

SELECTED TECHNOLOGIES

Technology Transfer Office



The Technology Transfer Office at National Jewish Health accelerates the development of laboratory research towards clinical application by identifying and protecting the institution's intellectual property and facilitating business partnerships for technology licensing and commercialization.

National Jewish has more than 150 technologies in its active portfolio and owns more than 80 issued U.S. patents plus additional corresponding foreign patents.

Attached is a non-exhaustive list of technologies available for licensing from National Jewish.

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TABLE OF CONTENTS

ANTI-CD79 ANTIBODY OFFERS NOVEL APPROACH TO THERAPY IN AUTOIMMUNE DISEASE, TRANSPLANTATION AND LYMPHOMA (11-15)	3
NOVEL PIM 1 KINASE INHIBITOR THAT UPREGULATES RUNX3 FOR THE TREATMENT OF ALLERGIC DISEASES (11-06)	4
PTPN13: A NOVEL TARGET FOR THE TREATMENT OF PULMONARY FIBROSIS (11-09)	5
NOVEL ADJUVANT FOR INCREASING EFFECTIVENESS OF VACCINES (10-13)	6
USE OF THE LISTERIA MONOCYTOGENES P60 POLYPEPTIDE AND VARIANTS FOR STIMULATING NK CELLS (10-08)	7
TARGETING FGF2B FOR THE TREATMENT OF ADULT LUNG INJURY (09-20)	8
MOUSE STRAIN EXPRESSING A T CELL RECEPTOR SPECIFIC FOR A SCHISTOSOMAL ANTIGEN PLUS IAB (09-11)	9
SERCA2: NOVEL TARGET FOR THE TREATMENT OF CYSTIC FIBROSIS (09-05)	10
TARGETING A SUBSET OF B CELLS TO TREAT AUTOIMMUNE DISEASES (09-03)	11
C57BL/10 TARGETED MUTATION MOUSE STRAIN THAT DEVELOPS SPONTANEOUS KERATITIS (08-12)	12
ADENOSINE A2A RECEPTOR: A PROGNOSIS MARKER FOR LUNG CANCER (08-11)	13
NOVEL TLR INHIBITORS PREVENT RESPIRATORY SYNCYTIAL VIRUS INFECTION IN VIVO (07-07)	14
MAGP-2: AN EXTRACELLULAR FACTOR SHOWN TO HAVE PRO-ANGIOGENIC PROPERTIES IN VIVO (06-05)	15
METHOD TO PREVENT BIOFILM FORMATION IN VARIOUS CLINICAL SETTINGS (CONTACT LENSES, WOUNDS, CYSTIC FIBROSIS, ETC.) (04-08)	16
CYSTATIN C: AN EXTRACELLULAR PROTEIN THAT DIRECTLY BLOCKS THE TGF- β RECEPTOR. POTENTIAL THERAPIES FOR CANCER AND FIBROTIC DISEASES (04-05)	17
MODULATING THE TRANSPORT OF THIOL-CONTAINING MOLECULES FOR THE TREATMENT OF LUNG DISEASE AND CANCER (02-16)	18
LIPOSOMAL CLODRONATE AS A THERAPY FOR AUTOIMMUNE HEMOLYTIC ANEMIA (02-07)	19
HIGH-THROUGHPUT CELL BASED ASSAY FOR THE IDENTIFICATION OF DRUGS TARGETING THE NF-KB SIGNALING PATHWAY (02-05)	20
TALL-1 AND ITS RECEPTOR BCMA: MOLECULAR TARGETS FOR THE DEVELOPMENT OF THERAPIES AGAINST INFLAMMATORY DISEASES (02-01)	21
C57BL/6 TRANSGENIC MICE STRAIN EXPRESSING GFP UBIQUITOUSLY (01-05)	22
USE OF AEROSOLIZED MONOCLONAL ANTIBODIES AGAINST ALPHA BETA OR GAMMA DELTA T CELL RECEPTORS AS A THERAPY FOR AIRWAY HYPERRESPONSIVENESS (01-01)	23
CALCITONIN GENE-RELATED PEPTIDE FOR THE REDUCTION OF ALLERGEN-INDUCED AIRWAY HYPERRESPONSIVENESS (00-14)	24
CDK6 AS A MARKER FOR BREAST CANCER (00-11)	25

TABLE OF CONTENTS

Anti-CD79 Antibody Offers Novel Approach to therapy in Autoimmune Disease, transplantation and lymphoma (11-15)	3
Novel PIM 1 Kinase Inhibitor that Upregulates RUNX3 for the Treatment of Allergic Diseases (11-06)	4
PTPN13: A Novel Target for the Treatment of Pulmonary Fibrosis (11-09)	5
Novel Adjuvant for Increasing Effectiveness of Vaccines (10-13)	6
Use of the <i>Listeria Monocytogenes</i> p60 Polypeptide and Variants for Stimulating NK cells (10-08)	7
Targeting FgfR2b for the Treatment of Adult Lung Injury (09-20)	8
Mouse Strain Expressing a T cell Receptor Specific for a Schistosomal Antigen Plus IAb (09-11)	9
SERCA2: Novel Target for the Treatment of Cystic Fibrosis (09-05)	10
Targeting a Subset of B Cells to Treat Autoimmune Diseases (09-03)	11
C57BL/10 Targeted Mutation Mouse Strain that Develops Spontaneous Keratitis (08-12)	12
Adenosine A2A Receptor: A Prognosis Marker for Lung Cancer (08-11)	13
Novel TLR Inhibitors Prevent Respiratory Syncytial Virus Infection In Vivo (07-07)	14
MAGP-2: An Extracellular Factor Shown to have Pro-Angiogenic Properties <i>in vivo</i> (06-05)	15
Method to Prevent Biofilm Formation in Various Clinical Settings (Contact Lenses, Wounds, Cystic Fibrosis, etc.) (04-08)	16
Cystatin C: An Extracellular Protein that Directly Blocks the TGF- β Receptor. Potential Therapies for Cancer and Fibrotic Diseases (04-05)	17
Modulating the Transport of Thiol-Containing Molecules for the Treatment of Lung Disease and Cancer (02-16)	18
Liposomal Clodronate as a Therapy for Autoimmune Hemolytic Anemia (02-07)	19
High-Throughput Cell Based Assay for the Identification of Drugs Targeting the NF-kB Signaling Pathway (02-05)	20
TALL-1 and its Receptor BCMA: Molecular Targets for the Development of Therapies Against Inflammatory Diseases (02-01)	21
C57BL/6 Transgenic Mice Strain Expressing GFP Ubiquitously (01-05)	22
Use of Aerosolized Monoclonal Antibodies Against Alpha Beta or Gamma Delta T Cell Receptors as a Therapy for Airway Hyperresponsiveness (01-01)	23
Calcitonin Gene-Related Peptide For The Reduction Of Allergen-Induced Airway Hyperresponsiveness (00-14)	24
CDK6 as a Marker for Breast Cancer (00-11)	25

ANTI-CD79 ANTIBODY OFFERS NOVEL APPROACH TO THERAPY IN AUTOIMMUNE DISEASE, TRANSPLANTATION AND LYMPHOMA

NJH ID: #11-15

Background

B lymphocytes play fundamental roles in the pathogenesis of autoimmune disease as well as transplant rejection. Current technologies for treatment of many lymphomas, leukemias, transplant rejection and some autoimmune disorders include monoclonal antibodies (mAb) that target and deplete B cell populations. Recovery from these treatments requires an extended period of time during which patients are immunosuppressed and therefore susceptible to opportunistic infections. In addition, this modality does not eliminate all B lineage cells and thus may not be appropriate for all pathologic conditions involving B lymphocytes.

