Huntington's Disease (HD) is one of a number of neurological diseases in which excessive repetition of the CAG nucleotide sequence, which codes for glutamines, causes an abnormally shaped HD protein. This protein then interacts with other proteins produced by the cell thus preventing their normal functions. HD afflicts 1 in every 10,000 individuals in the United States, however HD's pathogenesis and mechanistic action is relevant to at least 13 other neurodegenerative diseases.

The mouse lines which are available for licensing show progressive neurobehavioral and neuropathological changes that resemble clinical findings found in HD patients. These include behavior such as running in circles, performing backflips and other abnormal movements which correlate with the loss of neurons in the striatum, cortex, and other brain regions. The transgenic mice have been genetically engineered to show widespread expression of full length human HD cDNA with either 16, 48, or 89 CAG repeats. It is the mice containing the 48 or 89 CAG repeats which manifest the HD symptoms, the other modified mice are useful as controls. The mouse lines are able to model the early events that occur in Huntington's Disease and how these events ultimately result in neurological cell death. The utility of these mouse lines can be found in screening potential pharmaceutical treatments for HD and other neurodegenerative diseases, as well as testing therapies, including those used to assist neuronal survival.

Inhibition of T-Type Voltage-Gated Calcium Channels by a New Scorpion Toxin

K Swartz, H Jaffe (NINDS)
Serial No. 60/101,158 filed 21 Aug 98
Licensing Contact: Marlene Shinn, 301/496–7056 ext. 285; e-mail: ms482m@nih.gov

The T-Type calcium channel is found in neurons, cardiac and vascular smooth muscle and is thought to be important for generative specific patterns of electrical activity. We have identified, isolated, and determined the chemical composition of an inhibitor (named Kurtoxin-1) of the T-type calcium channel. Kurtoxin-1 (or drugs developed using it as a probe) may be useful therapeutic reagents to control heart rate (e.g., antiarrhythmic drugs), vascular smooth muscle tone (e.g., controlling blood pressure) or epileptic discharges in the central nervous system. T-type calcium channels may also be important for transmission of pain stimuli and therefore inhibitors of these channels may have analgestic properties.

Kurtoxin is from the venom of the *Parabuthus transvaalicus* scorpion. It binds to the α_{1G} T-type Ca^{2+} channel with high affinity and inhibits the channel by modifying voltage-dependent gating. The biophysical properties of T-type voltage-gated Ca^{2+} channels make them well suited to serve important pacemaking roles, and to support c flux near the resting membrane potential in both excitable and non-excitable cells. Until now, no selective high affinity ligands were available for T-type Ca^{2+} channels. Kurtoxin distinguishes between the α_{1G} T-type Ca^{2+} channels and other types of voltage-gated Ca^{2+} channels, such as α_{1E}, α_{1C}, α_{1B} and α_{1A}. Its primary amino acid sequence indicates it belongs to a family of ŧ-scorpion toxins that slow inactivation of Na^{+} channels. It is foreseen that kurtoxin will facilitate characterization of the molecular composition of T-type Ca^{2+} channels and will help delineate their involvement in electrical and biochemical signaling.

Composition and Methods for Identifying and Testing Tyrosine Kinase Substrates and Their Agonists and Antagonists

LE Samelson, W Zhang (NICHD)
Serial No. 60/068,690 filed 23 Dec 97
Licensing Contact: Susan S. Rucker; 301/496–7056 ext. 245; e-mail: sr156v@nih.gov

This application relates to T cell receptors (TCRs) and TCR mediated signal transduction. More particularly, the application describes the isolation, purification and cloning of an integral membrane protein, Linker for Activation of T cells (LAT), a tyrosine kinase substrate for ZAP–70/Syk protein tyrosine kinases (PTKs). LAT is phosphorylated by ZAP–70/Syk and this phosphorylation is necessary for the recruitment of multiple signaling molecules, such as Grb2, PLC-γ1, the p85 subunit of PI3K and other critical signaling molecules. Thus, LAT plays a role in linking the TCR to cellular activation. Tissues which express LAT are limited to the thymus, peripheral blood, and at low levels, the spleen. Cells, found in these tissues, which express LAT and T cells, NK cells and mast cells. In addition recent work has also demonstrated that LAT is expressed in megakarocytes. B cells and monocytes do not express LAT. This pattern of expression and its role in cell signaling suggest that LAT may be a specific target for the development of drugs for allergy and other T cell associated diseases. Such drugs may include antibodies which recognize LAT and inhibit its action.

In addition to the isolation, purification and cloning of LAT the application describes antibodies which specifically recognize LAT. Recent work has shown that LAT is palmitoylated and this palmitoylated LAT localizes to glycolipid-enriched microdomains (GEMs). The palmitoylation of LAT is necessary for the tyrosine phosporylation of LAT and for the targeting of LAT to the GEMs. Other recent work includes the generation of LAT knockout mice.

This research has been published in *Cell* 92(1): 83–92 (Jan 9, 1998) and *Immunity* 9(2): 239–46 (Aug 1998).

Probe To Identify Enteroinvasive *E. coli* and *Shigella* Species

KA Lampel, JA Jagow (FDA)
Serial No. 07/266,038 filed 02 Nov 88; U.S. Patent 5,041,372 issued 20 Aug 91
Licensing Contact: Carol Salata, 301/496–7735 ext. 232; e-mail: cs253n@nih.gov

Standard means for detecting pathogenic organisms in food or clinical specimens rely on animals or large DNA fragments, such as the 17 kb *Eco*RI fragment of Boileau. These methods are expensive, time-consuming, difficult to use, and have not been able to distinguish between nonvirulent enteroinvasive *E. coli* and *Shigella*. This invention described DNA probes for enteroinvasive *E. coli* and *Shigella* species, including the sequence of the 2.5 kb fragment (*Sma*II and Falkow's) on which the probe is based.

