The following document contains non-confidential summaries of innovations from Purdue University. These innovations are divided into several categories and are in the order indicated by the proceeding table of contents. Please reach out to Clayton Houck (Licensing Associate – Life Sciences ; cjhouck@prf.org) for additional information.

Cell and Gene Therapy (page 48)

▪ Engineering NK Cells to Treat Cancers Driven by Adenosine Immunosuppression
2019-MATO-68613 led by Matosevic, Sandro (note: *in vivo* data)
▪ Targeted Therapeutic for Metastatic Prostate Cancer
2020-FIGU-68875 led by Figueiredo, Marxa L (note: *in vivo* data)
▪ Off-the-shelf Chimeric Antigen Receptor (CAR) NK Cell Production and Application in Cancer Immunotherapy
2022-BAO-69890 led by Bao, Xiaoping
▪ A Chemically Modified MicroRNA as an Anticancer Agent
2023-KASI-70078 led by Kasinski, Andrea L (note: *in vivo* data ; inventor is starting company)

Neurobiology Innovations (page 57)

▪ Treatment of Lowe Syndrome with Repurposed Drugs
2017-AGUI-67722 led by Aguilar, Ruben C
▪ Small Molecule Proteasome Stimulators of Proteasome for Protein Degradation to Treat Alzheimer's and Parkinson's Diseases
2020-TRAD-68744 led by Trader, Darci Jones
▪ Kinase Inhibitors for Treating Cancer, Inflammation, and Neurological Diseases
2022-SINT-69859 led by Sintim, Herman O
▪ Treatment of Alzheimer's and Parkinson's through Aminoindole Carboxamide Derivatives
2023-FORT-69967 led by Fortin, Jessica
▪ Small Molecules for Reduction of Fibril Formation in Prone-to-aggregate Protein
2023-FORT-69996 led by Fortin, Jessica
▪ Therapeutic Strategy for Treatment of Lowe Syndrome and Dent-2 disease
2023-AGUI-69998 led by Aguilar, Ruben C
▪ Novel Small Molecule Inhibitors for Alpha-Synuclein and Tau Isoform 2N4R for the Treatment of Alzheimer's Disease
2023-FORT-70004 led by Fortin, Jessica
▪ Development of AMPylation Activators and Inhibitors for the Treatment of Neurodegenerative Diseases and Discovery of Novel Inhibitor of HYPE-directed AMPylation
2023-MATT-70064 led by Mattoo, Seema
▪ Cyclic Peptide Stimulators of the Proteasome for the treatment of Alzheimer's and Parkinson's
2023-PARK-70287 led by Parkinson, Elizabeth Ivy

Infectious Disease Therapeutic Innovations (page 76)

▪ Antibacterial Agents Against Methicillin- and Vancomycin-Resistant Bacteria
2018-SINT-68199 led by Sintim, Herman O
▪ Novel Inhalation Formulation of Antimicrobials
2018-ZHOU-68233 led by Zhou, Qi
▪ Nanoparticles for Intracorporeal Sepsis Treatment
2019-YEO-68355 led by Yeo, Yoon
▪ Antimicrobial Peptides Targeting Intracellular Bacteria
2019-CHMI-68405 led by Chmielewski, Jean Anne (note: *in vivo* data)
▪ Selective Antibiotics for Highly Resistant Enterococcus
2019-FLAH-68419 led by Flaherty, Daniel P
▪ Bactericidal and Bacteriostatic Agents against Drug-Resistant Bacteria
2019-SINT-68535 led by Sintim, Herman O (note: *in vivo* data)
▪ Carbonic Anhydrase Inhibitors as Treatment for Gonorrhea
2020-FLAH-68832 led by Flaherty, Daniel P
▪ Composites with Ivacaftor and Colistin for Cystic Fibrosis and Bacterial Lung Infection Treatment
2020-ZHOU-68954 led by Zhou, Qi

▪ Novel inhalation formulations of polymyxins
2020-ZHOU-68990 led by Zhou, Qi
▪ Low-toxicity Formulations of Polymyxins for Inhaled Treatment of Gram-negative Bacterial Lung Infections
2021-ZHOU-69256 led by Zhou, Qi
▪ Sustained Release Silver Nanoparticulate Compositions for Treating Microbial Infections
2023-RISS-70028 led by Risselada, Marije
▪ Novel Potent and Selective PRMT Inhibitors for Developing Therapeutic Agents
2023-HUAN-70160 led by Huang, Rong
▪ Novel Covalent Protein Inhibitors for Treating Malaria
2023-FLAH-70246 led by Flaherty, Daniel P

Drug Delivery Innovations (page 103)
▪ Carrier-Free Nanoparticle Formulation with Good Circulation Stability
2016-YEO-67581 led by Yeo, Yoon (note: *in vivo* data)
▪ Improved Nanoparticle Based Targeted Drug Delivery to Cancerous Cells and Tissues
2017-YEO-67767 led by Yeo, Yoon
▪ Radiation-Controlled Release of Drugs for Chemo-Radiotherapy
2018-WON-68028 led by Won, You-Yeon
▪ Liposomal Carriers with High Drug Loading Capacity
2019-YEO-68485 led by Yeo, Yoon
▪ Nanoparticle Chemotherapeutic Delivery System that Aids in Development of Antitumor Immunity
2020-YEO-68760 led by Yeo, Yoon
▪ Soft, Flexible Non-Cationic Nanocapsules for Systemic Delivery of Nucleic Acids
2020-YEO-68868 led by Yeo, Yoon (note: *in vivo* data)
▪ Cancer Therapy Using an Immunoactive Nanocarrier of Immunogenic Cell Death Inducers
2022-YEO-69546 led by Yeo, Yoon (note: *in vivo* data)
▪ Novel Nanoparticles applied to Pancreatic Adenocarcinoma Treatment
2023-HAN-70164 led by Han, Bumsoo
▪ Nanopuff: A New Class RNA Therapeutic Carrier
2023-YEO-70458 led by Yeo, Yoon

Excipient Innovations (page 122)
▪ Sustained Release Formulation of Griseofulvin for Treatment of Wet Macular Degeneration
2020-YEO-69132 led by Yeo, Yoon
▪ Sequence-Controlled Polymers for Sustained Release of Pharmaceutical Ingredients
2022-WON-69547 led by Won, You-Yeon
▪ Nanoparticle-based Opioid Abuse Deterrent Formulations
2022-YEO-69643 led by Yeo, Yoon
▪ Method for Excipient-free Lyophilization of Drugs for Respiratory Treatment
2023-WON-69925 led by Won, You-Yeon
▪ Innovative Polymeric Excipients for Enhancing Stability and Shelf-Life of Protein Therapeutics
2024-WON-70668 led by Won, You-Yeon

Diagnostic Innovations (page 133)
▪ Diagnostic Panel of Modified Proteins for Breast Cancer
2017-TAO-67681 led by Tao, Weiguo Andy
▪ Liquid Biopsy for Determining Breast Cancer Subtypes
2019-TAO-68555 led by Tao, Weiguo Andy
▪ Assessing In Vivo Efficacy of Drug Therapeutics by Monitoring Proteins from Extracellular Vesicles
2020-TAO-69103 led by Tao, Weiguo Andy

▪ Direct Isolation of Exosome and Other Extracellular Vesicle Particles for Chemotherapeutic Outcomes Assessment, Disease Diagnosis, and Monitoring Disease Progression
2022-TAO-69815 led by Tao, Weiguo Andy

Pharmaceutical Manufacturing Innovations (page 142)
▪ Completely Continuous Plug Flow Crystallization Process of Pharmaceutical Production
2016-KOSW-67539 led by Nagy, Zoltan Kalman
▪ Micro-scale Powder Process for Drug Particle Filled Capsules
2018-REKL-68230 led by Reklaitis, Gintaras "Rex" V
▪ Crystallization Method to Reduce Filtration Time of Agrochemical Products
2020-NAGY-69085 led by Nagy, Zoltan Kalman
▪ Mixed Solvent Micelle Formation Procedure
2020-WON-69093 led by Won, You-Yeon
▪ Polymer Salts for Improved Drug Delivery from Amorphous Solid Dispersions
2022-TAYL-69671 led by Taylor, Lynne S
▪ Precision 3D Printing Method for Customizable Pharmaceutical Mini-Tablets
2023-SUND-70094 led by Sundarkumar, Varun

Research Tool Innovations (page 154)
▪ Reagent for Measurement of Protein Phosphorylation by Gel Electrophoresis
2014-TAO-66895 led by Tao, Weiguo Andy
▪ Direct Contact Blood Brain Barrier Triculture
2015-KNIP-67191 led by Knipp, Gregory Thomas
▪ Reporter Molecule for 20S Proteasome Stimulators for Parkinson's and Aging
2017-TRAD-67888 led by Trader, Darci Jones
▪ Live Cell Conjugation Chemistry for Imaging, Sensing, Biomanufacturing, and Cell Therapy
2018-CHOP-68209 led by Chopra, Gaurav
▪ Tool to Identify Host Proteins Involved in Viral and Bacterial Pathogenesis
2019-TAO-68397 led by Tao, Weiguo Andy
▪ Selective Fluorescent Probe for the Immunoproteasome
2019-TRAD-68454 led by Trader, Darci Jones
▪ Reporter Molecule for Study of Alzheimer's Disease
2019-CHOP-68541 led by Chopra, Gaurav
▪ In vitro Model for Testing Efficacy and Neurotoxicity of Neurotherapeutic
2020-KNIP-68758 led by Knipp, Gregory Thomas
▪ Activity-Based Probes with Unnatural Amino Acids to Monitor the Proteasome in Living Cells
2020-TRAD-68937 led by Trader, Darci Jones
▪ Fluorescent Probes for Monitoring Serine Ubiquitination by Bacterial Enzymes
2020-DAS-69098 led by Das, Chittaranjan
▪ Peptide crystal formulation for room temperature storage of biopharmaceuticals and other proteins
2021-CHMI-69348 led by Chmielewski, Jean Anne
▪ pH-Activable Fluorescent Probes for Targeting Cell Organelles
2021-CHOP-69413 led by Chopra, Gaurav
▪ A Fluorescence-based Assay Benefitting PROTAC Drug Discovery and Development
2023-DAS-69989 led by Das, Chittaranjan

Software Research Tool Innovations (page 180)
▪ Patch-Surfer 2.0: A Protein-Ligand Modeling and Prediction Tool
2015-KIHA-67110 led by Kihara, Daisuke
▪ PatchSurfer: Software for Exploring Protein-Ligand Interactions
2015-KIHA-67111 led by Kihara, Daisuke

▪ IDP-LZerD, a Software that Models Disordered Protein Assembly
2021-KIHA-69433 led by Kihara, Daisuke
▪ LZerD, a Computational Method for Modeling Protein Pairwise Assembly
2021-KIHA-69434 led by Kihara, Daisuke
▪ Computational Method for Modeling Protein Assembly with More Than Two Protein Subunits
2021-KIHA-69437 led by Kihara, Daisuke
▪ Accurate Software-Assisted Laser Scanning Imaging and Optical Manipulation System for Biological and Pharmacological Samples
2024-ZHAN-70384 led by Zhang, Chi