Cluster of Differentiation 79 (CD79) is a transmembrane protein found exclusively in B cells that is the transducer component of B-cell receptor (BCR), generating a signal following recognition of antigen by the BCR. As a consequence CD79 is an ideal candidate molecule for B cell-targeted therapy.

Technology

Dr. Cambier and his laboratory discovered that in certain circumstances, subunits of the B cell antigen receptor (BCR) become dissociated rendering the receptor incompetent to transduce activating signals. Based on these observations they produced antibodies against the BCR transducers, CD79a and b, and found that they “desensitize” the BCR and suppress the immune response, autoimmunity, and growth of non-Hodgkin’s B lymphoma. These anti-CD79 mAbs show therapeutic potential to induce reversible inhibition of BCR signaling and B cell function. This technology exploits the unique qualities of the BCR to reversibly suppress signaling for therapeutic use in autoimmunity, cancer and transplantation. Receptor desensitization and therapeutic efficacy has been demonstrated *in vitro* and *in vivo*.

Potential Applications

- Treatment of autoimmune conditions such as rheumatoid arthritis, lupus, and diabetes.
- Treatment of B cell neoplasias
- Prevention of tissue rejection

State of Development

Investigators have shown that administration of an anti-mouse CD79 targeting BCR in a mouse model of lupus, decreased autoantibody production (suppressed B cell responses), decreased skin pathology, and increased survival from 20% to 80%. Furthermore they established that anti-CD79a/b antibodies (intact, or mutants incompetent to bind IgG receptors and activate the complement cascade) block the development of disease and ameliorate ongoing target organ injury in mouse models of Rheumatoid Arthritis and Type 1 Diabetes.

In later experiments they developed a proprietary monoclonal antibody against human CD79 (Curly 14) that has the capacity to desensitize the BCR *in vitro*.

Further experiments will involve the characterization of the effectiveness of Curly 14 for modulating immune disease, understanding Curly 14 binding affinity, determination of the antibody binding site and the ability to destabilize and/or desensitize B cells in huSCID and human CD79 knockin mouse models.

Patents

Issued U.S. Patent #6,503,509 and #7,825,224; Issued patents in France, Germany, UK, Australia and New Zealand; Pending in Canada, and Japan Human CD79 mAb-related patent pending worldwide.

Publications

- Vilen et al. 1997. J Immunol. 159(1):231-43
- Vilen et al. 1999. Immunity 10:239-248.
- Li et. al. 2008 J Immunol. 1;181(5):2961-72.

Inventors

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Licensing Status

This technology is available for licensing.



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PTPN13: A NOVEL TARGET FOR THE TREATMENT OF PULMONARY FIBROSIS

NJH ID: #11-09

Background

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive fibrosing interstitial pneumonia, primarily occurring in older adults. It is caused by injury and aberrant repair of the lower lung resulting in accumulation of fibroblasts. These cells produce abundant amounts of collagen and contribute to the formation of scar tissue. In normal wound repair, fibroblasts die and are removed at the completion of the repair process. In IPF, fibroblasts persist and accumulate in the lung, leading to progressive fibrosis, dyspnea, hypoxemia, and death within 5 years of diagnosis.

Technology

Dr. Riches and his group have previously shown that fibroblasts normally die through apoptosis following stimulation of a receptor called Fas. Furthermore they showed that these cells will not die when Fas becomes associated with an inhibitory protein, the PTPN13 molecule. They were able to demonstrate that by blocking the association between Fas and PTPN13, fibroblast cells are once again able to undergo Fas-receptor induced death. These findings suggest that the development of a compound that blocks the Fas/PTPN13 interaction could serve as a therapeutic modality to treat IPF.

Potential Applications

Therapeutic uses for treatment of idiopathic pulmonary fibrosis. Other fibrotic conditions are being explored.

State of Development

Investigators are currently screening libraries to identify molecules that will interfere in the binding of PTPN13 to Fas.

Publications

- “TNF- α Sensitizes Normal and Fibrotic Human Lung Fibroblasts to Fas-induced Apoptosis”. Frankel et al 2006 Am J Resp Cell Mol Biol 34(3): 293-304.
- “Increased Cell Surface Fas Expression Is Necessary and Sufficient To Sensitize Lung Fibroblasts to Fas Ligation-Induced Apoptosis: Implications for Fibroblast Accumulation in Idiopathic Pulmonary Fibrosis”. Wynes, MW et al. The Journal of Immunology, July 1, 2011 vol. 187 no. 1 527-537.
- “PTPN13 is an inhibitor of Fas-induced apoptosis in idiopathic pulmonary fibrosis”, in preparation.

Patent Status

US and International Patents pending.

Inventors

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Licensing Status

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NOVEL PIM 1 KINASE INHIBITOR THAT UPREGULATES RUNX3 FOR THE TREATMENT OF ALLERGIC DISEASES

NJH ID: #11-06

Background

It is estimated that 50 million people in North America are affected by allergic conditions with an associated cost of more than \$10 billion dollars yearly.

The most common form of allergy, allergic rhinitis (nasal allergies), affects about 35 million Americans, 6 million of whom are children. The number of cases of asthma has doubled over the last 20 years affecting 15 million Americans, 5 million of whom are children. Even greater proportionate increases have been seen in atopic dermatitis and food allergy. Several antagonistic drugs are used to block the action of allergic mediators, or to prevent activation of cells and degranulation processes. These include antihistamines, glucocorticoids, epinephrine (adrenaline), and theophylline. Anti-leukotrienes, such as Montelukast (Singulair) or Zafirlukast (Accolate), are FDA approved for treatment of allergic diseases. Anti-cholinergics, decongestants, mast cell stabilizers, and other compounds thought to impair eosinophil chemotaxis, are also commonly used. Although these drugs help to alleviate the symptoms of allergy, to some extent, but they play a limited role in chronic treatment of allergic disorders.

Runx-related transcription factors (Runx) are a novel family of transcription factors which are key regulators of lineage-specific gene expression. The data suggest that Runx3 plays a critical role in regulating T-cell development, the differentiation of Th1/Th2 cells and Th1/Th2 cytokine production, and the development of an allergic disease.

Technology

Dr. Gelfand's laboratory at National Jewish Health has shown that the proto-oncogene serine/threonine-protein kinase (PIM-1) increases upon allergen sensitization and is responsible for the downregulation of Runx3. Further, they have shown in mouse models of allergy that the upregulation of Runx3 can be achieved by inhibiting PIM-1 kinase. This strategy substantially reduced allergic responses in mice.

Therefore, upregulating Runx3 by targeting PIM-1 kinase represents a novel approach for treating allergic diseases. Scientists at National Jewish Health and the University of Colorado have also developed novel PIM-1 kinase inhibitors because existing ones suffer from a lack of specificity and problems associated with distribution, metabolism and excretion.

Potential Applications

Treatment of allergic disease by upregulating or sustaining the expression of Runx3.

State of Development

Investigators are currently testing a series of proprietary and novel PIM-1 kinase inhibitors in experimental models of asthma, allergic rhinitis and peanut-induced food allergy in mice.

Publication

Inhibition of Pim1 Kinase Prevents Peanut-Induced Allergy by Enhancing Runx3 Expression and Suppressing Th2 and Th17 Differentiation. In preparation.

Patent Status

US and International patent pending.

