

As part of the invention, the inventors contemplate the following:

(i) a method of detecting an increased risk for abnormal cellular proliferation in a subject via detection of overexpression of the *Sema 5* gene product;

(ii) methods and compositions for treating abnormal cellular proliferation in a subject by administering a molecule that decreases or prevents expression of a *Sema 5* gene product or a molecule that binds to *Sema 5* antigen on the surface of the cell and targets the cell for destruction.

This technology is available for licensing on an exclusive or a non-exclusive basis.

Novel Antisense Oligonucleotides Targeting Folate Receptor Alpha

Mona S. Jhaveri, Patrick C. Elwood, Koong-Nah Chung (NCI).

U.S. Provisional Application No. 60/274,249 filed 09 Mar 2001 (DHHS Reference No. E-321-2000/0-US-01).

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Ovarian cancer is the fifth leading cause of cancer death for women in the United States. Drug resistance of ovarian tumors to chemotherapy is a common problem resulting in only 20 to 30 percent overall 5-year survival rates. Folate is a vitamin that is absolutely necessary for cell survival. Some cancer cells, including ovarian carcinomas, have an abundance of a folate-binding protein termed the human alpha folate receptor (ahFR). It is believed that the elevated levels of ahFR contribute to the cells' cancerous state by mediating increased folate uptake or by generating positive regulatory growth signals. This invention comprises a genetic therapy that diminishes the levels of ahFR using antisense oligonucleotides that block the transcription of the gene. Studies have shown that this invention significantly decreases proliferation of cultured cancer cells and sensitizes these cells to treatment with chemotherapeutic drugs. Further development of receptor-targeted antisense oligonucleotides and related compounds have potential therapeutic value for a range of difficult-to-treat cancers including cancers of the ovary, cervix, uterus, and brain.

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Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent application listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: (301) 496-7057; fax: (301) 402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent application.

Compositions and Methods for Enhancing Differential Gene Expression

I Horikawa, JC Barrett (NCI).

DHHS Reference No. E-008-2001/0-US-01 filed 05 Jun 2003.

Licensing Contact: Susan S. Rucker; 301/435-4478; ruckersu@mail.nih.gov.

This application describes compositions and methods useful in enhancing the differential expression of heterologous nucleic acids. In particular, the application claims inventions that encompass artificial promoters derived from the human telomerase reverse transcriptase promoter (hTERT) and their use. More particularly, this application describes artificial hTERT promoters that minimize the expression of a heterologous nucleic acid sequences operably linked thereto in normal cells while providing for high levels of expression of the heterologous nucleic acid in cancer cells. The heterologous nucleic acid sequence preferentially encodes a product that will have cytotoxic activity upon expression in the cell.

The hTERT promoter has been characterized and research has demonstrated that small portions thereof are responsible for the cancer-

specific expression of the hTERT gene. The cancer-specific nature of hTERT promoter activity suggests that it is a target for the development of specific anti-cancer therapeutics and other strategies for cancer treatment.

In order to improve therapeutic strategies for delivering cytotoxic nucleic acid sequences that are expressed in cancer cells artificial hTERT promoters have been constructed that, when operably linked to the cytotoxic nucleic acid sequence, minimize expression of the cytotoxic nucleic acid sequence in normal cells while maintaining high levels of expression of the cytotoxic nucleic acid sequence in cancer cells. This differential regulatory control is accomplished by operably linking particular E-box nucleic acid sequences in cis with the regulatory elements of the hTERT promoter associated with gene expression in cancer cells and a nucleic acid sequence encoding a product that is cytotoxic upon expression. Cytotoxic substances include, for example, *Pseudomonas* exotoxin (polypeptide toxin), HSV thymidine kinase (pro-drug converting) or bax (apoptosis inducing).

Experimental work related to this invention has been published at Horikawa, I *et al.*, *Mol Biol Cell* 13(8): 2585-97 (Aug 2002).

Leukoregulin, An Antitumor Lymphokine, and Its Therapeutic Uses

JH Ransom (NCI), RP McCabe, M Haspel, N Pomato.

U.S. Patent Application No. 06/906,353 filed 11 Sep 1986, which issued as U.S. Patent 4,849,506 on 18 Jul 1989 (DHHS Reference No. E-537-1983/2-US-01); U.S. Patent Application No. 07/350,879 filed 11 May 1989, which issued as U.S. Patent 5,082,657 on 21 Jan 1992 (DHHS Reference No. E-970-1997/0-US-01).

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These patents claim compositions and methods for using the lymphokine/cytokine known as leukoregulin. In particular, leukoregulin is useful in methods of treating cancer. The NIH is the exclusive licensee of these patents.

Leukoregulin, a cytokine derived from T lymphocytes, is a glycoprotein hormone. Leukoregulin interacts with target cells to regulate cellular activity with its effects being pleiotrophic and dependent on the type of target cell. Among other roles, leukoregulin has been demonstrated to influence the synthesis of collagenase, stromelysin-1, collagen, and hyaluronan in human fibroblasts. These properties make it important in maintaining the