



OFFICE OF TECHNOLOGY TRANSFER



McGill

TECHNOLOGY OPPORTUNITY

Antisense Inhibitors of MBD2 Demethylase for Cancer Therapy

McGill University is seeking a company interested in commercializing an antisense oligonucleotide inhibitor of MBD2 Demethylase for the treatment of cancer and cancer metastasis. The total oncology market is \$60-70 billion per year. We expect a DNA demethylation inhibitor to be a major component of all cancer therapy cocktails, and therefore expect a market share of 10-15% (\$6-10 billion) per year at full maturity. This potential is likely significantly larger if this antisense is also used as antimetastatic therapy. The first indications to be developed will be liver cancer and liver cancer metastases. Worldwide the liver cancer market is currently estimated at around \$500M annually and will continue to grow along with the increasing incidence of Hepatitis C and liver cirrhosis.

Applications

Treatment of lung, liver and colorectal cancers and prevention and treatment of metastatic cancers.

Advantages

- MBD2 inhibition in cancer cells leads to inhibition of metastasis thereby offering a solution to the unresolved problem of metastatic cancer.
- Antisense oligonucleotides accumulate in the liver, lungs and kidneys which makes them ideal treatment for cancer of these organs.
- The antisense inhibitor of MBD2 Demethylase, AS10, has shown a reduction of the malignancy and invasiveness properties of liver cancer cells thereby confirming its effectiveness as treatment for liver cancer and prevention of metastasis.
- The antisense can be administered intravenously which makes it easy to incorporate into the current treatment protocols.

Technology

One of the hallmarks of cancer cells is an aberrant pattern of methylation; hypermethylation of selected genes and global hypomethylation have been documented. The DNA methylation machinery is composed of DNA methyltransferases, demethylases and methylated DNA binding proteins (MBDs) that interpret the DNA methylation signal. A newly characterized methylated binding protein, MBD2b isoform has been shown to possess demethylase activity. We have cloned and purified the cDNA encoding this MBD2 demethylase enzyme. We have also developed antisense oligos and identified small molecule inhibitors of this MBD2 demethylase. MBD2 is characterized by unique features: 1) MBD2 is not essential to normal cells, 2) MBD2 inhibition in normal cells does not cause toxicity, 3) MBD2 expression is essential for cancer cells and 4) MBD2 inhibition in cancer cells leads to inhibition of metastasis. This has been validated *in vitro* in HEK 293 human embryonal kidney cells, A549 non-small cell lung cancer cells, MCF-7 breast cancer cells, HepG2 human liver cancer cells and CaCo colon cancer cells and *in vivo* in nude mice treated with H1299 non-small cell lung cancer cells with pHis MBD2 antisense or empty vector.

The Inventor



Dr. Moshe Szyf is James McGill Professor in the Department of Pharmacology of McGill University. He received his PhD in Biochemistry from Hebrew university. Dr Szyf is a world renowned researcher in the field of epigenetics. Dr. Szyf's research focuses on understanding the basic principles of the DNA methylation machinery and its involvement in cancer as well as applying this research towards identifying novel anticancer targets.

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