Inventors

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NOVEL ADJUVANT FOR INCREASING EFFECTIVENESS OF VACCINES

NJH ID: #10-13

Background

Most current vaccines, including those against influenza, act via the generation of specific antibodies that can either neutralize or otherwise inactivate the pathogen. These vaccines induce the production of antibodies against viral surface proteins to prevent viral cellular entry. However, as far as influenza is concerned, these viral surface proteins tend to mutate over time and as a result a new vaccine against influenza must be developed every year. To avoid this problem, the ideal vaccine would be pan-specific across strains of influenza virus.

Targeting CD8 T cell mediated immunity could be the right strategy to reach this goal. The portions of influenza virus that are recognized by cytotoxic CD8 T cells are much less variable than those recognized by antibodies. Thus a vaccine designed to activate CD8 T cells has the potential to protect against yearly and newly emerging pandemic viral subtypes.

Technology

Dr. Marrack's laboratory at National Jewish Health has discovered how to prime a second arm of the immune system to boost the effectiveness of influenza vaccines. They demonstrated that the combination of two adjuvants (alum and monophosphoryl lipid A, MPL), already approved for patient use, with a viral nuclear protein can maintain long-lived memory CD8 T cells and protect mice from influenza viral challenge.

Potential Applications

A combination of two adjuvants, such as alum and MPL, with an internal viral protein can be used to induce CD8, (killer) T cells to join antibodies in response to viral infection. CD8 T cell epitopes are much less variable and thus a vaccine designed to activate protective CD8 T cells has the potential to protect against yearly and newly emerging pandemic viral subtypes. This new approach could be applicable to infectious disease such as the flu and malaria.

State of Development

Investigators have tested the combination of adjuvants (alum and MPL) in a mice model of Influenza A infection. Mice primed with nucleoprotein of influenza A (NP) and both adjuvant lost less weight and quickly regained their original weight in contrast to mice primed with NP/protein and either adjuvant.

Publication

Vaccine adjuvants aluminum and monophosphoryl lipid A provide distinct signals to generate protective cytotoxic memory CD8 T cells McLeod, MK et al. PNAS May 10, 2011 vol. 108 no. 19 7914-7919

Patent Status

US patent pending. Published international patent WO 2011/057267.

Inventors

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USE OF THE *LISTERIA MONOCYTOGENES* P60 POLYPEPTIDE AND VARIANTS FOR STIMULATING NK CELLS

NJH ID: #10-08

Background

Natural killer cells (or NK cells) are a type of cytotoxic lymphocyte that constitutes a major component of the innate immune system. NK cells play a major role in the rejection of tumors and cells infected by viruses. They kill cells by releasing small cytoplasmic granules of proteins called perforin and granzyme that cause the target cell to die by apoptosis (programmed cell death). Stimulation of NK cells can be used to treat infections and tumors, to improve adaptive immune responses to these agents and vaccines, and possibly to promote successful full-term pregnancy.

Toll-like receptors (TLRs) are a class of proteins that play a key role in the innate immune system. Current technologies that use TLR agonists have been showed to elicit toxicity. Others lack the ability to stimulate NK cell responses. Antibodies to NK cell surface markers in some cases activate only specific NK cell subsets and may not work in all patients due to allelic differences in NK cell surface proteins recognized by the antibodies. Antibodies may also cause depletion of NK cells or only activate specific functions of NK cells. Therefore a more effective approach to activate the innate immune system through NK cells is currently lacking.

Technology

All species of the genus *Listeria* secrete a major extracellular protein called p60. The laboratory of Dr. Lenz at National Jewish Health has purified the wildtype p60 protein and created a mutant form of p60 that lacks endopeptidase activity. They found that both forms of p60 contribute to the activation of dendritic cells (DC) in a manner that permits the activation of naïve NK cells. The enzymatically-null mutant p60 protein lacks the potential “off-target” effects, thus is an improvement over the wildtype p60 protein.

Potential Applications

Treatment of diseases that will benefit from NK cells activation:

- **Cancer.** Evidence point to a positive association between NK cell activation and positive outcomes in solid, metastatic and hematologic cancers.
- **Infectious diseases.** NK cells are implicated in resistance to numerous viral infections prevalent in the US and other countries; including upper respiratory infections, HSV, EBV, VZV, HPV, CMV.
- **Vaccines.** P60 appears to act directly on naïve DCs to stimulate their maturation in a manner that permits activation of NK cells. Both activated DCs and IFN γ that is produced by NK cells can boost cellular (Th1-type) immune responses. P60 may be useful to improve immune responses elicited by vaccines and thus be useful for vaccinating large numbers of people world wide.
- **Pregnancy.** NK cells are found in the placenta and their activation has been associated with positive pregnancy outcome. There may be utility in stimulating NK cell function with p60 to prevent pre-eclampsia and improve pregnancy success in individuals suffering recurrent miscarriages.

State of Development

Investigators at NJH have identified a region of the p60 protein that is necessary and sufficient to elicit NK cell activation. Small polypeptides that contain this region retain functionality and can be used in animals. Modified versions of these polypeptides may show increase stability (and thus activity).

Publication

Schmidt RL, Filak HC, Lemon JD, Potter TA, Lenz LL, 2011 A LysM and SH3-Domain Containing Region of the *Listeria monocytogenes* p60 Protein Stimulates Accessory Cells to Promote Activation of Host NK Cells. *PLoS Pathog* 7(11): e1002368. doi:10.1371/journal.ppat.1002368.

Patent Status

US patent pending. Published international patent WO 2011/060093.

Inventors

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Licensing Status

This technology is available for licensing.



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TARGETING FGFR2B FOR THE TREATMENT OF ADULT LUNG INJURY

NJH ID: #09-20

Background

The epithelial cells that line the airways are constantly exposed to potential toxic agents and pathogens in the environment, and they must therefore be able to respond quickly and effectively to both cellular damage and local inflammation. The cellular hallmark of lung repair after injury of lung epithelial cells is a rapid proliferative response ultimately leading to restoration of the airway epithelium and function.

Remodeling of the airway epithelium is a common pathological feature in chronic lung disease and a predisposing factor in the development of lung cancer. In young animals, tissue damage can usually be repaired quickly, but this natural capacity may fail after persistent injury and with age. Diseases such as cancer exploit the mechanisms by which the body normally rebuilds itself.

Technology

Dr. De Langhe, Assistant Professor for National Jewish Health has shown the importance of Fibroblast Growth Factor 10 (FGF10) signaling through FGFR2b for lung regeneration, lung tumor formation as well as goblet/mucus cell differentiation. His group has identified FGFR2b as a marker for lung stem cells. This discovery creates an enormous potential for diagnostic and treatment of several of the most critical lung diseases.

Potential Applications

- **Diagnostic:** The ex-vivo detection of lung stem cells on histological samples using monoclonal antibodies (mAb) against FGFR2b. The presence of these stem cells is an indicator of lung injury and/or tumor development. This diagnostic approach could also prove useful to establish which subgroup of patients will benefit from anti-FGFR2b drugs.
- **Therapeutic:** The isolation of live lung airway stem cells from a biopsy sample using mAb against FGFR2b. These cells can be amplified ex-vivo and intratracheally instill back to the same patient to repair injured lungs or treatment of fibrosis. Also an aerosolized mAb that blocks FGFR2b could be used to inhibit the proliferation of airway stem cells in the case of lung cancer or their transdifferentiation into goblet cells/mucous producing cells in the case of asthma. Alternatively, agonist FGFR2b antibodies could be used to increase proliferation of airway stem cells after a lung injury and to protect against and/or cure lung fibrosis.

State of Development

Proof of concept that FGFR2b can be used to isolate lung stem cells and that FGFR2b signaling is important for lung stem cell activation and therefore epithelial regeneration, tumor development as well as mucous cell hyperplasia.

