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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, HHS

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. 209 and 37 CFR Part 404 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.

FOR FURTHER INFORMATION: 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.

SUPPLEMENTARY INFORMATION: Technology descriptions follow.

Interferon Alpha Hybrids

Description of Technology: Available for licensing are hybrid interferon alpha (INF-alpha) polypeptides constructed by combinations of INFalpha21b and INFalpha2c, and mutants of these hybrids. These hybrid constructs have resulted in novel IFNs that either combine different biological properties from the parent proteins or have significantly different biological activity from both the parents in anti-proliferative, anti-viral, or competitive binding properties. For instance, the hybrid designated HY-3 has higher anti-proliferative activity in Daudi, WISH, and primary human lymphocyte cells exhibiting approximately 6 times higher anti-proliferative activity than either parent IFN. These IFN hybrids provide a powerful tool for studying the structure-function relationship of these molecules. The engineered IFN-alpha proteins may have important new therapeutic applications and may provide greater insights into understanding of the clinical activities of existing IFN-alphas.

Also available for licensing are hybrid INF-alpha nucleic acids encoding the hybrid polypeptides as well as cells, vectors, pharmaceutical compositions with these nucleic acid sequences.

Potential Commercial Applications:

- Anti-viral and cancer therapeutics

- Research tool to study IFN-alpha functions

Competitive Advantages:

- Ease of manufacture
- Strong anti-viral activity

Development Stage: In vitro data available

Inventors: Kathryn C. Zoon (NIAID), Joseph B. Bekisz (NIAID), Mark P. Hayes (FDA), Renqiu Hu (FDA)

Publications:

1. Hu R, et al. Protein engineering of interferon alphas. *Methods Mol Med.* 2005;116:69-80. [PMID 16000855]
2. Hu R, et al. Human IFN-alpha protein engineering: the amino acid residues at positions 86 and 90 are important for antiproliferative activity. *J Immunol.* 2001 Aug 1;167(3):1482-9. [PMID 11466368]
3. Hu R, et al. Divergence of binding, signaling, and biological responses to recombinant human hybrid IFN. *J Immunol.* 1999 Jul 15;163(2):854-60. [PMID 10395679]

Intellectual Property: HHS Reference No. E-068-1998/0 -

- US Patent No. 6,685,933 issued 03 Feb 2004
- US Patent No. 7,235,232 issued 26 Jun 2007

Licensing Contact: Peter Soukas; 301-435-4646; ps193c@nih.gov

Novel Treatment for Anemia and Polycythemia: AVPR1B Molecules Modulating Erythropoiesis

Description of Technology: Anemia can be caused by chronic diseases, chemotherapy, or radiation. Erythropoietin is commonly used to stimulate red blood cell production for anemia treatment, but it takes about a week to manifest its clinical effect. The subject invention describes the arginine vasopressin receptor 1B (AVPR1B) stimulatory molecules that can be used to stimulate hematopoietic stem cell proliferation. Preliminary results from animal studies suggest that the number of red blood cells and their precursors significantly increased on day 2 following AVP administration, an onset time much faster than erythropoietin. The AVPR1B stimulatory molecules can be used to jumpstart the system and erythropoietin can be used to sustain the effect. In addition, the AVPR1B inhibitory molecules can be used to suppress hematopoietic stem cell proliferation to treat polycythemia (overproduction of red blood cells).

Potential Commercial Applications:

- Treatment of anemia caused by chronic diseases, chemotherapy, or radiation.
- Anemia patients who do not respond to erythropoietin.
- Polycythemia treatment.

Competitive Advantages: AVPR1B stimulatory molecules act faster than the commonly used erythropoietin for anemia treatment.

