



## Office of Patents and Licensing THERAPEUTICS

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**A Novel Family of Cytokines: IFN $\lambda$**  (*Gallagher & Kotenko, NJMS 01-50 & 02-76*)  
Therapeutics

**Background**

Interferons are a group of cytokines produced in response to viral infections. There are three main types of well characterized interferons: IFN $\alpha$ , IFN $\beta$ , and IFN $\gamma$ . Interferons  $\alpha$  and  $\beta$  are produced mainly by white blood cells and IFN $\gamma$  mainly by activated T cells and natural killer cells in response to other cytokines such as IL-2 and IL-12. The induction of interferon production results in the expression of many antiviral proteins. **The present invention relates to the identification and characterization of a novel class of interferons as well as their cognate receptor complexes. These novel interferons have been shown to mediate antiviral responses.**

**Description of the Technology**

UMDNJ researchers have cloned and characterized a new class of interferons, named IFN $\lambda$  family of cytokines, which is comprised of three homologous proteins termed IFN $\lambda$ 1, IFN $\lambda$ 2, and IFN $\lambda$ 3. These interferons were expressed in response to viral infections indicating their role in the antiviral responses. The functional receptor complex for this new family of cytokines has also been cloned and characterized. Initial characterization has demonstrated that IFN $\lambda$ s mediate their antiviral activity through a novel receptor complex composed of two subunits, a novel subunit termed CRF2-12 and a second subunit, IL-10R2, which is also a component of the IL-10 and IL-22, and induce signaling through the Jak-Stat signal transduction pathway.

**Applications**

- For the treatment of viral infections
- In the induction of apoptosis in virus infected cells and in cancer
- For the treatment of hyper-proliferative diseases
- In gene therapy

**Patent Status**

PCT application published on August 14, 2003 (Publication Number WO 03/066002)

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**Novel Class of Compounds to Control Chronic Hepatitis C Virus** (Dr. Neerja Kaushik-Basu, 06-49 UMDNJ) Therapeutic

**Background**

Chronic Hepatitis C virus (HCV) infection is the leading cause of severe hepatitis that often progresses to cirrhosis, stasis, and hepatocellular carcinoma. Current therapies against HCV are limited in efficacy and have adverse side effects thus necessitating the development of new antiviral agents against this pathogen. The HCV RNA-dependent RNA polymerase (NS5B) is the key enzyme involved in the replication of the viral genome is unique to the virus and therefore represents an attractive target for drug development. **The present technology relates to a discovery of a novel class of compounds to control chronic Hepatitis C virus by inhibiting its replication.**

**Description of the Technology**

Researchers at UMDNJ have identified a class of compounds capable of inhibiting HCV NS5B. This has been shown utilizing a purified, functionally active recombinant NS5B in *in vitro* RNA dependent RNA polymerase (RdRp) activity of HCV NS5B on homopolymeric poly rA-U12 template primer. UMDNJ researchers have addressed the mechanism of inhibition by these compounds and identified that they compete with the template-primer in order to inhibit NS5B RdRp activity. In addition to inhibiting the HCV replicase, this family of compounds can potentially inhibit other RNA-dependent RNA/DNA polymerases of viral origin such as HIV-1RT, BVDV NS5B, Poliovirus RdRp, etc. Further studies are under way utilizing cell cultures and animal models.

**Applications**

- For the treatment of chronic Hepatitis C viral infection

**Patent Status**

United State provisional patent application filed

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**Glucono-delta-lactone as an Anticoagulant/ Anti-inflammatory Drug**  
(Charles Spillert, NJMS 05-40) Therapeutic

**Background**

About 80% of all deaths in the US involve a disease in which there is dysfunction in the blood coagulation and/or immune systems. The monocyte, an essential immune cell, when activated generates tissue factor (TF), the initiator of blood clotting. This cell may, in part, enhance the immune-clotting system synergy in promoting atherothrombosis. This process will eventually lead to reduction of blood flow to the essential organs with resultant injury and death. Diseases in which accelerated atherosclerosis reveal its devastating effects include heart disease, diabetes and the majority of strokes. The need for an effective, safe pharmaceutical intervention suggests the evaluation of Glucono-delta-lactone (GDL).