Publication

Parabronchial smooth muscle constitutes an airway epithelial stem cell niche in the mouse lung after injury. Thomas Volckaert, Erik Dill, Alice Campbell, Caterina Tiozzo, Susan Majka, Saverio Bellusci, Stijn P. De Langhe. J Clin Invest. 2011; doi:10.1172/JCI58097.

Patent Status

US patent pending. International Patent Publication WO/2011/025814.

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MOUSE STRAIN EXPRESSING A T CELL RECEPTOR SPECIFIC FOR A SCHISTOSOMAL ANTIGEN PLUS IAB

NJH ID: #09-11

Summary

Schistosomiasis is a major health problem in the developing world with about 2 million people infected world wide and about 400,000 people infected in the USA. The infected host clears this parasitic worm by means of schistosome-specific T cells. This is also true in infected mice.

Although mice are used as a model for the disease, so far no useful tools exist for following the protective T cells in mice. Such tools would be of great value to laboratories in the basic research and biotechnology industry in the USA and elsewhere that are trying to understand the disease and develop methods to immunize against the parasite, understand the disease and develop drugs to counteract the parasite.

We have developed a mouse that expresses as transgenes the genes for a T cell receptor that recognizes an antigen form schistosomes plus IAB. These transgenic mice will provide a source of T cells that can recognize, respond to and reject the parasite.

Potential Applications

- Understand Schistosomiasis
- Develop immunization methods
- Schistosomiasis diagnostics/personalized medicine/immunization tools

Advantages of Invention

These transgenic mice will provide a source of T cells that can recognize, respond to and reject the parasite.

State of Development

We have developed a mouse that expresses as transgenes the genes for a T cell receptor that recognizes an antigen form schistosomes plus IAB.

Publication

In preparation

Inventors

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SERCA2: NOVEL TARGET FOR THE TREATMENT OF CYSTIC FIBROSIS

NJH ID: #09-05

Summary

Modulation of the activity of sarcoendoplasmic reticulum calcium ATPase (SERCA2) can profoundly affect Ca(2+) homeostasis. Although altered calcium homeostasis is characteristic of cystic fibrosis (CF), the role of SERCA2 has never been explored. Our scientists have shown that SERCA2 expression was decreased in the airway epithelium of CF patient samples. Decreased SERCA2 expression causes enhanced susceptibility to oxidants and oxidative stress to airway epithelium and can be an important component of disease pathogenesis and exacerbations. Therefore increasing SERCA2 expression or activity could be a valuable approach for the treatment of respiratory diseases like CF or asthma.

Potential Applications

Treatment of airway inflammatory diseases like cystic fibrosis and asthma.

Advantages of Invention

Various SERCA2 activators are currently being tested as drug candidates by third parties.

State of Development

Our scientists have found that:

- SERCA2 is decreased in the epithelium of proximal and distal airways of CF subjects.
- SERCA2 is required for survival of airway epithelial cells under oxidant stress such as those caused by ambient concentration of ozone and concentrations of H₂O₂ and TNF found in CF airways.
- Increasing SERCA2 activity reduces ozone-mediated proinflammatory cytokine production.
- SERCA2 activity can be modulated/enhanced in CF airway epithelial cells by drug treatment.

Publications

- Am J Respir Crit Care Med 2009, May 179 (9):816-826 (PMID: 19201925).
- PLoS ONE 2011 Nov., 6(11): e27451. doi:10.1371.0027451.

Patent Status

U.S. patent application #20100087374. International Patent Publication #WO2010/040130.

Inventors

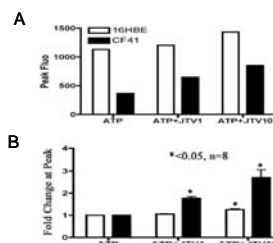
Shama Ahmad, Ph.D and Carl White, MD.

Licensing Status

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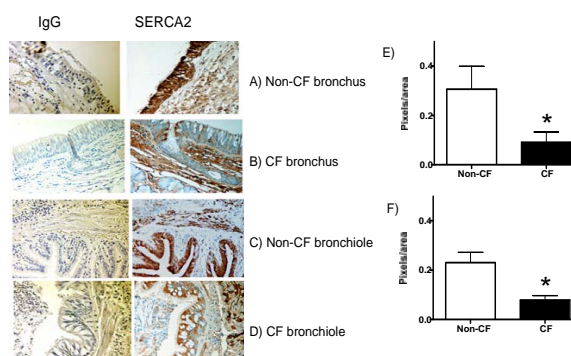


Calcium signaling can be modified by SERCA activator treatment in CF airway epithelial cells



Non-CF 16HBE and CF CF410 cells plated in a 96-well plate were treated with either 0, 1 or 10 μ M of JTV-519 in culture media. After 24 h of treatment cells were loaded with calcium sensing dye Fluo-4 in calcium buffer. ATP stimulations were performed and fluorescence was recorded for 18 mins in a Biotek Fluorimeter. Panel A shows the peak of intracellular calcium and Panel B shows fold change in the intracellular calcium release upon JTV-519 treatment in non-CF and CF cells.

SERCA2 expression is decreased in CF bronchial and bronchiolar epithelium *in vivo*



Sarcoplasmic/endoplasmic reticulum Ca²⁺-ATPase (SERCA2) expression in the epithelium of proximal and distal cystic fibrosis (CF) and non-CF airways. Immunohistochemical localization of SERCA2 was performed as described in METHODS using identical conditions for non-CF and CF tissue. Left panel: Nonspecific IgG control. Right panel: SERCA2 staining in epithelium (arrowheads). SERCA2 staining was found predominantly in the epithelium of non-CF bronchi (n = 5 donors) (A) and bronchioles (C), and it was significantly less intense in the epithelium of CF airways (n = 5 donors) (B and D). (E) Quantitation of SERCA2 staining (SERCA2-IgG) in the non-CF and CF bronchi. The regions containing mucus were excluded during quantitation. For each tissue, two SERCA2 and two IgG-stained sections were analyzed, and 10 nonmucus areas per section were randomly selected for quantitation using Image-Pro Plus version 4.0 (Media Cybernetics, Silver Spring, MD). Similarly, SERCA2 staining in the non-CF and CF bronchioles was quantified (F).

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TARGETING A SUBSET OF B CELLS TO TREAT AUTOIMMUNE DISEASES

NJH ID: #09-03

Background

It is estimated that 23.5 million Americans suffer from autoimmune disease (AD) and that the prevalence is rising. Researchers have identified 80-100 different ADs and suspect at least 40 additional diseases of having an autoimmune basis. These diseases are chronic and can be life-threatening with an annual direct health care costs in the range of \$100 billion. AD is one of the top 10 leading causes of death in female children and women in all age groups up to 64 years. Current therapies for autoimmune diseases such as immunosuppressant treatments, anti-CD20 and anti-TNF monoclonal antibodies (mAb) have very profound effects on the whole immune system leading to substantial long-term side effects. These therapies deplete patients of large populations of immune cells that are important for maintaining the integrity of the host response to pathogens.

Technology

Researchers at National Jewish Health have identified a new population of autoimmune associated B cells(ABCs) that appears in the blood and lymphoid organs as the mice develop an autoimmune disease.

They further demonstrated that ABCs secrete autoantibodies and depletion of these cells in mice with ongoing autoimmunity leads to reduction of autoreactive antibodies, suggesting that ABCs play a direct role in the development of autoimmunity. This population of cells also increase in female mice as they get older, possibly explaining why females are more likely to develop autoimmunity compared to males. Furthermore, they were able to identify B cells in the blood of autoimmune patients with a phenotype almost identical to those of ABCs in mice.