MedTech Innovations (page 191)
▪ Surgical Tool for Minimally Invasive Lumbar Discectomy
2015-CAPP-67213 led by Cappelleri, David John
▪ Wearable Biometric to Predict and Prevent Preeclampsia and Hypertension
2018-GOER-68042 led by Goergen, Craig Jonathan
▪ Strain Gauge Integrated Magnetic Microactuator for Smart Self-Clearing Catheter
2019-LEE-68342 led by Lee, Hyowon
▪ Novel Robotic Cannula for Minimally Invasive Lumbar Discectomy Surgery
2020-CAPP-68748 led by Cappelleri, David John
▪ Bioresorbable Materials for Unobtrusive, Sustained Topical Delivery of Therapeutics
2020-LEE-68893 led by Lee, Chi Hwan
▪ Resorbable Surgical Mesh Impregnated with Calcium Peroxide
2020-RAHI-68984 led by Rahimi, Rahim
▪ Wearable Ozone Generating System for Treatment of Infected Dermal Wounds
2020-RAHI-69057 led by Rahimi, Rahim
▪ A Wireless Implantable Passive Intra-Abdominal Pressure Sensing Scheme via Ultrasonic Imaging of a Microfluidic Device
2021-RAHI-69409 led by Rahimi, Rahim
▪ Microneedle Patch for Wound Oxygenation and Biofilm Eradication
2021-RAHI-69535 led by Rahimi, Rahim
▪ Device for Ocular Drug Delivery
2022-LEE-69581 led by Lee, Chi Hwan
▪ Low-cost, Wireless Radiation Sensor
2022-RAHI-69718 led by Rahimi, Rahim
▪ Titanium Implants with Enhanced Cell Integration and Antimicrobial Properties
2022-RAHI-69768 led by Rahimi, Rahim
▪ Image Recognition Integrated Service (IRIS) Prosthetic Arm
2023-WEIB-69953 led by Weibel, Justin A
▪ Remote Sensing Platform to Monitor Urine Bags in a Medical Environment
2023-RAHI-70178 led by Rahimi, Rahim
▪ Design for a Portable, Low-Cost, Magnetic Microrobot Control and Imaging System for Medical Use on Humans and Large Animals
2024-CAPP-70412 led by Cappelleri, David John

MedTech Research Tool Innovations (page 221)
▪ Cellular Model of Parkinson's Disease
2016-ROCH-67263 led by Rochet, Jean-Christophe
▪ Method of Thin Flexible Electrode Insertion for Deep Brain Neural Recording and the Design of Electrode Insertion Device
2018-IRAZ-68150 led by Irazoqui, Pedro P.
▪ Ultrasensitive Biosensor

2019-ZUO-68465 led by Zuo, Fan
▪ High-performance Platinum Neurostimulation Electrode with 97% Reduction in Corrosion
2019-LEE-68525 led by Lee, Hyowon
▪ Artificial Retina Based on Photon-Assisted Electrochemical Doping
2022-MEI-69888 led by Mei, Jianguo
▪ Light Pipe Microscope for large-scale dynamic imaging
2023-CUI-69962 led by Cui, Meng
▪ Novel Patient-Specific Method to Predict Prostate Cancer Relapse after Radiation Therapy
2023-DIAZ-70044 led by Gomez Diaz, Hector
▪ Photonic-organic Electrochemical Transistor
2023-MEI-70196 led by Mei, Jianguo
▪ Formulation for Novel, Blood Catalyzed Conductive Polymer for use in Bioelectronics, Bioimaging, and Biosensors
2024-MEI-70435 led by Mei, Jianguo

The following section contains non-confidential summaries of small molecule innovations from Purdue University. These summaries are of the following innovations:

▪ Targeted Therapeutic Against Bladder Cancer
2014-AGUI-66886 led by Aguilar, Ruben C
▪ EGF-Targeted Bladder Cancer Therapeutic
2016-AGUI-67476 led by Aguilar, Ruben C
▪ Potent and Non-toxic Molecules for Castration-resistant Prostate Cancer
2019-CHOP-68534 led by Chopra, Gaurav (note: *in vivo* data)
▪ Potent Small Molecule PD-1/PD-L1 Interaction Inhibitors for Cancer Immunotherapy
2020-CHOP-68949 led by Chopra, Gaurav (note: *in vivo* data)
▪ Kinase Inhibitors Optimized for Lung, Pancreatic, and Colon Cancer Therapy
2020-SINT-69073 led by Sintim, Herman O (note: *in vivo* data)
▪ Cell-potent and Selective Inhibitors of Nicotinamide N-methyltransferase for Disease Treatment
2021-HUAN-69352 led by Huang, Rong
▪ Enhanced Cell-potent Inhibitors for NTMT1/2 for Treating Cancers
2022-HUAN-69636 led by Huang, Rong
▪ Dual Inhibitors of MNK1/2 and p706SK as Potent Anticancer Drugs for Solid Tumors
2022-SINT-69726 led by Sintim, Herman O
▪ Novel Small Molecule Inhibitor for the Treatment of Prostate Cancer
2022-DYKH-69819 led by Dykhuizen, Emily C
▪ Kinase Inhibitors for Treating Cancer, Inflammation, and Neurological Diseases
2022-SINT-69859 led by Sintim, Herman O (note: *in vivo* data)
▪ Novel RET Protein Tyrosine Kinase Inhibitors
2023-SINT-70021 led by Sintim, Herman O
▪ Combination of a Phosphatidyl Serine Blocker and STING Stimulant for Cancer Immunotherapy
2023-YEO-70023 led by Yeo, Yoon
▪ Novel Photosensitizers as a Chemotherapeutic Against Triple Negative Breast Cancer
2023-ISAA-70121 led by Isaac-Lam, Meden F
▪ STING Antagonists for Treating Inflammatory Diseases and Diseased States
2023-SINT-70181 led by Sintim, Herman O
▪ Novel Anticancer Covalent Inhibitors of SHP2 Tyrosine Phosphatase Inspired from Natural Products
2023-DAI-70254 led by Dai, Mingji
▪ Novel FLT3 Inhibitor for Multiple Myeloma
2024-SINT-70378 led by Sintim, Herman O
▪ Novel 2,3'cGAMP analogs as a STING antagonist
2024-SINT-70418 led by Sintim, Herman O
▪ Potent, Highly Selective Anticancer Dual Degrader of PTP1B and TC-PTP
2023-ZHAN-70087 led by Zhang, Zhong-Yin (note: *in vivo* data)
▪ Potent, Highly Specific TC-PTP Degrader for Treatment of Skin Cancer and Enhancement of CAR-T Therapy
2024-ZHAN-70394 led by Zhang, Zhong-Yin
▪ Potent, Highly Selective SHP2 Degrader as Novel Anticancer Agent
2024-ZHAN-70417 led by Zhang, Zhong-Yin (note: *in vivo* data)

TARGETED THERAPEUTIC AGAINST BLADDER CANCER

TRACK CODE:
2014-AGUI-66886

Bladder cancer is the fourth most common cancer among men and eleventh among women. Bladder cancer has a high rate of recurrence post-surgery. Despite its obvious high impact on public health, the available therapies are still of limited efficacy. Instillation of therapeutics in the lumen of the bladder assures access to the tumor without affecting normal cells, but dilution of the therapeutic agent by urine flow and its elimination by periodic emptying of the bladder, greatly reduces the treatment efficacy. The market for new technologies related to novel therapeutics to support the treatment of such cancers includes pharmaceutical companies and cancer research centers.

Purdue University researchers have developed a novel strategy using an epidermal growth factor (EGF) targeted toxin, which can be used for elimination of both superficial and invasive bladder tumors. This is a highly efficient, targeted strategy that reduces treatment time from hours (current therapies) to minutes. Further, this agent can be administered by a pharmaceutically acceptable delivery system in the lumen of the bladder for treatment. In addition to being easily used against bladder cancer, this strategy is also applicable to other EGF receptor-dependent cancers such as lung and skin cancer.

Advantages:
-High efficacy and fast action
-Targets superficial and invasive bladder tumors
-EGF targeting and internalization of the toxin

Potential Applications:
-Bladder cancer treatment
-Lung and Skin cancer treatment

International Journal of Cancer Research Article -
https://onlinelibrary.wiley.com/doi/abs/10.1002/ijc.32719
A Novel, Safe, Fast, Efficient Treatment for Her2-positive and Negative Bladder Cancer Utilizing an EGF-Anthrax Toxin Chimera. October 4, 2019.

INTELLECTUAL PROPERTY:

Application Date: December 16, 2016
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: June 16, 2015
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 16, 2014

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Aguilar, Ruben C (Project leader)

CATEGORIES:
Biotechnology

KEYWORDS:
Assays, Biotechnology, Bladder Cancer, Cancer, Cell Targeting, Drug Delivery, Melanoma, Pharmaceuticals

EGF-TARGETED BLADDER CANCER THERAPEUTIC

TRACK CODE:
2016-AGUI-67476

The American Cancer Society (ACS) annually issues estimates for new cancer diagnoses and cancer deaths. For 2016, ACS estimates for bladder cancer is 76,960 new diagnoses and 16,390 deaths. Bladder cancer is the fourth and eleventh most common cancer in men and women respectively. The average age at diagnosis is 73 and 90 percent of patients are over the age 55. It is estimated that the annual national cost of bladder cancer care will reach $5.25 billion in 2020. Approximately 70 percent of newly diagnosed patients suffer disease recurrence after surgical treatment and more than 20 percent develop invasive bladder cancer. There is a need to develop efficient therapeutic strategies against this pathology.

Researchers at Purdue University have developed a therapeutic strategy using a modified bacterial toxin to target the EGF receptor and destroy bladder cancer cells. This agent proved to be superior due to its specificity and high efficacy at eliminating cancer cells, taking only minutes for treatment with enhanced safety. In animal studies, there were no toxic side effects and it was very effective against treatment-resistant tumors in dogs.

Advantages:
-Non-surgical treatment option
-Treatment takes minutes vs. hours
-Promising results in animal studies

Potential Applications:
-Bladder cancer treatment

INTELLECTUAL PROPERTY:

Application Date: May 9, 2017
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,588,939
Issue Date: March 17, 2020

Application Date: January 17, 2020
Type: DIV-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: May 9, 2016
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Aguilar, Ruben C (Project leader)

Ratliff, Timothy L

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Bladder Cancer, Cancer, Cancer Therapy, Pharmaceuticals, Treatment Methods

POTENT AND NON-TOXIC MOLECULES FOR CASTRATION-RESISTANT PROSTATE CANCER

TRACK CODE:
2019-CHOP-68534

Researchers at Purdue University have developed potent synthetic small molecules with high potential as drugs against castration-resistant prostate cancer (CRPC) that are non-toxic in normal human cell lines. To address the heterogeneity of cellular pathways in cancer, the source of a cancer's ability to become resistant to therapy, the investigators designed these molecules using a machine learning approach that targets the protein network implicated in the disease state to guide compound selection and synthesis. The series of compounds developed inhibits proliferation of C4-2 androgen-insensitive human prostate adenocarcinoma cells with IC50 as low as 0.72 nM, and the compounds are much more potent than a control, the current steroidal CRPC drug, abiraterone (ABI). The most potent compound and other active leads were also more metabolically stable than ABI in a mouse liver microsome assay. Further, these compounds promise to combat metastasis; they slow migration of cells relative to untreated cells in both LNCaP and C4-2 cell lines.