**Description of the Technology**

GDL is a stable, low molecular weight, natural product often used as an anti-oxidant and anti-microbial agent in the preparation of foods and cosmetics. GDL is on the FDA's GRAS (Generally Recognized As Safe) list. According to the methods disclosed in the present invention, GDL may effectively potentiate the anticoagulant effects of unfractionated and low molecular weight heparins. GDL also prolongs the clotting time of human blood spiked with TF and reduces the erythrocyte sedimentation rate (ESR) test values. The former shows GDL's anticoagulant properties, whereas the latter is indicative of an anti-inflammatory action.

**Applications**

- To anticoagulate patients with a variety of diseases and conditions in which increased thrombotic risk is present.
- To treat the inflammatory state generated by an activated immune system. These conditions could include arthritis and autoimmune conditions.

**Patent Status**

United States Provisional Application filed 2006.

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**Translational Control of Longevity** (*Dr. Alexey Ryazanov, 04-27 RWJMS*) Therapeutic & Drug Target

**Background**

The progressive decrease in protein synthesis and degradation leading to an increase in the concentration of damaged proteins is one of the major factors controlling aging. Thus, by regulating the rate of protein turnover, the rate of aging can be modulated. The present invention relates to increasing the life span in mice by modulating the function of eukaryotic elongation factor 2 (eEF-2) kinase, a negative translational regulator that phosphorylates and inactivates elongation factor-2. eEF-2 kinase is regulated by IGF-1/mTOR pathway and plays a role in the control of rate of protein synthesis at the elongation stage.

**Description of the Technology**

Knockout mice lacking a functional eEF-2 kinase gene were generated to study the effect of loss of eEF-2 kinase activity on longevity. These mice were viable, lacked any phenotypic abnormalities and produced normal progeny. Interestingly, male mice exhibited a 30% (36.6 months) increase in life span compared to normal mice. Furthermore, the complete elimination of eEF-2 kinase was not required for extension of life span. Thus, downregulation of eEF-2 kinase could be used as a means to increase lifespan.

**Advantages**

- eEF2-kinase has no homology to the majority of eukaryotic protein kinases and is not required for viability
- Complete elimination of eEF-2 kinase is not essential for life span extension

**Applications**

- eEF-2 Kinase can be used as a target for the design of therapeutic reagents to overcome aging
- To retard aging

**Patent Status**

United States Provisional Patent application filed

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**Non-Antibiotic Intervention of Chlamydial Infection** (Dr. Huizhou Fan, 03-38 RWJ)  
*Infectious Diseases/Therapeutic*

**Background**

Chlamydial infection is caused by Chlamydia trachomatis bacterium and is common among sexually active adolescents and young adults in the United States and in the developing world. As per U.S. Centers for Disease Control and Prevention estimates, there are 4 million new cases of Chlamydial infections each year. Chlamydial infection often results in abnormal discharge from female and male sexual organs and pain while urinating. If left untreated the infection may spread to other organs of the body causing pelvic inflammatory disease (PID) in women and epididymitis in men, inflamed rectum and inflammation of the eye. In women, PID is often asymptomatic and if left untreated, can lead to infertility. Current treatment methods include the use of antibiotics such as azithromycin or doxycycline or erythromycin or ofloxacin. The use of prescription antibiotics poses the risk of developing antibiotic resistance and disruption of normal microbial floras. Thus, there is a long felt medical need for alternative treatment strategies that overcome the aforementioned limitations. **The present technology represents a novel strategy to effectively prevent and eliminate C. trachomatis infection.**

**Description of the Technology**

UMDNJ researchers have discovered that the use of certain metalloprotease inhibitors prevent the production of infectious chlamydial progenies when used at both early and late stages of infections. In addition to preventing chlamydial growth, these compounds were found to enable host cells to resume chlamydia-blocked cell division.

**Advantages**

- Non-antibiotic treatment
- Normal microbial flora will not be destroyed

**Applications**

Prevention and treatment of chlamydial infection

**Patent Status:**

US Patent Application 11/572,546 filed 7/23/2004

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**Sepsis Prevention through Adenosine Receptor Modulation** (*Hasko, RWJ 05-03*)  
*Therapeutic/Infectious Disease*

**Background**

Sepsis is the single greatest cause of non-cardiac death in the hospital setting. Approximately 800,000 episodes of sepsis occur throughout the US leading to more than 200,000 deaths annually. Sepsis is a complex systemic syndrome that involves infection, inflammation, and ultimately multiorgan system failure. At present, there are limited therapeutic options for improving patient outcome in sepsis beyond, antibiotics, fluids, vasopressors, supportive intensive care, and occasionally low-dose corticosteroids.