Potential Applications

- **Diagnostic:** early detection of ABCs in blood will make possible for physicians to identify patients developing autoimmunity before the onset of symptoms, allowing for earlier and more successful therapeutic interventions.
- **Therapeutic:** targeted depletion of ABC cells with a bispecific (CD19/CD11c) mAb could lead to the development of a treatment for autoimmune diseases.

State of Development

These scientists are currently developing bi-specific mAbs that targets the ABC population and will test their efficacy in mouse models of autoimmunity. These bi-specific antibodies will recognize two different proteins (CD19 and CD11c) on the surface of ABCs. This therapeutic approach will lead to the specific elimination of ABCs with no effect over other B cells, modeling a potential treatment in which the individuals being treated are much less immune compromised than with current treatments where all B cells are depleted.

Publication

Toll-like receptor 7 (TLR7)–driven accumulation of a novel CD11c⁺ B-cell population is important for the development of autoimmunity, *Blood* 2011;118(5):1305-1315.

Patent Status

US patent pending. Published international patent WO 2010/054288.

Inventors

John W. Kappler Ph.D., Philippa Marrack Ph.D., Anatoly Rubtsov, Ph.D. and Julia Rhiannon, M.D.

Licensing Status

Available for licensing.



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C57BL/10 TARGETED MUTATION MOUSE STRAIN THAT DEVELOPS SPONTANEOUS KERATITIS

NJH ID: #08-12

Summary

Research scientists at National Jewish Health have developed a C57BL/10 targeted mutation mouse strain that expresses defective T cell receptors and spontaneously develop keratitis. Genes from mice of the C57BL/6 background, which carry existing genetically engineered mutations that prevent the development of $\gamma\delta$ or $\alpha\beta$ T cells, were transferred onto the C57BL/10 background.

Potential Applications

Animal model for keratitis where the development is spontaneous

A model to test compounds developed to treat keratitis or influence angiogenesis

Advantages of Invention

B10.TCR $\delta^{-/-}$ and B10.TCR $\beta^{-/-}$ female mice show a high frequency of spontaneous keratitis. The B10.TCR $\beta/\delta^{-/-}$ females have a lower incidence of spontaneous keratitis.

State of Development

To establish new C57BL/10 background mouse strains, ten or more backcrosses were carried out. The B10.TCR $\delta^{-/-}$ mice have defective T cell receptor-C δ gene; the B10.TCR $\beta^{-/-}$ mice have defective T cell receptor C β gene. These mice were intercrossed to establish the B10.TCR $\beta/\delta^{-/-}$ strain.

Publication

O'Brien et.al. Invest Ophthalmol Vis Sci. 2009 Jul;50(7):3266-74. Epub 2009 Jan 17.

Inventors

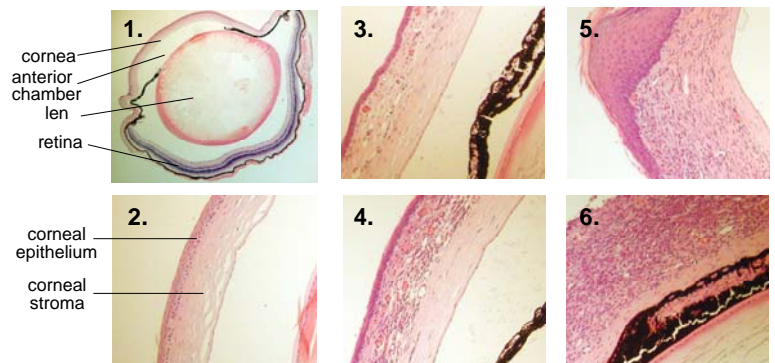
Rebecca O'Brien, PhD and Willi Born, PhD

Licensing Status

This technology is available for licensing.



B10.TCR $\delta^{-/-}$ and B10.TCR $\beta^{-/-}$ mice develop a spontaneous eye disease at a high frequency. Left - normal C57BL/10 eye. Right - B10.TCR $\delta^{-/-}$ mice showing corneal opacity. Note the central thickening.



Histological sections (H&E stained) showing that the corneal opacity in these mice is due to keratitis. 1 and 2, normal C57BL/10 eye shown for comparison. Panels 2-6 are close-ups of the corneal area only, and examples of increasing severity are shown. Note the inflammatory infiltrates in the corneal stroma, also the presence of blood vessels in the stroma, and the occasional thickening of the corneal epithelium.

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ADENOSINE A2A RECEPTOR: A PROGNOSIS MARKER FOR LUNG CANCER

NJH ID: #08-11

Summary

The role of angiogenesis in tumor survival and metastasis is now well recognized. Hypoxia-inducible transcription factors HIF-1alpha and HIF-2alpha are both known to induce angiogenesis by upregulating a common set of cytokines, including VEGF, but only the activation of HIF-2alpha has been associated with poor prognosis in lung cancer. However, since HIF-2alpha is highly labile, it is a poor candidate for a biomarker.

Scientists at National Jewish Health have discovered that the receptor Adenosine A2A (ADORA2A) is expressed only in response to HIF-2alpha activation and more importantly that the expression of ADORA2A is increased in later stage lung tumors.

This receptor could therefore be used as a prognosis marker for lung cancer as well as a potential new target for an anti-angiogenic approach to treating lung cancer.

Potential Applications

- A biomarker for HIF-2alpha activation and therefore for poor prognosis in lung cancer.
- A target for anti-angiogenic therapy in lung cancer

Advantages of Invention

Since HIF-2alpha is too labile to be used as a marker, ADORA2A instead can be used as readout of HIF-2alpha activation and can be easily measured at the RNA level in biopsy samples.

State of Development

Our scientists have found that

- Hypoxia increases ADORA2A *in vitro*
- HIF-2alpha and not HIF-1alpha regulates ADORA2A expression
- Overexpression of ADORA2A or its activation through agonists leads to an increase in endothelial cell proliferation, migration, and branching
- ADORA2A expression increases in later stage tumor samples collected from lung cancer patients

Publication

Ahmad et.al. *Proc Natl Acad Sci U S A*. 2009 Jun 30;106(26):10684-9. Epub 2009 Jun 17.

Patent Status

U.S. patent application #20090155796. International Patent Publication #WO2009/065044.

Inventors

Aftab Ahmad, Ph.D. and Carl White, MD

Licensing Status

Available for licensing.



NOVEL LIPID INHIBITORS OF TLR EFFECTIVE AT REDUCING RSV AND INFLUENZA A INFECTION IN VIVO

NJH ID: #07-07

Background

Respiratory Syncytial Virus (RSV) is the most common cause of hospitalization for respiratory illness in young children and 90% of children under the age of 2 will be infected by this virus. RSV infection and associated inflammation have also been shown to be a substantial contributing factor in the exacerbation of chronic lung diseases in adults and the elderly. Influenza A virus (IAV) is a worldwide public health problem causing 500,000 deaths each year with the highest death rates among newborns, the elderly and adults with chronic lung diseases.

Technology

Dr. Voelker's lab at National Jewish Health has demonstrated the anti-inflammatory and anti-viral properties of unsaturated phosphatidylglycerols (PGs). PGs markedly attenuate pro-inflammatory cytokine production (IL-6, IL8) induced by RSV, and prevent viral replication in human bronchial epithelium. In addition these researchers have shown that PGs prevent the intercellular spreading of the RSV virus, after infection is established. Studies with mice reveal that treatment with PGs at the time of viral challenge, dramatically reduces RSV infection.

