Technology Portfolio Listing

Life Sciences

Biomarkers and Diagnostics

Method for Detecting Invasive Microvesicles Derived from Tumor Cells

Dr. Crislyn D'Souza-Schorey — ND # 10-006

A number of disease states, such as ovarian and other cancers, do not have reliable or accurate diagnostic tests. Biologic elements such as microvesicles associated with diseased cells can provide an early indication of the condition. Microvesicles are small, membrane-enclosed structures and are believed to facilitate various processes, including tumor invasion and metastasis. Isolation, identification and analysis of populations of microvesicles can serve to detect and predict disease.

High Performance Near Infrared Photothermal Dyes

Dr. Bradley Smith — ND # 13-057

The identified dye molecules absorb light around the 800nm wavelength and outperform other photothermal dyes. The dyes generate the same amount of heat as gold nanoparticles while maintaining excellent chemical stability. These dyes are superior candidates for photothermal imaging, photothermal therapy, tissue welding, or drug delivery applications where heat generation due to photothermal absorption produces the desired effect.

Cathepsin E as a Marker of Colon Cancer

Dr. Rudolph Navari — ND # 311

The identification of molecular markers and proteomic patterns in the inception and progression of colon cancer is a major goal in the management of this disease. Elevated levels of cathepsin E are detectable in urine and a diagnostic/screening method for detecting colorectal is disclosed. A method for transcriptionally profiling an patient to monitor the progression of colorectal disease is provided.

Exosomes and Diagnostic Biomarkers

Dr. Jeffery Schorey — ND # 10-037

The invention provides methods for the detection of *M. tuberculosis* proteins in or on exosomes derived from infected individuals. The methods can use a proteomic approach including mass spectroscopy, data mining and multiplex reaction monitoring to quickly examine a large amount of *M. tuberculosis* proteins to determine the best biomarkers for use in diagnostic tests to identify active TB patients.

Expressive Robots for Improving Medical Education

Dr. Laurel Riek — ND # 13-003

Human Patient Simulator (HPS) can exhibit highly realistic facial expressions and provides high fidelity, realistic, repeatable learning experiences to clinicians in training. New techniques employed in this HPS include the use constrained local model facial feature tracking to provide more accurate motion. Additionally, the invention utilizes "patient masks", which are models of different patient physiologies (e.g., stroke, dystonia, cerebral palsy) and affective states (e.g., pain, drowsiness, disorientation) that can be computationally applied by an operator controlling the HPS system. By providing simulations on lifelike mannequins, clinicians can move their learning curve away from the patient and avoid potentialy life threatening and costly mistakes. In the United States, medical errors that harm patients cost an estimated $17.1 billion dollars per year, and kill as many as 98,000 people per year.

Therapeutic Design, Dev

A New Class of Quinazolinone Antibiotics

Dr. Mayland Chang ND # 13-023

Staphylococcus aureus is responsible for a number of human diseases, including skin and soft tissue infections. Annually, 292,000 hospitalizations in the US are due to *S. aureus* infections, of which 126,000 are related to methicillin-resistant *Staphylococcus aureus* (MRSA), resulting in 19,000 deaths. A novel structural class of Quinazolinone Antibiotics has been discovered. The lead compound in this class shows high *in vitro* potency against Gram-positive bacteria comparable to those of linezolid and superior to vancomycin (both considered gold standards) and shows excellent *in vivo* activity in mouse models of MRSA infection.

Matrix Metalloproteinases in Wound Healing

Dr. Mayland Chang ND # 15-018

A complication of diabetes is the inability of wounds to heal in diabetic patients. Diabetic wounds are refractory to healing due to the involvement of activated matrix metalloproteinases (MMPs), which remodel the tissue resulting in apoptosis. There are no readily available methods that identify active unregulated MMPs. With the use of a novel inhibitor-tethered resin that binds exclusively to the active forms of MMPs, coupled with proteomics, we quantified MMP-8 and MMP-9 in a mouse model of diabetic wounds. Topical treatment with a selective MMP-9 inhibitor led to acceleration of wound healing, re-epithelialization, and significantly attenuated apoptosis. In contrast, selective pharmacological inhibition of MMP-8 delayed wound healing, decreased re-epithelialization, and exhibited high apoptosis. The MMP-9 activity makes the wounds refractory to healing, whereas that of MMP-8 is beneficial. The treatment of diabetic wounds with a selective MMP-9 inhibitor holds great promise in providing heretofore-unavailable opportunities for intervention of this disease.

