doses of cocaine. In a cocaine self-administration reinstatement model in monkeys that may model relapse following a period of abstinence in humans, a D1 agonist can reduce the effect of a priming dose of cocaine that might lead to relapse. In humans, a D1 agonist blunted the subjective effects of cocaine, and reduced craving for cocaine and other drugs.

Rationale for Kappa-Opioid Antagonists

Kappa-opioid antagonists block receptors for the endogenous opioid ligand dynorphin, which is up-regulated by chronic opioid use and has been linked to dysphoric states that can lead to opioid relapse. There is also evidence that kappa antagonists have anti-stress effects, which may make them useful in the prevention of relapse to drugs of abuse like cocaine.

Rationale for Compounds Not Named Above To Be Considered

The possibility exists that compounds that have mechanisms of action other than those described in items 1–7 above may be potentially useful in the treatment of drug dependence. NIDA will consider candidate compounds from other classes if, and only if, scientific evidence exists to support a compelling rationale for testing and/or development.

Potential for Collaborative Development

NIDA does not currently own or have adequate access to compounds representing the referenced classes. To this end, NIDA is seeking to enter into a CRADA collaboration with entities that may qualify as CRADA collaborators. These would include, but not be limited to pharmaceutical companies, academic research institutions with company affiliations, and other commercial entities with adequate capacity to participate in the evaluation and development of candidate compounds from the classes listed for the treatment (reduction in use in drug dependent persons and prevention of relapse in formerly drug dependent individuals). NIDA will consider proposals from all qualified entities and will, subject to negotiation of the details of a mutually agreed upon research plan and CRADA, provide the CRADA collaborator access to services and data generated from its comprehensive preclinical and clinical trials facilities. CRADA Collaborators will be able to utilize data derived from the CRADA to pursue regulatory filings in the U.S. and abroad. Compounds of the representative classes at all stages of development will be considered. NIDA's Medications Development Program possesses the capacity to perform pharmacological and toxicological testing, pharmacokinetics, dosage form development, regulatory management, and clinical testing from Phase I through Phase III testing and is willing to apply these capacities in the assessment of specified compounds as may be warranted.

Following classical drug development schema, decisions to proceed to each subsequent preclinical or clinical study will be based on data derived from previous or ongoing studies. Assuming adequate safety can be demonstrated, it is NIDA's intention to provide clinical trials services sufficient to permit, subject to FDA approval, research and development up to and including Phase II hypothesis testing. Assuming demonstration of safety and efficacy at the conclusion of Phase II trials and subject to negotiation, NIDA will, in some cases, also consider collaborations to undertake Phase III trials sufficient to permit collaborator to seek a U.S. New Drug Approval (NDA).

No funding may be provided to a collaborator under a CRADA: all assistance is provided ''in-kind''. Therefore the collaborator will bear the financial and organizational costs of meeting its obligations under collaborator's portion of any research plan that may be negotiated. Benefits of collaborating with NIDA beyond access to NIDA's clinical and preclinical resources include the option to an exclusive license to any subject inventions made by NIDA scientists during the course of the collaboration, and exclusivity with respect to submitting data from the collaboration for regulatory filings.

Selection Factors and Considerations

Selection factors and considerations of importance of NIDA include:

1. It is mandatory that collaborators possess commercialization rights to the compound sufficient to permit research and commercial development for the intended field of use, *i.e.*, treatment of drug dependence. In the event the collaborator does not own the compound or composition, collaborator must provide appropriate documentation of a license permitting research and commercialization for the field of use sufficient to permit the CRADA to proceed.

2. NIDA will consider the amount of research and development documentation and experience already in the collaborator's possession. NIDA will sign appropriate confidential disclosure agreements in order to review confidential and unpublished data. While NIDA will review all proposals concerning candidate compounds representative of the listed classes, it will give a higher priority to proposals that can document a more advanced level of development with the proposed compound(s).

3. NIDA will consider the amount and type of research and development resources the collaborator proposes to undertake as part of a proposed CRADA.

4. NIDA will consider the background, experience, and expertise in medications development of the proposed collaborator.

Dated: August 27, 2004.

Steven M. Ferguson,

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

[FR Doc. 04–20290 Filed 9–7–04; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute: Cooperative Research and Development Agreement (''CRADA'') Opportunity and Licensing Opportunity: Scientific and Commercial Drug Development To Exploit Antiangiogenic Activity Targeting Adrenomedullin Gene Products

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

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) is currently seeking Cooperative Research and Development Agreement (CRADA) collaborator(s) to work with investigators in the Center for Cancer Research (CCR) to explore, for drug development and clinical testing, novel antiangiogenic agents that target adrenomedullin gene products. Research and development may include development of blocking reagents (humanized antibodies, peptide antagonists, small molecules), formulation for systemic and topical application, preclinical animal studies, and clinical trials. Licensing is available for background inventions related to this technology.