**Description of the Technology**

The novel technology provides a new way to treat sepsis by modulating adenosine A2a receptor subtype by a novel small molecule antagonist, named ZM241385. Adenosine receptors play an important role in modulating the innate immune response. Adenosine is a potent endogenous anti-inflammatory and immunosuppressive molecule that is released from cells into the extra-cellular space at sites of inflammation and tissue injury. Once released, adenosine diffuses to the cell membrane of surrounding cells and binds specific cell-surface receptors. The four known adenosine receptors are G-protein coupled receptors. Each adenosine receptor has its unique signal transduction mechanism, ligand affinity, and tissue distribution.

**Applications**

- The technology provided a new therapeutic strategy to treat sepsis by modulating the Adenosine A2a receptor sub-type.
- The technology includes a novel small molecule Adenosine A2a receptor sub-type antagonist prototype.
- The technology provides a novel target to discover additional therapeutic agents for the treatment of sepsis.

**Patent Status**

International Application for Patent (PCT/US2006/003523) was filed on February 1, 2006.

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**A novel class of mTOR inhibitors** (Zheng, RWJ 06-34) Therapeutics/Drug Target

**Background**

Mammalian target of rapamycin (mTOR) is an important drug target for many human diseases, including graft rejection, autoimmunity, restenosis, cancer, heart disease, diabetes, obesity, aging, and also Alzheimer, Parkinson and Huntington diseases. mTOR is a conserved regulator of cell growth and metabolism that integrates energy, growth factor, and nutrient signals. TOR is a phosphatidylinositide 3-kinase-related kinase (PIKK). It forms two multiprotein complexes mTORC1 and mTORC2. Only mTORC1 is sensitive to rapamycin. mTOR localizes to the endoplasmic reticulum (ER) and Golgi. Dysregulation of mTOR signaling occurs in diverse human tumors. Preclinical studies indicate that rapamycins are potent inhibitors of the proliferation of numerous tumor cell lines in culture and of murine syngeneic tumor models or human Xenografts.

**Description of Technology**

A novel class of mTOR inhibitors targeting both mTORC1 and mTORC2 were identified. The inhibitors are more potent than and distinct from rapamycin and rapamycin-derivatives in their mechanism of action. They block localization of mTOR to the ER and Golgi. They also induce apoptosis in tumor cells a distinctive advantage for cancer therapy. Moreover, because mTORC2, an important regulatory kinase in the aging pathway is inhibited, they can be useful agents to treat aging and aging-related illness.

**Applications**

- These new inhibitors can be used to develop drugs with clinical utility in the treatment of many human diseases involving mTOR dysregulation.
- This technology can also be used for drug discovery targeting ER and Golgi localization of mTOR.
- The technology can also be applied in the research area to target molecules to the ER and Golgi.

**Patent Status**

United States Provisional Application for Patent was filed on December 8, 2006

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**Localized Insulin Delivery for Bone Healing** (*Dr. Sheldon Lin, NJMS 05-43*) Device

**Background**

Fracture healing is a complex process that involves the sequential recruitment of cells and the specific temporal expression of factors essential for bone repair. Previous studies have shown that diabetes impairs bone healing clinically and experimentally due to low insulin levels. The effect of insulin on bone metabolism has been also been previously investigated using a non-diabetic model and been shown to increase histomorphologic indices of bone formation *in vivo*.

**Description of the Technology**

The present invention relates to the local administration of insulin as an anabolic agent to accelerate bone healing in non-diabetic patients and a drug delivery system comprising insulin and a pharmaceutically active carrier, wherein said system is adapted for localized administration of insulin to a patient in need thereof. The insulin delivery system comprises at least one biocompatible carrier and may also include additional growth factors. The insulin can be delivered via implant or coating.

**Advantages**

The advantages of this technology are an increase in bone formation, compared with the control group, as well as an indication of improved mechanical properties such as torsional rigidity, torque to failure, shear stress, and maximum shear stress.

**Applications**

This invention is applicable to the treatment of bone conditions including bone fracture, bone trauma, arthrodesis, and bone deficit conditions associated with post-traumatic bone surgery, post-prosthetic joint surgery, post-plastic bone surgery, post-dental surgery, bone chemotherapy treatment, congenital bone loss, posttraumatic bone loss, post surgical bone loss, post infectious bone loss, allograft incorporation or bone radiotherapy treatment.