Development Stage:

- Early-stage
- In vivo data available (animal)

Inventors: Eva Mezey and Miklos Krepuska (NIDCR); Balazs Mayer and Krisztian Nemeth (Semmelweis University Medical School)

Intellectual Property: HHS Reference No. E-619-2013/0 -

- US Application No. 61/885,258 filed October 01, 2013 (E-619-2013/0-US-01)
- PCT Application No. PCT/US2014/058613 filed October 01, 2014 (E-619-2013/0-PCT-02)

Licensing Contact: Sally Hu, Ph.D., M.B.A.; 301-435-5605; hus@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize treatment for anemia and polycythemia. For collaboration opportunities, please contact David Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

Modified AAV5 Vectors for Enhanced Transduction and Reduced Antibody Neutralization

Description of Technology: Adeno-associated viruses (AAVs) are small nonpathogenic viruses and can integrate into the cellular genome. AAV vectors are among the most frequently used viral vectors for gene therapy because AAV vectors can infect both dividing and non-dividing cells, and can establish long-term transgene expression. Two major issues in gene therapy are the ability to efficiently transduce the target cells and to evade the immune response to vectors. The subject invention describes a mutated AAV serotype 5 by modifying sialic acid binding regions which mediate viral entry into host cells. Preliminary results from animal studies suggest that this modification can increase transduction by 3-4 folds in salivary glands and muscle, and can significantly decrease the potential of being neutralized by preexisting antibodies

compared to the wild type. Thus, the modified AAV5 vectors seem to be optimal for gene therapy.

Potential Commercial Applications: Genetically engineered AAV5 vectors for gene therapy.

Competitive Advantages:

- Enhanced transduction activity.
- Reduced the potential for being neutralized by preexisting antibodies.

Development Stage:

- Early-stage
- In vivo data available (animal)

Inventors: John Chiorini and Sandra Afione-Wainer (NIDCR); Mavis Agbandje-Mckenna and Sujata Halder (University of Florida)

Publications:

1. Afione S, et al. Identification and mutagenesis of the adeno-associated virus 5 sialic acid binding region. *J Virol.* 2015 Feb; 89(3): 1660-72. [PMID 25410855]
2. Chiorini J, et al. AAV4 Vector and the uses thereof. U.S. Patent 6,468,524, issued on October 22, 2002.
3. Chiorini J, et al. AAV5 Vector and the uses thereof. U.S. Patent 7,479,554, issued January 20, 2009, and U.S. Patent 6,984,517, issued on January 10, 2006.
4. Chiorini J, et al. AAV5 Vector for transducing brain cells and lung cells. U.S. Patent 6,855,314, issued on February 15, 2005.

Intellectual Property: HHS Reference No. E-097-2015/0 - US Application No. 62/143,524 filed April 6, 2015

Related Technologies:

- E-175-2015: US 62/160,552.
- E-736-2013: PCT/US14/59825.
- E-142-2011 family: PCT/US12/34268, CA, EP and US.
- E-087-2011 family: PCT/US12/33556, EP and US.
- E-232-2011: US 14/428,929.
- E-194-2010: US 8,808,684.
- E-179-2005: US 8,283,151.
- E-227-2004: US 7,407,801.
- E-329-2003 family: US 8,137,960, US 8,685,722.
- E-105-2003: US 8,927,269.
- E-308-2001: US 7,419,817.
- E-071-2000: US 6,468,524.
- E-127-1998 family: US 6,984,517, AU, CA, EP, and JP.

Licensing Contact: Sally Hu, Ph.D., M.B.A.; 301-435-5606; hus@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize modified AAV5 vector for gene therapy. For collaboration opportunities, please contact David Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

A Novel Adeno-Associated Virus for Gene Therapy

Description of Technology: Adeno-associated viruses (AAVs) are small nonpathogenic viruses and can integrate into the cellular genome. AAV vectors are among the most frequently used viral vectors for gene therapy because AAV vectors can infect both dividing and non-dividing cells, and can establish long-term transgene expression. The subject invention describes a novel AAV termed “44-9.” AAV44-9 based vectors have high gene transfer activity in a number of cell types, including salivary gland cells, liver cells, and different types of neurons (e.g., cells of the cortex, olfactory bulb, and brain stem, and Purkinje cells of the cerebellum). These vectors can deliver heterologous genes to particular target cells through site-specific administration. Preliminary results from animal studies suggest that AAV44-9 vectors can efficiently deliver genes of interest, and the protein products of the delivered genes can be detected in bloodstream and at the local tissues. Therefore, these vectors are suitable for gene therapy for cells/tissues that are not efficiently targeted by other vectors.

