National Institutes of Health
Office of Technology Transfer

Medical Devices
Available for Licensing

National Institutes of Health (NIH) Office of Technology Transfer
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INTRODUCTION

NIH has an extensive intellectual property portfolio of early-stage technologies[†] and also invests substantially in their development. Roughly 10 percent of the annual NIH budget is dedicated to intramural research and development activities -- resulting in inventions that form the basis of a variety of new medical technology and therapies in the areas of medical devices, software, vaccines, diagnostics, and reagents. Similar to university research, commercial partners are needed to make sure that the long hours at the lab bench and the public investment pay off in the end in marketed products.

NIH believes that the future development of its innovative, early stage research lies largely with innovative, early stage companies. While the increasingly consolidated pharmaceutical industry remains a steady customer of research reagents and clinical collaborations with NIH, the more exciting therapeutic developments increasingly seem to come from NIH licenses signed with small and medium-sized life science companies early in their growth phase.

To further attract such early-stage concerns and start-ups, NIH affords favorable treatment to small firms and tries to provide IP agreements that facilitate new areas of product development based upon NIH research. For example, financially-burdened smaller companies can benefit from flexibility on patent costs and license execution fees in license agreements. Of particular note for venture-backed firms is that companies do not give up equity or management control nor are their future development or marketing rights compromised by signing NIH license agreements. Finally, once the product is in development, NIH is often able to assist with clinical trials, follow-on research collaborations, and even eventual purchase of the product as a customer.

We have collected some medical technologies your company might be interested in for further discussion with our licensing specialists.

Once you have picked the technology of interest, we urge you to apply for a License. A copy of the License Application template can be found at the NIH OTT website at: http://www.ott.nih.gov/forms_model_agreements/forms_model_agreements.html#LAP.

[†] *The NIH Office of Technology Transfer cannot guarantee that the listed technologies are still available for licensing. Please contact the Technology Licensing Specialist (listed under each technology) for the current status and for other complementary technologies.*

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DIAGNOSTIC DEVICES

Title: **A Cytokine Gene Signature Of Lung Adenocarcinoma And Its Tissue Environment Predicts Lymph Node Metastasis And Prognosis**

Reference: E-085-2007

Inventor(s): Curtis C. Harris (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is a novel method for determining the prognosis of a subject with adenocarcinoma in an organ, such as the lung, and to aid in the selection of a specific therapeutic regimen. Lung adenocarcinoma (AC) is the predominant histological subtype of lung cancer, which is the leading cause of cancer deaths worldwide. The risk of metastasis remains substantial in AC patients, even when a curative resection of early-stage AC is performed. The prognosis includes the determination of the likelihood of survival, the likelihood of metastasis, or both. The method includes quantization of the expression of a plurality of Th1 and Th2 cytokines of interest in the adenocarcinoma and in non-cancerous tissue in the organ. Altered expression of one or more of the Th1 and Th2 cytokines in the adenocarcinoma as compared to the non-cancerous tissue determines the prognosis for the subject. The method is capable of distinguishing patients with lymph node metastasis versus those with short term survival. Furthermore, methods are provided for evaluating the effectiveness of anti-cancer agents.

Applications: Prognosis of adenocarcinoma, aid in the selection of specific therapeutic regimens and evaluation of the effectiveness of anti-cancer agents.

Title: **A Novel Algorithm For The Molecular Diagnosis Of Lymph Node Metastasis And Prognosis In Early-stage Lung Adenocarcinoma By Profiling The Expression Of Unique Cytokines In Tumor And Non-tumor Specimens**

Reference: E-263-2006

Inventor(s): Curtis C. Harris (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is a novel method for determining the prognosis of a subject with adenocarcinoma in an organ, such as the lung, and to aid in the selection of a specific therapeutic regimen. Lung adenocarcinoma (AC) is the predominant histological subtype of lung cancer, which is the leading cause of cancer deaths worldwide. The risk of metastasis remains substantial in AC patients, even when a curative resection of early-stage AC is performed. The prognosis includes the determination of the likelihood of survival, the likelihood of metastasis, or both. The method includes quantization of the expression of a plurality of Th1 and Th2 cytokines of interest in the adenocarcinoma and in non-cancerous tissue in the organ. Altered expression of one or more of the Th1 and Th2 cytokines in the adenocarcinoma as compared to the non-cancerous tissue determines the prognosis for the subject. The method is capable of distinguishing patients with lymph node metastasis versus those with short term survival. Furthermore, methods are provided for evaluating the effectiveness of anti-cancer agents.

Applications: Prognosis of adenocarcinoma, aid in the selection of specific therapeutic regimens and evaluation of the effectiveness of anti-cancer agents.

Title: **Aviden-Rhpdaminex (AV-3ROX) As A Self-Quenching Fluorophore Useful In Imaging Technology**

Reference: E-255-2006

Inventor(s): Hisataka Kobayashi (NCI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

Available for licensing and commercial development is an optical imaging method capable of detecting living cancer cells in vivo. The method increases sensitivity and reduces the background signal to extremely low levels. In contrast to conventional fluorescent imaging, the strategy activates the probe after it binds to and is internalized within cancer cells. Using antibodies, reagent-receptor systems, or cytokines to target the agent to the cancer, the agent is internalized by the normal cellular process of endocytosis which in turn, leads to molecular changes within the probe itself; fluorophores are activated only in the living targeted cells. An activatable fluorophore is one that is normally self-quenched by attachment to a peptide backbone but which can be activated by specific proteases which degrade the peptide resulting in 8de-quenchinge. For example, self-quenching avidin-rhodaminex, which has affinity for lectin on cancer cells, is activated after endocytosis and degradation within the lysosome. Cellular internalization of receptor-ligand pairs with subsequent activation of fluorescence via 8de-quenchinge provides a generalizable and highly sensitive method of detecting cancer microfoci in vivo and has practical implications for assisting surgical and endoscopic procedures.

Applications: Optical detection of tumor cells and metastatic nodules

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Title: **Ghost Native-PAGE Using A Colorless Compound (dihydro-Coomassie, C47H51N2O7S2), Generated By The Chemical Reduction Of Coomassie Brillant Blue G, That Enhances The Charge Difference Of Macromolecular Strututures And Complexes For Isolation And Characterization Using Ionophoretic Techniques.**

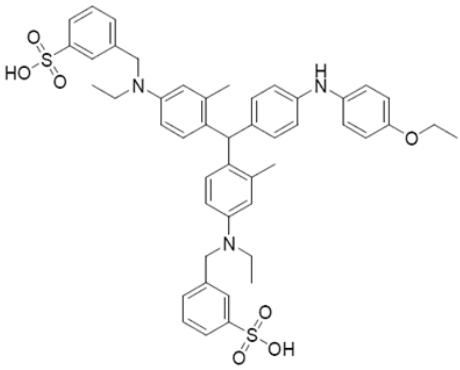
Reference: E-218-2006

Inventor(s): Robert Balaban (NHLBI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Protein staining dyes such as serva blue G or Coomassie blue are used to enhance the separation of protein complexes by binding to the proteins and differentially enhancing the net charge of the complexes improving the separation of the complexes using electrophoresis procedures. However, the intense blue color of Coomassie stains interferes with immunobloting and in gel colormetric or fluorescent studies. Available for licensing and commercial development is a colorless molecule that will bind and enhance the differential surface charge on protein complexes. The molecule has been demonstrated to work as well as Coomassie blue but will not interfere in gel assays critical for most investigations. This approach provides biochemists interested in protein complexes in biological tissues with the ability to separate protein complexes and perform in gel assays saving time and resources in this important emerging field.

The compound and methods of its use is for polyacrylamide gel electrophoresis (PAGE) and related gel techniques for the analysis of protein complexes and defects in the same. Such analysis can be extended to the detection of various diseases, e.g., Alzheimer's disease or Parkinson's disease. One such compound has the following formula:



Applications: Alzheimer's and Parkinson's disease diagnostic.

Title: **Detection And Subtyping Of Influenza Strains (including All Known Human And Avian Strains) With Genome-tiling Oligonucleotide Microarray**

Reference: E-208-2006

Inventor(s): Xiaolin Wu (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development are a novel influenza virus microarray and methods for using the microarray for the identification of existing and new types and subtypes of human influenza viruses. There are three types of influenza viruses, type A, B and C. Influenza types A or B viruses cause epidemics of disease almost every winter, with type A causes major pandemic periodically. Influenza type A viruses are further divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (H) and neuraminidase (N). There are 16 known HA subtypes and 9 known NA subtypes of influenza A viruses. Each subtype may have different combination of H and N proteins. Although there are only three known A subtypes of influenza viruses (H1N1, H1N2, and H3N2) currently circulating among humans, many other different strains are circulating among birds and other animals and these viruses do spread to humans occasionally. There is a requirement for sensitive and rapid diagnostic techniques in order to improve both the diagnosis of infections and the quality of surveillance systems. This microarray platform tiles the genomes of all types/subtypes of influenza viruses, and is capable of correctly identifying all 3 types/subtypes of influenza viruses from an influenza vaccine sample. More specifically, the invention consists of: 1) microarrays comprising a solid support with a plurality of n-mer influenza viral nucleotide segments of influenza Types A, B and C, including each respective subtypes, and 2) methods of detecting and identifying known and unknown influenza viral types and subtypes by: a) using hybridization microarrays to known influenza viral nucleotide sequences, b) sequencing the nucleotides which hybridize to the microarrays and c) analyzing the hybridized sequences using existing databases, thus identifying existing or new subtypes of influenza viruses.