**Patent Status**

A worldwide PCT (P32,656-A PCT) and US Provisional Application (Serial No. 60/775,076) have been filed.

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**Oligonucleotide Compositions for the inhibition of Transcription Factors** (Beverly E. Barton, NJMS 03-02) Therapeutic

**Background**

The STAT (signal transducers and activators of transcription) family of transcription factors is involved in the signal transduction pathway of growth factors and cytokines. STATs are known to be activated by phosphorylation of tyrosine and serine residues. Phosphorylation of STAT3 is via IL-6 signaling and is tightly regulated in normal cells. However, aberrant signaling of STAT3 is found in many types of malignancies. The persistent activation of STAT3 leads to over-expression of genes involved in anti-apoptotic factors and cellular proliferation. Inhibition of STAT3 has been found to lead to apoptosis of malignant cells. **The present invention provides oligonucleotide compositions for the inhibition of STAT family of transcription factors and, thus, for treatment of diseases wherein aberrant STAT expression plays a critical role in pathophysiology.**

**Description of the Technology**

Oligonucleotide compounds containing sequences capable of binding to transcription factors and inhibiting activity of transcription factors have been shown to modulate cellular responses mediated by STAT family of transcription factors. In the presence of excess amounts of the binding sequences, STAT transcription factors were prevented from binding to genes. These oligonucleotide binding sequences were tested for their ability to inhibit tumor growth in an *in vivo* mouse model for human prostate cancer. Mice injected with these oligonucleotides had significantly smaller tumors compared to control mice. Taken together, these data support the use of these oligonucleotides in the treatment of diseases wherein STAT transcription have a pathophysiological role.

**Applications**

For the treatment of diseases wherein STAT family of transcription factors have a pathophysiological role. Specific applications include:

- Cancer
- Autoimmune diseases
- Chronic inflammatory diseases
- Alopecia, cosmetic hair removal or suppression

**Patent Status**

United State provisional patent application filed

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## **PNA-Neamine Conjugates for use as Therapeutic agents and Research Tools**

*(Virendra N. Pandey, NJMS 03-37) Therapeutic*

### **Background**

Peptide nucleic acids (PNAs) are analogs of nucleic acid with peptide backbone replacing sugar phosphate backbone in a nucleic acid. These analogs bind to both single stranded and double stranded RNA or DNA in sequence specific manner to inhibit translation and replication. They are gene-specific, nontoxic, and non-immunogenic. However, their therapeutic potential has been limited because of their poor uptake into mammalian cells. Thus, new methods for efficient transfer of therapeutic agents and artificial nucleases with improved cell permeation properties have been extensively investigated.

Aminoglycoside antibiotics such as neomycin B, which are specific to 16S bacterial rRNA, also bind HIV RNA recognition elements, RRE (Rev Responsive Element) and TAR and block HIVRev and HIV-Tat RNA-protein interactions. However, the toxicity of neomycin B and the risk of developing antibiotic resistance due to modification by aminoglycoside-modifying enzyme limits its use as a therapeutic agent. Neamine derivatives with increased affinity to RNA targets or resistance to aminoglycoside modifying enzymes have been prepared by mimetics. **The present invention discloses new methods and compositions for the synthesis of improved PNA-aminoglycoside derivatives.**

### **Description of the Technology**

The aminoglycoside neamine was conjugated to a PNA sequence specific to the TAR region of HIV-1 RNA genome. The TAR specific PNA-neamine conjugate had improved cellular uptake and enhanced binding with the target sequence resulting in robust inhibition of viral replication. Furthermore, the conjugate was also able to block the production of HIV-1 in lymphocyte CEM cells infected with pseudotyped HIV-1 virions. One of the conjugates disclosed in the present invention showed RNA cleavage activity in the absence of magnesium ions. Taken together, these results indicate that aminoglycoside-PNA conjugates could be used as antiviral agents.

### **Applications**

- Therapeutics: PNA-aminoglycoside conjugates can be used as antiviral and anticancer agents.