Further studies by these scientists have also shown that PG attenuates influenza virus induced cytokine production in human bronchial epithelial cells; and intranasal administration of PG suppresses influenza A virus infection in mice.

The Voelker laboratory has also created 4 novel compounds with similar activity to that of PGs. These novel compounds block RSV and influenza A attachment to epithelial cells in vitro without apparent toxicity.

Potential Applications

Respiratory Syncytial Virus (RSV), influenza A virus, rhinovirus, sepsis-induced ARDS, asthma, reducing the effects of inflammation during mechanical ventilation, chronic bronchitis, COPD, cystic fibrosis, idiopathic pulmonary fibrosis

State of Development

Four novel compounds are undergoing a toxicology study with a mouse model of RSV infection.

Publications

- Kuronuma et al. J Biol Chem. 2009 Sep 18;284(38):25488-500. Epub 2009 Jul 7. PMID: 19584052.
- Numata et al. Proc Natl Acad Sci U S A. 2010 Jan 5;107(1):320-5. Epub 2009 Dec 22. PMID: 20080799.
- Kandasamy et al. J Biol Chem 286:7841 2011 PMID: 21205826.
- Numata et al. Am J Respir Cell Mol Biol. 2011 PMID: 22052877.

Patent Status

Published U.S. Patent application #20080242640. International patents pending.

Inventors

Dennis R. Voelker, PhD

Licensing Status

Available for licensing.



MAGP-2: AN EXTRACELLULAR FACTOR SHOWN TO HAVE PRO-ANGIOGENIC PROPERTIES IN VIVO

NJH ID: #06-05

Summary

Excessive angiogenesis has emerged as an essential feature of tumor development and appears to be regulated in part by extracellular matrix proteins. Scientists at National Jewish Health have identified an extracellular matrix protein (designated MAGP-2) that acts as a pro-angiogenic agent in vivo.

Potential Applications

- A target for inhibiting angiogenesis in cancer and other angiogenesis-dependent diseases
- Stimulating neovascularization by administration of MAGP-2 to ischemic tissues in coronary artery disease, stroke, and delayed wound healing
- A diagnostic biomarker, especially for cancer

Advantages of Invention

Because of its extracellular nature, MAGP-2 can be easily detectable and targetable by antibody-based technologies for example.

State of Development

Our scientists have shown the following:

In vitro:

- MAGP-2 is over expressed in human uterine tumor samples
- Endothelial cell expression of MAGP-2 increases during angiogenesis in vitro
- MAGP-2 stimulates angiogenic sprouting in 3-dimensional collagen cultures
- MAGP-2 increases endothelial cell proliferation and invasion in vitro

In vivo:

- Significant enhancement of neovascularization when MAGP-2 was implanted into mice through matrigel plugs
- MAGP-2 increases tumor size and angiogenesis in mice

Patent

U.S. Patent #8,158,107.

Publications

- Albig AR, et al. *Angiogenesis*. 2007;10(3):197-216.
- Albig AR, et al. *Microvasc Res*. 2008 May; 76(1): 7-14.

Inventors

William P. Schiemann, Ph.D. and Allan Albig, Ph.D.

Licensing Status

This technology is available for licensing.



METHOD TO PREVENT BIOFILM FORMATION IN VARIOUS CLINICAL SETTINGS (CONTACT LENSES, WOUNDS, CYSTIC FIBROSIS, ETC.)

NJH ID: #04-08

Summary

Researchers at National Jewish Health have determined that actin originating from necrotized human neutrophils serve as a biological matrix in the formation of microbial biofilms in the airways of cystic fibrosis (CF) patients. Since biofilm formation allows for the survival of microbial organisms in the airways of CF patients and is also associated with increased morbidity and mortality, targeting actin and/or neutrophils could be the basis for the development of a potential therapy for CF.

Potential Applications

- Targeted therapy for preventing or reducing biofilm formation in cystic fibrosis, infectious kidney stones, cystitis, dental caries, chronic otitis media, bacterial endocarditis, osteomyelitis, wounds, and acne
- Prevention of microbial biofilm development on contact lenses, orthopedic implants, stents, catheters and other medical devices
- An assay to test compounds for their ability to prevent/reduce biofilm formation by assessing the ability of microbial organizations to bind actin

Advantages of Invention

This therapy, focused on biofilm prevention or degradation, is particularly applicable for early stage CF in young patients when antimicrobial agents are only partially effective at best.

State of Development

Our scientists have shown the following in vitro:

Biofilm development of *P. aeruginosa* is enhanced with:

- the addition of human viable neutrophils and correlates with an increase in the number of necrotic neutrophils.
- the addition of neutrophils lysates and particularly with monomeric actin (G-actin).

Biofilm development of *P. aeruginosa* is reduced with:

- the addition of neutrophils lysates depleted of actin microfilaments (F-actin).
- the addition of compounds that promotes the depolymerization of F-actin, such as gelsolin or charged poly(amino acids).

Further R&D Required

Using the state grant to identify the most effective charged poly(amino acids) at disrupting biofilms and testing such compounds on infected contact lenses, and in animal models of eye and skin infections.

Patent

Published U.S. Patent Application #20060030539; Published U.S. Patent Application #20080207556; Published U.S. Patent Application #20080199509; International Patent Application #WO2006/017816.

An additional patent application pending.

Publications

- Walker et al. *Infect. Immun.* (2005) 73: 3693-3701.
- Parks et. al. *Med. Micro.* (2009) 58(Pt 4):492-502.
- Robertson et. al. *Invest. Ophthalmol. Vis. Sci.* (2011) 10.1167/iovs.10-6469.

Inventors

Jerry A. Nick, M.D.; Travis S. Walker; G. Scott Worthen, M.D.; and Quinn Parks, Ph.D.

Licensing Status

This technology is available for licensing.



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CYSTATIN C: AN EXTRACELLULAR ANTAGONIST OF THE TGF- β RECEPTOR. POTENTIAL THERAPIES FOR CANCER AND FIBROTIC DISEASES

NJH ID: #04-05

Summary

Aberrant TGF- β signaling is often associated with tumor malignancies in humans. Scientists at the National Jewish Health have discovered that cystatin C, an extracellular protein, acts as a TGF- β receptor antagonist and is capable of inhibiting TGF- β signaling. Therefore, cystatin C and molecules derived from it can be a source of drug development for the treatment of some cancers or diseases regulated by TGF- β .

Potential Applications

Method to regulate or prevent tumor growth and metastasis
Therapies for proliferative and fibrotic diseases regulated by TGF- β

Advantages of Invention

No direct TGF- β receptor antagonist currently exists.

State of Development

- Our scientists have shown the following in vitro:
- cystatin C is downregulated in human tumors
- Overexpression of cystatin C in highly malignant human HT1080 fibrosarcoma cells inhibits their invasion through matrices and the expression of TGF- β -responsive genes
- TGF- β treatment of 3T3-L1 fibroblasts stimulates their invasion through matrices
- Overexpression of cystatin C in these TGF- β -treated cells inhibits this invasion process
- Cross-linking assays show that recombinant cystatin C dose-dependently inhibits the binding of TGF- β to its cell surface receptor
- Other assays show that cystatin C physically interacts with the TGF- β receptor but not with TGF- β

In vivo, our scientists have found that cystatin C (and d14-CystC, a mutant of cystatin C) inhibits TGF- β signaling and breast tumor growth in mice.

Patent

U.S. Patent #7,282,477. An additional patent application pending. International Patent Publication #WO2005/037221.