Applications: Detection and identification of human influenza viruses and efficient discovery of new subtypes of influenza viruses

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Title: **Monoclonal Antibody Microarray**

Reference: E-207-2006

Inventor(s): Cassio S. Baptista (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

The present invention provides methods for constructing and using a novel Monoclonal Antibody Microarray which allows high-throughput determination of protein expression profiles from serum, tissue, and cultured cells. The Monoclonal Antibody Microarray consists of more than 1000 different antibodies immobilized on a glass slide, which recognize antigens from several groups of proteins, including cytokines, kinases, apoptotic proteins, growth factor receptors, tumor suppressors, and oncoproteins. Protein samples to be identified and quantified are labeled with fluorescence and hybridized to the antibodies immobilized on the arrays. By differentially labeling two protein samples (dual-color labeling) and co-hybridizing to the same microarray, a direct comparative analysis of protein expression can be performed using as little as 100 -g of total protein. This method allows a large number of samples to be screened in parallel on identical arrays.

Applications: High-throughput analysis of protein expression and direct measurement of protein expression at the gene product or post-translational levels.

Title: **Virus Microarray**

Reference: E-206-2006

Inventor(s): Cassio S. Baptista (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

The spectrum of pathogenic viruses of importance in human disease, agriculture and biology is not only large and diverse, but continually evolving. The identification or isolation of viral pathogens, in correlation with the presence of specific disease phenotypes, is of paramount importance both to diagnosis of disease and the subsequent management or treatment of viral infection. The limitations of current viral detection methods, such as PCR and immunoassays, led to the development of a novel microarray system for specific detection of viruses. The technology offered here for licensing provides a method for high-throughput screening of known pathogenic viruses along with identification of "new" disease-associated viruses.

The novel method is based on a viral microarray containing 10,000 immobilized DNA oligonucleotide features, representing all known mammalian and avian pathogenic viruses (approximately 600). Software was also developed to analyze the viral microarray results. The oligonucleotide features in this system are 60-mer long and distributed across both conserved and non-conserved regions of known viral sequences. This design serves the dual purpose of: (1) facilitating validation via redundant signals associated with each represented virus and (2) allowing for the discovery of new viruses, which arise due to recombination. In addition, positive and negative controls against human and mouse housekeeping genes are included along with software for analysis of virus microarray results.

Further advantages of the viral microarray include: (a) the use of sample inputs as little as 10ng of either total DNA or RNA extracted from virus infected cells, representing as few as 20 viral particles; (b) detection of viruses of both DNA and RNA classes; (c) a capacity for high-throughput screening of various sample types including serum, saliva and biopsy tissues; and (d) analysis of a large number of samples in

parallel on identical arrays.

The detection of viral DNA is unique to this technology, as other available technologies only detect viral genomic RNA or viral mRNA transcripts. Additionally, the viral chip was found to be highly specific and sensitive for detecting different viral genomic sequences in cell lines and multiple viral constructs co-infection in cultured cells.

Applications: Detection and identification of viruses that cause disease. Efficient discovery of new pathogenic viruses.

Title: **Gene Panel For Intracerebral Hemorrhage: Panel Of Genes For The Diagnosis Of Intracerebral Hemorrhage Developed From Gene Expressing Profiling Of The Peripheral Blood**

Reference: E-197-2006

Inventor(s): Alison Baird (NINDS)

Licensing Contact: Fatima Sayyid; 301-435-4521, sayyidf@mail.nih.gov

Stroke affects 15 million people worldwide each year, and is the number three leading cause of morbidity in the United States. Although most forms of stroke are ischemic in nature, approximately 10-15% of strokes are hemorrhagic. At present, clinical applications for distinguishing between these two forms of stroke do not exist. The present invention describes a highly predictive, cost-effective diagnostic assay capable of detecting whether an individual has suffered from an intracerebral hemorrhagic stroke and the likelihood of neurological recovery. It comprises a rapid screening device for measuring differential expression patterns of nucleic acid molecules or proteins of at least four hemorrhagic stroke-related genes. Accurate prediction of hemorrhagic stroke will improve rapid diagnosis and aid in determining early treatment regimens.

Applications: Gene expression profile assay for determining hemorrhagic stroke victims and means of differentiating between hemorrhagic stroke and ischemic stroke thereby optimizing patient response to stroke therapies.

Title: **Tomographic Reconstruction Of The 3-D "average Propagator" From Diffusion Weighted MR Data Using An Iterative Scheme**

Reference: E-164-2006

Inventor(s): Peter J. Basser and Valery Pickalov (NICHD)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

This invention relates to diffusion-weighted magnetic resonance imaging (DW-MRI) and describes a novel method for estimating the 3-D average propagator from DW-MRI data. The average propagator measures the probability that water molecules move from one place to another during a given diffusion time. This quantity provides local information about the tissue microstructure and the microenvironment in which water diffuses without making any a priori assumptions about the underlying diffusion process itself. Several methods, such as 3D q-space magnetic resonance imaging (MRI) and diffusion spectrum imaging

have been developed to measure the average propagator, but these techniques currently require acquisition of large numbers of DW images, making them infeasible for routine animal and clinical imaging. The proposed methodology introduces a new data reconstruction concept, which involved using computer tomography (CT) algorithms to estimate the average propagator from the MR data. The proposed CT reconstruction requires many fewer DW-MRI data than conventional methods consistent with a clinically feasible period of MR image acquisition. The novel technique can be used to diagnose medical disorders that are associated with alterations in water diffusion, such as stroke and several neurodegenerative diseases and other disorders for which diffusion tensor MRI is currently used. Additional applications include drug development (screening drug candidates), material science (testing the quality of materials that have restricted and hindered compartments, e.g. porous media, gels and films) and food processing (testing structural changes in food).

Applications: In vivo Functional MRI of humans and animals.

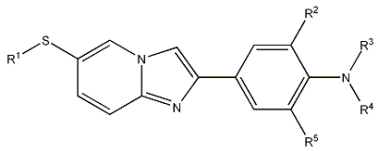
Title: **Beta-amyloid PET Imaging Agents Based On Thioether Derivatives**

Reference: E-156-2006

Inventor(s): Lisheng Cai (NIMH)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development are two novel classes of compounds useful as radioligands for in vivo imaging of beta-amyloid peptides and plaques in humans.



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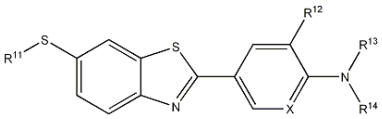

(II)

Beta-amyloid peptide deposition in the brain is a pathological feature of Alzheimer's disease (AD). Early detection of beta-amyloid load in patients with suspected AD is vital to initiating early treatment, which can improve cognitive function and quality of life for many patients. The invention describes novel derivatives of imidazopyridinylbenzeneamine (IMPY) and benzothizolylbenzeneamine (BTA), which demonstrate high in vitro binding affinity to human beta-amyloid. The difference between existing IMPY compounds and the novel derivatives is the substitution of an aryl halide with an aryl thioether group and replacement of a sulfur group of the pyridine ring with a nitrogen group. The new classes of compounds have the potential of providing improved amyloid imaging agents for Positron Emission Tomography (PET) with higher specificity for amyloid, low background noise, better entry into the brain and improved labeling efficiency. In addition to the novel compounds, the invention also includes: 1) a new method of synthesizing the IMPY derivatives, using palladium as a catalyst, 2) methods of imaging beta-amyloid deposits in the brain by in vivo PET, magnetic resonance imaging (MRI) and other imaging methods involving the use of these compounds, and 3) and methods of labeling these compounds with radiotracers.

Title: **Inductive Decoupling Of Multiple RF Coils Using Passive Transformers**

Reference: E-099-2006

Inventor(s): George C. Nascimento and Afonso C. Silva (NINDS)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

Parallel magnetic resonance imaging (MRI) techniques employ RF coil arrays for faster data acquisition, and have been shown to reduce the overall length of MRI procedures, improve signal-to±noise ratio (SNR) and image quality, thus making MRI more attractive and less costly. Elimination of inductive coupling is an essential step in designing RF coil arrays for parallel MRI. If mutual inductance remains among coils in the RF coil array, the MR signal obtained from one coil may disturb the flux in another coil, making it difficult to match the impedance of each individual element to the input impedance its preamplifier. This non-optimal matching can lead to degradation of MR signal thereby yielding images with low quality. The most common strategy for inductive decoupling involves the use of preamplifiers with very low input impedance and decoupling networks with lumped elements. However, the construction of preamplifiers with low input impedance is not easy to accomplish, and these preamplifiers impose technical restrictions on coil design, requiring the use of overlapping loops to further minimize the amount of mutual inductance between the coils. The present invention describes a novel RF coil circuitry scheme to remove inductive coupling and to overcome the limitations of having to use overlapping geometries and low-impedance preamplifiers. The coil array employs a transformer to match the input impedance of the preamplifier. The signal that reaches the preamplifier is coupled in an inductive fashion to the RF coil decoupling network through the transformerfs primary coil. Because primary and secondary coils in the transformer are isolated, the preamplifier circuit (and the MRI scanner electronics) is electrically isolated from the MR pickup coil. This arrangement provides a perfect electrical balance and isolation between the array channels, thus making it unnecessary to use traps and balluns in the circuit. At 7T, a 4-channel small animal coil array implementing the novel circuitry provided images with excellent SNR and demonstrated isolation of all individual RF coils and immunity to standing waves and other parasitic signals.

Applications: MR imaging of humans, including imaging of brain.