### **Patent Status**

- PCT Patent Application filed

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**Novel Combretastatin A-4 Analogues with Potent Cytotoxicity and Anti-Tubulin Polymerization Activities** (*William J. Welsh, RWJ 04-29*) Therapeutic

**Background**

The microtubule system of eukaryotic cells is considered to be a target for the development of anti-cancer agents. The  $\alpha$ - and  $\beta$ -tubulin heterodimer is the building block of microtubules and, as such, is the biochemical target for several clinically used chemotherapeutics. Colchicine, paclitaxel and other clinically used anti-tubulin drugs often face limitations such as neural and systemic toxicity, poor water solubility and bioavailability, and complex synthetic pathways and isolation procedures. The present invention describes five novel small-molecule compounds that exhibit anti-tubulin polymerization and anti-cancer activity.

**Description of the Technology**

The present invention describes the rational design, synthesis and biological evaluation of a series of novel small-molecule compounds that exhibit strong *in vitro* anti-tubulin polymerization activity as well as cytotoxicity in the low nM range against four cancer cell lines isolated from cervical, breast and colon tumors. Moreover, these compounds show significant cytotoxicity in human cervix epithelial adenocarcinoma and colon carcinoma cells which overexpress multiple drug resistance. Furthermore, these novel inhibitors are water soluble and predicted to exhibit good bioavailability. These compounds and their analogues are also attractive from the standpoint of medicinal chemistry and large-scale chemical synthesis, by virtue of the absence of chiral (stereochemical) centers and the efficient 5-step reaction scheme which renders the desired product in high yield employing inexpensive starting materials.

**Applications**

- Compounds of this invention can be used as anti-cancer agents

**Patent Status**

- PCT patent application filed

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## **Identification of a Myeloid Precursor Cell for Modulations of Immune Responses**

*(Yacov Ron, RWJ 98-08) Therapeutic*

### **Background**

Pluripotential stem cells (PSC) are found in the bone marrow and spleen in mice and are cells that are capable of self-renewal and differentiation into all lineages of the hematopoietic system. Only one in 2,000-5,000 cells in bone marrow are PSC and are present within a narrow subset (Thy-1.1lo LinSca-1+) of bone marrow cells. The current dogma concerning the kinetics of hematopoiesis is that only primitive pluripotential bone marrow stem cells can support hematopoiesis, whereas lineage-committed stem cells can support only a particular lineage. The present invention provides long-lived myeloid-committed stem cell population that can replenish the mature myeloid lineage.

### **Description of the Technology**

Researchers at UMDNJ have identified long-lived myeloid-committed stem cells in spleen which replenish the mature myeloid lineage for at least 12 months. Evidence for these findings is provided by the discovery that these cells do not home back to the bone marrow. These stem cells can be targeted with a retroviral vector following LPS stimulation of T-cell depleted spleen cells. The ability to introduce exogenous genes into myeloid lineage has several advantages over current methods of retroviral-mediated gene transfer techniques using bone marrow stem cells. For example, the efficiency of gene transfer using bone marrow stem cells is very low (5%), while the efficiency with the present method is extremely high. Another disadvantage of using bone marrow cells includes expression of the exogenous gene in all hematopoietic cell lineages.

**Gene transfer using the cells identified in the present invention results in the targeted expression of the exogenous gene in the desired subset of the myeloid compartment.**

### **Applications**

- Gene therapy-based treatment of genetic disorders linked to myeloid lineage such as Gaucher's disease
- Selective immune response against tumor or viral antigens.

### **Patent Status**

- United States patent application filed (Application Number: 09/830,176)
- PCT Application published on May 11, 2000 (Publication Number: WO 00/26393)

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**Method of Improving Drugs with Anti-Retroviral and Anti-Cancer Activity** (*Harmut M. Hanauske-Abel, NJMS 04-39, 04-46*) Therapeutic

**Background**

This invention relates to a method of inhibiting the generation of infections viral progeny, or suppressing the proliferation of malignant cells, which comprises interrupting the eIF5A-dependent cellular pathway essential for cellular proliferation. eIF5A is a eukaryotic translation initiation factor 5A, an intracellular protein with two isoforms. eIF5A requires posttranslational modification in order to become biologically active. It has been shown to be over-expressed in cancers and is thought to play an essential role in virally-induced proliferation of cells. This protein is unique in that it contains hypusine, a lysine derivative, which is formed by posttranslational hydroxylation, catalyzed by the non-heme ferrous dioxygenase deoxyhypusine hydroxylase (DOHH). The active site architecture of DOHH can be characterized by an active site cage entombed inside the apoenzyme ('fireplace-with-chimney' model). This invention relates to the discovery that the 'chimney' segment of the DOHH active site can accommodate large hydrophobic moieties which can serve as an anchor for a smaller inhibitor in the 'fireplace' segment of DOHH thereby significantly improving the efficacy of the inhibitor.