Advantages:
-Non-toxic
-Potent
-Addresses drug resistance

Potential Applications:
-Disease Research
-Cancer Therapy

INTELLECTUAL PROPERTY:

Application Date: August 27, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: August 26, 2021
Type: NATL-Patent
Country of Filing: Japan
Patent Number: (None)
Issue Date: (None)

Application Date: August 25, 2021
Type: NATL-Patent
Country of Filing: India
Patent Number: (None)
Issue Date: (None)

Application Date: September 28, 2020
Type: NATL-Patent
Country of Filing: Europe

Patent Number: (None)
Issue Date: (None)

Application Date: February 28, 2020
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: February 28, 2020
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: February 28, 2020
Type: NATL-Patent
Country of Filing: China
Patent Number: (None)
Issue Date: (None)

Application Date: February 28, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Chopra, Gaurav (Project leader)

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Androgen, Cancer, Castration-resistant Prostate Cancer, drugs, Oncology, Pharmaceuticals, Prostate Cancer

POTENT SMALL MOLECULE PD-1/PD-L1 INTERACTION INHIBITORS FOR CANCER IMMUNOTHERAPY

TRACK CODE:
2020-CHOP-68949

Purdue University researchers have developed a potent small molecule for use in cancer immunotherapy which acts by inhibiting the Programmable Cell Death Protein 1/Programmable Death-Ligand 1 (PD-1/PD-L1) interaction. Cancer cells express PD-L1, a cell surface protein that binds to PD-1 on T-cells, debilitating anti-cancer immunity. Antibodies targeting the PD-1/PD-L1 interaction have proven to be a viable therapeutic strategy toward mitigating cancer growth but suffer from high production costs, limited administration techniques, and low therapeutic indices. To address these limitations, Purdue University researchers created a small molecule inhibitor of the PD-1/PD-L1 interaction that specifically target PD-1 dimerization. The researchers developed the new molecule through robust computational modeling of publicly available PD-1/PD-L1 inhibitory data. In homogenous time-resolved fluorescence binding assays the Purdue compound exhibited about 1.6 fold increased potency in inhibiting the PD-1/PD-L1 interaction compared to a positive control molecule known from the patent literature (IC50 = 339.9 nM and 521.5 nM, respectively). Further medicinal chemistry optimization promises to increase potency and yield an excellent preclinical candidate for use in small molecule immune checkpoint blockade therapy.

Advantages:
-Increased Potency to PD-1/PD-L1 Interaction
-Combined Scaffolds of BMS Compounds

Potential Applications:
-Immune Checkpoint Blockade
-Cancer Therapeutics

Related Publication:
Combined Molecular Graph Neural Network and Structural Docking Selects Potent Programmable Cell Death Protein 1/Programmable Death-Ligand 1 (PD-1/PD-L1) Small Molecule Inhibitors
Preprint available at chemrixiv.org
DOI: 10.26434/chemrxiv.12083907.v1

INTELLECTUAL PROPERTY:

Application Date: August 31, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)

Issue Date: (None)

Application Date: March 5, 2021
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: NATL-Patent
Country of Filing: China
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: NATL-Patent
Country of Filing: India
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: NATL-Patent
Country of Filing: Japan
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: NATL-Patent
Country of Filing: Mexico
Patent Number: (None)
Issue Date: (None)

Application Date: March 11, 2020
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Chopra, Gaurav (Project leader)
Fine, Jonathan
Jethava, Krupal P.
Wijewardhane, Prageeth

CATEGORIES:

Pharmaceuticals

KEYWORDS:

Bootstrapping, Cancer, Computer Aided Drug Design, HTRF, ICB, Immune Checkpoint Blockade, immunotherapy, PD-1, PD-1/PD-L1 Interaction, PD-L1, Pharmaceuticals, small molecules, Therapy

KINASE INHIBITORS OPTIMIZED FOR LUNG, PANCREATIC, AND COLON CANCER THERAPY

TRACK CODE:
2020-SINT-69073

Purdue University researchers have synthesized kinase inhibitors that display potent anti-proliferative effects when dosed into lung, pancreatic, and colon cancer cells. Overactive kinases are a primary driver of cancer cell proliferation. Accordingly, many chemotherapeutic regimens contain kinase inhibitors; however, current kinase targeting compounds are not effective in treating aggressive forms of lung, pancreatic, and colon cancers. Purdue University researchers have optimized previously identified kinase inhibitors to achieve a higher potency against many lung, pancreatic, and colon cancer cell lines. These compounds were tested against the NCI-60 cancer cell panel and have low sub micromolar GI50 values. For example, the GI50 against some colon cancers are as low as 5 nM. These compounds also have IC50 values of 25 nM against proliferation of the MiaPaCa-2 pancreatic cancer cell line. The potency of the compounds toward multiple aggressive cancer cell lines makes them promising cancer therapeutic candidates for future development.

Technology Validation: The compounds were tested against the NCI-60 cancer cell line panel and exhibit nanomolar GI50 values in some cell lines.

Advantages
-Inhibits Growth of Multiple Cancer Cell Lines
-Increased Potency versus Previously Identified Molecules

Applications
-Cancer Therapies
-Cancer Relapse
-Kinase Inhibitors

Related publications:
Targeting RET Solvent-Front Mutants with Alkynyl Nicotinamide-Based Inhibitors
https://doi.org/10.1158/1535-7163.MCT-22-0629

INTELLECTUAL PROPERTY:

Application Date: December 8, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2021
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2021
Type: NATL-Patent
Country of Filing: Europe

Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2021
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Sintim, Herman O (Project leader)
Dayal, Neetu
Hernandez, Delmis E.
Larocque, Elizabeth Anne

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Lung Cancer, Pharmaceuticals

CELL-POTENT AND SELECTIVE INHIBITORS OF NICOTINAMIDE N-METHYLTRANSFERASE FOR DISEASE TREATMENT

TRACK CODE:
2021-HUAN-69352

NCS: Researchers at Purdue University have synthesized a series of cell-potent and selective inhibitors of nicotinamide N-methyltransferase (NNMT) that can be used to treat cancer, metabolic and neurodegenerative diseases. NNMT plays an important role in regulating both epigenetics and metabolism by methylating nicotinamide. Elevated levels of NNMT have been associated with diseases like cancer, liver disease, diabetes, and obesity. The most potent compound (IC50 =3.4 nM) synthesized by the Purdue researchers had an IC50 value of 100 nanomolar for inhibiting N-methylated Nicotinamide in cells, over 1000-fold selectivity for NNMT compared to related methyltransferases. Moreover, cell-potent NNMT inhibitors exhibit a favorable pharmacokinetics profile.

Related Publications: Chen D, Li L, Diaz K, Iyamu ID, Yadav R, Noinaj N, Huang R. (2019) Novel propargyl-linked bisubstrate analogs as tight-binding Inhibitors for nicotinamide N-methyltransferase. Journal of Medicinal Chemistry. 62 (23), 10783-10797. PMID: 31724854; PMCID: PMC7296983. www.ncbi.nlm.nih.gov/pubmed/31724854

Iyamu ID, Vilseck JZ, Yadav R, Noinaj N, Huang R. (2022) Exploring unconventional SAM analogues to build cell-potent bisubstrate inhibitors for nicotinamide?N-methyltransferase. Angewandte Chemie International Edition.? https://doi.org/10.1002/anie.202114813

Advantages

- Selective

- Low concentration

Applications

-Metabolic disorders

-Cancers

-Neurodegenerative diseases

INTELLECTUAL PROPERTY:

Application Date: May 22, 2024
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: November 21, 2022

Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: November 22, 2021
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: (None)
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Huang, Rong (Project leader)
Iyamu, Iredia David

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Cell-potent Inhibitor, Nicotinamide N-methyltransferase, Pharmaceuticals, Selective

ENHANCED CELL-POTENT INHIBITORS FOR NTMT1/2 FOR TREATING CANCERS

TRACK CODE:
2022-HUAN-69636

NCS: Researchers at Purdue University have designed a series of new peptidomimetic inhibitors for protein alpha-N-terminal methyltransferases (NTMTs). NTMTs recognize a unique N-terminal of a protein and catalyze the addition of 1-3 methyl group(s) to it. The exact role and function of NTMTs is unknown, but NTMT1 plays an important role in mitosis, DNA damage repair, stem cell maintenance, glioblastoma, and cervical cell proliferation and migration. NTMT1 is a potential anti-cancer target as it is overexpressed in several cancers such as gastrointestinal, colorectal and melanoma. To improve the cellular inhibition activity of previously invented peptidomimetic inhibitors, the Purdue researchers designed several cell-potent peptidomimetic inhibitors of N-terminal methylation. These inhibitors displayed not only increased cellular inhibition, but they were also optimized for increased hydrophobicity which co-relates with increased cell permeability. The most potent inhibitor (IC50 = 0.9 uM) exhibited over 2-fold increased inhibition on cellular N-terminal methylation levels with a cellular IC50 value of ~50 μM compared to previously reported peptidomimetic inhibitors of NTMT1. It also exhibited over 300-fold selectivity to several other methyltransferases. These cell-potent inhibitors serve as valuable tools to study the function and role of NTMTs and the alpha-N-terminal methylation pathway in cancer and stem cell maintenance.

Technology Validation: In vitro cytotoxicity studies were conducted in normal and NTMT1 knock-out HCT116 cells.

Related Publications:

G Dong, ID Iyamu, JZ Vilseck, D Chen, R Huang. (2022) Improved Cell-Potent and Selective Peptidomimetic Inhibitors of Protein N-Terminal Methyltransferase 1. Molecules, 27, 1381. https://www.mdpi.com/1420-3049/27/4/1381

Chen D, Dong G, Deng Y, Noinaj N, Huang R. (2021) Structure-based Discovery of Cell-potent Peptidomimetic Inhibitors for Protein N-terminal Methyltransferase 1. ACS Medicinal Chemistry Letters. 12, 485-493. https://pubs.acs.org/doi/full/10.1021/acsmedchemlett.1c00012

Mackie BD, Chen D, Dong G, Dong C, Parker H, Schaner Tooley C, Noinaj N, Min J, Huang R. (2020) Selective Peptidomimetic Inhibitors of NTMT1/2: Rational design, synthesis, characterization, and crystallographic studies. Journal of Medicinal Chemistry. 63, 9512-9522. PMID: 32689795. PMCID: PMC74286280. https://pubs.acs.org/doi/10.1021/acs.jmedchem.0c00689

Advantages

- Fully characterized in biochemical and biophysical methods
- highly effective inhibition of N-terminal methylation
- high selectivity to a panel of methyltransferases

Applications

- novel cancer treatment for cervical cancer and glioblastoma
- stem cell therapy
- studying NTMTs and the alpha-N-terminal methylation pathway

INTELLECTUAL PROPERTY:

Application Date: December 2, 2022
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: February 3, 2022
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

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Dong, Guangping

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:

Biotechnology, Cell-potent Inhibitor, NTMT1/2, Peptidomimetic inhibitor, Pharmaceuticals, Selective

DUAL INHIBITORS OF MNK1/2 AND P706SK AS POTENT ANTICANCER DRUGS FOR SOLID TUMORS

TRACK CODE:
2022-SINT-69726

Researchers at Purdue University have designed molecules to concurrently inhibit two proteins important in tumorigenesis, MNK1/2 and p706SK. Pharmaceutical companies have pursued MNK1/2 and p706SK as individual targets; however, drugs targeting these proteins performed poorly as monotherapies. By inhibiting both MNK1/2 and p706SK with a single molecule, the Purdue researchers' orally bioavailable compounds potently inhibit several solid tumor cancer cell lines, including breast, ovarian, lung, and colon cancer cells.

Technology Validation: At 200 nM, one of the drugs designed by the researchers completely inhibited the growth of Caki-1 (renal cancer) and MDA-MB-231 (breast cancer) cells. Compounds were tested against the NCI-60 cell line panel.

Advantages
- Targets two oncogenic proteins with a single molecule
- Effective against multiple solid tumor cell lines
- Orally bioavailable

Applications
- Anticancer drugs

INTELLECTUAL PROPERTY:

Application Date: April 6, 2023
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: April 6, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Sintim, Herman O (Project leader)
Dayal, Neetu

CATEGORIES:

Pharmaceuticals

KEYWORDS:

Cancer, Kinase inhibitor, MNK, Oncology, p70S6K, Pharmaceuticals, Solid Tumor

NOVEL SMALL MOLECULE INHIBITOR FOR THE TREATMENT OF PROSTATE CANCER

TRACK CODE:
2022-DYKH-69819

Researchers at Purdue have synthesized a novel small molecule inhibitor (dubbed 2-77) specific to Bromodomain-containing protein 7 (BRD7). Compound 2-77 was found to reduce the cell viability of prostate cancer cell lines LNCaP and PC-3 in a dose-dependent manner. Prostate cancer (PC), the most diagnosed cancer for men in the US, can be treated in several different ways. Hormone-responsive PC is treated using androgen depravation therapy. Unfortunately, patients eventually become resistant to this treatment, leading to development of castration-resistant prostate cancer (CRPC) after which, the prognosis is grim. Further development of novel small molecule inhibitors targeting BRD7, a protein implicated in the progression of PC, is a promising path for new treatments of PC. While some dual inhibitors of BRD7 and BRD9 exist, none target only BRD7, limiting their efficacy.