Potential Commercial Applications: AAV44-9 can be used as a delivery vector in gene therapy.

Competitive Advantages:

- High gene transfer activity in a number of cell types including salivary gland cells, liver cells, and different types of neurons (e.g., cells of the cortex, olfactory bulb, and brain stem, and Purkinje cells of the cerebellum).
- As a gene transfer vector for cells that are not efficiently targeted by other vector.

Development Stage:

- In vitro data available

- In vivo data available (animal)

Inventors: John Chiorini and Giovanni Pasquale (NIDCR)

Publication: Schmidt M, et al. Identification and characterization of novel adeno-associated virus isolates in ATCC virus stocks. J Virol. 2006 May; 80 (10): 5082-5098. [PMID 16641301]

Intellectual Property: HHS Reference No. E-175-2015/0 - US Application No. 62/160,552 filed May 12, 2015

Related Technologies:

- E-097-2015: US 62/143,524.
- E-736-2013: PCT/US14/59825.
- E-142-2011 family: PCT/US12/34268, CA, EP and US.
- E-087-2011 family: PCT/US12/33556, EP and US.
- E-232-2011: US 14/428,929.
- E-194-2010: US 8,808,684.
- E-179-2005: US 8,283,151.
- E-227-2004: US 7,407,801.
- E-329-2003 family: US 8,137,960, US 8,685,722.
- E-105-2003: US 8,927,269.
- E-308-2001: US 7,419,817.
- E-071-2000: US 6,468,524.
- E-127-1998 family: US 6,984,517, AU, CA, EP, and JP.

Licensing Contact: Sally Hu, Ph.D., M.B.A.; 301-435-5606; hus@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize AAV44-9 vector for gene therapy. For collaboration opportunities, please contact David Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

WNT1-Induced Secreted Protein-1 Knockout Mouse Model

Description of Technology: WNT1-induced secreted protein-1 (WISP1) is expressed at high levels in osteoblasts and their precursors. WISP1 plays an important role in various aspects of bone formation. Scientists at the NIH generated *Wisp1*-deficient (*Wisp1*^{-/-}) mice. Deletion of *Wisp1* resulted in a decrease in bone mineral density, total bone volume, bone thickness, and biomechanical strength. *Wisp1* knockout mouse model can be used to study the molecular mechanisms of bone turnover and patho/physiology of tissues that express WISP1.

Potential Commercial Applications:

- To study the molecular mechanisms of bone formation and osteodifferentiation.
- To study the patho/physiology of tissues that express WISP1, including cartilage during osteoarthritis, healing skin, and other soft tissues including lung, pancreas, and heart.

Development Stage: In vivo data available (animal)

Inventors: Marian F. Young, Mitsuaki Ono, Azusa Maeda (all of NIDCR)

Publication: Maeda A, et al. WNT1-induced secreted protein-1 (WISP1), a novel regulator of bone turnover and Wnt signaling. J Bio Chem. 2015 May 29;290(22):14004-18. [PMID 25864198]

Intellectual Property: HHS Reference No. E-234-2015/0 - Research Tool.
Patent protection is not being pursued for this technology.

Licensing Contact: Sally Hu, Ph.D., M.B.A.; 301-435-5606; hus@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize WNT1-Induced Secreted Protein-1 Knockout Mouse Model. For collaboration opportunities, please contact David Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

Dated: July 30, 2015

Richard U. Rodriguez, M.B.A.
Acting Director
Office of Technology Transfer
National Institutes of Health

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