**Description of the Technology**

This invention discloses a method used to obtain a suppressive effect on the proliferation of cells occurring within a non-metastatic or metastatic malignancy. The preferred embodiment of the pharmacologically relevant DOHH inhibitor is a compound of a disclosed formula or a derivative thereof with a hexane backbone and a hydrophobic anchor as (C<sub>5</sub>-C<sub>12</sub>) alkyl, (C<sub>3</sub>- C<sub>12</sub>) cycloalkyl, or a hydrophobic aromatic moiety. Other side chains can be hydrogens; alkyl, alkenyl, alkynyl or alkoxy groups; or a peptide or a peptidomimetic moiety containing 10 to 50 carbon atoms particularly positioned on the hexane ring. The disclosed formula for the proposed pharmaceutical agent has been shown to have an improved efficacy as compared to the currently existing DOHH inhibitors.

**Application**

- The compounds of this invention can be used in systemic or topical application as anti-neoplastic agents in combination with existing anti-cancer drugs of various clinically introduced chemotypes, as well as, a part of cancer treatment protocols also comprising surgery and radiation.

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**Activated CDC42-Associated Kinase (Ack) as a Therapeutic Target for Ras Induced Cancer** (*Nur-E-Kamal, RWJ 04-49*) Therapeutic Target

**Background**

Activation of Ras GTPase function has been shown to be associated with various types of cancer identifying Ras as a target for cancer therapeutics. However, Ras GTPase activity is also essential for multiple normal signaling pathways involved in controlling growth and differentiation of mammalian cells. Thus targeting Ras directly may have deleterious effects on non-cancer cells. This invention is based on the discovery that Ras signal for transformation transduces through the activated CDC42-associated kinase (Ack). This invention validates Ack kinase as an attractive therapeutic target for Ras-induced cancer.

**Description of the Technology**

The present invention discloses the fact that CDC42 and activated CDC42 associated kinase (Ack) act downstream of Ras signaling in cancer cells. To prove this, the expression of Ack was knocked down using siRNA in v-Ha-Ras NIH 3T3 transformed cells. siRNA knocked down the expression of Ack in a dose-dependent manner in v-Ha-Ras transformed NIH 3T3 and parental NIH 3T3 cells. Additionally, Ack-deficiency in the v-Ha-Ras transformed cells was shown to induce apoptosis. Therefore Ras signals transduced through Ack protect v-Ha-Ras transformed cells from apoptosis. PD 158780 tyrosine kinase inhibitor inhibits the kinase activity of Ack *in vitro* and affects the growth of v-Ha-Ras transformed NIH3T3 cells in a dose-dependent manner. Thus Ras-CDC42-Ack signaling pathway is required for survival of Ras-transformed mammalian cells and Ack kinase is an attractive target to develop a chemotherapeutic agent for Ras-induced cancer.

**Applications**

- CDC42-Ack can be used as a target in search of novel therapeutic agents for Ras-induced cancers, i.e. brain tumors, breast and prostate cancers.

**Patent Status**

- United States Provisional Patent Application filed on 08/09/2005
- Provisional Patent Application Number 60/706,655

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**New Erythropoietin Molecule: Erythropoietic Without Immunosuppression** (*Yuan, Rui Rong RWJ 06-73*) *Oncology*

**Background and Description of the Invention**

Anemia is a common complication in patients with cancer, especially in those with advanced disease or who are under intensive chemotherapy or radiotherapy. Erythropoietin (EPO) is a 165 amino acid glycoprotein and the recombinant Human EPO (rHuEPO) has been used extensively for the treatment of anemia in humans. EPO treatment is capable of alleviating therapy-related anemia and improves cancer patient's quality of life (QOL). It represents a safe and effective means to increase the red cell mass and avoid blood transfusions in >50% of the cancer patients with chronic anemia.