Title: **Real-time Correction Of Magnetic Field Fluctuations In MRI**

Reference: E-085-2006

Inventor(s): Jozef H. Duyn (NINDS)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

Available for licensing is a new MRI technique that will markedly improve the diagnostic potential of the rendered images. This is a method for applying real-time corrections to prevent image distortions caused by field variations that are due to the patient's respiratory cycle or instrument instability. These field variations reduce the B_0 homogeneity in a non-uniform and spatially-dependent manner. They may lead to a variety of image artifacts such as ghosting and blurring. This method provides a way of calculating the correct electrical currents that must be applied to a set of gradients and shims, smaller magnets that are used to make fine-tune adjustments to the magnetic field in a spatially-dependent manner. As the MRI subject breathes, changes in the B_0 field occur. During a brief training session, the amplitude of these changes as a function of chest motion is recorded in a phase map. Similarly, changes in B_0 as a function of chest motion is recorded in a phase map. Similarly, changes in B_0 as a function of current intensity is available from calibration data containing B_0 as a function of coil current. As the subject undergoes a scan, compensatory

currents are applied to the x, y, or z axis of the gradients and the shims coils in order to correct for the effect of respiration on the B_0 homogeneity. The shim values can be updated every 10 to 80 milliseconds during an experiment. This method results in a substantial decrease in artifacts that can obscure the overall image quality. It can be used for virtually all types of scans and MRI instruments.

Applications: Real-time correction of magnetic fluctuations in MRI experiments.

Title: **Small Molecules For Imaging Protein-protein Interactions In Alzheimer's Disease**

Reference: E-046-2006

Inventor(s): King C. Li and S. Narasimhan Danthi (CC)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Imaging techniques like positron emission tomography and photon emission computerized tomography are often used with imaging agents to detect the presence and accumulation of amyloid plaques within the human brain. These imaging agents have high specificity for beta amyloid peptides, and administration of such agents aids in the early detection of amyloid plaques in brains of Alzheimer's victims. However, currently available imaging agents have limited success for detecting pre-plaque beta amyloid proteins because they are small and reside within the tissue for a short period of time. Therefore, new imaging agents are needed for enhanced identification of amyloid deposits.Available for licensing and commercial development are small molecules for imaging protein-protein interactions in Alzheimer's disease. This technology describes a bifunctional molecule with high specificity for beta amyloid proteins that is applicable for in vivo imaging. The molecule contains two moieties with different binding affinities, one moiety has an affinity for amyloid beta proteins, and the other moiety has an affinity for a tissue-specific chaperone. The different moieties of the subject invention are conjoined by an inert linkage group, typically comprised of a hydrocarbon chain, peptide, or carbohydrate. The subject invention is affixed with a label, such as a fluorophore or radioisotope, which adheres to the binding site of the beta amyloid protein, the chaperone, or the linkage group. The choice of label makes the subject invention versatile and employable in several types of imaging modalities such as single photon emission computed tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI), and computerized tomography (CT) scans.

Applications: Applicable for identification of beta amyloid plaques in patients with or at risk for Alzheimer's disease and pre-plaque amyloid beta proteins, in vivo imaging protein-protein interactions using small molecules, and image guided therapy of Alzheimer's disease.

Title: **A Minimally Invasive Microdialysis Probe For In-vivo Sampling And Drug-delivery**

Reference: E-024-2006

Inventor(s): Jay Shah (NIHCC)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is a microdialysis probe. This device permits *in-vivo* measurement of bioavailable substances (e.g., cytokines, growth factors, neuropeptides, inflammatory mediators, etc.) at picogram levels of concentration directly from soft tissue and organ systems. The probe may also serve as an *in-situ* drug delivery vehicle of micro doses of medication to specific anatomical sites by slow diffusion. It also permits measurement of efficacy of drug delivery, whether given orally, systemically or topically, at the local tissue level. It can be utilized in a variety of patient populations and conditions. For example, the probe can be used to monitor the local biochemical milieu in soft tissue and organ systems to provide insights into the pathophysiology of musculoskeletal, neuromuscular, rheumatic, gastrointestinal, renal, cardiovascular and endocrinologic diseases, cancers, dermatological conditions, and pediatric disorders, especially in premature newborns.

The probe is made from a small-bore (32 gauge) needle, whose probe surface has been fashioned to permit near trauma-less entry, containing both a fluid delivery and recovery tube within the bore. A molecular exchange membrane is positioned about 200 microns from the tip. Fluid flows across the membrane removing diffused molecules to a collection device. The rounded tip of the needle is designed to cause minimal tissue damage while allowing investigations to be performed on local tissue fluids. Additionally, this device allows simultaneous delivery of small concentrations of drug. In summary, this unique apparatus provides a minimally invasive means for sampling biological fluids in any human or animal organ or tissue and for *in-situ* drug-delivery, in continuous or incremental dosing, of extremely small doses.

Applications: Measurement of bioavailable substances in organs and soft tissues.

Title: **All-hollow-waveguide Laser Delivery System For Digital Particle Image Velocimetry**

Reference: E-015-2006

Inventor(s): Ilko K. Ilev (FDA)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is an all-hollow-waveguide laser delivery system used for effective digital particle image velocimetry (DPIV) illumination. The system incorporates two key optical hollow waveguide components: an uncoated funnel-shaped hollow glass taper for a direct laser-to-taper coupling and a flexible hollow core waveguide for precise high-peak-power laser delivery. The principle of operation of the uncoated hollow taper is based on grazing-incidence effect. The optical taper is used for direct lens-free launching of laser radiation including from powerful lasers into fibers and waveguides. Because of the mutual action of the direct parallel laser excitation, the mode coupling process and mode filtering effect, the hollow taper serves as a mode converter that transforms the highly multimode profile of the input laser emission into a high-quality Gaussian-shaped profile at the taper output. Moreover, because of the lower power density of the output laser beam and its high quality profile, the taper ensures higher damage threshold for the delivery waveguide in comparison to the conventional lens laser-to-fiber coupling. To improve the high-peak-power delivery capability of the proposed all-hollow-waveguide DPIV illumination system, instead of a conventional solid-core fiber link, we have used a cyclic olefin polymer (COP)-coated hollow glass waveguide which is designed to minimize the waveguide attenuation losses at a typical DPIV laser wavelength of 532-nm. This waveguide provides a significantly higher laser power delivery capability and higher damage threshold. The all-hollow-waveguide DPIV laser delivery system offers essential advanced features over conventional bulk-optics-based delivery techniques in terms of formatting thin (0.5-1.0 mm), wide (10 mm or wider) and uniform laser illumination sheet; high-peak-power laser delivery without damaging effects (>1 GW/cm2), flexibility, miniaturization, simplified alignment, immunity to external influence (including vibrations and angular laser beam drift), and safe and confined laser delivery.

Applications: Optics, Particle imaging, Velocimetry.

Title: **Novel Infrared (IR)-Transparent Hydrophilic Membrane That Can be Used for Filtration, Printing or Microarrays, and Cultivation of Bacteria and Other Microorganisms for Reagent-Free IR Spectroscopic Identification**

Reference: E-174-2005

Inventor(s): Magdi M. Mossoba (FDA)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is a novel, disposable infrared (IR)-transparent, microporous, plasma treated polyethylene hydrophilic membrane, as well as methods for making and using this membrane to identify bacterial and other micoorganism impurities in food using IR spectroscopy. Further applications include: filtering dilute aqueous bacterial suspensions, and growing bacterial colonies when the PE membrane is placed over an agar medium and incubated. The patent also describes a novel high-throughout technique, as an alternative to manual filtration, where the PE membrane is used for microarray printing of intact microorganisms in pre-enriched medium on the treated PE substrate. Furthermore, the invention relates to a method of detecting mixtures of food-borne pathogens E. sakazakii and K. pneumonia, by using the treated PE membranes. Because this unique membrane is transparent to infrared light, isolated microcolonies of bacterial cells grown on this PE substrate can be fingerprinted directly by IR microspectroscopy, followed by multivariate analysis for the identification of the pathogens. The method can be applied to other cell types as well.

Applications: Identify presumptive pathogen colonies, in screening tests for a large number of pathogens, isolate microorganisms from aqueous suspensions as well as spores, including airborne ones.

Title: **Fluorescent Imaging and Photodynamic Treatment of Tumors**

Reference: E-335-2005/0

Inventor(s): Hisataka Kobayashi (NCI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

Available for licensing and commercial development are methods and compositions for optically detecting tumors, in particular disseminated intraperitoneal cancers. Unlike existing detection methods using avidin and/or galactosyl serum albumin (GSA), the current invention allows tumors to be visualized in situ, with high sensitivity and without hazardous radioactive probes. The invention also provides methods of treating tumors.

The invention describes the labeling of avidin and GSA with fluorophores. The fluorescently labeled agents selectively bind to cells expressing asialoglycoprotein receptors on the surface of tumor cells, such as in tumors of the ovary, stomach, colon or pancreas. Metastatic tumor cells can then be detected endoscopically, laparoscopically, or during surgery with an appropriate imaging system.

The fluorescently labeled avidin and GSA can be used diagnostically, but also have an application for treating cancer. Using photoactivatable fluorophores linked to avidin or GSA, free radicals can be produced which results in localized death of tumor cells upon exposure to excitation with the appropriate wavelength.

Applications: Optical detection of tumor cells and metastatic nodules. Photodynamic treatment of tumors

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Title: **Image Guided Systems and Methods for Organ Viability Assessment**

Reference: E-098-2005/0

Inventor(s): Alexander M. Gorbach (NCI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

The number of patients for organ transplants continues to grow, without an increase in the number of organs available for transplant. This has increased interest in transplanting organs from non-traditional sources, such as donations after cardiac death. However, there are currently no methods to objectively measure the effects of resuscitation and ischemia damage on organ viability.