Inhibitors of Matrix Metalloproteinases

Dr. Mijoon Lee ND # 326

Specific interactions of cells within the extracellular matrix are critical for the normal function of organisms. The alterations are carried out in various cellular processes such as organ development, ovulation, fetus implantation in the uterus, embryogenesis, would healing and angiogenesis. Inhibition of the MMPs can be useful in the treatment of various diseases such as cancer, neurological conditions, inflammations, and autoimmune diseases.

Antibiotics of a Novel Class-I and Class-II

Dr. Shahriar Mobashery ND # 07-038 & 07-039

Infections caused by hard-to-treat methicillin-resistant Staphylococcus aureus (MRSA) are a serious global public-health concern, as MRSA has become broadly resistant to many classes of antibiotics. Researcher at the University of Notre Dame discovered a new class of non-β-lactam antibiotics, the oxadiazoles, which inhibit penicillin-binding protein 2a (PBP2a) of MRSA. The oxadiazoles show bactericidal activity against vancomycin and linezolid-resistant MRSA and other Gram-positive bacterial strains, in-vivo efficacy in a mouse model of infection, and have 100% oral bioavailability.

MMP Inhibitors that Cross the Blood-brain Barrier

Dr. Mayland Chang ND # 15-023

Matrix metalloproteinase play and important role in the pathology of many neurological diseases. Disclosed as part of this invention are novel small molecule therapeutic candidates which are capable of crossing the blood-brain barrier. These compounds may be effective treatments for chronic wounds, certain forms of cancer, traumatic brain injury, and neurological diseases.

Gelatinase Inhibitors and Prodrugs

Dr. Mayland Chang ND # 09-022

Compounds, compositions, and methods for the treatment of diseases, disorders, or conditions that are modulated by matrix metalloproteinase (MMPs) can be useful in the treatment of stroke and neurological disorders . Providing a prodrug compound that metabolizes to an active MMP inhibitor in vivo. MMP inhibition can be selective, thus non-mutagenic prodrug compounds and formulas can be developed.

Treatment for Diabetic Wounds

Dr. Shahriar Mobashery ND # 12-006

Matrix metalloproteinase (MMPs) is responsible for the turnover and degradation of the extracellular matrix, including collagen. We have evidence that certain selective MMP inhibitors are effective in the treatment of chronic wounds. We have evaluated three such inhibitors in a mouse model of diabetic wounds and have shown that the compounds are efficacious in speeding the healing process.

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elopment, and Discovery

Non-beta Lactam Antibiotics

Dr. Mayland Chang ND # 15-017

The newly discovered oxadiazole class of antibiotics impairs cell-wall biosynthesis and exhibits activities against the Gram-positive bacterium *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant and linezolid-resistant *S. aureus.* They are efficacious in a mouse model of MRSA infection, exhibiting a long half-life, a high volume of distribution, and low clearance. This class of antibiotics hold great promise in recourse against infections by MRSA.

A Genetic Engineering Method for the Production of Peptide Therapeutics

Dr. Shaun Lee ND # 14-046

Novel peptide therapeutics which specifically target to and kill certain types of cancer cells are provided. Also an overall method for the synthesis of small, bioactive peptide therapeutics is developed using a primer-based gene synthesis approach coupled with *E. Coli*-based heterologous protein expression and purification. The genetic engineering method could decrease the cost of producing the novel peptide therapeutics as well as provide a method for building a peptide therapeutic library for further screening.

Inhibition of EGFR as a Strategy to Eliminate ECM-detached, Metastatic Breast Cancer Cells

Dr. Zachary T. Schafer ND # 15-012

The metastasis of cancer cells from the site of the primary tumor to distant sites in the body represents the most deadly manifestation of cancer. Notre Dame researchers have discovered that ECM-detached ErbB2 expressing cells may be uniquely susceptible to therapeutics approaches aimed at blocking EGFR activity. Thus a method for specific elimination of ECM-detached cancer cells is developed by applying the therapeutic approaches aimed at blocking EGFR activity.

ER PI3P function as a Target of Pathogenic Secretion

Dr. Kasturi Haldar ND # 12-010

PI3P is a signaling lipid usually found in the cytoplasm of cells. PI(3)P is present within a cellular organelle called the ednoplasmic reticulum which regulates protein secretion from the cell. In the case of the malaria parasite, PI3P regulates secretion of hundreds of pathogenic proteins and thus may be the target to block infection and disease.

Non-Aqueous Electrophoretic Separation System for Bioanalysis and Pharmaceutical Screening

Dr. Paul W. Bohn ND # 13-018

A diagnostic system capable of in-vivo analysis of biomolecular samples. The microfluidic platform utilizes label-free, non-aqueous separation solvent enabling the detection of biomarkers. This device could be used in medical diagnostic application for real-time monitoring or in a pharmaceutical target screening process.