In recent years, EPO has received considerable attention because it may have the capability of inducing broad neuroprotective effects in animals following CNS injury. However, long-term use of EPO therapy remains an elusive because EPO treatment may overly stimulate erythropoiesis. To overcome this excessive red cell production, we have created a library of EPO-derived fragments for tissue protection based on the hypothesis that two distinct functions (erythropoiesis and tissue protection) reside in different domains of the molecule. Our studies on small EPO-derived peptides have provided strong evidence to support the notion that there are at least two distinct functional domains co-existing within the whole EPO molecule and that sequences and/or structures within the EPO amino acid sequence will dictate their biological functions. Since we have identified the amino acid sequence of the immunosuppressive EPO-derived small peptides, we hypothesize that the amino acid sequence(s) responsible only for erythropoiesis can be created and characterized. The new type of EPO (EPO-new or EPO-N) for anemia treatment is thus being developed for future clinical use.

**Patent Status**

United States Provisional Application for Patent Filed

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**Local Combination Immunotherapy for Solid Tumors** (*Rui-Rong Yuan, UMDNJ 04-03*) Oncology

**Background**

Despite the significant progress in cancer treatment made over the last two decades, many patients with malignant solid tumors, especially patients with metastatic disease or locally advanced unresectable tumors, die of disease progression. Both SCLC and neuroblastoma are of neuroendocrine origin and express high-levels of the neuron specific nuclear antigen-HuD protein. The HuD-antigen is a neuronal RNA-binding protein. Hu proteins are expressed in the nucleus and cytoplasm of neurons and are thought to play roles in neurogenesis and neuronal maintenance. All SCLC cells express HuD antigen, while there is no expression in normal lung tissue. The HuD-antigen is also expressed in 80% of all human neuroblastomas. A strong correlation between the presence of high titer polyclonal anti-HuD antibodies and occasional spontaneous remissions of SCLC in some patients has suggested that the HuD-antigen might be a good molecular target for specific immunotherapy against SCL.

**Description of the Technology**

We have created a new immunotoxin (named BW-2) using anti-HuD Antibody in complex with a toxin. (For future clinical application, other immunotoxins can be created utilizing humanized SCLC tumor specific monoclonal antibodies or a fragment that can enter into the targeted tumor cells.) We have demonstrated that the immunotoxin aggressively killed SCLC cells in vitro with high specificity while exhibiting minimal toxicity against control cell lines. In contrast to conventional immunotoxin therapy, we injected the immunotoxin compound directly into tumors (subcutaneous) in a nude mouse model of human SCLC. We found that this immunotoxin killed targeted SCLC tumor cells and significantly delayed tumor progression compared to all the control groups. There was no toxicity in the immunotoxin treated animals. Furthermore, following local tumor specific immunotoxin therapy, additional autologous DCs injections into the immunotoxin treated tumor site should improve tumor antigen presentation resulting in a more robust shrinking of the tumor.

**Patent Status**

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**IFN antagonists** (*Sergei Kotenko, NJMS 06-46*) *Therapeutics*

**Background**

Cytokines are small proteins, which are produced by cells in response to various stimuli and, in turn, regulate a broad array of cellular functions. Importantly, they are involved in regulating proper immune response to various bacterial and viral pathogens, and to diverse pathologies including cancer, autoimmune and inflammatory diseases. One group of cytokines, the interferons (IFNs) is involved in antiviral activities and deregulation of IFN expression and/or function can play a role in the establishment and/or maintenance of various pathological conditions. More specifically, type I and type III IFNs are produced and secreted in response to viral infections. Binding of IFNs to their corresponding cellular receptor complexes induces a signaling cascade that leads to the expression of important mediators of antiviral response. These antiviral mediators inhibit protein synthesis, cleave viral RNA or interfere with protein/RNA trafficking. These enzymatic activities are directed toward suppressing virus replication, making the IFN system one of the most important defense mechanisms against viral infections. In turn, viruses have developed many strategies to circumvent IFN-induced antiviral protection, generally interfering with IFN signaling. The present invention relates to a discovery by UMDNJ researchers of a first viral defense mechanism that directly targets type I and type III IFNs.

**Description of the Technology**

The *Poxviridae* are a family of large dsDNA viruses that encode numerous immunomodulatory proteins. *Vaccinia virus* (VACV), the smallpox vaccine, encodes two secreted proteins that function as IFN antagonists. One of these proteins is able to suppress the biological activity of all type I IFNs while the other can inhibit both, type I and type III IFN-induced signaling and biological activities.

**Applications**

- Neutralizing antibodies against these virus-encoded IFN antagonists can be used for the treatment of poxvirus infections
- The compositions of the present inventions can be used for the treatment of pathological conditions where IFN activity should be inhibited/reduced

**Patent Status**

Provisional patent application was filed in September 2006.

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