The present invention relates to systems and methods for evaluating the status and characterization of organs, determining their suitability for transplants, as well as restoring the viability of organs intended for transplants. Particularly, this method is based on using optical (infrared or near infrared) imaging to guide the resuscitation of the donor organs and predict the recovery of grafts challenged with several hours of preservation. This method allows for localization of ischemic areas and guiding targeted resuscitation of the organ.

For example, the inventors have shown that by combining a kidney reperfusion system with infrared imaging equipment, it is possible to differentiate between ischemic and non-ischemic tissue and restore the viability of the kidney. This method can potentially be used to evaluate the viability of any body part or organ intended for transplantation, such as extremities, heart, lungs, and liver. This approach can lead to the utilization of donation-after-cardiac-death organs and can substantially increase the donor pool of organs. Hence, this new method can identify organs that may be considered unsuitable for transplant, and help prevent transplantation of organs whose function may be considered impaired, as well as help guide resuscitation efforts.

Title: **Method for Improved Phase Contrast MRI Resolution**

Reference: E-134-2005/0

Inventor(s): Reza Nezafat (NHLBI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

This invention is a method to significantly improve the temporal or spatial resolution in a phase contrast MRI (PC-MRI) study. In general, conventional PC-MRI involves encoding the motion information of spins in the phase of the image. The velocity of the spin motion can be extracted by calculating the phase difference between two consecutive images acquired with two different bipolar encoding gradients. Two scans are required in order to reconstruct flow velocity data, resulting in an increase in image acquisition

and reconstruction time by a factor of two compared to that of a standard anatomical image. As a means of reducing the PC-MRI scan time, the inventors propose a method of acquiring only a fraction of k-space data. The k-space is sampled using an under-sampled spiral or single projection, radial scheme. Subsequently, the two data sets in the PC-MRI are subtracted to extract the motion information from undersampled data without any aliasing artifacts. This method of partial-field of view acquisition and reconstruction of PC-MRI results in an increased temporal resolution, while maintaining high spatial resolution. The increase in image acquisition efficiency could be used to increase the spatial resolution while maintaining the temporal resolution.

Title: **Biofunctionalized Quantum Dots for Biological Imaging**

Reference: E-325-2003/0

Inventor(s): Joseph Barchi (NCI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing is intellectual property covering carbohydrate-encapsulated quantum dots (QD) for use in medical imaging and methods of making the same. Certain carbohydrates, especially those included on tumor glycoproteins are known to have affinity for certain cell types. One notable glycan used in the present invention is the Thomsen-Freidenreich disaccharide (Galb1-3GalNAc) that is readily detectable in 90% of all primary human carcinomas and their metastases. These glycans can be exploited for medical imaging. Quantum Dots (QDs) are semiconductor nanocrystals (CdSe or CdTe) with detectable luminescent properties. Encapsulating luminescent QDs with target-specific glycans permits efficient imaging of the tissue to which the glycans bind with high affinity. Accurate imaging of diseased cells (e.g., primary and metastatic tumors) is of primary importance in disease management. The inventors describe a method for enhancing the luminescence of carbohydrate-encapsulated QDs by addition of specific functional units in a novel synthesis of hybrid CdTe-based core-shell semiconductor nanocrystals.

Title: **New Method for Quantification of Allele-Specific RNA Expression, that Can be Used for Detection of Various Genetic Disorders**

Reference: E-146-2005/0

Inventor(s): Marjan Huizing (NHGRI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is a new method for quantification of allele-specific RNA expression. This invention describes methods for simultaneously detecting the levels of expression of a plurality of different RNA transcripts expressed from a gene of interest in a subject or a cell. This is a simple assay to validate and quantify allele-specific silencing, by applying a combination of a fluorescent primer/probe set that specifically recognizes the targeted allele where the probe is labeled with one fluorophore, and a primer/probe set that specifically recognizes the normal allele, where the probe is labeled with another fluorophore in the same reaction tube. Furthermore, this method can be run on most real time PCR machines and requires very small amounts of RNA, less than 100 ng. This novel method, by comparing alleles within the same gene, expands on current real time PCR methods which compare one gene with another gene.

The invention also describes methods for validating the effectiveness and specificity of allele-specific

siRNAs, kits for performing such assays, as well as methods for diagnosis of autosomal-dominant disorders, in which mutations in one allele result in a disease phenotype, such as Hutchinson-Gilford progeria, incontinentia pigmenti, neurofibromatosis, myotonic dystrophy, sialuria, Machado-Joseph disease, spinocerebellar ataxia, frontotemporal dementia, amyotrophic lateral sclerosis, slow channel congenital myasthenic syndrome, spinobulbar muscular dystrophy, as well as compound heterozygous autosomal recessive disorders. Other diseases that can be diagnosed include diabetes, cystic fibrosis, homocystenuria, Hermansky-Pudlak syndrome, cystinosis, Zellweger syndrome, beta-thalassemia, alkaptonuria, and cancer.

A variety of diseases appear to be mediated or accompanied by aberrant expression of one allele, often a mutant of a gene. Such differences in allelic expression can serve as the basis for diagnostic test for such conditions, and the ability to specifically silence the expression of detrimental alleles could be a therapeutic method for treating the disease, hence this novel method has very wide applications.

Title: **A Novel MRI Adiabatic T_2 Preparation Sequence with Reduced B1 Sensitivity**

Reference: E-073-2005/0

Inventor(s): Reza Nezafat (NHLBI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

This invention relates to a novel magnetic resonance angiography (MRA) method that accomplishes uniform contrast enhancement between coronary arteries and the surrounding tissue across the entire imaging volume. The disclosed technique utilizes an adiabatic refocusing transverse relaxation time (T_2)-preparation pulse sequence, in which the magnetization is tipped into the transverse plane with a hard radio-frequency (RF) pulse and refocused using a pair of adiabatic fast-passage RF pulses. The isochromats are subsequently returned to the longitudinal axis using a hard RF pulse. Simulations and in vivo images acquired with the T_2-Prep sequence illustrate excellent suppression of artifacts originating from B_1 inhomogeneity while achieving contrast-to-noise (CNR) enhancement between coronary arteries and surrounding tissues. Furthermore, images acquired with the T_2-Prep sequence show suppression of the banding artifacts and improvement of the visual sharpness of distal segments of the coronaries as compared to images acquired without the T_2-Prep sequence.

Title: **New Surrogate Marker for Diagnosis of HIV/AIDS Infection and for Evaluation of Treatment Effectiveness**

Reference: E-045-2004/2

Inventor(s): Gene M. Shearer (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

This technology describes the identification of a new surrogate marker, TNF-related apoptosis-inducing ligand (TRAIL), that can be universally employed to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation and immunoassays for assessing the amount of TRAIL in a biological sample. In the case of HIV infection, measuring levels of this surrogate marker can distinguish among infected individuals with high viral load, infected individuals with low viral

load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4+ T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new surrogate marker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods.

Title: **Nanoprobes for Detection or Modification of Molecules**

Reference: E-195-2005/0

Inventor(s): Ilya G. Lyakhov (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development are the "Rod-tether Nanoprobes", devices consisting of a rigid molecular rod with a flexible molecular tether attached at each end that can be used to detect and/or modify molecules. Each tether tip has a functional group, such as an antibody or oligonucleotide, that recognizes a target molecule. In addition, one tip carries a donor fluorophore and the other carries an acceptor fluorophore. The fluorophores form a pair for Forster Resonance Energy Transfer (FRET). In the absence of the target molecule, the rod keeps the tether arms apart most of the time, while in the presence of the target molecule, both recognizers bind to the target. This holds the donor and acceptor fluorophores close together. Illumination with light excites the donor and the energy is transferred by FRET to the nearby acceptor, which emits a detectable signal. By reducing an ELISA-like assay entirely to the molecular level, complex macroscopic or microfluidic washing and pumping systems can be eliminated. Rod-tether Nanoprobes can detect a wide variety of clinical and biowarfare reagents. The nanoprobes can also be used to rapidly and simply detect, modify and/or destroy endogenous molecules such as proteins and mRNA involved in a broad range of diseases. The simplest ssDNA-detecting nanoprobe has been created.

The benefits of the Rod-Tether Nanoprobes include: a) simplicity, only one reagent required and complicated and expensive microfluidic chips are eliminated (see BioTechniques Jan 2006, 40:1:85-90); b) reduction of ELISA, Southern, Northern and Western assays to single molecules; c) speed, only a single molecular reaction is required to detect a target molecule; d) exceptionally low cost per device; e) could be used in the clinic to instantaneously analyze patient's blood and detect genetic diseases; and f) could be used to detect biowarfare agents instantaneously.

The technology is further described at http://www.ccrnp.ncifcrf.gov/~toms/patent/nanoprobe/.

Title: **The Medusa™ Sequencer: A Sequencing Machine the Size of a Molecule that Could Sequence RNA in a Living Cell**

Reference: E-194-2005/0

Inventor(s): Thomas D. Schneider (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is the Medusa™ Sequencer, a single-molecule sequencing device that consists of a DNA (or RNA) polymerase attached to a set of four flexible arms. The tip of each arm carries a nonhydrolyzable nucleotide and a spectrally distinct Forster Resonance Energy Transfer (FRET) acceptor fluorophore. A donor fluorophore attached to the polymerase can excite the acceptor fluorophores by FRET. A Medusa™ Sequencer binds to a DNA primer hybridized to the DNA or RNA to be sequenced. The four arms with nucleotide tips "test" the polymerase pocket and the arm that has the nucleotide tip complementary to the unknown base of the sequence will dwell longer than the other three that are not complementary. However, the polymerase will not incorporate the nucleotide on the tip of the arm into the nascent strand because the nucleotide is nonhydrolyzable. FRET between the donor and the acceptor fluorophore at the arm tip produces a characteristic spectrum that identifies the bound base. Free hydrolyzable dNTPs (or NTPs) allow the Medusa™ Sequencer to step forward. The series of FRET signals reveals the unknown nucleotide sequence. A Medusa™ Sequencer could also be injected into a cell to read mRNA sequences inside a living organism. Coded versions of the Medusa™ Sequencer can signal when the device has been damaged.

