute is making strides in the new 440,000-square-foot facility, bringing us even closer to medical breakthroughs in cardiovascular disease, cancer, infectious disease, neurosciences, diabetes and more.

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