regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug and biological product development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations, the Japanese Ministry of Health and Welfare, the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, the Canadian Health Protection Branch, and the European Free Trade Area.

To facilitate the process of making ICH guidances available to the public, the agency is changing its procedures for publishing ICH guidances. Beginning April 2000, we will follow the same procedures we follow with other agency guidances. Rather than including the text of ICH guidances in the **Federal Register**, we will publish a notice in the **Federal Register** announcing the availability of an ICH guidance. The ICH guidance will be placed in the docket and can be obtained through regular agency sources (see the **ADDRESSES** section). The draft guidance will be left in the original ICH format. The final guidance will be reformatted to conform to GGP style before publication.

In March 2000, the ICH Steering Committee agreed that a draft guidance entitled ''E12A Principles for Clinical Evaluation of New Antihypertensive Drugs'' should be made available for public comment. The draft guidance, which is the product of the Efficacy Expert Working Group of the ICH, was designated an ICH principle document. Because requirements of the three ICH regions differ in some specifics, this ICH principle document will not be subject to the usual ICH step procedures leading to a fully harmonized document. Comments about this draft will be forwarded to the three regulatory parties for consideration.

In accordance with FDA's good guidance practices (GGP's)(62 FR 8961, February 27, 1997), this document is being called a guidance, rather than a principle document.

The draft guidance is intended to provide general principles for the clinical evaluation of new antihypertensive drugs. It describes core principles that are accepted in the three ICH regions for the evaluation of antihypertensives, including assessments of efficacy and safety and choice of study population. The draft guidance is meant to be used together with other ICH clinical guidances.

This draft guidance represents the agency's current thinking on the clinical evaluation of new antihypertensive drugs. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

Interested persons may submit to the Dockets Management Branch (address above) written comments on the draft guidance by November 7, 2000. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: August 2, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00–20172 Filed 8–8–00; 8:45 am]

BILLING CODE 4160–01–F

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 agencies 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.

Methods for Reducing Tumor Growth and Metastasis by Inhibiting MCP–1 Activity

WJ Murphy, JJ Oppenheim, and R Salcedo (all of NCI)
Serial No. 60/205,757 filed 19 May 2000
Licensing Contact: Susan S. Rucker; 301/496–7056 ext. 245; e-mail: ruckers@od.nih.gov

This application relates to methods for the inhibition of tumor growth and metastasis. The inhibition of tumor growth and metastasis is based on the demonstration that certain inhibitors of the chemokine MCP–1 (monocyte chemotactic protein 1 also known as JE) inhibit angiogenesis in *in vitro* and *in vivo* model systems. In addition, methods for identifying other inhibitors are described. In addition to this application the NIH has other intellectual property related to MCP–1 which is available for license, including U.S. Patents 5,714,578, 5,532,144, 5,179,078, 5,212,073 and 5,278,287.

This work has been published, in part in Blood 96(1): July 1, 2000.

The Use of an Inducible Plasmid Vector Encoding for Active TGF–β for the Treatment of Autoimmune Diseases

A Kitani, I Fuss, K Nakamura and W Strober(NIAID)
DHHS Reference No. E–096–00/0 filed 20 Apr 2000
Licensing Contact: Susan S. Rucker; 301/496–7056 ext. 245; e-mail: ruckers@od.nih.gov

This application describes a composition and method for treating inflammatory bowel disease or other autoimmune diseases. The composition utilizes a vector which contains a first

promoter which controls the expression of a regulatory transcription factor and a second inducible promoter which controls the expression of the gene of interest. The preferred gene of interest encodes an isoform of TGF–β such as TGF–β_1 or TGF–β_3. The isoform of TGF–β does not have to be hTGF–β and can be a latent or active isoform of TGF–β. The preferred inducible promoter is TRE–CMV which can be induced using doxycycline. The usefulness of the composition for treating autoimmune diseases is demonstrated in the application in a murine model of inflammatory bowel disease in which intestinal inflammation was abrogated by the administration of a plasmid vector encoding active TGF–β. The composition may be administered by a variety of delivery systems and intranasal delivery is exemplified.