The benefits of the Medusa™ Sequencer include: a) simplicity, only one reagent required; b) accuracy for counting individual mRNAs or DNAs; c) low error rate per base, and this can be improved by modifying the polymerase; d) speed, a single microscope can be used to obtain many sequences in parallel; e) exceptionally low cost per sequencing device; and d) could be used in the clinic along with sequence walkers to analyze patient's genetic diseases (e.g. Medical Applications of Sequence Walkers: ABCR Mutation G863A, http://www.ccrnp.ncifcrf.gov/~toms/g863a.html).

The technology is further described at http://www.ccrnp.ncifcrf.gov/~toms/patent/medusa.

Title: **Measuring Fifteen Endogenous Estrogens Simultaneously in Human Urine by High-Performance Liquid Chromatography-Mass Spectrometry**

Reference: E-207-2005/0

Inventor(s): Xia Xu (NCI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is a patent-pending, validated high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry method for measuring the absolute quantities of fifteen endogenous estrogens and their metabolites in human urine. The method is sensitive, specific, accurate, and precise. It requires a single hydrolysis/extraction/derivatization step and only 0.5 mL of urine, yet is capable of simultaneously quantifying estrone, its 2- and 4-methoxy derivatives, and its 2-, 4-, and 16alpha-hydroxy derivatives; estradiol, its 2- and 4-methoxy derivatives, and its 2- and 16alpha-hydroxy derivatives; 2-hydroxyestrone-3-methyl ether; 16-epiestriol; 17-epiestriol; and 16-ketoestradiol in premenopausal and postmenopausal women as well as men. Standard curves are linear over a 103-fold concentration range with the relative standard error of the estimate for the linear regression line ranging from 1.2 to 7.3%, respectively. The lower limit of quantitation for each estrogen is 0.02 ng per 0.5-mL urine sample (only 2 pg placed on column). The percent recovery of a known added amount of estrogen metabolite ranges from 96 to 107%. The overall precision, including the hydrolysis, extraction, and derivatization steps, is 1-5% relative standard deviation for samples prepared concurrently and 1-12% relative standard deviation for samples prepared in separate batches.

Title: **Active MRI Compatible and Visible iMRI Catheter**

Reference: E-298-2005/0

Inventor(s): Ozgur Kocaturk (NHLBI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

Interventional magnetic resonance imaging (iMRI) has gained important popularity in many fields such as interventional cardiology and radiology, owing to the development of minimally invasive techniques and visible catheters under MRI for conducting MRI-guided procedures and therapies. This invention relates to a novel MRI compatible and active visible catheter for conducting interventional and intraoperative procedures under the guidance of MRI. The catheter features a non conductive transmission line and the use of ultrasonic transducers that transform RF signals to ultrasonic signals for transmitting RF signal to the MRI scanner. The unique design of this catheter overcomes the concern of patient/sample heating (due to the coupling between RF transmission energy and long conductors within catheter) associated with the design of conventional active MRI catheters.

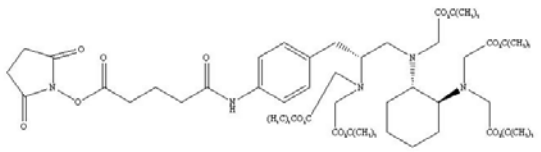
Title: **Metal Chelators and Target-Moiety Complexes for Imaging**

Reference: E-317-2004/1

Inventor(s): Martin W. Brechbiel (NCI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development are bifunctional metal chelators, metal chelator-targeting moiety complexes, metal chelator-targeting moiety-metal conjugates, kits, and methods of preparing them in a non-aqueous, automated peptide synthesizer system. These bifunctional chelators are useful for radiolabeling targeting moieties with SPECT and PET radioisotopes for molecular imaging for diagnosis and/or treatment of cancer. The metal chelators may be used in conventional synthetic methods to form targeting moieties [e.g., peptides, proteins, and Starburst polyamidoamine dendrimers (PAMAM)], capable of conjugating diagnostic and/or therapeutic metals. The formulae for two such chelators is shown below:



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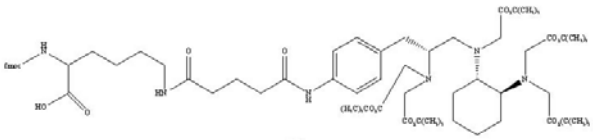

II

Title: **Fast Electron Paramagnetic Resonance Imaging (EPRI) Using CW-EPR Spectrometer with Sinusoidal Rapid-Scan and Digital Signal Processing**

Reference: E-221-2005/0

Inventor(s): Sankaran Subramanian (NCI)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

Electron Paramagnetic Resonance (EPR) Imaging is an indispensable tool that may be applied to a variety of disciplines for evaluation of chemical species having unpaired electrons such as free radicals and transition metal ions. In Continuous Wave (CW)-EPR the sample is continuously irradiated with weak RF radiation while sweeping the magnetic field relatively slowly. Existing CW-EPR techniques utilize a signal detection method known as phase-sensitive detection which results in data acquisition times that are too long for in vivo applications. The present technology represents significant improvements on conventional CW-EPR.

The subject technology includes three approaches to collecting image data with increased spatial, temporal and spectral resolution and improved sensitivity. Spectral data acquisition is performed by a direct detection strategy involving mixing a signal to base-band and acquiring data with a fast-digitizer. Projection data is acquired using a sinusoidal magnetic field sweep under gradient magnetic fields. Data collection times are decreased with the utility of rotating gradients. Further, the current technology improves sensitivity by employing Digital Signal Processing, which decreases background analog noise.

Increased speed and sensitivity makes CW-EPR a potentially useful and complementary tool to Magnetic Resonance Imaging for in vivo imaging. The presently described improvements to CW-EPR will allow changes of blood perfusion and oxygenation in tumors to be observed in nearly real-time, while improved resolution will permit angiogenesis in and around tumors to be carried out in a non-invasive manner. Additionally, rapid scan imaging provides excellent temporal resolution and will help quantify pharmaco-kinetics and metabolic degradation kinetics of bioactive free radicals.

Applications: Enhanced spatial, temporal, and spectral resolution of Continuous Wave-Electron Paramagnetic Resonance Imaging. Real-time assessment of changes in blood perfusion and oxygenation

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Title: **Systems and Methods for Intelligent Quality Control of Instruments and Processes**

Reference: E-042-1997/0

Inventor(s): James M. Deleo (CIT) and Alan T. Remaley (CC)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is a cost-effective system and method for evaluation of instruments and processes for real-time detection of error. The subject invention includes the capacity to identify imprecision in a variety of data analysis tools, which may be susceptible to malfunction. Such processes include instrumental analysis of patient specimens, assembly line manufacturing and general plant or factory operation. This system provides an automated platform for the dual purpose of 1) monitoring data to detect unusual events in real time and 2) enhancement of human and machine recognition and analysis of improper occurrences based on time-varying patterns of measured values.

The scheme of the current system is straightforward and in general the method involves the following steps: 1) collection of data elements from an instrument or process 2) counting data elements having values within predetermined intervals of the data range 3) applying counts of data to a neural network that monitors data trends and 4) production of an output based on the neural network, which demonstrates whether the instrument or process is generating results within an appropriate range. This system is advantageous because output is generated in real time and thus available without delay for immediate correction of malfunctions.

Applications: Quality control for processes and instruments. Automated system for real time notification of malfunctions in an instrument or process for immediate correction of the procedure

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THERAPEUTIC DEVICES

Title: **Targeting Of T-cell Regulatory Receptors Of The TIM Family Based On The Crystal Structure Of The Ligand-binding Domain**

Reference: E-098-2006

Inventor(s): Gerardo Kaplan (CBER/FDA)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development are methods to produce and/or enhance therapeutic agents based on models of the three-dimensional structures of the Ig-like domains of various TIM family members to a) develop agonists and antagonists of the T-cell immunoglobulin mucin (TIM) family of receptors and b) design specific TIM receptor-mutants with altered binding capabilities. The TIM receptors are involved in the regulation of immune responses, tissue regeneration, cancer, and viral cell entry. The invention provides models of the three-dimensional structures of the Ig-like domains of TIM family members developed after several crystal structures were resolved. The structures were further validated by mutagenesis and biochemical analysis. The TIM family comprises type 1 integral membrane glycoproteins containing a characteristic six-cysteine Ig-like domain extended above the cell surface by a mucin-like domain. The crystal structures revealed diverse homophylic interactions between TIM family members. The three-dimensional structure of all TIM family members can be used in the making of agonists and antagonists of homophilic, heterophilic, and ligand interactions of these receptors.

Applications: Therapies that target the interaction of TIM family members with their ligands, such as small molecules or monoclonal antibodies, can control immune responses and the development of a variety of diseases.