DATES: Parties interested in a CRADA collaboration should notify the Technology Transfer Branch of the NCI in writing of their interest no later than October 25, 2004. The written notice should briefly address the selection criteria listed below under Supplementary Information.

Licensing inquiries/applications are accepted by the NIH Office of Technology Transfer at any time.

ADDRESSES: For information on the CRADA Opportunity, please contact: Julianne Chappell, J.D., Technology Transfer Specialist, Technology Transfer Branch, National Cancer Institute, NIH, 6120 Executive Boulevard, Suite 450, Rockville, MD 20852; Phone: (301) 496–0477; Fax: (301) 402–2117; e-mail: *jchappel@mail.nih.gov.*

For information on the Licensing Opportunity, please contact: Pradeep Ghosh, J.D., Ph.D., M.B.A., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Blvd., Suite 325, Rockville, MD 20852; Phone: (301) 435–5282; Fax: (301) 402–0220; e-mail: *ghoshpr@mail.nih.gov.* Information about patent application(s) and pertinent information not yet publicly described can be obtained under the terms of a Confidential Disclosure Agreement. Respondees interested in licensing the technology will be required to submit an Application for License to Public Health Service Inventions.

SUPPLEMENTARY INFORMATION:

Scientific Background: Tumor growth requires a series of extracellular signaling molecules that induce cell proliferation and production of new blood vessels (angiogenesis) and reduce apoptosis (programmed cell death) of the tumor cells. Agents that block angiogenesis or tumor cell proliferation have been successfully used in the clinic to reduce tumor burden.

The regulatory peptide adrenomedullin (AM) is a multifunctional molecule that has been recently characterized by researchers at the CCR, through use of *ex vivo* and *in vivo* animal models, as a proangiogenic factor. In addition to inducing angiogenesis, AM functions in cancer cells as an autocrine growth factor, enhances thymidine incorporation, reduces apoptosis, and is induced by hypoxia, thus identifying this peptide as an important tumor cell survival factor and a potential target for antitumor therapy.

AM is synthesized as a prohormone that contains another biologically active peptide, proAM N-terminal 20 peptide. CCR has determined that PAMP is approximately one million times more potent than well-known angiogenic factors such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). CCR scientists have characterized PAMP's angiogenic activity in both *in vitro* and *in vivo* assays, including a chick aortic ring angiogenesis assay and a nude mouse angiogenesis assay. Inhibitors of PAMP have been shown to inhibit angiogenesis *in vivo.*

Current Status of the Technology: There is a continuing market need for new therapeutic interventions to inhibit angiogenesis in diseases dependent on the development of new vasculature, or to promote angiogenesis in conditions ameliorated by such development. In addition to the discoveries described above, CCR scientists have developed a method of screening small molecule libraries for AM agonists and antagonists and have identified a number of potential small molecule candidates for drug development; CCR has also identified antagonistic peptide fragments and monoclonal antibodies against AM and PAMP that may warrant development. These discoveries form the basis of the background intellectual property, identified below in the **Patent Status and Pertinent References** section. AM gene products and their agonists or antagonists may prove effective in areas such as cancer treatment, wound healing, diabetic retinopathy, endometriosis, psoriasis, arthritis, coronary artery disease, peripheral vascular disease, and cerebral ischemia.

CRADA Proposal: CRADA collaborative efforts will explore the specific and highly active pathway discussed above. Inhibition of either AM or PAMP *in vivo* with a variety of agents (monoclonal antibodies, peptide analogs, small molecule antagonists) results in significant reduction of tumor growth. Therefore, CRADA studies may focus on the utilization of that technology in tumor management, and the NCI proposal delineated below reflects that approach. The Institute, however, is open to proposals directed at other diseases and conditions in which angiogenesis may play a major role (arthritis, impaired wound healing, ischemia, retinal degeneration, coronary artery disease, etc).

Proposed NCI Contribution: The role of the NCI will include, but not be limited to, the following:

1. Conduct *in vitro* and *in vivo* analysis of the antitumor capabilities of the generated blocking reagents.

2. Test biological specimens from the animal and clinical phases to evaluate whether the intermediate endpoints (diminution of peptide contents) are reached.

Proposed CRADA Collaborator Contribution: The role of the CRADA collaborator(s) will include, but not be limited to, the following:

1. Manufacture enough of the blocking reagents (humanized monoclonal antibodies, peptide antagonists, small molecules) under FDA approved standards.

2. Formulate the initial lot of agent for topical and systemic administration.

3. Perform pharmacokinetic and pharmacodynamic evaluation in animal models.

4. Collaborate in the planning and support clinical development leading to FDA approval and marketing.

5. Conduct clinical trials.

Proposed Joint Contribution: NCI and CRADA collaborator(s) will:

1. Design a CRADA research plan and interpret the data generated under the research plan.

2. Publish the results and share all data as soon as they become available.

Selection Criteria for Choosing the CRADA Collaborator May Include:

1. A demonstrated background and expertise in conducting clinical trials, and in the generation of the blocking reagents.

