nearby residents during the operational phase of the project were evaluated. The risks were deemed to be negligible, and mitigable through adherence to guidelines outlined in Biosafety in Microbiological and Biomedical Laboratories, a joint publication of the NIH and Centers for Disease Control, as well as other standards for safe operational practices.

Conclusion

Based upon review and careful consideration, the NIH has decided to implement the Proposed Action, the construction of the Integrated Research Facility at the Rocky Mountain Laboratories in Hamilton, Montana.

The decision was based upon review and careful consideration of the impacts identified in the Final EIS; public comments received throughout the National Environmental Policy Act process, including comments on the Draft EIS and Supplemental Draft EIS and those provided during the required 30-day waiting period for the Final EIS. Other relevant factors included in the decision, such as NIAID's mandate to conduct research on agents of emerging and re-emerging infectious diseases were carefully considered. The unique scientific capabilities of the scientists at the RML, who require the selected alternative in order to perform their expanded research mission, was also a factor in the decision making process.

Dated: June 7, 2004.

Leonard Taylor, Jr.,

Acting Director, Office of Research Facilities Development and Operations, National Institutes of Health.

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BILLING CODE 4140–01–P

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 inventions listed below are owned by an agency of the U.S. Government and are 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 applications 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 applications.

Identification of a Tricyclic Amino Amide (NSC–644221) Inhibitor of the Hypoxic Signaling Pathway

Giovanni Melillo (NCI).

DHHS Reference Nos. E–185–2004/0–US–01 and E–185–2004/1–US–01.

Licensing Contact: George Pipia; 301/435–5560; *pipiag@mail.nih.gov.*

This invention describes the identification of a tricyclic (1,4-dioxane) amino amide with confirmed potent activity in inhibiting HIF–1 transcriptional activity.

HIF–1 is a transcription factor and plays an important role in adaptation of cancer cells to an hypoxic environment. HIF–1 significantly increases the ability of cancer cells to survive under strenuous conditions. It contributes to the ability of cancer cells to migrate and invade surrounding tissue, and is important for the formation of new blood vessels that are essential for growth and metastasis of cancer cells. Thus HIF–1 mediates survival and spreading of cancer cells. Previous studies have shown that HIF–1 is also important in human cancers, and therefore, inhibition of HIF–1 activity is contemplated in the field as a therapy for cancer patients.

The inventors, using a cell-based high throughput screen, identified a new compound, NSC–644221, with potent inhibitory activity of the HIF–1 pathway. The compound inhibits expression of HIF–1 and reduces its accumulation in the cell. This compound also inhibits expression of endogenous genes that are under control of HIF–1, such as Vascular Endothelial Growth Factor (VEGF) that is essential for the formation of new blood vessels. The NIH inventors currently are testing the compound in angiogenesis assays and are starting preclinical studies of the compound using animal cancer models.

SH2 Domain Binding Inhibitors

Terrence R. Burke, Jr., Zhen-Dan Shi, Kyeong Lee (NCI).

U.S. Provisional Application No. 60/504,241 filed 18 Sep 2003 (DHHS Reference No. E–315–2003/0–US–01).

Licensing Contact: George Pipia; 301/435–5560; *pipiag@mail.nih.gov.*

The present invention provides for ultra-potent Grb2 SH2 domain-binding compounds, or a pharmaceutically acceptable salt thereof. The compounds of the present invention represent tetrapeptide mimetics whose conformation is constrained through macrocyclization. Low picomolar binding affinity is achieved in *in vitro* Grb2 SH2 domain binding assays. Addition of covered agent to the extracellular media of erbB–2 over-expressing breast cancer cells at low nanomolar concentrations results in effective intracellular blockade of Grb2 association with activated cytoplasmic erbB–2 tyrosine kinase. Antimitogenic effects are observed in erbB–2-dependent breast cancer cells in culture at sub-micromolar concentrations. The present invention further provides a pharmaceutical composition comprising a pharmaceutically or pharmacologically acceptable carrier and a compound of the present invention. The present invention also provides a method for inhibiting an SH2 domain from binding with a phosphoproteins comprising contacting an SH2 domain with a compound of the present invention. The present invention also provides a method of preventing or treating a disease state or condition by the use of the compound. While the invention has been described and disclosed below in connection with certain embodiments and procedures, it is not intended to limit the invention to those specific embodiments. Rather it is intended to cover all such alternative embodiments and modifications as fall within the spirit and scope of the invention.

This research is described, in part, in: Z. Shi *et al.*, ''A novel macrocyclic tetrapeptide mimetic that exhibits low-picomolar Grb2 SH2 domain-binding affinity,'' Biochem. Biophys. Res. Commun. (2003 Oct 17) 310(2):378–383, doi:10.1016/j.bbrc.2003.09.029; Z. Shi *et al.*, ''Synthesis of a 5-methylindolyl-containing macrocycle that displays ultrapotent Grb2 SH2 domain-binding affinity,'' J. Med. Chem. (2004 Feb 12) 47(4):788–791, doi:10.1021/jm030440b.

Dated: June 4, 2004.

Steven M. Ferguson,

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

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