Serial Tissue ImmunohistoChemistry-Chip (STITCH-CHIP): High and Deep Throughput Characterization of Cancer Tumors and the 3D Microenvironment

Dr. Siyuan Zhang ND # 14-051

The disclosed invention aims to significantly reduce the amount of time taken to clear a tissue sample, and furthermore, enable the application of multiple, sequential washes and fluorophore labels *without* moving the sample, enabling each fluorescently labeled channel to be superimposed in a comprehensive 3D image of the TME. Our device, the highly-innovative STITCH-Chip combines cutting-edge tissue clearing, whole-mount imaging, developed in the modified CLARITY protocol with a microfluidic network architecture to automate the sequence of clearing, washings, antibody perfusion, and imaging steps. By bridging expertise from cancer biology and bioengineering, our goal is to develop a clinically translatable device for fast and high-thought multiplex staining of biomarkers in the whole tissue biopsy

Therapeutics Cont.

Functionalized Liposome Purification via Liposome Extruder Purification

Dr. Basar Bilgicer ND # 13-030

Liposome Extruder Purification (LEP) allows for the rapid purification of diverse liposome formulations using the same extrusion apparatus employed during liposome formation. The LEP process provides a means for purifying functionalized liposomes from non-conjugated drug or protein contaminants with >93% liposome recovery and >93% contaminant removal in a single step. Depending upon the desired liposomal properties, different preparation techniques can be used that include: extrusion, sonication, reversed phase evaporation, and

Antibody Purification Via Affinity Chromatography that Utilizes the Nucleotide Binding Site

Dr. Basar Bilgicer ND # 11-025

The metastasis of cancer cells from the site of the primary tumor to distant sites in the body represents the most deadly manifestation of cancer. Notre Dame researchers have discovered that ECM-detached ErbB2 expressing cells may be uniquely susceptible to therapeutics approaches aimed at blocking EGFR activity. Thus a method for specific elimination of ECM-detached cancer cells is developed by applying the therapeutic approaches aimed at blocking EGFR activity.

Disease Driven Engineering of Multifunctional Nanoparticles and Method of Use

Dr. Basar Bilgicer ND # 12-018

Engineered nanoparticles functionalized to target malignant cells such as those comprising multiple myeloma, lymphomas, and leukemia can be used in numerous cancer therapeutics. These nanoparticles can also be used to increase the effectiveness of current market therapeutics against cancers which exhibit drug resistance. The nanoparticles contain a cell penetrating peptide and a target specific peptide to facilitate drug entry. The nanoparticle target diseased cells to reduce the toxic effect of a drug on

Antibody Purification Via Affinity Chromatography that Utilizes the Nucleotide Binding Site

Dr. Basar Bilgicer ND # 11-025

Novel affinity chromatography method that utilizes the Nucleotide Binding Site (NBS) as a target for selectively purifying antibodies from complex mixtures. Antibodies can be selectively captured and retained on a NBS IBA column and can successfully eluted by applying a mild NaCl gradient. The NBS IBA column consistently yields >95% antibody recovery with >98% purity, even when the antibody was purified from complex mixtures such as conditioned cell culture supernatant, hybridoma media, and mouse ascites fluid..

Liposomal Drug Delivery of Proteasome Inhibitors for the Treatment of Cancers

Dr. Zihni Bilgicer ND # 13-022

Proteasomes are proteins responsible for the degradation of misfolded proteins and play a role in some cell signaling pathways. Bortezomib and carfilzomib are FDA approved first and second generation proteasome inhibitors for the treatment of multiple myeloma. Notre Dame researchers have incorporated these therapeutics, into stealth, long circulating liposomes for improved drug delivery and enhanced tumor accumulation. The drug loaded nanoparticles are internalized by and cytotoxic to multiple myeloma cell lines. Xenograph models show that the nanoparticles result in significantly reduced systemic toxicity with simultaneous improvements tumor cell uptake and growth inhibition when compared to the systemic free drug.

RESEARCH TOOLS

Mouse Models

Total fibrinogen deficiency useful for study of hemostasis and lung disorders

FXII-deficient useful for coagulation disorders, heart disease, coronary artery disease, etc.

Malaria models

Lobund-Wistar useful for prostate cancer studies

PA(iii) Cells Prostate adenocarcinoma (PA) cells

Zebra Fish Models

BlaR1 Plasmid - Staphylococcus aureus, useful for antibiotic sensing applications.

PiggyBac Transposon - "Cut and Paste" vector for insertion of genetic material to a host organism. Distribution through our commercial partner

IF YOU ARE INTERESTED IN LICENSING AND COMMERCIAL DEVELOPMENT OF NOTRE DAME TECHONLOGY . . .

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