Publications

- Sokol and Schiemann (2004) Molecular Cancer Research, 2:183-195.
- Sokol et al. (2005) Breast Cancer Research 7:R844-53.
- Tian & Schiemann, Transl Oncol.2009 August 18; 2(3): 174–183.

Inventor

William P. Schiemann, Ph.D.

Licensing Status

This technology is available for licensing.



MODULATING THE TRANSPORT OF THIOL-CONTAINING MOLECULES FOR THE TREATMENT OF LUNG DISEASE AND CANCER

NJH ID: #02-16

Summary

National Jewish scientists have identified families of compounds that can increase the transport of thiol-containing molecules, like glutathione, from the cell. Glutathione is a critical thiol used by a large number of repair and detoxification pathways, particularly in the lung. Cystic fibrosis and a number of inflammatory lung diseases share a diminished level of glutathione in the epithelial lining fluid and excessive lung inflammatory responses. The compounds identified increase endogenous glutathione in the epithelial lining fluid and therefore could decrease oxidative damage in these diseases. Increasing glutathione efflux is also beneficial in sensitizing cancer cells, which are characterized by increased intracellular levels of glutathione and increased levels of multidrug resistance-associated proteins (MRPs) that transport glutathione, to anti-cancer agents that cause oxidative damage. These discoveries form the basis of a novel drug discovery platform that modulates oxidative stress in human disease.

Potential Applications

- Lung diseases, such as cystic fibrosis, chronic beryllium disease, sarcoidosis, idiopathic pulmonary fibrosis, acute respiratory distress syndrome, chronic obstructive lung diseases, idiopathic interstitial pneumonia, and diffuse fibrosing alveolitis.
- Adjuvant therapeutic in radiation or chemotherapy treatment for cancer

Advantages of Invention

- Many of the compounds are well known and characterized, including one that is currently approved and marketed for unrelated indications
- Compartment and tissue specific secretion of thiol-containing molecules
- An improvement over treatment with exogenous glutathione, which has a short half-life, poor bioavailability, and a lack of stability

State of Development

In mice, treatment with these compounds increased the levels of glutathione in the extracellular compartment and the lung epithelial lining fluid (ELF). Significant MRP-specific efflux of glutathione has also been demonstrated in cancer cell lines with a concomitant potentiation of cisplatin cytotoxicity.

Further R&D Required - Will use the Colorado “proof of concept” grant to test two identified lead compounds in an acute lung inflammatory mouse model

Patent – Issued U.S Patent # 7,498,047

Published U.S. Patent Application # 20060135585; International Publication #WO2004/042020; other U.S. and international patents pending.

Publications

- Day BJ et al. *Infect Immun*. 2004 Apr; 72(4):2045-51. PMID: 15039325.
- Day BJ et al. *Am J Physiol Lung Cell Mol Physiol*. 2001 Jul; 281(1):L31-8. PMID: 11404242.
- Kachadourian et al. *Int J Oncol*. 2007 Jul; 31(1):161-8. PMID: 17549417.
- Kachadourian et al. *Biochem Pharmacol*. 2007 Dec 15; 74(12):1677-85. Epub 2007 May 21. PMID: 17585883.
- Kachadourian et al. *Free Rad Bio & Med* 2006; 41:65-76. PMID: 16781454.

Inventors - Brian Day, Ph.D., Leonard Velsor, Ph.D. and Remy Kachadourian, Ph.D.

Licensing Status - This technology is available for licensing.



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LIPOSOMAL CLODRONATE AS A THERAPY FOR AUTOIMMUNE HEMOLYTIC ANEMIA

NJH ID: #02-07

Summary

This invention is using liposomal bisphosphonate as a therapy for autoimmune hemolytic anemia.

Potential Applications

- Therapy for autoimmune hemolytic anemia
- The therapy is applicable to both humans and companion animals

Advantages of Invention

- The method is less invasive than surgery (splenectomy)
- Decrease use of steroids
- Decrease side effects

State of Development

- The efficacy of this therapy has been demonstrated by some strong in vivo data obtained in mice.
- Using a mouse model in which animals were given anti red blood cell antibodies, treatment with liposomal clodronate substantially decreased red blood cell destruction.
- In addition, this effect was detected within hours and lasted at least a week.
- This therapy has been tested in dogs and results show high efficacy and no toxicity.

Further R&D Required

Additional testing in dogs.

Patent

Issued U.S. Patent # 7,090,865.

Publications

- Jordan et al. (2003) Blood: 101(2): 594-601.
- Mathes et al. (2006) Exp Hematology 34:1393-1402.

Inventors

Mike Jordan, M.D., Philippa Marrack, Ph.D., and John Kappler, Ph.D.

Licensing Status

This technology is available for licensing.



HIGH-THROUGHPUT CELL-BASED ASSAY FOR THE IDENTIFICATION OF DRUGS TARGETING THE NF- κ B SIGNALING PATHWAY

NJH ID: #02-05

Summary

Researchers at National Jewish Health have developed a microscopy-based visual assay to measure the antigen-receptor activation of an intermediate molecule located upstream of NF- κ B

Potential Applications

Identification of compounds as potential agents against inflammatory diseases, immune diseases and cancer

Advantages of Invention

- The assay targets Bcl10, a specific intermediate protein of the NF- κ B pathway, and it is compatible with epifluorescence/confocal microscopy

State of Development

Using cell lines developed in-house, National Jewish scientists have demonstrated that T cell receptor activation of NF- κ B involves the dynamic relocalization of the signaling intermediate Bcl10. This protein movement can be visualized by confocal or epifluorescence microscopy using a fluorescent marker (such as GFP) or antibodies.

Publication

Proc Natl Acad Sci 2004 Jan 27;101(4):1004-9.

Patent

Issued US Patent # 7,169,570

Inventors

Brian Schaefer, Ph.D., Philippa Marrack, Ph.D. and John Kappler, Ph.D.

Licensing Status

This technology is available for licensing.



TALL-1 AND ITS RECEPTOR BCMA: MOLECULAR TARGETS FOR THE DEVELOPMENT OF THERAPIES AGAINST INFLAMMATORY DISEASES

Tech ID: 02-01

Summary - Researchers at National Jewish Health have discovered that TALL-1, a member of the tumor necrosis factor (TNF), plays an important role in the modulation of immune responses by costimulating B lymphocyte proliferation. TALL-1 has been crystallized and its 3D structure resolved. In addition, the investigators have isolated a receptor at the surface of B lymphocytes, B cell maturation protein (BCMA), that specifically binds to TALL-1. Various TALL-1 induced genes have also been identified. Therefore, BCMA, the 3D structure of TALL-1 and TALL-1-induced genes can constitute several target routes for the development of treatments against inflammatory diseases.

Potential Applications - Therapy for inflammatory and immune-related diseases.

Advantages of Invention - Novel extracellular targets

State of Development - National Jewish Health scientists have demonstrated the following:

- TALL-1 is expressed specifically in monocytes and macrophages
- TALL-1 is down regulated by mytogens
- BCMA specifically binds to TALL-1 and activates NF- κ B through a TRAF5/TRAF-6 pathway
- The 3D structure of the TALL-1 monomer by crystallography
- 60 TALL-1 monomers can form a virus like structure in physiological conditions
- The TALL-1 region critical for the formation of this virus-like structure has been identified
- Deletion of such region disrupts the virus like assembly but does not affect the binding to BCMA and the NF-kappaB activation
- Several genes have been identified and shown to be induced by TALL-1 and NF-kappaB dependent

Further R&D Required - in vivo studies and ongoing work is assessing the potential to utilize the region of TALL-1 critical in the formation of virus like structure to enhance the potency of other TNF-family molecules.