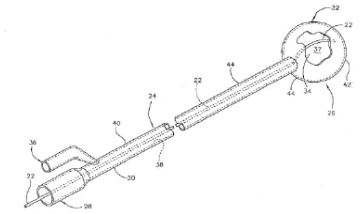
Title: **Singh Intracavitary Balloon Brachytherapy System (SIBBS)**

Reference: E-314-2005

Inventor(s): Anurag K. Singh (NCI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is a device for delivering targeted radiation brachytherapy to a portion of tissue in the cavity of a patient. The device includes an applicator with a balloon where in a deflated state is inserted into the body cavity and in an inflated state enlarges to fill the body cavity. The balloon moves from the deflated state into the inflated state upon introduction of pressurized fluid to the interior of the balloon. The apparatus also includes a catheter extending over at least a portion of the balloon for delivering treatment to the adjacent cavity (e.g., radiation or heat). A tracking device (e.g., a camera) is included in the apparatus for helping track the positioning of the balloon within the body cavity prior to inflation. The apparatus can be alternatively configured with a second balloon containing a therapeutic agent which is inflated after positioning and expansion with a first balloon first.



Applications: Brachytherapy, Radiation dosing, Cancer therapy

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Title: **Cell-nanofiber Composite Based Engineered Cartilage**

Reference: E-116-2005

Inventor(s): Wan-Ju Li and Rocky S. Tuan (NIAMS)

Licensing Contact: Peter A Soukas; 301-435-4646, soukasp@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. 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. 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, and support of chondrogenic differentiation as well as other connective tissue linage differentiation. The invention based on cell-nanofiber composite represents a candidate engineered tissue for cell-based approaches to cartilage repair.

Title: **Mucus Shaving Apparatus for Endotracheal Tubes**

Reference: E-061-2004/0

Inventor(s): Theodor Kolobow (NHLBI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

HHS seeks parties interested in manufacturing and commercializing an endotracheal tube cleaning apparatus for insertion into the inside of the endotracheal tube of a patient to shave away mucus deposits. This cleaning apparatus comprises a flexible central tube with an inflatable balloon at its distal end. Affixed

to the inflatable balloon are one or more silicone rubber shaving rings, each having a squared leading edge to shave away mucus accumulations implicated in bacterial accumulation. In operation, the un-inflated cleaning apparatus is inserted into the endotracheal tube until its distal end is properly aligned with the distal end of the endotracheal tube. After proper alignment, the balloon is inflated by a suitable inflation device (e.g., a syringe) until the balloon's shaving rings are pressed against the inside surface of the endotracheal tube. The cleaning apparatus is then pulled out of the endotracheal tube and in the process the balloon's shaving rings shave off the mucus deposits from the inside of the endotracheal tube.

Title: **The Mucus Slurper: A Novel Device to Keep the Endotracheal Tube (ETT) Free of All Mucus, Without Suctioning**

Reference: E-074-2005/0

Inventor(s): Theodor Kolobow (NHLBI)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is a mucus slurping device to remove all mucus, before mucus reaches the tip of the endotracheal tube (ETT); thus, no mucus ever enters the ETT, and the ETT remains always clean - without suctioning. A Mallinckrodt Hi-Lo® CASS (continuous aspiration of subglottic secretions) endotracheal tube is modified by appending to the distal-most tip of a cut-off CASS tube a molded, hollow, concentric plastic ring with 3 - 4 (or more) small (less than l mm in diameter) suction ports, the latter positioned in the most dependent part of the ETT (Figure 1). The CASS line was extended to the very tip of the ETT, and suction was activated for approximately 0.5 s, synchronized to the early part of expiration; and repeated once a minute, or as desired. All mucus was collected in a small in-line vial. Healthy, anesthetized and paralyzed sheep, were intubated with a modified 8 mm CASS ETT tube with attached “Mucus Slurper”; with sheep lying prone, trachea/neck oriented below horizontal. Never suctioned. At the end of the 72 h study, sheep were electively euthanized, and autopsied.

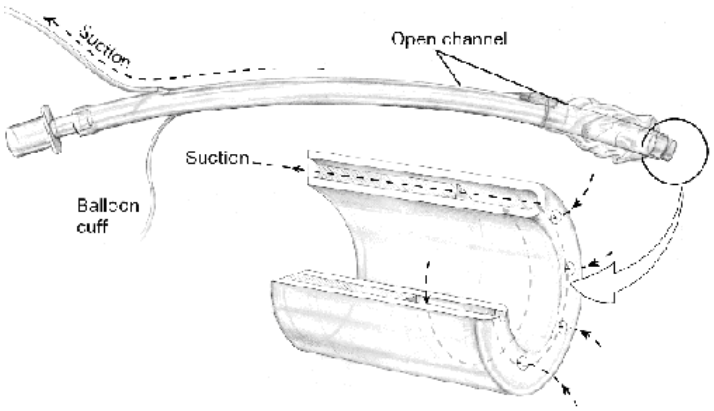

Figure 1. Normal arterial blood gases. No traces of mucus were found along the entire length of the ETT. There were no gross abnormalities of the tracheal mucosa; Bacterial cultures of the 5 lobes of the lungs were negative. The Mucus Slurper represents a new concept that may significantly contribute to improved care of patients intubated and mechanically ventilated; with no need for suctioning/cleaning, and free of ventilator associated pneumonia.

Applications: Prevention of ventilator associated pneumonia. Intubation. Mucus clearance.

RESEARCH TOOLS AND MATERIALS

Title: **Model for Study of Glomerular Disorders: Conditionally-Immortalized Mouse Podocyte Cell Line with Tet-on-Regulated Gene Expression**

Reference: E-049-2007/0

Inventor(s): Jeffrey B. Kopp (NIDDK)

Licensing Contact: Tara L. Kirby Ph.D., 301-435-4426, tarak@mail.nih.gov

Podocytes, cells of the visceral epithelium in the kidneys, are a key component of the glomerular filtration barrier. As such, they play a vital role in glomerular disorders, which are a major cause of chronic kidney disease. Examples of these disorders include focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, and diabetic nephropathy.

The inventors have developed a conditionally-immortalized mouse podocyte cell line with tightly controlled conditional gene expression. The cell line has been conditionally immortalized through the introduction of the H-2Kb-tsA58 transgene, which is a temperature-sensitive mutant of the SV40T antigen. Inducible gene expression is tightly controlled through two introduced transgenes, podocin-rtTA and CMV-tTS, that produce a "Tet-on" system wherein gene expression is induced by tetracycline or doxycycline. The combination of the two transgenes for Tet-on gene expression has resulted in much tighter regulation and lower background expression compared to cells carrying the podocin-rtTA transgene alone.

Applications: Model system for study of glomerular disorders. Model system for podocyte cell biology.

Title: **Methods and Systems for Identifying and Classifying Drug Targets**

Reference: E-268-2005/0

Inventor(s): Anatoly L. Mayburd (NCI)

Licensing Contact: Cristina Thalhammer-Reyero; 301-435-4507, thalhamc@mail.nih.gov

Available for licensing and commercial development is a novel method for a-priori evaluation of the therapeutic relevance of gene products for various diseases, in order to make drug development more cost-efficient. In addition, this technology may be used to identify novel therapeutic uses for known drugs. For example, the current invention has the potential to uncover the role of an established cancer drug target, in an alternative disorder such as Alzheimer’s disease, thus providing an additional use for the available cancer drug.

The multivariable model used by the method, which is based on a training set of targets that have already passed FDA review, is capable of ranking drug targets in terms of prospective clinical success. This innovative approach integrates multiple datasets that describe each single gene product from a broad range of analyses, such as microarrays, x-ray crystallography, and phylogenetics, to rapidly characterize a proteins structure, function, and gene regulation information. An algorithm subsequently scores a protein’s potential as a drug target for use in future drug design studies. The resulting set of targets is enriched 28-fold as compared to randomly selected gene products.

Applications: Early evaluation of a candidate drug target's potential to yield a therapeutic effect, given the target's inhibitor is provided.

Title: **Gene Cassette for Enhancement of Protein Production**

Reference: E-261-2003/0

Inventor(s): Shankar Adhya and Sudeshna Kar (NCI)

Licensing Contact: Tara L. Kirby Ph.D., 301-435-4426, tarak@mail.nih.gov

There is a continuing market need for expression systems that improve recombinant protein production for disease therapeutics or research materials. The present invention describes a "gene cassette" containing the *aadA1* (aminoglycoside adenylyltransferase) gene that increases protein expression levels when incorporated into a bacterial or eukaryotic host genome. In bacterial systems, the inventors have shown that this gene cassette induces enhancement of protein production and accumulation. This inducement is not restricted by the nature of the vector, induction system or nature of protein. In particular, this invention has yielded 3-fold upregulation of anti-HIV peptide expression levels in a microbial microbicide (see reference below). This technology offers an effective mechanism for increased product yield that can be utilized for pharmaceutical or biotechnological applications.

Applications: Affordable gene cassette that increases production of recombinant or native proteins with reduced culture volume and faster processing time.

Title: **Mice Lacking Expression of Chemokine Receptor CCR9 Generated by Gene Targeting (CCR9 KO Mice)**

Reference: E-328-2006/0

Inventor(s): Paul E. Love (NICHD)

Licensing Contact: Jennifer S Wong; 301-435-4633, wongje@mail.nih.gov

Chemokines and their receptors are key regulators of thymocytes migration and maturation in normal and inflammation conditions. The chemokine CCL25 is highly expressed in the thymus and small intestine. CCR9, the receptor for CCL25, is expressed on the majority of thymocytes, indicating that CCR9 and its ligand may play an important role in thymocyte development. To investigate the role of CCR9 during lymphocyte development, CCR9 knockout mice were developed. Knockout mice had increased numbers of peripheral gammadelta-T cells but reduced numbers of alphabeta-T cells. In competitive transplantation experiments bone marrow from CCR9 knockout mice was much less efficient at repopulating the thymus than control (wild type) bone marrow. Thus, CCR9 KO mice are a model for studying thymocyte development and trafficking in the body. Additionally, as the ligand for CCR9 is highly expressed in the small intestine, CCR9 potentially plays a role in the specialization of immune responses in the gastrointestinal tract.

