



## Office of Patents and Licensing Biomarkers and Diagnostics

### Technology Contact Information :

**Peter Golikov, MS, MBA**

Director, Ventures and Licensing  
University of Medicine and Dentistry of  
New Jersey

335 George Street,

New Brunswick, NJ 08901

Direct Phone: **(732)-235-9355**

Office Phone: (732)-235-9350

Fax: (732)-235-9358

[golikope@umdnj.edu](mailto:golikope@umdnj.edu)



TABLE OF CONTENTS

ASSESSMENT AND QUANTIFICATION OF RISK FOR THE DEVELOPMENT OF SCHIZOPHRENIA ( <i>JOHNSON, RWJ 96-16</i> ) .....	3
DUTPASE ENZYME A MARKER FOR CELLULAR PROLIFERATION BACKGROUND ( <i>ROBERT LADNER, SOM 94-12</i> ) .....	4
HEMATOPOIETIC GROWTH FACTOR INDUCIBLE NEUROKININ-1 GENE ( <i>PRANELA RAMESHWAR, NJMS 00-31 &amp; 02-47</i> ).....	5
A NOVEL TOPOISOMERASE 1 BINDING PROTEIN FOR USE IN CANCER DIAGNOSTICS AND THERAPEUTICS ( <i>ERIC H. RUBIN, CINJ 01-46</i> ).....	6
METHODS FOR DETERMINING AUTISM SPECTRUM DISORDER ( <i>MILLONIG, CABM 03-16</i> ).....	7
NOVEL MODIFICATION OF IMMUNOMODULATORY PROTEIN ( <i>ALEXEY G. RYAZANOV, RWJ 04-41</i> ).....	8
BONE MORPHOGENETIC PROTEIN -2 AND PROTEIN-4 IN TREATMENT AND DIAGNOSIS OF CANCER ( <i>JOHN LANGENFELD, RWJ 01-02</i> ).....	9
THYMIDYLATE SYNTHASE POLYMORPHISMS FOR USE IN SCREENING FOR CANCER SUSCEPTIBILITY ( <i>ROBERT LADNER, SOM 02-52</i> ).....	10
MONOCLONAL ANTIBODY FOR A PROSTATE-SPECIFIC TUMOR SUPPRESSOR GENE ( <i>CORY ABATE-SHEN, CABM 01-10</i> ) .....	11
A NOVEL HUMAN BRAIN DERIVED NEUROTROPHIC FACTOR AS A MARKER FOR THE PREDICTION OF REPRODUCTIVE POTENTIAL IN WOMEN ( <i>SEIFER, 01-17</i> ).....	12
A NOVEL BIOMARKER FOR DIAGNOSIS OF ULCERATIVE COLITIS AND COLON CANCER ( <i>KIRON DAS, 01-08 RWJ</i> ) .....	13
BIOMARKERS FOR BREAST CANCERS ( <i>KIRAN MADURA, 04-13RWJ</i> ) .....	14
PDJA1, A CARDIAC SPECIFIC BIOMARKER ( <i>STEPHEN VATNER, NJMS 02-17</i> ).....	15
IDENTIFICATION OF THE SECOND GENE OF NIEMANN-PICK C DISEASE ( <i>PETER LOBEL, 00-39 RWJMS</i> ).....	16
DETECTION OF MUTATIONS IN HETEROGENEOUS TISSUES ( <i>JAMES S. GOYDOS, CINJ 03-15</i> ) 17	
HUMAN PREPROTACHYKININ-I GENE PROMOTER ( <i>PRANELA RAMESHWAR, NJMS 97-16</i> ).....	18
METHOD OF QUANTIFYING DISEASE BIOMARKERS IN THE LENS OF THE EYE ( <i>FREDERIKSE NJMS 06-04</i> ).....	19
DIAGNOSTIC TEST FOR BIOLOGICAL AGENTS ( <i>CHARLES SPILLERTR, NJMS 05-42</i> ) .....	20



## **Assessment and Quantification of Risk for the Development of Schizophrenia** (Johnson, RWJ 96-16) CNS

### **Background**

Schizophrenia is a developmental disorder caused by brain damage in a fetus due to maternal genetic and environmental factors. The genetic factors have not been definitively identified due to several factors: 1) involvement of more than one gene 2) uncertainty in the mode of inheritance 3) a high frequency of the allele being tested in the population being screened. The environment around the developing fetus is contributed by maternal components and there is a growing appreciation that a combination of fetal environmental and maternal genetic factors during the second trimester of pregnancy contributes to the development of schizophrenia. A resolution of the precise nature, components, and manner of interaction of the genetic and environmental factors could lead to the prevention of this disease and other developmental disorders that are believed to share common etiological factors.