The researchers developed a series of possible hit compounds through an in silico virtual high-throughput screening. Using the best hit compounds, compound 2-77 was identified as the best at binding specifically to BRD7, and not BRD9 through a thermal shift assay. The anti-PC ability of 2-77 was quantified using an in vitro assay with PC cell lines that are androgen receptor positive and negative. It was found that compound 2-77 reduced the cell viability of androgen responsive PC cells in a dose-dependent manner, with a ~63 % reduction in viability at 5 uM compound 2-77. Furthermore, it was found that compound 2-77 reduced the cell viability of androgen nonresponsive CRPC cells by ~40 % at 5 uM.

Technology Validation:
Based on the assumption that a protein bound to a well-shaped ligand becomes more stable, it should increase the temperature at which the sample melts (Tm). Upon measuring the Tm of BRD7 protein alone, BRD7 with compound 2-77, BRD9 alone, and BRD9 with compound 2-77, (n=4) with differential scanning fluorimetry, it was found that the sample containing BRD7 with compound 2-77 had a significantly higher Tm shift than BRD9 with compound 2-77, indicating that 2-77 binds specifically to BRD7 and not BRD9. Anti-PC effectiveness of 2-77 evaluated by treating LNCaP cells (androgen responsive) and PC-3 cells (androgen nonresponsive CRPC cells) with 0.1, 1, and 5 uM 2-77 after 4 days of incubation. Cell viability measured using CellTiter-Glo® Luminescent Cell Viability Assay.

Advantages:
- Specific to BRD7 over BRD9
- More potent than previously described BRD7 inhibitor BI7273

Applications:
- Prostate cancer treatment and diagnostics
- Biological investigation of role of BRD7 protein

INTELLECTUAL PROPERTY:

Application Date: March 29, 2024
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)

Issue Date: (None)

Application Date: March 30, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
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CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Inhibitor, Prostate Cancer

KINASE INHIBITORS FOR TREATING CANCER, INFLAMMATION, AND NEUROLOGICAL DISEASES

TRACK CODE:
2022-SINT-69859

Researchers at Purdue University have developed new drugs to treat cancer, inflammation, and neurological diseases. The researchers' previous anticancer compound, HSD1217 a 4-(3H-pyrazolo[4,3-f]quinolin-7-yl)benzamide was only moderately effective at inhibiting Cyclin Dependent Kinases, CDKs. CDK2 and CDK12 are emerging as important therapeutic targets for cancer treatment. By modifying the Benzamide moiety of HSD1217, the researchers developed HSH2177 and HSD1993 analogs that have dramatically improved activity in inhibiting CDKs. By inhibiting CDK function, these compounds could be used as potential anti-cancer agents, anti-inflammatory agents, or agents against neurological diseases.

Technology Validation: The new drugs were validated in vitro. HSH2177 inhibited CDK2 and CDK12 with IC50 values of 7 nM and 27 nM, respectively. HSD1993 inhibited CDK2 and CDK12 with IC50 values of 4 nM and 9 nM respectively. These IC50 values are much lower than those of HSD1217, which inhibits CDK2 with an IC50 value of 185 nM.

Advantages:
- Highly specific at targeting CDK2 and CDK3
- Potently inhibits Tyrosine Kinase 3, FLT3

Applications:
- Treating cancer, inflammation, and neurological diseases

Related publication:
Dual FLT3/haspin kinase inhibitor based on 3H-pyrazolo[4,3-f]quinoline scaffold with activities against acute myeloid leukemia
https://doi.org/10.1039/D3MD00192J

INTELLECTUAL PROPERTY:

Application Date: June 2, 2023
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 2, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

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Kempen, Allison

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Cancer, Kinase inhibitor, Neurological diseases, Pharmaceuticals

NOVEL RET PROTEIN TYROSINE KINASE INHIBITORS

TRACK CODE:
2023-SINT-70021

Researchers at Purdue University have developed novel RET protein tyrosine kinase inhibitors (TKIs). RET is a transmembrane receptor protein-tyrosine kinase that activates multiple downstream pathways involved in cell proliferation and survival. Several small molecule TKIs that are specific to RET have been recently approved to treat RET-altered cancers. However, these compounds are inactive against RET mutations. Viable treatment options for treating mutated RET is direly needed.

Purdue researchers have identified molecules that potently inhibit a common RET mutation better than previously reported molecules. Aside from the increased activity, these molecules also exhibit better drug-like properties, such as solubility. The half maximal inhibitory concentration with mutated RET is as low as 1.5 nanomolar. Furthermore, the solubility of these molecules is 100 times greater than current treatments. This technology can be used to treat multiple forms of RET-altered cancers.

Technology Validation: This technology has been validated using in-vitro kinase assay. This method demonstrated the half maximal inhibitory concentration of the synthesized molecules.

Advantages:
-Potent
-Active against common RET mutation
-Highly soluble

Applications:
-RET-altered cancers
-Cancers with RET mutation

INTELLECTUAL PROPERTY:

Application Date: January 23, 2024
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: January 23, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Sintim, Herman O (Project leader)
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Larocque, Elizabeth Anne
Wu, Jie

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Cancer, Pharmaceuticals, RET mutations, tyrosine kinase inhibitor

COMBINATION OF A PHOSPHATIDYL SERINE BLOCKER AND STING STIMULANT FOR CANCER IMMUNOTHERAPY

TRACK CODE:
2023-YEO-70023

Immunotherapy is one of the most critical tools available for cancer treatment. However, tumor resistance to immunotherapy can develop over time due to the emergence of an immunosuppressive tumor microenvironment (TME). Phosphatidylserine (PS), a key cellular phospholipid, plays a role in this immunosuppression. Normally, PS present on apoptotic cell membranes attracts phagocytes for removal of the apoptotic cells and simultaneously triggers anti-inflammatory signals for homeostasis. Tumor cells hijack this pathway to avoid the surveillance of the immune system. Research has shown that an increase in PS occurs following radiation or chemotherapy treatment in patients. Counteracting this increase in PS is crucial for effective immunotherapy and reducing TME suppression.

Purdue Researchers have developed a pharmaceutical combination that is able to the block PS and boost the anti-tumor response within cells, allowing for enhanced immunochemotherapy of tumors. The pharmaceutical combination consists of a PS blocker, an immune stimulant, and a chemotherapeutic agent. The PS blocker can be composed of dipicolylamine (DPA) or its metal complex, a metal salt, Annexin V, or an anti-PS antibody. The PS blocker is coupled with an immune stimulant such as a STING agonist or granulocyte-macrophage colony-stimulating factor or any combination of the two. The anti-tumor efficacy of the developed formulation was tested in C57BL/6 mice bearing melanoma and successfully delayed tumor growth with an increase in immune stimulation. The PS blockade therapy can be used to enhance immunotherapy and other standard cancer therapies by circumventing immunosuppressive feedback to the treatment.

Technology Validation:
-Transmission electron microscopy images were taken to identify the coordination of cyclic dinucleotide (CDN) and Zn nanoparticles
-Isothermal titration calorimetry (ITC) was performed to calculate the binding affinity of DPA-Zn to PS
-ITC of CDN-Zn was used to calculate the stoichiometry and dissociation constant
-C57BL/6 mice were inoculated with melanoma for treatment with CDN DPA-Zn formulation
-In vitro release of DPA-Zn or CDN from hydrogels was performed

Advantages:
-Decrease in immune suppression by blockade of PS
-Increase in efficacy of standard cancer therapy drugs

Applications:
-Cancer treatment

INTELLECTUAL PROPERTY:

Application Date: October 10, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
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CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Anti-cancer, Biotechnology, Cancer, Medical/Health, Pharmaceuticals

NOVEL PHOTOSENSITIZERS AS A CHEMOTHERAPEUTIC AGAINST TRIPLE NEGATIVE BREAST CANCER

TRACK CODE:
2023-ISAA-70121

Researchers at Purdue University have developed a novel photosensitizer as a chemotherapeutic against triple negative breast cancer (TNBC). TNBC is the most prevalent form of cancer found in women and is considered the most aggressive form of breast cancer, comprising 15-20% of breast cancer cases. Current standard treatment for TNBC utilizes traditional chemotherapies. Unfortunately, traditional chemotherapies have high toxicity and often result in cancers with drug resistance. This has led to a dire need to discover novel treatments.

Purdue researchers have developed photosensitizers as a co-therapy with current chemotherapies. These compounds at 100 nanomolar were able to generate synergistic activity against TNBC cells with Taxol, Cisplatin, Fluorouracil, or Methotrexate. Furthermore, researchers discovered that the mode of action for the death of TNBC cells is mitotic catastrophe with slight autophagy. Combinational therapy with these photosensitizers not only shows a decrease in cell viability but the dosage of the chemotherapeutic is also reduced.

Technology Validation: This technology has been validated using a transmission electron microscope, fluorescence microscopy, and MTT assay. These methods demonstrated that the novel photosensitizer works synergistically with known chemotherapeutics and identified the mode of cell death.

Advantages:
-Known mechanism of death
-Reduced chemotherapy dosage
-Sensitize cancer cells to known chemotherapeutics

Applications:
-Triple negative breast cancer
-Chemotherapeutic
-Cancer therapy

Publication:
Chlorin Conjugates in Photodynamic Chemotherapy for Triple-Negative Breast Cancer
DOI: https://doi.org/10.21203/rs.3.rs-2894973/v1

INTELLECTUAL PROPERTY:

Application Date: May 3, 2024
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: May 5, 2023
Type: Provisional-Patent

Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
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CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Cancer, Chemotherapy, Combinational Therapy, Photosensitizer, Triple Negative Breast Cancer

STING ANTAGONISTS FOR TREATING INFLAMMATORY DISEASES AND DISEASED STATES

TRACK CODE:
2023-SINT-70181

Researchers at Purdue University have developed a class of novel stimulator of IFN gene (STING) inhibitors for inflammatory related diseases and diseased states. Persistent activation of STING is known to be the cause of STING-associated vasculopathy with onset infancy (SAVI) and activated STING is believed to play important roles in worsening various diseased states, such as traumatic brain injury, diabetic kidney disease, and colitis. Further, chronic activation of STING has been associated with autoimmune disorders, pulmonary inflammation, diabetes, fibrosis, and many other conditions.

The Purdue researchers have identified a STING inhibitor that suppresses STING mediated cytokine production in macrophages at low nanomolar concentrations. These compounds are orally bioavailable and have the potential to be translated in vivo. The researchers were able to identify the mechanism of which the molecules were able to inhibit STING activation. These compounds inhibit STING by attenuating type 1 interferon. This technology can be utilized to further understand the role of STING or be developed into a therapy for inflammatory diseases.

Technology Validation: This technology has been validated using a fluorescence polarization assay and western blot. These methods demonstrated that this novel class of proteins has a high affinity to STING and identified the mode of action.

