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.

Spatially Selective Fixed-Optics Multicolor Fluorescence Detection System for Microfluidic Device

Nicole Y. Morgan, Paul D. Smith, Edward Wellner (ORS).
U.S. Provisional Application No. 60/693,780 filed 27 Jun 2005 (HHS Reference No. E–223–2005/0–US–01).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

Available for licensing and commercial development is a new scheme for sensitive spatially resolved and spectrally resolved laser-induced fluorescence detection from multiple microfluidic channels. The prototype instrument has been developed and is versatile in that it contains only fixed optical parts and has simultaneous five-color detection from eight microchannels in a plastic microchip for DNA analysis. The detection scheme could be applied to fluorescence detection for any microchip-based analysis in a transparent substrate. The economies of parallel detection and the importance of spatial selectivity would make this method most useful for polymeric substrates with multiple microchannels. Free space laser excitation incident off-axis (about 60 degrees to normal on the chip) is used to minimize the coupling of laser light into the detection optical fiber. The emitted fluorescence is detected with an optical fiber-ball lens combination, one for each microchannel. The spatial selectivity is achieved by using a high refractive index 2 mm ball lens and a small-diameter (200 um) .22 NA optical fiber positioned to obtain focused light from the channel. There are no moving parts so this configuration is both more robust and more versatile than a scanning system. Furthermore, the detection optics can be freely positioned near the channel, placing minimal constraints on channel layout and design. After the emitted fluorescence is coupled into the fiber, the light is passed through a long pass filter (here, 510AELP, Omega Optics), and then spectrally dispersed using a compact imaging spectrograph (FICS, Oriel). The resulting spectra are imaged using a cooled monochrome CCD (Qimaging Retiga EXl) at 10 frames per second. This setup allows simultaneous detection of multiple dyes. The laser excitation is split into multiple spots with two cylindrical lenses and an array of spherical plano-convex lenses. The spacing of the plano-convex lenses is chosen such that the laser spots coincide with the microchannels in the chip. At each excitation spot, a ball lens and optical fiber is positioned underneath the microchannel. The other ends of the optical fiber are formed into a 1–D array and directed onto the slit of an imaging spectrograph.

In addition to licensing, the technology may be available for further development through collaborative research opportunities with the inventors.

Cell-Nanofiber Composite Based Engineered Cartilage

Wan-Ju Li and Rocky S. Tuan (NIAMS).
U.S. Provisional Application No. 60/690,998 filed 15 Jun 2005 (HHS Reference No. E–116–2005/0–US–01).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

Available for licensing and commercial development is a tissue-engineered cartilage derived from a cellular composite made from a biodegradable, biocompatible polymeric nanofibrous matrix having dispersed chondrocytes or adult mesenchymal stem cells. More particularly, tissue-engineered cartilage can be prepared where the cartilage has a biodegradable and biocompatible nanofibrous polymer matrix prepared by electrospinning and a plurality of chondocytes or mesenchymal stem cells dispersed in the pores of the matrix. The tissue-engineered cartilage possesses compressive strength properties similar to natural cartilage.

The electrospinning process is a simple, economical means to produce biomaterial matrices or scaffolds of ultra-fine fibers derived from a variety of biodegradable polymers (Li WJ, *et al.* J Biomed Mater Res 2002; 60:613–21). Nanofibrous scaffolds (NFSs) formed by electrospinning, by virtue of structural similarity to natural extracellular matrix (ECM), may represent promising structures for tissue engineering applications. Electrospun three-dimensional NFSs are characterized by high porosity with a wide distribution of pore diameter, high-surface area to volume ratio and morphological similarities to natural collagen fibrils (Li WJ, *et al.* J Biomed Mater Res 2002; 60:613–21). These physical characteristics promote favorable biological responses of seeded cells in vitro and in vivo, including enhanced cell attachment, proliferation, maintenance of the chondrocytic phenotype (Li WJ, *et al.* J Biomed Mater Res 2003; 67A: 1105–14), and support of chondrogenic differentiation (Li WJ, *et al.* Biomaterials 2005; 26:599–609) as well as other connective tissue linage differentiation (Li WJ, *et al.* Biomaterials 2005; 26:5158–5166). The invention based on cell-nanofiber composite represents a candidate engineered tissue for cell-based approaches to cartilage repair.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Method and Device for Catheter-Based Repair of Cardiac Valves

Robert J. Lederman (NHLBI).
U.S. Provisional Application No. 60/426,984 filed 15 Nov 2002 (HHS Reference No. E–010–2003/0–US–01); International Patent Application PCT/US03/36617 filed 14 Nov 2003 (HHS Reference No. E–010–2003/0–PCT–02); U.S. Patent Application No. 11/127,112 filed 12 May 2005 (HHS Reference No. E–010–2003/0–US–03).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