### **Description of the Technology**

A 19 base pair deletion in the enzyme dihydrofolate reductase (DHFR) has been shown to have a significant predictive value for the identification of individuals at risk for the development of schizophrenia. Models for the determination of gene inheritance pattern using patient derived tissue samples have been developed. Further, the dietary content of folate, cobalamin, and pyridoxine of pregnant and susceptible individuals has been determined to be predictive of the susceptibility to schizophrenia.

### **Applications**

- To screen and identify individuals genetically susceptible to give birth to schizophrenic individuals
- To screen and identify individuals susceptible to schizophrenia
- For the development of a database of environmental reference sets for the identification of environmental factors capable of triggering the disease in genetic carriers or genetically prone individuals or their off-springs
- For the development of treatment modalities for individuals identified as susceptible to developmental disorders

### **Patent Status**

United States patent issued 6,210,950 B1

### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**dUTPase Enzyme A Marker for Cellular Proliferation Background** (*Robert Ladner, SOM 94-12*) *Diagnostic/Therapeutic Target*

**Background**

dUTPase is an enzyme that hydrolyzes dUTP to dUMP and pyrophosphate. Since dUTPase levels increase during cell proliferation in a cell-cycle dependent manner, it is suggested that this enzyme could be used as a proliferation marker. Other human proteins such as Ki-67, C5F10 and DNA polymerase alpha, which increase during cell proliferation, have been reported to be useful as prognostic indicators of the status of a cell. For example, Ki-67 has been used as a proliferation marker for lymphoproliferative diseases, and central nervous system and breast tumors. The present invention describes the use of dUTPase enzyme as a marker for the determination of proliferation status of a cell in both neoplastic and normal tissues.

**Description of the Technology**

Scientists at UMDNJ have isolated and completely sequenced the human dUTPase gene. In addition, the dUTPase enzyme has been isolated and purified. The invention also provides methods for determining the proliferation status of a cell and the efficacy of antineoplastic agents using dUTPase. The dUTPase enzyme of the present invention can be used as a cellular proliferation marker to diagnose tumors and to determine responses to chemotherapy since dUTPase has been implicated as having a role in cellular response to fluorodeoxyuridine chemotherapy.

**Applications**

- For the determination of the proliferation status of a cell in both neoplastic and normal tissues.
- For the development of antimicrobial and antineoplastic agents
- To determine efficacy of antineoplastic drugs such as fluorodeoxyuridine or drugs that affect thymidylate synthesis.

**Patent Status**

- United States Pat. No. 5,962,246 granted on October 5, 1999

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**Hematopoietic Growth Factor Inducible Neurokinin-1 Gene** (*Pranela Rameshwar, NJMS 00-31 & 02-47*) Therapeutic Target/Diagnostic

**Background**

Neurokinin-1 (NK-1) belongs to a family of receptors known to bind neurotransmitters, tachykinins, with different affinities and mediate a range of physiological functions. These receptors are expressed differentially in bone marrow, mammary epithelial cells and neural tissues. While the expression of NK-1 is constitutive in neural tissues, in bone marrow cells its expression is inducible by hematopoietic regulators. NK-1 receptors and its ligands have been implicated in the pathology of several lymphoproliferative disorders such as Hodgkin's and non-Hodgkin's lymphoma, leukemia and inflammatory diseases. The present technology relates to a discovery of NK-1 variant in the bone marrow cells that is differentially expressed in mature hematopoietic cells and peripheral immune cells.

**Description of the Technology**

A novel gene was discovered, termed Hematopoietic Growth Factor Inducible Neurokinin-1 type (HGFIN), because of its expression in differentiated hematopoietic cells and peripheral immune cells and its absence in progenitor bone marrow mononuclear cells. Further research indicated that HGFIN is a cell cycle inhibitor. This reveals a role for HGFIN in hematopoietic proliferation and regulation, and suggests a potential application in the treatment of lymphoproliferative disorders. Human melanoma and breast cancer cell lines also showed expression of HGFIN.

HGFIN has been shown to bind substance P, a tachykinin peptide, and may play a role in substance P-mediated early integration of cancer cells to the bone marrow. Thus targeting NK-1 and other NK receptors in combination with HGFIN could be beneficial in the treatment of cancers.