Advantages:
-Activity in multiple cell lines
-Minimal cytotoxicity
-Known mechanism of action
Applications:
-Inflammatory diseases
-Diabetes
-Traumatic brain injuries
-Fibrosis

Related Publication:
STING antagonists, synthesized via Povarov–Doebner type multicomponent reaction
DOI: https://doi.org/10.1039/D3MD00061C
Tags: Inflammatory diseases, diabetes, STING, neurological

INTELLECTUAL PROPERTY:

Application Date: March 22, 2024
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 24, 2023

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Sintim, Herman O (Project leader)
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Lamptey, Jones
Ong, Wei Shiuan Wilson

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Chemistry and Chemical Analysis, Diabetes, Neurological diseases, Pharmaceuticals, STING

NOVEL ANTICANCER COVALENT INHIBITORS OF SHP2 TYROSINE PHOSPHATASE INSPIRED FROM NATURAL PRODUCTS

TRACK CODE:
2023-DAI-70254

Researchers at Purdue have developed a novel library of natural-product inspired covalent inhibitors of SHP2 tyrosine phosphatase. Misregulated SHP2 tyrosine phosphatase function is implicated in a variety of cancers, therefore, SHP2 is an emerging target for anti-cancer drug targets. Covalent inhibitors have high biochemical efficiency due to their ability to irreversibly bind to protein targets. This may allow for developing drugs and therapeutics with lower dosage and reduced side effects as compared to competitive inhibitor molecules, which reversibly bind to target proteins. However, current synthetic covalent inhibitor drug libraries lack structural diversity and are dominated by flat molecules, limiting their scope for targeting many desirable proteins.

Researchers at Purdue have designed covalent inhibitors of SHP2 tyrosine phosphatase based off natural products with many of these covalent inhibitors showing substantial inhibition. The researchers selected a family of natural products called ent-kaurene diterpenoids that have diverse structures and have a long history of research and medical applications in Eastern medicine. From this family, they identified and synthesized the bicyclo[3.2.1]octane ? -methylene ketone pharmacophore and attached to it a range of synthetic drug analogues. After testing the inhibitory activity of their natural-product inspired drug library with SHP2, they discovered a series of molecules that have from a 6 to 119-fold increase in inhibitory activity as compared to previously reported SHP2 covalent inhibitor phenyl vinyl sulfonate.

Technology Validation:
- Inhibitory activity of molecules tested in vitro by measuring the enzymatic cleavage of para-nitrophenyl phosphate with the SHP2 protein and selected covalent inhibitor.

Advantages:
- Many compounds from series show significant inhibition as compared to previous literature.
- Distinct chemical structure from other covalent inhibitor molecules.
- Pharmacophore was found to be easy to prepare on a large scale from readily available starting materials.

Applications:
- Cancer treatment
- Medical diagnostics

INTELLECTUAL PROPERTY:

Application Date: June 3, 2024
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 16, 2023
Type: Provisional-Gov. Funding

Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
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Liang, Weida
Zhang, Zhong-Yin

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Covalent Inhibitor, Pharmaceuticals, Phosphatase Inhibitor

NOVEL FLT3 INHIBITOR FOR MULTIPLE MYELOMA

TRACK CODE:
2024-SINT-70378

Researchers at Purdue University have developed a novel FLT3 inhibitor for multiple myeloma. FMS-like tyrosine kinase 3 (FLT3) is normally expressed in hematopoietic cells, lymphohematopoietic organs, and the brain. Overexpression of phosphorylated FLT3 results in cell maturation and proliferation in acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). Furthermore, FLT3 overexpression is correlated with a poor prognosis. There are currently three FDA approved FLT3 inhibitors, unfortunately these compounds struggle with on-target drug resistance and selectivity. There is a dire need to develop novel selective compounds to combat resistance.

Purdue researchers have identified a selective and potent molecule which inhibits FLT3. The synthesized molecules had a maximal inhibitory concentration against FLT3 at 1 nanomolar. After screening the compound against an array of common off target proteins, the molecule selectively inhibits FLT3. Furthermore, the compounds were active in Molm-14 cells with a concentration that reduces total cell growth by 50% at 2 nanomolar. As phosphorylated FLT3 overexpressed in AML and ALL, researchers demonstrated that there is a significant reduction of phosphorylated FLT3 at 5 nanomolar. This technology can be used to treat AML and ALL.

Technology Validation: This technology has been validated with ADP Glo kinase assay, CellTiter-Blue cell viability assay, and western blot. These methods demonstrated that these compounds can inhibit phosphorylation of FLT3 and inhibit growth of Molm-14 cells.

Advantages:
-Nanomolar activity
-Selective
-In cellulo activity in Molm-14 cells
-Reduces FLT3 phosphorylation

Applications:
-Acute myeloid leukemia
-Acute lymphoblastic leukemia

INTELLECTUAL PROPERTY:

Application Date: October 5, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Sintim, Herman O (Project leader)
Akwata, Desmond

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Cancer, Kinase inhibitor, Pharmaceuticals

NOVEL 2,3'CGAMP ANALOGS AS A STING ANTAGONIST

TRACK CODE:
2024-SINT-70418

Researchers at Purdue University have developed novel 2,3'cGAMP analogs as a STING antagonist. Targeting the c-GAS-STING pathway has been associated with multiple immune responses. The pathway is responsible for the synthesis of 2,3'cGAMP. 2,3'cGAMP promotes antitumor immune memory and antitumor immunity. The degradation of cGAS via ENNP1 advances cancer cell metastasis. Research has demonstrated that targeting the cGAS-STING pathway by synthesizing 2,3'cGAMP analogs leads to rapid tumor regression. Further joint ENPP1 and 2,3'cGAMP agonists are believed to further retain STING agonism.

Purdue researchers have identified molecules that associates with hSTING. These molecules have EC50 values as low as 4.3 μM in-cellulo. Furthermore, it is important that these compounds are stable against ENNP1 degradation. Studies demonstrated that after 24 hours the molecule is still intact. This technology can be used to for immunogenic tumor clearance, vaccine adjunctive, and antiviral therapy.

Technology Validation: Docking was initially utilized to identify the top analogs to be synthesized and tested for STING agonism. The binding affinity to STING was demonstrated using a fluorescent polarization assay. ENNP1 degradation assay was performed to demonstrate the stability of the analogs.

Advantages:
-Active in cells
-Stable against ENNP1
-Low micromolar affinity

Applications:
-Immunogenic tumor clearance
-Vaccine adjunctive
-Antiviral therapy

INTELLECTUAL PROPERTY:

Application Date: September 7, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Sintim, Herman O (Project leader)
Yeboah, Kofi Simpa

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:

antitumor, Cancer Therapy, immunotherapy, Vaccines

POTENT, HIGHLY SELECTIVE ANTICANCER DUAL DEGRADER OF PTP1B AND TC-PTP

TRACK CODE:
2023-ZHAN-70087

Researchers at Purdue have developed a dual degrader that is highly specific to two protein tyrosine phosphatases (PTPs) implicated in cancer, diabetes, and obesity. These PTPs - PTP1B and TC-PTP- have synergistic roles in negatively regulating insulin and T-cell activation, making them desirable targets for the design of small molecule inhibitors. While different small molecule inhibitors could be developed for each PTP, generally, there is an increased risk and unpredictability with multi-drug therapeutics compared with single drug systems.

Purdue researchers have designed a small-molecule drug that is multi-specific to PTP1B and TC-PTP. This small molecule drug is effective in the low nanomolar range. Further, the dual PTP drug includes a motif that activates the ubiquitin-proteasome pathway, which can selectively degrade the target proteins instead of only inhibiting them. The drug reversibly binds to proteins of interest, allowing the same drug molecule to bind to and activate the degradation of many PTP1B/TC-PTP's catalytically.

Technology Validation:
- Ability to degrade PTP1B and TC-PTP in vivo tested in MC38 syngeneic mice. The mice were split into three experimental groups, daily injection of saline, daily injection of 25 mg/kg of duel PTP degrader, and daily injection of 50 mg/kg of duel PTP degrader. Tumor growth was effectively halted for all mice treated with dual PTP degrader as compared to those injected with saline only.
- High selectivity of dual PTP degrader verified by administering the drug to HEK293 cells and measuring the level of other PTP's in cell lysate. Post treatment, PTP1B and TC-PTP were completely degraded and none of the other PTP's were affected.

Advantages:
- Potent degrader of target PTP's, effective in low nanomolar range
- Highly selective to two target PTP's
- Halts tumor growth in mouse model

Applications:
- Cancer treatment
- Diabetes treatment

Related Publication:
Small Molecule Degraders of Protein Tyrosine Phosphatase 1B and T-Cell Protein Tyrosine Phosphatase for Cancer Immunotherapy
https://doi.org/10.1002/anie.202303818

INTELLECTUAL PROPERTY:

Application Date: December 8, 2023
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: February 6, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
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Miao, Jinmin
Miao, Yiming

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Obesity, PTP

POTENT, HIGHLY SPECIFIC TC-PTP DEGRADER FOR TREATMENT OF SKIN CANCER AND ENHANCEMENT OF CAR-T THERAPY

TRACK CODE:
2024-ZHAN-70394

Researchers at Purdue have designed a small molecule degrader, effective at low nanomolar concentrations, that stimulates a cell's protein degradation system to catalytically degrade T-cell protein tyrosine phosphatase (TC-PTP). Currently, clinical approaches to treat cancer through immunotherapy have failed to have consistent results in many patients, requiring further research for developing therapeutics. One approach that has garnered significant interest is to develop therapeutics that target specific protein tyrosine phosphatases (PTPs) while having high selectivity and bioavailability.

The researchers developed a small molecule degrader (dubbed TP1L) that is highly selective for TC-PTP, leaving all other relevant PTPs unaffected. This is evident by TP1L having a > 110-fold selectivity of TC-PTP over PTP1B (a very similar homolog to TC-PTP). By degrading TC-PTP through the ubiquitin proteasome pathway, TP1L allows cells to properly regulate IFN-gamma signaling, promoting anti-tumor activity. Additionally, it was found that by co-incubating 4M5.3 CAR-T cells and KB tumor cells with TP1L, the tumor-killing efficiency was increased through stimulation of CAR-T cells.

Technology Validation:
Degradation ability of TP1L evaluated by treating HEK293 cells with a range of concentrations of TP1L for 16 hours and measuring the levels of TC-PTP via Western blot, the DC50 (concentration needed to induce TC-PTP degradation by 50%) measured was 35.8 nM. The specificity of TP1L for TC-PTP was confirmed by treating HEK293 cells with 0.5 micrometer TP1L for 16 hours and measuring the levels of TC-PTP, PTP1B, SHP2, PTP-MEG2, PTEN, and 7 other proteins. Complete degradation of TC-PTP and zero degradation of the other proteins was observed. Increases in IFN-gamma signaling due to TP1L treatment observed by measuring the levels of phosphorylated JAK1, phosphorylated STAT1, and MHC-1 expression in HEK293 cells, while these levels were not changed by the TP1L treatment in TC-PTP knockout HEK293 cells. The CAR-T cell activation ability of TP1L was validated by measuring the CD69 and CD25 levels after co-culturing KB cells and CAR-T cells for 48 hours.
A 26% and 100% increase of CD25 and CD69 respectively, was observed after treatment with TP1L.

Advantages:
- Potent at degrading TC-PTP at low nanomolar concentrations
- Highly specific to TC-PTP, > 110-fold selectivity of TC-PTP over PTP1B
- Promotes IFN-gamma signaling, activating CAR-T cells and increasing tumor-killing efficiency

Applications:
- Cancer treatment
- CAR-T Therapy
- Further investigation of TC-PTP's role in human biology

Related Publication:
Discovery of a selective TC-PTP degrader for cancer immunotherapy

DOI: 10.1039/D3SC04541B

INTELLECTUAL PROPERTY:

Application Date: October 6, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Zhang, Zhong-Yin (Project leader)
Dong, Jiajun
Miao, Jinmin
Miao, Yiming

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:

Cancer, Cancer Immunotherapy, PTP

POTENT, HIGHLY SELECTIVE SHP2 DEGRADER AS NOVEL ANTICANCER AGENT

TRACK CODE:
2024-ZHAN-70417

Researchers at Purdue have developed a small molecule degrader, effective at low nanomolar concentrations, that can degrade Src homology region 2 - containing protein tyrosine phosphatase (SHP2). SHP2 is a protein tyrosine phosphatase (PTP) that is implicated in cancer cell proliferation and survival, making it a desirable target for designing anticancer drugs. While some small molecule degraders specific to SHP2 have been tested, currently, none have strong enough efficacies in vivo.

