Inhibition of MTHFR (methylenetetrahydrofolate reductase) for cancer therapy

McGill is looking for a partner to commercialize an antisense to inhibit MTHFR (methylenetetrahydrofolate reductase) for the use in cancer. MTHFR is a critical enzyme in folate metabolism that generates the primary circulatory form of folate which is also used for methylation reactions. Inhibition of MTHFR with an antisense reduces survival of many cancer cell lines in vitro and reduces growth of colon, lung and prostate tumors in mice in vivo. This antisense also shows additive effects when combined with some standard chemotherapeutic agents both in vitro and in vivo. MTHFR inhibitors and uses have been protected under the US patent #7,319,145 issued on January 15, 2008 and the European patent #EP1307588 issued on April 21, 2009.

Applications

Antisense alone and in combination with standard chemotherapeutic drugs
- Colon cancer
- Prostate cancer
- Lung cancer

Advantages of MTHFR in Cancer Therapeutics

- MTHFR involved in folate and methionine/methylation metabolism, two critical pathways in tumor development
- Target validated by antisense technology in vitro and in vivo
- Additional validation by human pharmacogenetic data, mouse mutants
- Highly amenable to small molecule inhibition; leads available
- Well-characterized enzyme target, crystal structures available
The lead Inventor

Dr Rima Rozen is a James McGill Professor of Human Genetics and Pediatrics at Faculty of Medicine and Associate member, Department of Biology, Faculty of Science, McGill University. Her research is focused on the investigation of common genetic variants that influence the metabolism of folate, an important B vitamin. These variants, with or without nutritional imbalances, can modulate the risk for birth defects and cancer, and for brain and liver dysfunction.

Her laboratory uses cellular, molecular and in vivo approaches to understand the mechanisms by which genetic factors and nutrition influence these complex traits and to translate her work into the clinical sphere for identification of new avenues of diagnosis or treatment.

Research foci:
- Folate and homocysteine metabolism
- Polymorphisms and risk for disease
- Genetics and epigenetics
- Nutritional modulation
- Mild hyperhomocysteinemia and homocystinuria
- Gene regulation and functional studies.

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