The probe is more reliable, more sensitive, and less expensive than methods now is use.

Dated: January 25, 1999.

Jack Spiegel,

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

[FR Doc. 99–2245 Filed 1–29–99; 8:45 am]
BILLING CODE 4140–01–M

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.

Broad Spectrum Chemokine Antagonist and Uses Thereof

B Moss, I Damon-Armstrong (NIAID)
DHHS Reference No. E–065–98/1 filed 08 Jan 99 (based on Provisional U.S. Patent Application No. 60/070,945 filed 10 Jan 98)
Licensing Contact: Leopold Luberecki, Jr.; 301/496–7735 ext. 223; e-mail: 1187a@nih.gov

Chemokines are the small proteins involved in recruitment of leukocytes (white blood cells) to areas of tissue injury or infection, so they are also in part responsible for inflammation. There are two major classes of chemokines: CXC (α) and CC (β). Chemokines elicit leukocyte movement by binding to a receptor on the cell surface. Typically, CXC chemokines direct the movement of neutrophils and CC chemokines direct the movement of other types of leukocytes. Previously, the open reading frame of the recently sequenced molluscum contagiosum viral genome was predicted to encode a protein that would function as a CC chemokine antagonist by mimicking the chemokine and thus diverting it from its receptor. The inventors have cloned, expressed, purified, and demonstrated the broad-spectrum ability of this viral protein to inhibit chemotaxis of multiple different leukocyte classes to different chemokines in both the CXC and CC classes. Thus, the protein has potential use as an anti-inflammatory agent and as an antiviral agent to treat HIV.

Cell Expansion System for Use in Neural Transplantation

L Studer, V Tabar, J Yan, R McKay (NINDS)
Serial No. 60/093,991 filed 24 Jul 98
Licensing Contact: Leopold Luberecki, Jr.; 301/496–7735 ext. 223; e-mail: 1187a@nih.gov

Cell transplantation therapy typically involves transplanting primary cells or immortalized cells into patients. The promising but still inconsistent data stemming from those clinical trials using primary cells in Parkinson's disease are believed to be due to an insufficient number, function and uniformity of the transplanted cells. In an effort to overcome these problems an improved method for isolating, growing and differentiating precursor cells into dopaminergic neurons has been developed. The process described provides for an expansion of the cell number of primary cells by up to 1000 fold. This technique could assist in solving the problem of obtaining sufficient cells for a reliable, effective cell transplantation therapy. The process consists essentially in the isolation and in vitro numerical expansion of an early mesencephalic precursor population, the use of serum, cAMP, dopamine and ascorbic acid during differentiation and the development of an aggregation technique during cell differentiation that allows convenient grafting of dopaminergic neurons.

Real-Time Interactive Functional Magnetic Resonance Imaging

JA Frank, J Ostuni, JH Duyn (CC)
Serial No. 09/090,166 filed 04 Jun 98
Licensing Contact: John Fahner-Vihtelic; 301/496–7735 ext. 270; e-mail: jf35z@nih.gov

The present disclosure describes a device and methods for capturing whole brain raw data image files as they are being produced from a magnetic resonance (MR) system. The invention performs reconstruction of the data, registration, statistical analysis, and then displays the results within seconds after completion of the MR image acquisition. This invention provides the ability to have a quick look at the image maps produced of brain activity or brain perfusion. It gives the clinician or researcher performing the diagnosis or study, the flexibility to modify the procedure ''on the fly'' to produce a more meaningful image or data set.

Method of Reducing Perivascular Lesions Using Insulin-Like Growth Factor I

HD Webster, S Komoly, D Yao, X Liu, LD Hudson (NINDS)
Serial No. 08/705,820 filed 30 Aug 96 (based on Provisional U.S. Patent Application No. 60/003,055 filed 31 Aug 95)
Licensing Contact: Leopold Luberecki, Jr.; 301/496–7735 ext. 223; e-mail: 1187a@nih.gov

A perivascular lesion is a site near or surrounding a lesion in the blood vessel system that is accompanied by an accumulation of inflammatory leukocytes and/or damage to perivascular tissue. Although it is unclear how a perivascular lesion originates, the sequence of events leading to such lesions induce increased vascular endothelial permeability and induce toxic effects on the nervous system, which may lead to myelin injury. Myelin is a protein-lipid composite that insulates axons, which are the cellular processes by which electrical impulses travel through the nervous system. When myelin sheaths sustain injury, entire segments of myelin degenerate, thus affecting the ability of impulses to travel. Typically, perivascular lesions occur after or during: brain or spinal cord trauma, ischemic injury or insult; certain inflammatory diseases affecting the musculo-skeletal system, central nervous system, and peripheral nervous system; and certain autoimmune disorders. The application claims a method to reduce perivascular lesions by administering an effective amount of insulin-like growth factor I to treat diseases or disorders associated with demyelination, such as multiple sclerosis, experimental autoimmune encephalomyelitis, neuromyelitis optica, optic neuritis, acute encephalomyelitis, cervical myelopathy, and spinal cord injury.

Dated: January 25, 1999.

Jack Spiegel,

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

[FR Doc. 99–2246 Filed 1–29–99; 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 Diseases; Notice of 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 meetings of the National Diabetes and Digestive and Kidney Diseases Advisory Council.

The meetings will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.