The researchers developed a small molecule inhibitor with an IC50 of 90 nM and tested to find the optimal linker to the E3 ligand. The degrader (dubbed P9) was found to degrade SHP2 at a dose and time dependent basis, with a DC50 of 35.2 ± 1.5 nM, and highly specific targeting of SHP2 (no observed degradation of other PTP's and common cell proteins after incubation of 16 hours at 1 μM in HEK293 cells). Finally, the anticancer ability of P9 was quantified by dosing a mouse xenograft model of KYSE-520 cells either 25 or 50 mg/kg of P9 daily. A decrease in tumor size and growth was observed with 25 mg/kg of P9 and a nearly complete tumor regression was observed for mice dosed with 50 mg/kg of P9, all with no change in weight or observed side effects.

Technology Validation:
Degradation ability of P9 measured in vitro against HEK293 cells by dosing cultures with increasing concentrations of P9 and measuring the levels of SHP2 via Western blot. Specificity of P9 to degrade SHP2 verified by incubating 1 μM of P9 for 16 hours in HEK293 cells and observing the levels of SHP1, LYP, TC-PTP, PTP1B, PRL1, PRL2, AKT, ERK1/2, and Actin, after which, no degradation of other proteins was observed aside from SHP2. Anticancer ability of SHP2 degrader in vivo measured by injecting mice with KYSE-520 cancer cells on both of their flanks and measuring the tumor size with calipers according to the equation V = (W2 × L)/2. At 200 mm3, daily injections of 0 (control), 25, or 50 mg/kg of P9 was conducted, with 50 mg/kg inducing nearly complete tumor regression and a decrease in SHP2 levels to 34 ± 18 % compared to the control group.

Advantages:
- Potent, compound has DC50 of 35.2 ± 1.5 nM
- Highly selective for SHP2 protein
- Effective at arresting tumor growth

Applications:
- Anticancer agent
- Biological investigation of SHP2 protein

Related Publication:
Discovery of a SHP2 Degrader with In Vivo Anti-Tumor Activity
https://doi.org/10.3390/molecules28196947

INTELLECTUAL PROPERTY:

Application Date: October 2, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)

Issue Date: (None)

PEOPLE:
Zhang, Zhong-Yin (Project leader)
Bai, Yunpeng
Miao, Jinmin

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Oncology, PTP

The following section contains non-confidential summaries of cell and gene therapy innovations from Purdue University. These summaries are of the following innovations:

▪ Engineering NK Cells to Treat Cancers Driven by Adenosine Immunosuppression
2019-MATO-68613 led by Matosevic, Sandro (note: *in vivo* data)
▪ Targeted Therapeutic for Metastatic Prostate Cancer
2020-FIGU-68875 led by Figueiredo, Marxa L (note: *in vivo* data)
▪ Off-the-shelf Chimeric Antigen Receptor (CAR) NK Cell Production and Application in Cancer Immunotherapy
2022-BAO-69890 led by Bao, Xiaoping
▪ A Chemically Modified MicroRNA as an Anticancer Agent
2023-KASI-70078 led by Kasinski, Andrea L (note: *in vivo* data ; inventor is starting company)

ENGINEERING NK CELLS TO TREAT CANCERS DRIVEN BY ADENOSINE IMMUNOSUPPRESSION

TRACK CODE:
2019-MATO-68613

Researchers at Purdue University have developed a cell therapy capable of exerting a cytotoxic effect on CD73 expressing cancer cells. Adenosine immunosuppression is a regulatory mechanism of the immune system that protects against autoimmunity. However, this mechanism also drives cancers that express the enzyme, CD73. This enzyme produces adenosine, a molecule that inhibits immune cells. The Purdue technology circumvents this adenosine-mediated immunosuppression to treat cancer.

Purdue's researchers engineered a type of immune cell, the natural killer (NK) cell, to target and kill cancer cells. The cells are engineered to express a protein consisting of an extracellular CD73 antibody fragment for targeting and an intracellular signaling domain that activates the NK cell to destroy the cancer cell. This potential therapy circumvents adenosine immunosuppression in the solid tumor microenvironment, selectively targeting cancer cells with engineered immune cells. The engineered NK cells have been successfully tested against glioblastoma cell lines and in vivo in lung carcinoma models, supporting this technology as a transformative cancer treatment to effectively target solid tumors.

Advantages

-Selective cancer therapeutic
-NK cell mediated cytotoxicity

Potential Applications
-Cancer therapeutic
-Circumvent adenosine immunosuppression

INTELLECTUAL PROPERTY:

Application Date: November 23, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: October 25, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: April 27, 2020
Type: PCT-Patent
Country of Filing: WO

Patent Number: (None)
Issue Date: (None)

Application Date: April 25, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Matosevic, Sandro (Project leader)
Chambers, Andrea Marie

CATEGORIES:
Biotechnology, Pharmaceuticals

KEYWORDS:
CD73, cell therapy, Gene Construct, Immunosuppression, NK cells, solid tumors

TARGETED THERAPEUTIC FOR METASTATIC PROSTATE CANCER

TRACK CODE:
2020-FIGU-68875

Researchers at Purdue University have developed a targeted therapeutic option for treating metastatic prostate cancer, the second leading cause of cancer death for men in the United States. The cancer often metastasizes into the bone; however, treatment options targeting advanced metastatic prostate cancer are few, leaving patients with a poor prognosis. The Purdue researchers' technology targets both the primary tumor and the metastatic sites with the goal of patients' increased survival.
The Purdue technology is a gene therapy that delivers a protein conjugate combining a therapeutic cytokine suited for treating metastatic cancer with a peptide that specifically targets tumor tissue. This technology was tested in an ex vivo mouse model and showed 10-fold increase in binding to tumor cells relative to normal cells. Expression of this conjugate in a mouse model displays an 89 percent decrease in prostate tumor growth rate relative to the control. In addition, the researchers observed upregulation of genes associated with immune cell trafficking suggesting delivery of this conjugate has a beneficial impact on both targeted cells and neighboring cells at metastatic sites.

Advantages:
-Designed for Advanced Stage Cancer Treatment
-Targeted to Tumor Cells
-Enhances Expression of Immunogenic Genes

Potential Applications:
-Prostate Cancer
-Metastatic Control
-Bone Repair

Related Publication:
Ligand-Mediated Targeting of Cytokine Interleukin-27 Enhances Its Bioactivity In Vivo
Mol Ther Methods Clin Dev. 2020;17:739-751
doi:10.1016/j.omtm.2020.03.022

INTELLECTUAL PROPERTY:

Application Date: August 25, 2022
Type: NATL-Patent
Country of Filing: Republic of Korea
Patent Number: (None)
Issue Date: (None)

Application Date: July 22, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 21, 2021

Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: January 1, 2021
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: January 1, 2021
Type: NATL-Patent
Country of Filing: Australia
Patent Number: (None)
Issue Date: (None)

Application Date: January 1, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: January 1, 2021
Type: NATL-Patent
Country of Filing: Japan
Patent Number: (None)
Issue Date: (None)

Application Date: January 30, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Figueiredo, Marxa L (Project leader)

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Cancer, Cytokine, Gene Therapy, Heptapeptide, IL-27, IL-6, IL-6-Ralpha, Interleukin-27, Ligand-Mediated Targeting, Metastatic Cancer, Oncology, Prostate Cancer, Sonoporation, Targeted Therapeutic

OFF-THE-SHELF CHIMERIC ANTIGEN RECEPTOR (CAR) NK CELL PRODUCTION AND APPLICATION IN CANCER IMMUNOTHERAPY

TRACK CODE:
2022-BAO-69890

Purdue University researchers have developed an off-the-shelf treatment for targeted cancer immunotherapy. Natural killer (NK) cells are innate lymphoid cells that can be used as targeted immunotherapy for various cancers, but the lack of reliable resources for large scale production and supply of NK cells for clinical use has limited their application in cell therapy. Purdue researchers genetically engineered human pluripotent stem cells (hPSCs) that overexpress ID2, a transcription factor that greatly promotes NK cell generation, under a chemically-defined, feeder-free culture condition. The ID2-hPSC-derived NK cells contain NK cell-specific markers and show effective tumor-killing activity, comparable to NK cells derived from wild-type hPSCs. Further enhancements in antitumor activity were seen when hPSC-NK cells were engineered with a dual anti-PD-L1 CAR and universal anti-fluorescein (FITC) CAR. The use of the universal CAR design allows for targeting of solid tumors and a more widespread targeting of all cancers. The hPSC CAR-NK engineering platform provides a scalable strategy for enhanced generation of off-the-shelf NK cells for use in clinical applications for cancer treatment.

Advantages:
-Modular and scalable
-Off-the-shelf, no long waiting period for patients
-No autoimmune reactivity or cell rejection

Applications:
-Solid Tumor therapy
-Targeted immunotherapy

Publication:
Temporal Expression of Transcription Factor ID2 Improves Natural Killer Cell Differentiation from Human Pluripotent Stem Cells.
ACS Synth. Biol. 2022, 11, 6, 2001–2008
https://doi.org/10.1021/acssynbio.2c00017

INTELLECTUAL PROPERTY:

Application Date: August 16, 2023
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: August 17, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Bao, Xiaoping (Project leader)
Chang, Yun
Jung, Juhyung
Low, Philip Stewart

CATEGORIES:
Biotechnology, Medical/Health

KEYWORDS:
Cancer Drug, Cancer Therapy, cell therapy, Pharmaceuticals, Solid Cancers, Targeted Immunotherapy

A CHEMICALLY MODIFIED MICRORNA AS AN ANTICANCER AGENT

TRACK CODE:
2023-KASI-70078

Purdue researchers have developed a chemically modified microRNA (miRNA) that is an anticancer agent. Unmodified RNAs are subject to serum and intracellular nucleases leading to rapid degradation and a short half-life. This chemical instability has resulted in miRNA therapeutics often requiring high and repetitive dosing to achieve a therapeutic response.

Purdue researchers have a developed a fully modified miRNA, which has an over 400-fold increase in stability relative to its unmodified version and without compromising activity. This approach is particularly promising towards developing anticancer agents because certain miRNAs, such as miR-34a, are frequently overexpressed in cancer. Further, pertaining to miR-34a, downregulation of targets of miR- 34a have been shown to lead to inhibition of several types of cancers. With the aim of developing anticancer agents, researchers have been able to fully chemically modify miR-34a with 2'-O-methyl, 2'-fluoro ribose bases, and phosphorothioate linkages to create conjugates of miR-34a.

Administration of these conjugates, which are composed of fully modified miR-34a (FM-miR-34a) conjugated to folate, results in specific delivery to tumor tissue leading to a strong inhibition of tumor proliferation and delayed tumor growth. The FM-miR-34a robustly inhibits the activity of miR-34a targets, affecting repressing a greater number of them, as compared to partially modified miR-34a. Many of these developed conjugates have demonstrated notable inhibition of miRNA interactions within cells, as shown by their ability to disrupt pathways critical to the survival and proliferation of lung, breast, ovarian, and prostate cancer cells.