Applications: Evaluate drugs aimed at blocking or augmenting lymphocyte trafficking.

Title: **Preparative Two Dimensional Gel Electrophoresis System**

Reference: E-066-1994/0

Inventor(s): B. Alex Merrick (NIEHS)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

The National Institute of Environmental Health Sciences has developed procedures and a prototype device for isolation of proteins from complex mixtures for protein identification. The system serves as a one-step purification method for isolation of biologically relevant proteins affected by disease or experimental treatment and has been described in Electrophoresis 15, 735–745, 1994. The system includes a preparative isoelectric focusing device for separation of proteins by charge, a glass mold for preparative polyacrylamide gel separation by mass and a protocol for use.

The commercial advantage of the Preparative Two Dimensional Gel Electrophoresis system is to separate and isolate sufficient amounts of individual protein for sequencing in a powerful one-step purification method. The Preparative Two Dimensional Gel Electrophoresis system can resolve individual proteins by charge and mass from up to 1 to 2 mg of unpurified starting material from protein mixtures. Current devices for two dimensional gel electrophoresis are generally for analytical scale work and are not physically or procedurally adapted to accommodate preparative sample loads. Although other preparative electrophoresis devices do exist, they separate by either mass or charge alone and function as stand-alone units without ready integration into additional systems for resolution of individual proteins.

Applications: Protein sequencing, protein immunization for antibody production, immunostaining and other modes of protein characterization.

Title: **mFPR2 Transgenic and Knockout Mouse Models for Alzheimer's and Other Inflammatory Diseases**

Reference: E-303-2006/0

Inventor(s): Ji Ming Wang (NCI)

Licensing Contact: Tara L. Kirby Ph.D., 301-435-4426, tarak@mail.nih.gov

Human Formyl Peptide-Like Receptor 1 (hFPLR1) has been implicated in host defense for disease processes including Alzheimer's disease, infection, and other inflammatory diseases. hFPLR1 and its mouse homologue Formyl Peptide Receptor 2 (mFPR2) are G-protein coupled receptors that are expressed at high levels on phagocytic leukocytes, mediating leukocyte chemotaxis and activation in response to a number of pathogen- and host-derived peptides. Activation of hFPRL1/mFPR2 by lipoxin A4 may play a role in preventing and resolving inflammation. Also, hFPRL1/mFPR2 has been shown to mediate the chemotactic activity of amyloid beta 1-42, a key pathogenic peptide in Alzheimer's disease.

Available for licensing are mice expressing the mFPR2 transgene on either the FVB or C58BL background, as well as mFPR2 knockout mice on the C57BL background. These mice are anticipated to be highly useful in the study of a wide variety of inflammatory, infectious, immunologic and neurodegenerative diseases.

Applications: Drug development model for Alzheimer's disease and other inflammatory diseases. Tool to probe the role of hFPRL1/mFPR2 in host responses in a variety of disease processes, including inflammatory, infectious, immunologic, and neurodegenerative disease

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Title: **Bioreactor Device and Method and System for Fabricating Tissue**

Reference: E-042-2005/0

Inventor(s): Juan M. Taboas and Rocky S. Tuan (NIAMS)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is a millifluidic bioreactor system for culturing, testing, and fabricating natural or engineered cells and tissues. The system consists of a millifluidic bioreactor device and methods for sample culture. Biologic samples that can be utilized include cells, scaffolds, tissue explants, and organoids. The system is microchip controlled and can be operated in closed-loop, providing controlled delivery of medium and biofactors in a sterile temperature regulated environment under tabletop or incubator use. Sample perfusion can be applied periodically or continuously, in a bidirectional or unidirectional manner, and medium re-circulated.

Title: **Human Sweet and Umami Taste Receptor Variants**

Reference: E-099-2005/0

Inventor(s): Dennis Drayna and Un-Kyung Kim (NIDCD)

Licensing Contact: Susan Carson, D.Phil., 301-435-5020, carsonsu@mail.nih.gov

The complexity of taste discrimination (salty, sour, sweet, umami and bitter) varies between human individuals and populations. Sweet and umami (the taste of glutamate) tastes play a major role in the perception of calorically-rich and essential nutrients and there are well-documented differences in individual perception of sweet and umami flavorings, many of which appear to be genetic in origin. Studies of individuals within and between populations that vary in any of the taste receptors should be of direct interest to the multi-billion dollar food and flavoring industry as the characterization of such variants could be used to aid in the development of a variety of taste improvements in foods and orally administered medications. NIH researchers previously characterized bitter taste receptor variants in world wide populations [Human Mutation 26, 199-204; HHS Ref. No. E-222-2003/0] and have now extended their studies to the sweet and umami receptors in global populations.

The group of Dr. Dennis Drayna at NIDCD have now discovered novel coding sequence polymorphisms in the human TAS1R genes. These genes encode dimeric receptors that sense sweet taste (as TAS1R2+TAS1R3) and the taste of umami (as TAS1R1+TAS1R3). To achieve maximum genetic diversity, TAS1R receptors from a panel of 30 Europeans, 20 East Asian, 10 Native Americans, 8 South Asians and 20 sub-Saharan Africans were sequenced. Approximately 60% of the identified SNPs caused an amino acid substitution in the encoded receptor protein. This variation may account for individual preferences in sweet and umami tastes in foods and could be of use in the understanding and control of dietary preferences that lead to obesity and diabetes.

Title: **Susceptibility-Matched Multiwell Plates for High-Throughput Screening by Magnetic Resonance Imaging and Spectroscopy**

Reference: E-243-2005/0

Inventor(s): Kenneth W. Fishbein (NIA)

Licensing Contact: Chekesha S Clingman; 301-435-5018, clingmac@mail.nih.gov

This invention describes the development of a multi-well assay plate for high-throughput screening by magnetic resonance imaging (MRI) and nuclear magnetic resonance (NMR) spectroscopy. Multi-well plates are used in a wide variety of high-throughput measurements in clinical chemistry and immunology, as well as in drug discovery and other research applications. Magnetic resonance imaging (MRI) of multi-well plates offers the possibility of performing new kinds of high-throughput assays, including the detection of magnetic nanoparticles attached to or within cells. Moreover, MRI-guided localized nuclear magnetic resonance (NMR) spectroscopy could be used to perform detailed chemical analysis of complex mixtures of metabolites not possible by any other common analytical technique. Best of all, conventional MRI techniques exist which would permit all samples in one or more multi-well plate(s) to be analyzed simultaneously. Unfortunately, conventional multi-well plates typically give poor performance for MRI-based assays since they provide inadequate matching of magnetic susceptibility between the plate, the sample and their surroundings. This results in distortion of the magnetic field within the scanner and thus reduces the sensitivity for detecting magnetic particles and the resolution of NMR spectra. This invention relates to a new multi-well plate design incorporating one-piece polyetherimide plastic construction for improved magnetic susceptibility matching for aqueous samples. This design can easily be extended to non-aqueous samples by the selection of an appropriate, commercially-available plastic resin or resin blend. Further enhancement in susceptibility matching can be accomplished by combining the new plate design with plugs for each well constructed from the same plastic as the plate. These plugs would allow the entire thickness of each sample to be scanned in chemical analyses, improving signal-to-noise ratio and sensitivity. These plugs can be integrated into a single “cap mat” so that the entire assembly can be filled and manipulated by standard robotic laboratory equipment already in wide use in the pharmaceutical industry. Alternatively, spherical wells, accessed by narrow fill holes, may be molded into a solid plate, eliminating the need for individual plugs to seal each well. The new multi-well plate/plug design reduces magnetic field distortions and should dramatically improve spectral resolution and sensitivity for NMR and MRI-based high-throughput screening.

Title: **Transformation-Associated Recombination (TAR) Cloning**

Reference: E-121-1996/0

Inventor(s): Vladimir Larionov (NCI)

Licensing Contact: Susan Carson D.Phil., 301-435-5020, carsonsu@mail.nih.gov

Transformation-Associated Recombination (TAR) cloning in yeast is a unique method for selective isolation of large chromosomal fragments or entire genes from complex genomes without the time-consuming step of library construction (PNAS (1996) 93, 491-496). The technique involves homologous recombination during yeast spheroplast transformation between genomic DNA and a TAR vector that has short (approximately 60bp) 5’ and 3’ gene targeting sequences (hooks). Further, because up to 15% sequence divergence does not prevent recombination in yeast, TAR cloning is highly efficient for isolation of gene homologs and synthenic regions. Using this technology, chromosomal regions up to 250kb can be rescued in yeast as circular YACs within 3-5 working days (NAR (2003) 31, e29; Current Protocols in Human Genetics (1999) 5.17.1).

NIH researchers Drs. Larionov, Kouprina and Resnick have championed the use of this technology and TAR cloning has been used to efficiently isolate haplotypes, gene families (Genome Research (2005) 15, 1477) as well as genomic regions which are not present in existing BAC libraries. Known mutations and new modifications, including point mutations, deletions and insertions, can easily be introduced into DNA

fragments hundreds of kilobases in size without introducing any unwanted alterations. The modified DNAs can then be tested functionally in mammalian cells and transgenic mice. TAR has also been used for structural biology studies, long-range haplotyping, evolutionary studies, centromere analysis and analysis of other regions which cannot be cloned by a routine technique based on in vitro ligation (Kouprina and Larionov (2005) Recent Developments in Nucleic Acids Research, in press). In particular, construction of human artificial chromosome vectors and the combining of a HAC vector with a gene of interest can be effectively performed using the TAR methodology. Human genes isolated by TAR for expression in HACs include HPRT (60kb), BRCA1 (84kb), BRCA2 (90kb), PTEN (120kb), hTERT (60kb), KA11 (200kb), ASPM (70kb), SPANX-C (83kb) among others. TAR is a flexible and efficient means for employing in vivo recombination in yeast in order to clone entire genomic loci which can then be used for structural and functional analysis and for expression in HAC vectors for a variety of uses including for potential use in gene therapy.