**Applications**

- For the development of small molecule inhibitors, RNAi, gene therapy, peptides or proteins for therapies in the treatment of cancers, inflammatory, neurological or hematopoietic diseases.
- For use as a transdifferentiation marker to follow the path of cells from bone marrow.
- For the development of antibodies for research use.

**Deliverables**

- Sequence of HGFIN; Vectors and Expression Systems; Purified Protein

**Patent Status**

United States patent granted on 9/6/2005 No. 6,939,955.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **A Novel Topoisomerase 1 Binding Protein for Use in Cancer Diagnostics and Therapeutics** (*Eric H. Rubin, CINJ 01-46*) *Diagnostic/Therapeutic Target*

### **Background**

Topoisomerase 1 is a DNA binding protein that regulates DNA topology and is used as a target of antineoplastic agents camptothecins. Several other proteins are presumed to be necessary for top1 functions. Previous studies at UMDNJ have identified a novel topoisomerase 1 and p53 binding protein called topors. This protein was characterized to be a RING protein rich in serine and arginine domains. The RING domain was shown to be similar to SUMO and E3 ubiquitin ligases. Post-translational modification of proteins via covalent attachment of SUMO is known to be important in cell cycle progression, stress response and signal transduction. **The present invention relates to further characterization of the novel topors protein and its uses in cancer diagnostics and therapeutics.**

### **Description of the Technology**

Expression of topors protein is down-regulated in tumors from kidney, colon, endometrium and lung, as compared to normal tissue samples. Consistent with the protein data, endometrium and colon tumor tissue samples lacking topors protein did not reveal measurable mRNA levels. Furthermore, over-expression of Topors in cervical cancer cell lines leads to cell death. Thus, lack of topors in cancer cells appears to contribute to the selection and persistence of mutant phenotype and progression to tumorigenesis. Additionally, it has been shown that topors functions as an E3-type ubiquitin ligase and E3-type SUMO ligase for topoisomerase and p53. Thus, topors is a dual function ubiquitin and SUMO ligase. Collectively these data indicate that topors is a candidate tumor suppressor gene similar to p53 and the loss of topors SUMO ligase activity could lead to cancer. It is feasible that modulation of topors ubiquitin and/or SUMO ligase activities may be useful in diseases associated with alterations in ubiquitin or SUMO pathways, including cancer.

### **Applications**

- For screening of cancer tissues
- In gene therapy to re-introduce topors gene into cells lacking the gene
- For use in modulation of DNA repair process
- For development of small molecule inhibitors

### **Deliverables**

- Expression vectors; Purified protein; Polyclonal antibody

### **Patent Status**

United States patent application filed

### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing



**Methods for Determining Autism Spectrum Disorder** (*Millonig, CABM 03-16*)  
*CNS/Biomarker/Diagnostic*

**Background**

Despite intense research in Autism field, there is no known cause for autism; however, abnormalities in brain structure or function are generally associated with the disease. Diagnosis is often based on observation of patient's communication, behavior, and developmental levels. Due to the fact that there are no reliable diagnostic tests, there is a critical need for the development of such tests for accurate diagnosis of autism. Since research to date indicates a possible genetic basis for susceptibility to the disease, a genetic marker would be a valuable diagnostic tool to detect individuals at risk. The present invention relates to the identification of genes for use as diagnostic tools for autism and methods for identifying subjects susceptible to autism.

**Description of the Technology**

The homeobox transcription factor, Engrailed2 (En2), was investigated for possible association with autism spectrum disorder. Linkage/disequilibrium tests in En2 in 137 triads of autistic individuals and their parents indicated that two single nucleotide polymorphisms, Intron A/G and Intron C/T, are critical. The A allele of Intron A/G and the C allele of Intron C/T were transmitted preferentially to autistic individuals, indicating that EN2 locus predisposes individuals to autism. Studies conducted in 29 additional families, confirmed that there is a statistically significant association between susceptibility to autism and the presence of these polymorphisms. Thus, A, C haplotype could be used as a diagnostic marker in the identification and screening of individuals at risk for developing autism.