The invention provides a system and method for catheter-based repair of cardiac valves. The technique may permit non-surgical repair of regurgitant valves using percutaneous catheters in awake patients. The intervention is intended to discontinue/lessen regurgitation of the mitral valve and should provide a viable alternative to

the conventional treatment with vasodilator medications and open heart surgery. The technology involves re-apposing of mitral valve leaflets by percutaneous annuloplasty delivering circumferential tensioning devices. Under appropriate imaging guidance (such as fluoroscopic MRI) a circumferential device trajectory is navigated through anatomic (coronary sinus) and non-anatomic spaces to deliver a circumferential tensioning device. Provided are also designs of various catheters, systems that would be necessary to perform the repair of cardiac valves. Imaging methods, like fluoroscopic (real time MRI), could be used to assist the operator for placement and orientation purposes.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Variable Curve Catheter

Robert J. Lederman, Parag Karmarkar (NHLBI).

U.S. Provisional Patent Application 60/426,542 filed 15 Nov 2002 (HHS Reference No. E–035–2003/0–US–01); International Patent Application PCT/US03/36210 filed 14 Nov 2003 (HHS Reference No. E–035–2003/0–PCT–02).

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

The invention provides a deflectable tip guiding device, such as a catheter, that enables the operator to vary the radius of curvature of the tip of the catheter. This is a novel variation on the classic ''fixed fulcrum,'' tip deflectors used in minimally invasive procedures in open surgical treatments. The described device permits a more comprehensive ability to navigate complex geometric pathways in patient's body and enables better access to target structures (*e.g.*, to all endomyocardial walls from a transaortic approach). The guiding device can be made compatible with imaging methods like MRI. The described technology can be used as a platform for a variety of interventional devices for delivery of drugs, cells, energy, or sutures through complex trajectories of the body.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Dated: August 5, 2005.

Steven M. Ferguson,

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

[FR Doc. 05–16137 Filed 8–12–05; 8:45 am]

BILLING CODE 4140–01–P

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Benztropinamine Analogs as Dopamine Transport Inhibitors

Amy H. Newman *et al.* (NIDA).

U.S. Provisional Application No. 60/689,746 filed 10 Jun 2005 (HHS Reference No. E–089–2005/0–US–01).

Licensing Contact: Marlene Shinn-Astor; 301–435–4426; *shinnm@mail.nih.gov.*

Dopamine is a neurotransmitter that is directly involved in locomotor activity, motivation and reward, and cognition. The dopamine transporter is expressed on the plasma membrane of dopamine neurons and is responsible for clearing dopamine released into the extracellular space, thereby regulating neurotransmission. The dopamine transporter plays a significant role in neuropsychiatric diseases, such as Parkinson's disease, drug abuse (especially cocaine addiction), Attention Deficit Disorder/Attention Deficit Hyperactivity Disorder (ADD/ADHD), narcolepsy and a number of other CNS disorders. Therefore, the dopamine transporter is a target for research and potential therapeutics for the treatment of these indications.

Benztropine and its analogs are an important class of dopamine transport inhibitors that are indicated for the treatment of cocaine abuse and ADHD. They bind with high affinity to the dopamine transporter and block dopamine uptake, but generally do not produce behavioral effects comparable to those produced by cocaine. In animal models of drug abuse, many benztropine analogs have been shown to (1) reduce cocaine-induced locomotor stimulation, (2) have long-lasting effects, and (3) lack a significant abuse liability. This suggests they may be useful medications for the treatment of human diseases where dopamine-related behavior is compromised, especially in situations in which an (partial) agonist treatment is indicated.

However, some of the reported analogs have limited or poor solubility in aqueous systems or poor stability characteristics. To remedy this, the 3-position benzhydrylether moiety of the benztropine analogs was replaced with the isosteric benzhydrylamine system in order to reduce hydrolysis of the less stable ether function, observed in the benztropine series, and further reduce lipophilicity to ultimately increase water solubility and bioavailability for improved therapeutic formulation and utility.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Inhibition of SMAD-Signaling Leads To Enhanced Insulin Production and Better Glucose Control: A Potential Therapy for Diabetes and Associated Complications Due to Hyperglycemia

Sushil G. Rane *et al.* (NCI).

U.S. Provisional Application No. 60/665,204 filed 25 Mar 2005 (HHS Reference No. E–235–2004/0–US–01).

Licensing Contact: Marlene Shinn-Astor; 301–435–4426, *shinnm@mail.nih.gov.*

TGFβ and related proteins, activins and bone morphogenetic proteins (BMPs), are critical during pancreas development. Alterations in the TGFβ pathway are observed in diseases of the pancreas, including diabetes and cancer, although the precise ramifications of altered TGFβ functions are unclear. The *DPC4* (deleted in pancreas cancer 4) locus that encodes the TGFβ-signaling intermediate, SMAD 4, is mutated in 55–70% of pancreatic cancers and