associated with hematopoietic malignancies of lymphoid, myeloid, and erythroid lineage. Additionally, strikingly increased expression of notch-1 has been documented in a number of human tumors including cervical cancer, colon tumors, lung tumors, and pre-neoplastic lesions of the uterine cervix.

Notch antisense oligonucleotides (or other molecules that interfere with the expression or function of notch) could be therapeutically administered to treat or prevent tumors. It has not been found that administration of notch antisense oligonucleotides alone is effective as an anti-neoplastic treatment. The present invention has overcome this problem by combining the administration of a cell differentiation agent with an antibody that antagonizes the function of a notch protein and hence interferes with the expression or function of a notch protein (such as the notch-1 protein). This combination of approaches has unexpectedly been found to induce apoptosis in neoplastic cells, and provide a useful therapeutic application of this technology.

In particular the tumor cell is one that is characterized by increased activity or increased expression of a notch protein, such as a notch-1 or notch-2 protein. Examples of tumor types that over express notch-1 include cervical cancer, breast cancer, colon cancer, melanoma, seminoma, lung cancer and hematopoietic malignancies, such as erythroid leukemia, myeloid leukemia, (such as chronic or acute myelogenous leukemia), neuroblastoma and medulloblastoma. The differentiation inducing agent to which the cell is exposed can be selected from a broad variety of agents, including retinoids, polar compounds (such as hexamethylene bisacetanmide), short chain fatty acids, organic acids, Vitamin D derivatives, cyclooxygenase inhibitors, arachidonate metabolism inhibitors, ceramides, diacylglycerol, cyclic nucleotide derivatives, hormones, hormone antagonists, biologic promoters of differentiation, and derivatives of any of these agents.

Technology

This invention provides compositions, pharmaceutical compositions, and methods for stimulating/increasing cell differentiation, and is particularly related to the treatment of tumors which have increased notch-1 expression. A polyclonal and/or monoclonal antibody generated against human Notch-1 Epidermal Growth Factor (''EGF'') that recognizes an extracellular epitope of notch-1 and that stimulates target cell differentiation in the presence of an effect amount of differentiation inducing agent is disclosed as is the hybridoma which produces these antibodies. At a time during which differentiation has been promoted, and the cell is susceptible to interference with the anti-apoptosis effect of notch, the function of the notch protein is disrupted. Disruption of notch function can be achieved, for example, by the expression of antisense oligonucleotides that specifically interfere with expression of the notch protein on the cell, or by monoclonal antibodies that specifically bind to notch and inactivate it. This technology represents a novel method to induce apoptosis in tumor cells.

The above mentioned Invention is available, including any available foreign intellectual property rights, for licensing.

Dated: November 24, 1999.

Jack Spiegel,

Director, Division of Technology Development & Transfer, Office of Technology Transfer.

[FR Doc. 99–31343 Filed 12–2–99; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel. ZDK1 GRB–7 J3 P.

Date: December 6–8, 1999.

Time: 7:00 p.m. to 12:00 p.m.

Agenda: To review and evaluate grant applications.

Place: Radisson Hotel at Gateway, 651 Huron Road, Cleveland, OH 44115.

Contact Person: Lakshmanan Sankaran, Scientific Review Administrator, Review Branch, DEA, NIDDK, Natcher Building Room 6AS25F, National Institutes of Health, Bethesda, MD 20892–6600, (301) 594–7799.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel. ZDK1 GRB C (J1).

Date: December 7–9, 1999.

Time: 7:30 p.m. to 11:00 a.m.

Agenda: To review and evaluate grant applications.

Place: New Haven Hotel, 229 George Street, New Haven, CT 06510.

Contact Person: Dan E. Matsumoto, Scientific Review Administrator, Review Branch, DEA, NIDDK, Natcher Building Room 6AS37B, National Institutes of Health, Bethesda, MD 20892–6600, (301) 594–8894.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel. ZDK1 GRB–C J3 P.

Date: December 16–18, 1999.

Time: 7:00 p.m. to 12:00 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn, 5 Blossom Street, Boston, MA 02114.

Contact Person: Dan E. Matsumoto, Scientific Review Administrator, Review Branch, DEA, NIDDK, Natcher Building Room 6AS37B, National Institutes of Health, Bethesda, MD 20892–6600, (301) 594–8894.

(Catalogue of Federal Domestic Assistance Program Nos. 93.847, Diabetes, Endocrinology and Metabolic Research; 93.848, Digestive Diseases and Nutrition Research; 93.849, Kidney Diseases, Urology and Hematology Research, National Institutes of Health, HHS)

Dated: November 24, 1999.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 99–31340 Filed 12–2–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Disease; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The contract proposals and the discussions could disclose