**Applications**

- The A/C haplotype can be used in diagnostic tests for the identification individuals that have autism spectrum disorder.
- Screening tests can enable early diagnosis and prognosis of autism and lead to better healthcare outcome

**Patent Status**

United States Provisional Patent application filed.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**Novel Modification of Immunomodulatory Protein** (*Alexey G. Ryazanov, RWJ 04-41*)  
*Diagnostic/Therapeutic Target*

**Background**

TRPM7 is a bifunctional molecule consisting of an ion channel fused to a protein alpha-kinase domain and plays an important role in magnesium homeostasis, proliferation and cell death. Although this channel kinase has been characterized using electrophysiological techniques, the function of the kinase domain as well as its endogenous substrates still remains unknown. Research at UMDNJ has revealed that annexin 1, a member of annexin family of Ca<sup>2+</sup>-regulated phospholipids binding proteins, is a substrate for TRPM7 kinase. This protein has been shown to play a role in proliferation, inflammation, apoptosis and cancer.

**Description of the Technology**

UMDNJ researchers have discovered a novel modification of annexin 1 protein. This protein consists of a Ca<sup>2+</sup> and membrane-binding core and N-terminal tail preceding the core. The N-terminal region is crucial for its interaction with both intracellular and extracellular targets responsible for regulating proliferation and inflammation. TRPM7 phosphorylates annexin at the conserved Ser5 residue within the N-terminus. Since N-terminus is known to interact with other proteins and membranes, phosphorylation of N-terminus may be pivotal in modulating its function.

**Applications**

- The development of new therapeutics for modulation of inflammation, cancer, heart diseases, arthritis, skin diseases, and anoxic neuronal cell death
- As a marker of diagnosis of cancer, heart diseases, arthritis, and skin diseases

**Patent Status**

- United States Patent application filed

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **Bone Morphogenetic Protein –2 and Protein-4 in Treatment and Diagnosis of Cancer** (*John Langenfeld, RWJ 01-02*) Diagnostic/Therapeutic Target

### **Background**

BMP-2 expression is linked to cancer invasion and. BMPs are synthesized as inactive proteins of variable length. The precursor BMP-2 and BMP-4 proteins are proteolytically cleaved, producing mature C-terminal proteins of a little more than 100 residues. BMP-2 and BMP-4 interact with the same binding sites: mature BMP-2 and BMP-4 protein signaling is mediated by transmembrane serine/threonine kinases called type IA, IB, and type II receptors. The receptor phosphorylates cytoplasmic targets, which include the Smad family of proteins. In addition, the same molecules including noggin, chordin, DAN, gremlin, and Cerberus 1 homolog, inhibit both BMP-2 and BMP-4, thereby preventing their ability to bind to the receptors. While BMP expression has been noted in a few cancers, such as sarcomas and in pancreatic cancer and in cancer cell lines, the inhibition of BMP-2 activity and/or BMP-4 activity as a potential cancer treatment has never been mentioned.

### **Description of the Technology**

BMP-2 expression is linked to cancer invasion and growth and inhibiting BMP-2 activity reduces the size of cancerous tumors in nude mice and down regulates the expression of VEGF and sonic hedgehog in lung cancer cell lines. The present technology provides amino acid sequence of inhibitors to BMP-2 and BMP-4 and the receptor site for BMP-2 and BMP-4 antibodies.

### **Advantages**

- Allows for early detection of metastases and treatment
- Technology provides novel sequences and receptor sites

### **Patent Status**

3 U.S. patents are in prosecution

### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **Thymidylate Synthase Polymorphisms for Use in Screening for Cancer Susceptibility** (*Robert Ladner, SOM 02-52*) *Diagnostic/Therapeutic*

### **Background**

Thymidylate Synthase (TS) is an important enzyme in the nucleotide synthesis pathway and converts dUMP to dTMP. TS is a target for a variety of chemotherapeutic agents such as 5-FU, raltitrexed (Tomudex and pemetrexed (Alimta)) and inhibition of TS leads to cytotoxicity due to depletion of dTTP pool, a phenomenon dubbed as “thymine-less death.” TS also plays a critical role in cardiovascular diseases and other defects. TS and methylenetetrahydrofolate reductase (MTHFR) compete for folate in the generation of homocysteine. Folate and homocysteine have been associated with cardiovascular risk. Polymorphisms consisting of 28 base pair repeats in the 5'-untranslated region of the TS gene have been identified in certain African and Asian populations and have been shown to predict patient response to 5-FU chemotherapy. **The present invention discloses a novel single nucleotide polymorphism which could be added to existing screening tests thereby enhancing the predictive value of the tests.**

### **Description of the Technology**

A novel single nucleotide polymorphism (SNP) in the 5' tandem repeats of the TS gene has been discovered. Individuals with wild-type form had higher transcription of TS than those with the variant form. In addition, the present invention also discloses a six base pair deletion in the 3' gene of TS which results in mRNA instability and decreased production of TS. It has been shown that in cancer tissues, the reduced production of TS prevents the growth and metastasis of cancerous cells. Taken together, these studies demonstrate that identification of these polymorphisms would enable the prediction of a patient's response to chemotherapy and cardiovascular disease treatments.