Serum Free Medium

F Luyten, L Erhlacher (NIDCR)

Serial No. 09/468,562 filed 21 Dec 1999

Licensing Contact: Susan S. Rucker; 301/496–7056 ext. 245; e-mail: ruckers@od.nih.gov

The technology described and claimed in this application relates to the development of a serum-free medium which is particularly useful for the culture, both growth and expansion, of chondrocytes. More particularly, the medium allows chondrocytes to maintain their cartilaginous phenotype. Chondrocytes cultured in this medium may be used to repair joints having cartilage damage from diseases such as rheumatoid arthritis.

This work has been published, in part, at L Erhlacher, et al. ''Presence of cartilage-derived morphogenetic proteins in articular cartilage and enhancement of matrix replacement in vitro'' Arthritis Rheum. 1998 Feb;41(2):263–73. The material found in the patent application has been published as WO 98/59035 (Dec 30, 1998).

PHS also owns additional intellectual property, related to cartilage derived morphogenetic proteins 1 and 2 (CDMP–1/GDF5 and CDMP–2/GDF6) which may be used in conjunction with this technology. The work related to CDMP–1 and CDMP–2 has been published as WO 96/14335 (May 17, 1996) and at originally at Chang, *et al.*, ''Cartilage-derived morphogenetic proteins. New members of the transforming growth factor-beta superfamily predominantly expressed in long bones during human embryonic development'' J Biol Chem. 1994 Nov 11;269(45):28227–34.

Mutant of RAD51 Gene and Its Use in the Diagnosis of Predisposition to Breast Cancer

Jeffery P. Struewing, Weiching Wang (NCI)

DHHS Reference No. E–231–99/0 filed 10 Sep 1999

Licensing Contact: Vasant Gandhi; 301/496–7056 ext. 224; e-mail: gandhiv@od.nih.gov

This invention relates to a mutant of the RAD51 gene and its use in diagnosing individuals predisposed to breast cancer involving BRCA1 and/or BRCA2. The mutant contains a guanine-to-cytosine transversion at nucleotide position 135 in the 5′ untranslated region of the RAD51 gene. The invention relates to the nucleotide sequence of the mutant RAD51 gene, associated vector constructs and host cells, and diagnostic methods. Epidemiological and in vitro biochemical characterization studies are in progress.

Dated: July 31, 2000.

Jack Spiegel,

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

[FR Doc. 00–20036 Filed 8–8–00; 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.

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Mouse Strain Deficient for the Protein MT1–MMP (MMP14)

Kenn Holmbeck *et al.* (NIDCR)

DHHS Reference No. E–191–00/0

Licensing Contact: Marlene Shinn; 301/496–7056 ext. 285; e-mail:shinnm@od.nih.gov

Matrix metalloproteinases (MMPs) constitute a family of zinc endopeptidases that are capable of degrading most of the structural components of the extracellular matrix. The NIH announces a new mouse model deficient in MT1–MMP activity. This mouse model demonstrates the necessity of MT1–MMP for normal development of cranial bones, long bones and general housekeeping of connective tissues throughout the body. Since studies in the pharmaceutical industry are currently aiming at inhibiting the MMP family at large for purposes of cancer and arthritis treatment, this mouse model provides a valuable demonstration of the possible side effects that such treatment may lead to. As such this mouse model may also provide a test bed for the substances that can alleviate the unwanted side effects of MMP inhibitor treatments.

HIV Protease Inhibitors, Ritonavir and Saquinavir Are Potent Inhibitors of Calcium Activated Neutral Peptidases, Calpains

Paolo DePetrillo, Wenshuai Wan (NIAAA)

DHHS Reference Number E–041–00/0 filed 04 May 2000

Licensing Contact: John Rambosek, Ph.D.; 301/496–7056 ext. 270; e-mail: rambosej@od.nih.gov

This invention discloses a novel use for compounds that are inhibitors of the HIV Protease: specifically, the invention shows that HIV protease inhibitors are also potent inhibitors of Calcium Activated Neutral Proteases (Calpain). Activation of calpain plays a central role in tissue destructive processes following tissue trauma caused by, for example, stroke, heart attack, brain trauma, and spinal cord injury. Thus specific inhibition of calpain is an important therapeutic target in these disease processes. The estimated total market for these classes of therapeutic agents is on the order $500 million to 1 billion annually. The inventor has specifically demonstrated that *in vitro* the HIV protease inhibitors ritonavir and saquinavir are also potent inhibitors of calpain. This technology has a variety of practical applications: (1) Existing HIV