Licensing Potential - Available for licensing.

Patent Status - U.S. Patents #6,475,987, #7,825,089 and #7,994,115, other U.S. and foreign patents pending covering TALL-1 and its 3D structure, BCMA and homologues, and methods of use. Published U.S. Patent Application #20070015695 and published International Patent Application #WO2003/35846.

Publications

- Shu et al. (1999) *J. Leukoc. Biol.* 65(5): 680-683
- Shu and Johnson (2000) *Proc. Natl. Acad. Sci.* 97(16): 9156-9161
- Liu et al. (2002) *Cell.* 108: 383-394
- Xu et al. (2002) *J. Leukoc. Biol.* 72(2): 410-416
- Liu et al. (2003) *Nature.* 423: 49-56

Inventors - Hong-Bing Shu, PhD, Gongyi Zhang, PhD

Licensing Status - This technology is available for licensing.



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C57BL/6 TRANSGENIC MICE STRAIN EXPRESSING GFP UBIQUITOUSLY

NJH ID: #01-05

Summary

Research scientists at National Jewish Health have developed an UBI-GFP/BL6 transgenic mouse (C57BL/6 strain) that expresses GFP in all cell types. This characteristic is particularly useful to identify and follow the identification and fate of cells transplanted into another mouse.

Potential Applications

- Organ and tissue transplantation
- Tissue development, regeneration and repair
- Immunology

Advantages of Invention

- The UBI-GFP/BL6 transgenic mice are healthy and can be bred to homozygosity.
- The UBI-GFP/BL6 transgenic mice were made directly in the C57BL/6 mouse strain.
- The UBI-GFP/BL6 transgenic mice show remarkably uniform expression of GFP for each cell type studied.
- No loss of GFP fluorescence due to metabolism or partitioning can be detected.
- The GFP gene of these UBI-GFP/BL6 transgenic mice is expressed regardless of tissue type and developmental stage.

State of Development

Scientists have demonstrated by FACS analysis and microscopy that GFP is expressed throughout the mice and that the level of GFP expression is uniform for each cell type studied.

Publication

Schaefer et al. 2001 Cellular Immunology 214:110.

Inventors

Brian Schaefer, Ph.D.; Philippa Marrack, Ph.D. and John Kappler, Ph.D.

Licensing Status

Available for licensing.

An additional license from GE Healthcare for the original GFP technology will also be necessary.



USE OF AEROSOLIZED MONOCLONAL ANTIBODIES AGAINST ALPHA BETA OR GAMMA DELTA T CELL RECEPTORS AS A THERAPY FOR AIRWAY HYPERRESPONSIVENESS

NJH ID: #01-01

Method proven in mice

Summary

Researchers at National Jewish Health have discovered that the targeted delivery of anti alpha/beta or gamma/delta T cell monoclonal antibodies can be used as a means to manipulate T cell-dependent regulation of airway reactivity. They have demonstrated that the use of such antibodies can significantly decrease airway hyperreactivity (AHR) in a mouse model of asthma. Therefore, the use of monoclonal antibodies anti-alpha beta or gamma delta T cells could constitute a treatment for asthma and other allergic diseases of the airways.

Potential Applications

Therapy for asthma and chronic obstructive pulmonary disease

Advantages of Invention

- Monoclonal antibodies are specific and therefore various subsets of T cell population can be targeted.
- Low doses of antibody are required.
- The therapeutic effects of such techniques are rapid.
- The delivery of these antibodies is confined to the airways and does not affect the peripheral immune system.

State of Development

National Jewish scientists have demonstrated in a mouse model of asthma that targeted delivery of monoclonal antibodies anti-alpha beta or gamma delta T cells alleviate AHR. In addition, the same decrease in AHR was demonstrated in mice genetically-deficient in cells targeted by these antibodies. They have also shown that the cellular effects of these antibodies are localized exclusively to the airways and do not spread systemically.

Experiments in primates found that treatment with anti-human CD3 delivered directly to the lung was well tolerated and produced a 20-fold decrease in sensitivity to methacholine (a measure of AHR) in hypersensitive allergic animals.

Further R&D Required

Using the state grant to extend testing from mice to a nonhuman primate animal model.

Patent

Published U.S. Patent Application # 20020172677.

Publications

- Lahn et al. *Int Arch Allergy Immunol.* 2004;134(1):49-55;
- Lahn et al. *Proc. Natl. Acad. Sci. USA*, Vol. 99, Issue 13, 8850-8855, June 25, 2002

Inventors

Willi Born, Ph.D., Erwin W. Gelfand, M.D., Michael Lahn, M.D. and Arihiko Kanehiro, M.D.

Licensing Status

This technology is available for licensing.



CALCITONIN GENE-RELATED PEPTIDE FOR THE REDUCTION OF ALLERGEN-INDUCED AIRWAY HYPERRESPONSIVENESS

NJH ID: #00-14

Summary

Calcitonin gene-related peptide (CGRP) is a sensory neuropeptide which expression is reduced after allergen challenge in sensitized mice. The same mice develop eosinophilic airway inflammation and airway hyperresponsiveness (AHR). Scientists at National Jewish Health have shown that administration of CGRP to sensitized and challenged mice resulted in the normalization of AHR.

Potential Applications

Treatment of AHR

State of Development

Administration of CGRP to sensitized and challenged mice resulted in the normalization of AHR. This potential therapy for AHR was tested in phase II of clinical trials however the trial was never completed.

Publications

- Dakhama A et al. *Respir Physiol Neurobiol*. 2008 Jan 1;160(1):28-36. Epub 2007 Aug 10.
- Dakhama A et al. *Am J Respir Crit Care Med*. 2002 Apr 15;165(8):1137-44.

Patent Status

Issued US patent #6,743,429 and International Patent Application publication #WO/2001/068118: pending in Canada and Europe, and issued in Australia (#2001249207).

The IP is owned by the National Jewish Health and the Universite de Sherbrooke.

Inventors

Erwin Gelfand, MD, Azzedine Dakhama, PhD (National Jewish Health) and Alain Cadieux, PhD (Universite de Sherbrooke)

Licensing Status

Available for licensing.



CDK6 AS A MARKER FOR BREAST CANCER

NJH ID: #00-11

Summary

Many cell cycle regulatory molecules have been shown to be present in higher amounts in tumor cells. In contrast, researchers at National Jewish Health discovered that the important cell cycle kinase, cdk6, plays an important role in tumor cell growth and was absent or present in decreased amount in all breast tumor-derived cell lines and human breast tumor samples examined. Therefore, cdk6 may be useful as a marker of tumor cell growth especially in patients with breast cancer.

Potential Applications

- Diagnostic assay for breast cancer
- Diagnostic assays for evaluating the efficacy of anti-cancer treatments and for determining the stage of tumor malignancy
- Method to regulate tumor cell growth

Advantages of Invention

New marker for breast cancer and possibly other cancers

State of Development

In vitro:

- No cdk6 or considerably lower levels of cdk6 were detected in breast tumor-derived cell lines compare to healthy breast cells.
- 3T3 cells overexpressing cdk6 exhibited a much reduced growth rate compare to normal 3T3 cell lines.

In vivo:

- Histologic studies using tissue samples from breast cancer patients show a decrease in cdk6 expression.

Further R&D Required

Demonstrating reliability of cdk6 as a predictor of *in vivo* tumor cell growth.

Patent

Issued U.S. Patent # 7,160,681.

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Licensing Status - This technology is available for licensing.