### **Applications**

- To assess the risk of cancer and cardiovascular diseases
- To develop screening methods for the base pair deletion in the 3' gene of TS
- To predict the clinical outcome of chemotherapy and anti-cardiovascular treatments

### **Patent Status**

PCT application filed.

### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**Monoclonal Antibody for a Prostate-Specific Tumor Suppressor Gene** (*Cory Abate-Shen, CABM 01-10*) *Diagnostic/Research Tool*

**Background**

Relatively little is known about the molecular mechanisms involved in prostate carcinogenesis due to the lack of animal models that mimic human prostate carcinoma. Mutant mouse models lacking genes critical for prostate development could be utilized to understand the molecular pathways involved in prostate cancer initiation and progression. Thus, identification of prostate-specific oncogenes would be extremely valuable in studying prostate carcinogenesis. The present invention relates to: (1) the identification of a prostate-specific tumor suppressor gene, (2) generation of monoclonal antibodies (mouse and human) to the tumor suppressor protein, and (3) mutant mouse models of prostate cancer.

**Description of the Technology**

Knockout mice lacking the functional homeobox gene Nkx3.1 and the lipid phosphatase Pten were generated to study the molecular factors involved in prostate carcinogenesis. These studies showed that the loss of Nkx3.1 protein expression is a hallmark of prostate cancer in mice and humans, and occurs in early stages of the disease. Thus the resultant mouse models mimic early stages of human prostate cancer. Monoclonal antibodies against human NKx3.1 regulatory protein have been produced. A method for detecting the presence of Nkx3.1 in biopsy tissue samples has been developed.

**Applications:**

- Mouse anti-human and anti-mouse polyclonal as well as monoclonal antibodies with specificity for the tumor suppresser Nkx3.1 protein are available. These antibodies can be used:
  - As tumor marker for early detection of prostate cancer.
  - Pre- and post-treatment monitoring of prostate cancer
  - As a marker to distinguish between indolent versus aggressive prostate cancer.
- The knockout mice can be used to study the molecular mechanisms involved in prostate cancer initiation and progression.

**Patent Status:**

- US patent applications filed.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **A Novel Human Brain Derived Neurotrophic Factor as a Marker for the Prediction of Reproductive Potential in Women** (*Seifer, 01-17*) Diagnostic

### **Background**

Neurotrophins are a family of growth factors expressed in the mammalian nervous system. Some examples of neurotrophins include nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin-4/5 (NT-4/5), and neurotrophin-3 (NT-3). These neurotrophins have also been found to be expressed in a variety of non-neuronal tissues such as cardiovascular, immune, endocrine and reproductive systems. NGF, BDNF, NT-4/5, NT-3 and their corresponding receptors have been shown to be expressed in murine ovaries. Their presence in the ovaries has been shown to be critical for ovarian function such as ovulation.

**The present invention, for the first time, demonstrates that BDNF is expressed in human ovarian follicles and offers methods for a definitive way to measure human ovarian reserve, and consequently, represents a useful method for the prediction of the success of assisted reproductive techniques.**

### **Description of the Technology**

BDNF was detected in human follicles derived from women undergoing in vitro fertilization (IVF). Further studies with mouse models, revealed a critical role for BDNF in human oocyte maturation allowing for development of a definitive way to predict the reproductive capability of women undergoing IVF. Currently, serum markers such as FSH and ultrasound are used to measure ovarian reserve. These approaches do not measure the ovarian reserve directly. BDNF can be used for the direct assessment of ovarian reserve and thereby predict the success of Assisted Reproductive Technologies. Furthermore, current methods attempt to stimulate oocyte induction through the use of fertility drugs such as clomiphene citrate (Serophene), HMG (human menopausal gonadotropin), FSH (follicle stimulating hormone), or hCG (human chorionic gonadotropin). By contrast, the present invention would entail the use of small molecules such as cAMP and other signal transduction agents in oocyte induction.

### **Applications**

- To predict the reproductive potential of women undergoing IVF
- To stimulate oocyte production and maturation as a way to treat infertility
- To promote oocyte maturation in women during IVF prior to transfer of embryos

### **Patent Status:**

- United States patent No. 7,097,984.

### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**A Novel Biomarker for Diagnosis of Ulcerative Colitis and Colon Cancer** (*Kiron Das, 01-08 RWJ*) *Diagnostic*

**Background**

Tropomyosins are microfilament-associated proteins found in all eukaryotes and have been implicated in autoimmune diseases such as ulcerative colitis (UC). To date, eight different isoforms (hTM1, hTM2, hTM3, hTMsm $\alpha$ , hTM5a, hTM5b, hTM4, and hTM5) have been identified. Although anti-tropomyosin autoantibodies have been detected in the sera of patients with ulcerative colitis, the autoantigen triggering the autoantibody response has not been definitively identified. Previous studies at UMDNJ have identified hTM5 as the predominant immunogen in ulcerative colitis patients. UC is difficult to diagnose because its symptoms are similar to other intestinal disorders. About 5% of patients with ulcerative colitis develop colon cancer. **The present invention identifies the autoantigen(s) that trigger ulcerative colitis and colon related diseases and dysfunction.**

**Description of the Technology**

A new isoform of tropomyosin, named TC22, that predominates in human colon carcinoma has been identified and completely sequenced. Monoclonal antibodies, TC22-2, TC22-4, TC22-6 and TC22-7, specific for this distinctive protein have been generated. A significantly large percentage (83%) of colon cancer tissues obtained from colon cancer patients showed strong reactivity with TC22-4 monoclonal antibody compared with normal colon epithelial cells or normal colonic mucosa tissue from patients with Crohn's disease. Thus, this novel biomarker can be used for screening and detection of patients at risk of developing colon cancer and other colon related diseases, and ulcerative colitis.

**Applications**

- To develop in vitro diagnostics for ulcerative colitis and colon cancer
- To develop assays for the screening of novel agents capable of modulating the activity of TC22 for therapeutic applications
- For selecting patients for enrolment in clinical trials.

**Patent Status:**

United States and PCT patent applications filed.

**Licensing Opportunity:**

This technology is available for licensing non-exclusively or exclusively.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **Biomarkers for Breast Cancers** (*Kiran Madura, 04-13RWJ*) *Diagnostic*

### **Background**

The current methods for early detection of breast cancer include self-examination and routine mammography. However, a typical self-examination is imprecise and normally reveals a growth of approximately one inch, while a mammogram can reveal smaller masses but is considered to be an invasive method. Because early detection is critical for improving the prognosis for the patient, the availability of diagnostic methods that can identify abnormal growth at an early stage, and distinguish between cancer and non-malignant growth is crucial. Two methods that are currently available are based on polymerase chain reaction (PCR). One of these can identify mutations in the BRCA1 gene present in familial forms of breast cancer, which affects 5% of patients. A second method measures expression levels of the Her2 gene, which is indicative of increased potential for developing breast cancer. Nonetheless, this marker is also representative of a minor fraction of patients. Since most breast cancers occur spontaneously without a genetic/familial origin, a proteomic method that can reveal altered expression of specific proteins, rather than genetic alterations would be more desirable.

### **Description of the Technology**

Researchers at UMDNJ have identified several protein markers, whose expression levels are strongly correlated with the incidence of breast cancer. The measurement of these proteins using conventional antibody-based kit can be carried out. Because the levels of multiple proteins (four) can be simultaneously examined, the veracity of the readout is correspondingly strengthened.

### **Applications**

- Early diagnosis of breast cancer
- For monitoring breast cancer patients undergoing treatment

### **Patent Status**

United States and PCT patent applications filed.

### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**pDJA1, a Cardiac Specific Biomarker** (*Stephen Vatner, NJMS 02-17*) *Diagnostic*

**Description of the Technology**

The present invention provides novel nucleic acid and protein sequences for methods and compositions for treating, screening, and diagnosing cardiovascular disease and methods for using these genes and gene products for prevention of cardiac cell death and prevention of cardiac tissue damage resulting from ischemic events in cardiac tissue, as well as other tissue that is subject to damage resulting from an ischemic event. The genes, gene products and agents of the invention are also useful for treating other related clinical or coronary events such as angina, myocardial infarct (MI), and stroke, for monitoring the effectiveness of their treatment, and for drug development. The genes, gene products and agents of the present invention are also provided as pharmaceutical compositions for treatment of cardiovascular disease, ischemic heart disease, myocardial infarct and related conditions. Kits are also provided for the diagnosis, treatment and prognosis of cardiac diseases and related conditions.