Technology Validation:
- MB-231 cells were transfected with PM-miR-34a or FM-miR-34a for measurement of tumor inhibition
- Significant decrease in tumor volume was seen for tumors harvested from mice implanted with transfected breast cancer cells
- Western blot analysis following a single 1.5 nmol intravenous injection of folate-FM-miR-34a highlights decreases expression of miR-34a targets (MET, CD44 and AXL) in comparison to folate-PM-miR-34a and Fol-NC
- Intravenous injection of four 1 nmol doses of folate-FM-miR-34a at six day intervals reduced preformed MB-231 breast cancer xenografts, leading to complete cures in some mice.

Advantages:
- Allows for the specific targeting of miRNA-cancer cell interactions, resulting in a more personalized and precise approach to cancer treatment
- Treatment can be tailored to specific types of cancers, leading to more effective treatments
- Full modification of miRNA enhances stability, increasing resistance to serum nucleases and boosting the intracellular half-life, making the treatment more durable and longer lasting

Applications:
- Treatment of various types of cancers

INTELLECTUAL PROPERTY:

Application Date: March 22, 2024

Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 23, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Kasinski, Andrea L (Project leader)
Abdelaal, Ahmed Mansour Abdelbaky
Sohal, Ikjot Singh

CATEGORIES:
Biotechnology, Pharmaceuticals

KEYWORDS:
Cancer, Cancer Drug, Cancer Therapy, Cell Biology, Medical Health, Medicinal Chemistry, Pharmacology, Therapeutics

The following section contains non-confidential summaries of neurobiology therapeutic innovations from Purdue University. These summaries are of the following innovations:

▪ Treatment of Lowe Syndrome with Repurposed Drugs
2017-AGUI-67722 led by Aguilar, Ruben C
▪ Small Molecule Proteasome Stimulators of Proteasome for Protein Degradation to Treat Alzheimer's and Parkinson's Diseases
2020-TRAD-68744 led by Trader, Darci Jones
▪ Kinase Inhibitors for Treating Cancer, Inflammation, and Neurological Diseases
2022-SINT-69859 led by Sintim, Herman O
▪ Treatment of Alzheimer's and Parkinson's through Aminoindole Carboxamide Derivatives
2023-FORT-69967 led by Fortin, Jessica
▪ Small Molecules for Reduction of Fibril Formation in Prone-to-aggregate Protein
2023-FORT-69996 led by Fortin, Jessica
▪ Therapeutic Strategy for Treatment of Lowe Syndrome and Dent-2 disease
2023-AGUI-69998 led by Aguilar, Ruben C
▪ Novel Small Molecule Inhibitors for Alpha-Synuclein and Tau Isoform 2N4R for the Treatment of Alzheimer's Disease
2023-FORT-70004 led by Fortin, Jessica
▪ Development of AMPylation Activators and Inhibitors for the Treatment of Neurodegenerative Diseases and Discovery of Novel Inhibitor of HYPE-directed AMPylation
2023-MATT-70064 led by Mattoo, Seema
▪ Cyclic Peptide Stimulators of the Proteasome for the treatment of Alzheimer's and Parkinson's
2023-PARK-70287 led by Parkinson, Elizabeth Ivy

TREATMENT OF LOWE SYNDROME WITH REPURPOSED DRUGS

TRACK CODE:
2017-AGUI-67722

Researchers at Purdue University have developed a therapeutic strategy for Lowe Syndrome (LS), a currently untreatable genetic disorder characterized by cognitive deficiencies, bilateral congenital cataracts and renal dysfunction that leads to the early death of those affected, often from kidney failure. The Purdue treatment method has the potential to reverse symptoms and offer patients a higher quality of life. The researchers designed this treatment regimen using rapamycin and statins, drugs approved by the FDA for other indications because of on those drugs' ability to target two molecular pathways implicated in LS. The drugs produced a phenotype similar to normal cells in a variety of tests on LS patient cells. This technology addresses the molecular basis of LS and promises to ameliorate symptoms. This strategy also has the potential to help those suffering from other genetic conditions in which the same cellular pathways are affected.

Related Publication:
Lowe syndrome patient cells display mTOR- and RhoGTPase-dependent phenotypes alleviated by rapamycin and statins
Hum Mol Genet. 2020 Jun 27;29(10):1700-1715
doi: 10.1093/hmg/ddaa086

Advantages:
- Uses FDA Approved drugs with low risk of adverse effects
- Addresses the molecular basis of symptoms in Lowe Syndrome

Applications:
- Therapeutic for Lowe Syndrome
- Strategy could be applied to other genetic conditions

Technology Validation:
The Purdue researchers analyzed the effect of rapamycin and statins on the cellular and molecular phenotypes of Lowe Syndrome patient cells.

INTELLECTUAL PROPERTY:

Application Date: July 8, 2021
Type: Utility-Gov. Funding
Country of Filing: United States
Patent Number: 11,857,549
Issue Date: January 2, 2024

Application Date: November 14, 2023
Type: CON-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: September 17, 2020
Type: Provisional-Gov. Funding

Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Aguilar, Ruben C (Project leader)

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Children, drug therapeutics, genetic disease, Genetic Diseases, kidney, Lowe Syndrome, Neurological, ocular, Pediatric, rare disease, Rare Pediatric, renal, Therapeutics

SMALL MOLECULE PROTEASOME STIMULATORS OF PROTEASOME FOR PROTEIN DEGRADATION TO TREAT ALZHEIMER'S AND PARKINSON'S DISEASES

TRACK CODE:
2020-TRAD-68744

Researchers at Purdue University have developed small molecule stimulators of the enzyme responsible for routine protein degradation, the 20S core particle of the proteasome (20S CP). The researchers were motivated to develop 20S CP stimulators as a pharmaceutical intervention to degrade the damaged and disordered proteins associated with a variety of disease states including Alzheimer's and Parkinson's. The hit compound discovered by Purdue's researchers stimulates catalytic activity of the 20S CP. This stimulator molecule increased the degradation of a peptide probe as well as several full-length proteins by the 20S CP versus a control without the stimulator. In a cell line expressing alpha-synuclein, a protein found aggregated in neurodegenerative diseases, the stimulator enhanced degradation of this protein 200-300 percent. The researchers are now developing derivatives of the hit compound towards a new therapeutic lead. These new molecules pave the way for a drug to prevent debilitating and life-threatening diseases like Alzheimer's and Parkinson's Diseases.

Advantages:

-Stimulates 20S core of the proteasome
-Selective for 20S CP versus 26S proteasome

Potential Applications

-Treatment of Alzheimer's and Parkinson's diseases
-Treatment for aging and disease processes associated with protein aggregation

INTELLECTUAL PROPERTY:

Application Date: January 14, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: August 14, 2020
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: August 14, 2020
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)

Issue Date: (None)

Application Date: August 14, 2020
Type: NATL-Patent
Country of Filing: China
Patent Number: (None)
Issue Date: (None)

Application Date: August 16, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: (None)
Type: NATL-Patent
Country of Filing: Japan
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Trader, Darci Jones (Project leader)
Coleman, Rachel Anne
Salazar-Chaparro, Andres

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Aging, Alzheimer's Disease, Biopharmaceutical Manufacturing, Biotechnology, Chemical Synthesis, Chemistry and Chemical Analysis, Drug Development, Drug Manufacturing, Molecular Biology, Molecular Chemistry, Molecules, Neurodegenerative Disease, Parkinson's Disease, Pharmaceutical Analysis, Pharmaceutical Research, Pharmaceuticals, Pharmaceutics, Pharmacology, protease, Proteasome, Protein Aggregation, Proteins, small molecules

KINASE INHIBITORS FOR TREATING CANCER, INFLAMMATION, AND NEUROLOGICAL DISEASES

TRACK CODE:
2022-SINT-69859

Researchers at Purdue University have developed new drugs to treat cancer, inflammation, and neurological diseases. The researchers' previous anticancer compound, HSD1217 a 4-(3H-pyrazolo[4,3-f]quinolin-7-yl)benzamide was only moderately effective at inhibiting Cyclin Dependent Kinases, CDKs. CDK2 and CDK12 are emerging as important therapeutic targets for cancer treatment. By modifying the Benzamide moiety of HSD1217, the researchers developed HSH2177 and HSD1993 analogs that have dramatically improved activity in inhibiting CDKs. By inhibiting CDK function, these compounds could be used as potential anti-cancer agents, anti-inflammatory agents, or agents against neurological diseases.

Technology Validation: The new drugs were validated in vitro. HSH2177 inhibited CDK2 and CDK12 with IC50 values of 7 nM and 27 nM, respectively. HSD1993 inhibited CDK2 and CDK12 with IC50 values of 4 nM and 9 nM respectively. These IC50 values are much lower than those of HSD1217, which inhibits CDK2 with an IC50 value of 185 nM.

Advantages:
- Highly specific at targeting CDK2 and CDK3
- Potently inhibits Tyrosine Kinase 3, FLT3

Applications:
- Treating cancer, inflammation, and neurological diseases

Related publication:
Dual FLT3/haspin kinase inhibitor based on 3H-pyrazolo[4,3-f]quinoline scaffold with activities against acute myeloid leukemia
https://doi.org/10.1039/D3MD00192J

INTELLECTUAL PROPERTY:

Application Date: June 2, 2023
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 2, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Sintim, Herman O (Project leader)
Dayal, Neetu

Hernandez, Delmis E.
Kempen, Allison

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Cancer, Kinase inhibitor, Neurological diseases, Pharmaceuticals

TREATMENT OF ALZHEIMER'S AND PARKINSON'S THROUGH AMINOINDOLE CARBOXAMIDE DERIVATIVES

TRACK CODE:
2023-FORT-69967

Alzheimer's and Parkinson's are neurodegenerative diseases with symptoms that encompass cognitive decline, movement disorders, functional incapacitation, and often premature death. These diseases arise from the protein fibrillization processes where the tau protein and alpha-synuclein aggregates form neurofibrillary tangles (NFTs) and Lewy bodies. Current treatment methods for these diseases focus mainly on the alleviation of symptoms rather than treating underlying causes.

Purdue researchers have developed a pharmaceutical strategy that involves aminoindole carboxamide-based compounds for the treatment of Alzheimer's and Parkinson's. These compounds can modify the tau protein and alpha-synuclein without altering their fundamental structure. Furthermore, they have shown efficacy at therapeutic doses. This strategy allows researchers to combine the developed compounds with pharmaceutical carriers, which can be pharmaceutical additives like lactose, mannitol, and microcrystalline cellulose for the administration of the carrier via various pathways. Researchers have also further developed multiple formulations for oral intake, spanning from tablets to syrups, optionally augmented with sugar or gastric/enteric coatings for enhanced adaptability. This strategy shows promise as a next step treatment therapy for Alzheimer's and Parkinson's and exhibits potential adaptability for other analogous neurodegenerative diseases.

Technology Validation:
- Anti-fibrillary activity using tau isoform 2N4R in ThT fluorescence assay was confirmed
- Structural analogs were tested at various concentrations in the presence of tau 2N4R
- Alpha-syn and tau oligomer formation with aminoindole carboxamides by photo-inducing cross uncoupled protein (PICUP) assay was tested
- Various amide compounds at different concentrations tested demonstrated protein oligomerization inhibition
- Alpha-syn and tau oligomer formation by transmission electron microscopy was examined.
- Direct changes in alpha-syn and tau isoform 2N4R fibril morphology were observed, showing a significant inhibition of fibril formation in tau isoform 2N4R

Advantages:
- Strategy effectively targets and reduces fibrillization in specific proteins like tau isoform 2N4R and alpha-syn
- Minimal toxicity in neuroblastoma cells was shown for developed compounds
- Strategy can evaluate both fibrillary and oligomer formation, lending itself for applications in various stages of protein aggregation

Applications:
- Neurodegenerative Disease Therapeutics for Parkinson's Disease and Alzheimer's Disease

INTELLECTUAL PROPERTY:

Application Date: March 22, 2024
Type: PCT-Gov. Funding

Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: April 24, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 24, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Fortin, Jessica (Project leader)

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biomedical Engineering, Carrier, Therapeutics

SMALL MOLECULES FOR REDUCTION OF FIBRIL FORMATION IN PRONE-TO-AGGREGATE PROTEIN

TRACK CODE:
2023-FORT-69996

Researchers at Purdue University have developed a portfolio of small molecules that can reduce protein misfolding associated with the development of various diseases. A plethora of known diseases are classified as protein misfolding diseases with subsequent fibril formation. These diseases include Alzheimer's disease, Parkinson's disease, Huntington's disease, Type 2 diabetes, Lewy body dementia, and spongiform encephalopathy. There are currently limited general strategies that have emerged for developing small molecules capable of inhibiting the formation of fibrils, or to disaggregate amyloid deposits. Further, there are no effective therapies for resolving or halting neurodegenerative diseases associated with protein disorders.