2. The demonstration of adequate resources to perform the research and development necessary for commercialization of the technology and any inventions.

3. A demonstrated record of success in the commercial development and production of products related to this area of technology.

4. The level of financial and staffing support the CRADA collaborator will provide for CRADA-related activities.

5. The willingness to cooperate with the NCI in the collection, evaluation, and maintenance of data from preclinical and clinical trials of investigational agents; and in the timely publication of research results.

6. The agreement to be bound by the Department of Health and Human Services (DHHS) regulations involving the use of human and animal subjects, and human tissue.

7. The willingness to accept the legal provisions and language of the CRADA. These provisions govern the distribution of future patent rights to CRADA inventions. Generally, the rights of ownership are retained by the organization which is the employer of the inventor, with (a) the grant of a license for research and other Government purposes to the Government when the CRADA collaborator's employee is the sole inventor, or (b) the grant of an option to elect an exclusive or non-exclusive license to the CRADA collaborator when the Government employee is the sole inventor.

8. The willingness to obtain any necessary background licenses to NIH technology.

Terms/Licensing Potential/Patent Status:

1. No funding from the Government is available to collaborator under a CRADA.

2. Non-exclusive license option available for background rights. Exclusive license rights may be available in a specified field of use.

3. One patent has been issued related to Adrenomedullin and PAMP and other related patent applications are pending.

4. In case, as a result of the CRADA work, a joint intellectual property is developed, the CRADA partner may have a right to file a joint patent application.

Patent Status and Pertinent References:

U.S. Provisional Patent Application Number 60/425,018, filed November 7, 2002, ''A New Target for Angiogenesis and Anti-angiogenesis Therapy.''

Patent Application Number PCT/US2003/035633, filed November 7, 2003, ''A New Target for Angiogenesis and Anti-angiogenesis Therapy.''

U.S. Provisional Application Serial No. 60/500,650 filed on 09/08/2003; ''A new method to screen small molecule libraries and biologically active compounds that modulate adrenomedullin and gastrin releasing peptides.'' International Publication Number WO 2004/043383 A2, published May 27, 2004, ''A New Target for Angiogenesis and Anti-angiogenesis Therapy.''

López J, Martínez A. Cell and molecular biology of the multifunctional peptide, adrenomedullin. *International Review of Cytology* 221:1–92 (2002).

Martínez A, Vos M, Guédez L, Kaur G, Chen Z, Garayoa M, Pío R, Moody T, Stetler-Stevenson WG, Kleinman HK, Cuttitta F. The effects of adrenomedullin overexpression in breast tumor cells. *Journal of the National Cancer Institute* 94: 1226–1237 (2002).

Cuttitta F, Pío R, Garayoa M, Zudaire E, Julián M, Elsasser TH, Montuenga LM, Martínez A. Adrenomedullin functions as an important tumor survival factor in human carcinogenesis. *Microscopy Research and Technique* 57:110–119 (2002).

Pío R, Martínez A, Cuttitta F. Cancer and diabetes: two pathological conditions in which adrenomedullin may be involved. *Peptides* 22:1719–1729 (2001).

Pío R, Martínez A, Unsworth EJ, Kowalak JA, Bengoechea JA, Zipfel PF, Elsasser TH, Cuttitta F. Complement factor H is a serum binding protein for adrenomedullin. The resulting complex modulates the bioactivities of both partners. *Journal of Biological Chemistry* 276:12292–12300 (2001).

Martínez A, Julián M, Bregonzio C, Notari L, Moody TW, Cuttitta F. Identification of vasoactive non-peptidic positive and negative modulators of adrenomedullin using a neutralizing monoclonal antibody-based screening strategy. *Endocrinology* 145:3858–3865 (2004).

Martínez A, Zudaire E, Portal-Núnez S, Guédez L, Libutti SK, Stetler-Stevenson WG, Cuttitta F. Proadrenomedullin—terminal 20 peptide is a potent angiogenic factor and its inhibition results in reduction of tumor growth. *Cancer Research* in press (2004).

Dated: August 25, 2004.

Karen Maurey,

Acting Chief, Technology Transfer Branch, National Cancer Institute, National Institutes of Health.

Dated: August 30, 2004.

Steven M. Ferguson,

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

[FR Doc. 04–20291 Filed 9–7–04; 8:45 am]

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.

Integrin Alpha-V Beta-3 Antagonists for Use in Imaging and Therapy

S. Narasimhan Danthi *et al.* (CC), U.S. Patent Application filed 04 Aug 2004 (DHHS Reference No. E–170–2004/0–US–01).

Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov*.

Available for licensing are compounds as shown below for imaging and therapy. These compounds are integrin $\alpha_v\beta_3$ receptor antagonists and are described and claimed in a patent application available for review. The patent application also includes claim coverage for the administration of these compounds containing a detectable moiety or pharmaceutical compositions of such imaging agents as part of the imaging of cells that express integrin $\alpha_v\beta_3$.