**Patent Status**

United States Patent No. 7,009,038

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**Identification of the Second Gene of Niemann-Pick C Disease** (*Peter Lobel, 00-39 RWJMS*) *Diagnostic/Therapeutic*

**Description of the Technology**

Niemann-Pick type C2 (NP-C2) disease is a fatal lipid storage disorder characterized by massive lysosomal accumulation of cholesterol. The present invention identifies HE1 as the gene responsible for NP-C2. Treatment of NP-C2 fibroblasts with an exogenous HE1 genetic element ameliorated the cholesterol accumulation phenotype. HE1 functions in intracellular cholesterol transport. The present invention provides therapeutic compositions consisting of HE1 polynucleotide and polypeptide sequences, as well as an expression system for expressing HE1 in target cells. These therapeutic compositions can be used to target diseases involving faulty cholesterol transport and regulation, including NP-C2, atherosclerosis, Alzheimer's, diabetes, and cardiovascular disease. In addition, the present invention provides methods of diagnosing both NP-C2 and the ability of a subject to genetically transmit the disease by detecting mutations in the HE1 gene sequence.

**Patent Status**

United States and PCT patent applications filed.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **Detection of Mutations in Heterogeneous Tissues** (*James S. Goydos, CINJ 03-15*)

### Diagnostic

#### **Background**

The detection of point mutations in genes from heterogeneous biological samples is often complicated by the presence of both mutated and wild type cells. Methods currently in use such as DNA chips, single strand conformation polymorphism (SSCP), and Denaturing Gradient Gel Electrophoresis (DGGE), are expensive, cumbersome, not amenable to high throughput analyses, and involve the performance of electrophoresis. Other methods such as immunohistochemistry and Western blotting approaches used to detect the mutant protein, although useful, require diagnostic antibodies. Thus, there is a long felt need for techniques that can rapidly distinguish a normal allele from a disease causing allele in a specific and sensitive manner. **The present invention relates to a diagnostic strategy for the detection of mutant alleles in heterogeneous tissue sample.**

#### **Description of the Technology**

UMDNJ researchers have developed a method to detect point mutations in genes derived from heterogeneous biological samples containing both mutated and wild type cells. Normally, point mutations introduce new restriction site(s) in genes, which could then be identified using restriction enzymes that cut PCR products at specific sites of the DNA. Thus, the ability to detect these mutations depends on the presence of restriction sites within the site of mutation. However, the three most commonly found point mutations (Q61K, Q61R N-Ras and V599E B-Raf) in the N-Ras and B-Raf components of the MAPK pathway do not introduce restriction sites. Based on this observation, a strategy that introduces restriction sites via site directed mutagenesis has been developed to enable the detection of as low as 100 copies/ $\mu$ l of the mutant mRNA

#### **Applications**

- For the diagnosis of cancers and genetically determined diseases.
- For the screening of disease carriers.
- To predict patient outcome and plan therapy.

#### **Patent Status**

United States Provisional Patent application filed

#### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**Human Preprotachykinin-I Gene Promoter** (*Pranela Rameshwar, NJMS 97-16*)  
Diagnostic/Therapeutic Target

**Background**

Neurokinins belong to a family of receptors known to bind neurotransmitters, tachykinins, with different affinities and mediate a range of physiological functions such as neurotransmission, hematopoietic homeostasis, angiogenesis, cell transformation and immune modulation. The Preprotachykinin-I (PPT-I) gene encodes the tachykinin family of neurotransmitters. Further, PPT-I gene has been shown to be over-expressed in breast and other endocrine cancers that metastasize to the bone marrow. Since tachykinins are involved in the maintenance of homeostasis and neoangiogenesis, imbalance in SP and NK-A can lead to tumor metastasis. **The present invention relates to the use of PPT-I as a novel target in the development of therapies and diagnostics for a multitude of diseases.**

**Description of the Technology**

Using vectors and expression systems containing promoter regions involved in transcription for the PPT-I, NK-2 and SP-R genes, a role for PPT-I encoded gene products and corresponding receptors, in breast cancer has been established. Certain mutations in the promoter region that could be associated with breast cancer and breast cancer metastasis have been identified. Knock-out and knock-in studies with breast cancer cells revealed that PPT-I is important in cell transformation and also in having a central role in the integration of cancer cells as part of the bone marrow microenvironment. The present invention provides vectors with PPT-I promoter regions and receptor genes NK-1 and NK-2; deletion mutants; expression systems; vectors containing RNAi for PPT-I, NK-1 or NK-2; knock-in and knock-out breast cancer cell lines.