Title: **Rapid Methods for Human Artificial Chromosome (HAC) Formation**

Reference: E-128-2005/0

Inventor(s): Vladimir Larionov (NCI)

Licensing Contact: Susan Carson D.Phil., 301-435-5020, carsonsu@mail.nih.gov

Human artificial chromosomes (HACs) provide a unique opportunity to develop a new generation of vectors for therapeutic use as gene expression and delivery systems. The advantages of a high-capacity, non-integrating chromosome-based vector capable of autonomous replication and long-term gene expression are evident for potential use in gene therapy and this area is one of active research. In particular, the generation of a functional centromere (a complex structure needed for segregation at cell division) has been recognized as key in the production of synthetic chromosomes. However, a typical human centromere extends over many millions of base pairs containing mainly alphoid satellite DNA (171 bp repeating units) organized into higher order repeats (HORs), which have been difficult to fully characterize or modify readily. There remains a need to elucidate the structural requirements of alphoid DNA arrays for efficient de novo assembly of centromere structure in order to construct HAC vectors able to carry intact mammalian genes capable of fully regulated gene expression and which can be stably maintained in the host nucleus for use in gene therapy.

The group of Dr. Larionov at the NCI and colleagues have recently developed a novel strategy to rapidly construct large synthetic alphoid DNA arrays with a predetermined structure by in vivo recombination in yeast (Nucleic Acids Res., Sep 2005; 33: e130). The invention is a two step method involving 1) rolling-circle amplification (RCA) of a short alphoid DNA multimer (e.g. a dimer) and 2) subsequent assembly of the amplified fragments by in vivo homologous recombination during transformation with a Transformation-Associated Recombination targeting vector (TAR-NV) into yeast cells. This method or Recombinational Amplification of Repeats (RAR) has been used to construct sets of different synthetic alphoid DNA arrays varying in size from 30 to 120 kb which were shown to be competent in HAC formation. Thus, these long arrays are engineered centromere-like regions that permit construction of mammalian artificial chromosomes with a predefined centromeric region structure. As any nucleotide can be easily changed into an alphoid dimer before its amplification, this new system is optimal for identifying the critical regions of the alphoid repeat for de novo centromere seeding.

Title: **R On-Demand Protein Microarrays: In Vitro Assembly of Protein Microarrays**

Reference: E-244-2005/0

Inventor(s): Deb K. Chatterjee (NCI)

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Protein microarrays are becoming an indispensable biomedical tool to facilitate rapid high-throughput detection of protein-protein, protein-drug and protein-DNA interactions for large groups of proteins. The novel Protein Microarray of this invention is essentially a DNA microarray that becomes a protein microarray on demand and provides an efficient systematic approach to the study of protein interactions and drug target identification and validation, thereby speeding up the discovery process. The technology allows a large number of proteins to be synthesized and immobilized at their individual site of expression on an ordered array without the need for protein purification. As a result, proteins are ready for subsequent use in binding studies and other analysis.

The Protein Microarray is based on high affinity and high specificity of the protein-nucleic acid interaction of the Tus protein and the Ter site of E. coli. The DNA templates are arrayed on the microarray to perform dual function: (1) synthesizing the protein in situ (cell-free protein synthesis) in the array and (2) at the same time capturing the protein it synthesizes by DNA-protein interaction. This method utilizes an expression vector containing a DNA sequence which serves a dual purpose: (a) encoding proteins of interest fused to the Tus protein for in vitro synthesis of the protein and (b) encoding the Ter sequence, which captures the fusion protein through the high affinity interaction with the Tus protein.

Applications: Simultaneous analysis of interactions of many proteins with other proteins, antibodies, nucleic acids, lipids, drugs, etc, in a single experiment. Efficient discovery of novel drugs and drug targets.

Title: **A Nurr1-Knockout Mouse Model for Parkinson's Disease and Stem Cell Differentiation**

Reference: E-024-1999/0

Inventor(s): Dr. Vera Nikodem (NIDDK)

Licensing Contact: Tara L. Kirby Ph.D., 301-435-4426, tarak@mail.nih.gov

The researchers have generated Nurr1-knockout mice via genomic locus inactivation using homologous recombination.

Transcription factor Nurr1 is an obligatory factor for neurotransmitter dopamine biosynthesis in ventral midbrain. From a neurological and clinical perspective, it suggests an entirely new mechanism for dopamine depletion in a region where dopamine is known to be involved in Parkinson's disease. Activation of Nurr1 may be therapeutically useful for Parkinson's disease patients; therefore, the mice would be useful in Parkinson's disease research.

Additionally, Nurr1 has been shown to be critical for development of midbrain dopaminergic neurons, and thus may contribute to stem cell-based therapies for neurological disorders. Nurr1 is also important for osteoblast differentiation, suggesting a general role in stem cell differentiation and growth.

Applications: Research and drug testing for Parkinson's disease and other neurological disorders. Stem cell research relating to neurological and other disorders and bone formation.

Title: **Devices for Aseptic Lyophilization of Biological Samples**

Reference: E-015-1995/2

Inventor(s): Geoffrey Kidd (NCI)

Licensing Contact: Tara L. Kirby Ph.D., 301-435-4426, tarak@mail.nih.gov

Biological materials are often lyophilized and stored in small aliquots for long-term preservation as a means of improving stability and expanding shelf life. At present, sterility of solutions cannot be preserved throughout the lyophilization process, and reconstituted samples must be filtered to remove contaminants such as fungi or bacteria, resulting in considerable loss of expensive sample via absorption by the filter. Thus, there exists a need for a device that eliminates microbial contamination throughout the lyophilization process and provides materials that are ready to use following lyophilization.

This technology offers a functional method to prevent microbial contamination during lyophilization and a simple means to prevent contamination. It affords a convenient system for gas venting and exchange utilizing a microcentrifuge tube fitted with a cap incorporating a filter membrane. In a related technology, a unique, cost-effective multi-well plate assembly provides for simultaneous lyophilization of small sample volumes for high-throughput operations. Thus, these technologies are well-suited for researchers concerned about contamination during the lyophilization process. Given the spillage often occurring within centrifugal freeze-dryers, these technologies are also useful even when sterility is not needed, as they prevent contamination from the often-dirty interiors of laboratory centrifugal freeze-dryers, as well as cross-contamination between samples undergoing lyophilization. In addition, by extending shelf-lives, these technologies enable researchers to purchase expensive biomolecules and pharmaceuticals in money-saving bulk quantities. Furthermore, these technologies permit cells to be grown and stored axenically, in small quantities, with or without lyophilization.

Applications: Maximizes the shelf-lives of expensive biomolecules and pharmaceuticals. Makes practical the bulk purchase of expensive biomolecules and pharmaceuticals by extending shelf-lives. Makes possible the axenic storage of cells via aseptic freeze-drying.

Title: **Dissection Tools and Methods of Use**

Reference: E-272-2005/0

Inventor(s): Soojung Shin (NIA)

Licensing Contact: Fatima Sayyid; 301-435-4521, sayyidf@mail.nih.gov

Available for licensing is a dissection tool for cutting cell aggregates into smaller portions for further colony propagation. It is comprised of a handle attached to a rotatable shaft fitted with a cutting blade. The technology describes a safe and practical device that provides maximum product yield by preventing material from accumulating between the cutting surfaces. It also provides for more uniform cut colonies using lesser number of cuts than existing stem cell cutting instruments.

Applications: Makes possible the sectioning of cultured embryonic stem cells into smaller fractions for their transfer to new culture medium and subsequent incubation.

MANUFACTURING

Title: **Poly-saccharide-derived Nitric Oxide-releasing Carbon-bound Diazeniumdiolates**

Reference: E-279-2005

Inventor(s): Joseph A. Hrabie (NCI)

Licensing Contact: John Stansberry; 301-435-5286, stansbej@mail.nih.gov

The invention discloses a method for producing nitric oxide (NO)-releasing derivatives of any material containing a reducing sugar component. It may be used to produce NO-releasing cotton bandages or surgical fabrics, cellulose filters or dialysis membranes, and drug formulating/compounding agents to prevent stomach irritation. The method involves incorporation of a diazeniumdiolate ($-N_2O_2$) group at one or more carbons via the base-catalyzed replacement of acidic hydrogens and is thus compatible with traditional polysaccharide processing techniques. Monosaccharides such as glucose may also be derivatized.

OTHER

Title: **Hand Puncture Protector for Nurses**

Reference: E-104-1992/0

Inventor(s): Bonnie C. Thornton (CC)

Licensing Contact: Michael A Shmilovich; 301-435-5019, shmilovm@mail.nih.gov

Available for licensing and commercial development is a device that provides nurses or other health care workers with protection against accidental needle sticks. Specifically, a device has been created which protects the most susceptible areas on the back and sides of the thumb, forefinger and the area of the hand there between. This offers the notable advantage of preventing infections from accidental needle sticks. This invention is particularly useful during the risky task of inserting a twisted or kinked needle (such as a Huber needle) into a pot-a-cath.