**Applications**

- For development of therapeutic and diagnostic applications in cancer and hematopoietic diseases
- For the development of small molecules, antisense molecules, antibodies, peptide or proteins for therapeutic interventions in the treatment of cancers, inflammatory diseases, neurological disorders, and hematopoietic diseases.

**Patent Status**

United States patent application filed.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



**Method of Quantifying Disease Biomarkers in the Lens of the Eye** (*Frederikse NJMS 06-04*)  
*CNS/Medical Device/Biomarkers*

**Background**

Age related neurodegenerative disease is a growing problem due to the aging of the population. Alzheimer's and other related diseases, associated with the aging process, are difficult to diagnose in early stages; despite the fact that early detection is the key to prophylactic treatment. To further complicate assessment of disease state or progression, many of the currently available diagnostic methods are qualitative. However, recent studies have shown that changes in the eye can provide information about corresponding changes in the brain related to the presence of age-related degenerative disease. Further, there is also evidence that the presence and concentration of specific disease-related biomarkers in the eye can be measured and that a correlation exists with the levels of such biomarkers in the brain.

**Description of the Technology**

The invention consists of disease related biomarkers and a non-invasive, non-contact optical method and instrument for the measurement of those biomarkers that have been shown to be indicative of the disease state. The instrument uses standard light source and CCD detection optics. A compact prototype has been built and tested on animals and human cadaver lenses.

**Advantages**

- Non-invasive, non-contact
- Short measurement time
- Can be performed in physician's office
- Relatively low-cost instrumentation
- Quantitative
- Allows measurement of progression over time

**Applications**

The applications for this technology include early detection of senile cataracts, complications of diabetes, Alzheimer's disease, and Wilson's disease.

**Patent Status**

U.S. Provisional patent has been filed.

**Licensing Opportunity**

This technology is available for exclusive or non-exclusive license. For more information, please contact Judith Ladd at the Office of Patents and Licensing.

**Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing



## **Diagnostic Test for Biological Agents** (*Charles Spillertr, NJMS 05-42*)

### Diagnostic

#### **Background and Description of the Technology**

Recent world events regarding the alarming threat of bioterrorist attacks have drawn attention to prevention, detection, and treatment methods for highly virulent diseases such as anthrax, plague, and glanders. Plague, once thought to be a disease of the Middle Ages, is now being recognized by bioterrorism experts as a potentially disastrous agent in biological warfare. The bacillus, *Yersinia pestis*, invades the lymphatic and vascular systems, causing a severe bacteremia that progresses into sepsis, disseminated intravascular coagulopathy (DIC), and eventually death. This final pathway of sepsis leading to shock and death is shared by *Bacillus anthracis*, the pathogen that causes anthrax, another bioterrorist weapon whose devastating potential was amply demonstrated in recent mail attacks in the US. *Burkholderia mallei*, the agent that produces the disease glanders, has also been extensively studied by the United States and the Soviet Union as a possible weapon of biological warfare. During World War II, glanders was utilized as a bioweapon against horses, civilians, and prisoners of war. Like plague and anthrax, glanders causes overwhelming septicemia often leading to death once the bacteria is disseminated in the vasculature.

Rapid detection of biological agents is the critical first step in bioterrorism prevention and response. Many common and emerging detection methods are dependent upon antibody-antigen or gene chip assays that operate via specific biochemical interactions. Genetic modification of recognition sequences or surface protein expression may therefore subvert these screening methods. Additionally, these types of tests are costly and complex, requiring highly trained technicians and expensive equipment. Thus, there remains a need for a simplified, rapid, cost-effective diagnostic test that monitors an individual's risk potential for coagulopathy to determine the presence of a pathogen. The coagulation-inflammation cascades are common pathophysiological mechanisms affected by bioterrorism agents that cause anthrax, plague, and glanders, and eventually converge to cause sepsis. Accordingly, the vascular system may be affected by these agents in significant ways that could compromise the clotting cascade. **The present invention describes a rapid, cost-effective, clinically relevant bioassay to serve as a biomarker for pathogen-induced coagulopathy.**

#### **Patent Status**

United States Provisional Application filed 2006.

#### **Contact Information**

Peter Golikov, MS, MBA  
Director, Ventures and Licensing  
Office of Patents and Licensing