Researchers at Purdue University evaluated a set of 4-(2-benzothiazolyl) aniline (BTA) and its derivatives on their ability to modulate the folding of prone-to-aggregate proteins such as islet amyloid polypeptide (IAPP), amyloid-beta (A?1-40, A?1-42), transthyretin (TTR81-127, TTR101-125), ?-synuclein (?-syn), and tau isoform 2N4R (tau 2N4R). By utilizing various biophysical methods, researchers were able to study compounds and identify the compounds that held the most promise for treating protein misfolding disorders. This study provides an initial platform to generate more potent inhibitors of ?-syn, tau 2N4R, and TTR fibril formation in the future.

Technology Validation: Transmission electron microscopy was used to confirm anti-fibrillary activity. The photoreactive cross-linking assay identified the most promising compound in reducing oligomerization. The most promising compound reduced the inclusions based on the cell-based assay using M17D neuroblastoma cells that express inclusion-prone ?S-3K::YFP. A Thioflavin-T fluorescence assay was used to monitor fibril formation after treatment with the BTA compounds and its derivatives. The most promising compound identified by this research abrogated the fibril, oligomer, and inclusion formation in a dose-dependent manner.

Advantages:
-Potent inhibition of fibril formation

Applications:
- Drug development
- Drug discovery

Related Publications:
5-Nitro-1,2-benzothiazol-3-amine and N-Ethyl-1-[(ethylcarbamoyl)(5-nitro-1,2-benzothiazol-3-yl)amino]formamide Modulate a-Synuclein and Tau Aggregation

DOI: https://doi.org/10.1021/acsomega.3c02668?urlappend=%3Fref%3DPDF&jav=VoR&rel=cite-as

INTELLECTUAL PROPERTY:

Application Date: February 2, 2024
Type: PCT-Gov. Funding

Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: April 24, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: February 3, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Fortin, Jessica (Project leader)

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Chemistry and Chemical Analysis, Drug Development, Pharmaceutical Development

THERAPEUTIC STRATEGY FOR TREATMENT OF LOWE SYNDROME AND DENT-2 DISEASE

TRACK CODE:
2023-AGUI-69998

Lowe Syndrome (LS) and Dent-2 (D2) are incurable genetic diseases with treatment options focusing on symptoms and having limited effectiveness. The symptoms of these diseases are severe and include ocular, neurological, and renal abnormalities, with culmination in early death. The diseases arise from mutations in the OCRL1 (oculo-cerebro-renal syndrome of Lowe) gene, leading to dysfunctions in the inositol 5-phosphatase Ocrl1 enzyme. Allosteric activators, through their ability to stabilize the enzymatically active conformer of the Ocrl1 enzyme, have emerged as a potential component in developing therapies for these diseases.

Purdue Researchers have utilized allosteric activators to develop a therapeutic strategy that leverages the changes in Ocrl1 enzyme that do not directly impact the enzyme's catalytic site but lead to phosphatase domain inactivation. Researchers have developed a variety of allosteric activators that can be combined into effective pharmaceutical compositions that show promise when administered in therapeutic quantities. These compositions, which include carriers, excipients, and other common pharmaceutical additives like lactose, mannitol, glucose, hydroxypropylcellulose, and microcrystalline cellulose, can be administered via various routes. Researchers have also developed various formulations suitable for oral administration, some of which are tablets, powders, syrups, and others, with options for sugar or gastric/enteric coating for tablets and pills as needed. This approach shows potential for providing a first-of-a-kind treatment for LS or D2 disease and could also be adapted to tackle other similar genetic diseases.

Technology Validation:
- Suppression of the Golgi/OCRL1 fragmentation phenotype in specific cell lines (HK2 OCRL KO cells stably expressing OCRL10451G) was shown
- Restoration of enzymatic function was seen when 4-PBA (4-Phenyl Butyric Acid) was used as well as suppression of the phenotypes of other OCRL1 mutated variants (D451G, V508D or I393F)
- High-throughput screening process involving three compound libraries (LOPAC1280, the ChemBridge 30Klibrary, and the 7.2Kfragmented library) was used to assess the impact on the enzymatic activity of the OCRL10451G variant

Advantages:
- Targeted application towards restoration of enzymatic activity of proteins
- High-throughput screening for screening of large number of compounds
- Personalized treatment for LS or DS through identification of different mutated variants of a protein.

Applications:
- Treatment of LS or DS
- Drug discovery for related diseases
- Personalized medicine

INTELLECTUAL PROPERTY:

Application Date: November 7, 2023
Type: PCT-Gov. Funding

Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: November 8, 2022
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Aguilar, Ruben C (Project leader)

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biomedical Engineering, Carrier, Therapeutics

NOVEL SMALL MOLECULE INHIBITORS FOR ALPHA-SYNUCLEIN AND TAU ISOFORM 2N4R FOR THE TREATMENT OF ALZHEIMER'S DISEASE

TRACK CODE:
2023-FORT-70004

Researchers at Purdue have developed several small molecule inhibitors active at the low micromolar level for alpha-synuclein (alpha-syn) as well as tau isoform 2N4R (T-2N4R) to a limited degree. Both alpha-syn and T-2N4R are heavily associated with the development of Alzheimer’s disease in humans. This disease is believed to occur due to accumulation of plaques and intraneuronal neurofibrillary tangles within the brain, causing neural degeneration and eventually death. Currently, no drug exists to treat Alzheimer's disease entirely, only managing some symptoms.

The researchers synthesized a library of compounds with similar chemical motifs and measured their inhibitory activity against development of alpha-syn and T-2N4R oligomers in vitro. Of the 25 compounds synthesized, two significantly inhibited oligomer formation at the low micromolar level.

Technology Validation:
Oligomer inhibition of alpha-syn and T-2N4R measured via photo-inducing cross uncoupled protein (PICUP) assay. It was found that concentrations of 6.25 μM - 50 μM of the 1st compound and 25 μM – 50 μM of the 2nd compound significantly reduced alpha-syn oligomer formation. Additionally, a concentration of 50 μM of the 1st compound had limited inhibition of T-2N4R oligomers. The 1st compound is capable to disaggregate plaques and tangles isolated from AD patient brains at 50 μM.

Advantages:
- Inhibition of oligomer formation and seeding at low micromolar level
- Disaggregation of pre-formed fibrils
- Novel

Applications:
- Alzheimer’s and Parkinson’s disease treatment
- Medical diagnostics

INTELLECTUAL PROPERTY:

Application Date: March 21, 2024
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 24, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Fortin, Jessica (Project leader)

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Alzheimer's Disease, Inhibitor

DEVELOPMENT OF AMPYLATION ACTIVATORS AND INHIBITORS FOR THE TREATMENT OF NEURODEGENERATIVE DISEASES AND DISCOVERY OF NOVEL INHIBITOR OF HYPE-DIRECTED AMPYLATION

TRACK CODE:
2023-MATT-70064

Fic enzymes are known for catalyzing AMPylation, a posttranslational modification essential for cell signaling, involving the addition of adenosine monophosphate (AMP) to serine, threonine, or tyrosine residues on proteins. This process is facilitated by a conserved Fic motif within the enzyme's active site, where a histidine residue initiates the transfer of AMP from adenosine triphosphate (ATP) to the target protein. The sole human Fic protein, HYPE, located in the endoplasmic reticulum, specifically AMPylates the chaperone protein Binding Immunoglobulin Protein (BiP), regulating its activity. Under normal conditions, AMPylated BiP is inactive, but it becomes active (deAMPylated) in response to misfolded proteins in the ER. HYPE has additionally been found to AMPylate alpha-synuclein, which leads to a reduction in harmful phenotypes linked to Parkinson's disease and affects the aggregation of proteins associated with various neurodegenerative diseases. Following this, more potential substrates of HYPE-mediated AMPylation have been identified, implicating HYPE in a variety of diseases including cancer, diabetes, and neurodegeneration.

Purdue researchers have developed a method for screening pharmaceutical compositions for treating neurodegenerative diseases that are impacted by HYPE-mediated AMPylation. Researchers were able to complete a high throughput small molecule screen, which included over 30,000 compounds, to identify activators and inhibitors of HYPE. This developed method can be used for optimizing and scaling dual screening assays for the identification of novel modulators of in vitro HYPE AMPylation. Furthermore, this has allowed for the discovery of a novel inhibitor of HYPE-directed AMPylation in I2.10. I2.10's specificity for HYPE was confirmed through validations, showing that the inhibitor was effective without affecting other cellular targets. Additionally, the inhibitor demonstrated minimal toxicity in human cell lines, showing viable candidacy for further development.

Technology Validation:
- Fluorescence polarization (FP) of Fl-ATP was used to monitor HYPE- mediated AMPylation
- FP AMPylation assay was performed to confirm both WT HYPE activator and inhibitor validation
- In-gel autoAMPylation assay with WT HYPE and E234G HYPE validated WT HYPE activators and showed fluorescence for direct AMPylation and Coomassie staining for protein loading
- Fluorescence quantification was normalized to DMSO controls with data from four experiments; showing direct protein AMPylation
- Radioactive in-gel AMPylation assay used WT IbpA-Fic2, Cdc42, and a-32P-ATP to assess cross-reactivity and control activation with T229A BiP-AMP
- Phosphor screen and Coomassie staining confirmed direct AMPylation and protein loading.
- MTT cell viability assay of HeLa cells were incubated with inhibitor compounds demonstrating low cellular toxicity

Advantages:
- High-throughput screening allows for rapid identification of potential inhibitors or activators

- Precise and scalable method to measure enzyme activity
- High-quality and reproducible selection process for inhibitors and activators
- Low cytotoxicity of discovered compounds

Applications:
- Developing therapies for neurodegenerative diseases such as Parkinson's, Alzheimer's, and Huntington's by targeting protein misfolding
- Identifying novel compounds that can serve as either activators or inhibitors of HYPE-mediated AMPylation
- Potentially discovering treatments for diseases that involve proteostasis imbalances, like certain cancers and diabetes

INTELLECTUAL PROPERTY:

Application Date: May 15, 2024
Type: Utility-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: May 16, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Mattoo, Seema (Project leader)

CATEGORIES:

Biotechnology, Pharmaceuticals

KEYWORDS:

Alzheimer's, Biomedical Engineering, Therapeutics

CYCLIC PEPTIDE STIMULATORS OF THE PROTEASOME FOR THE TREATMENT OF ALZHEIMER'S AND PARKINSON'S

TRACK CODE:
2023-PARK-70287

Cyclic Peptide Proteasome Stimulators (CyPPS) have gained prominence for their ability to selectively catalyze the degradation of disordered proteins, leaving structured proteins untouched. CyPPS address proteinopathies—conditions arising from structurally misfolded proteins that impact cellular, tissue, and organ functions. Some of these diseases include neurodegenerative disorders like Alzheimer's and Parkinson's. Various small molecules and peptides have been found to stimulate the proteasome; however, these proteasome stimulators are disadvantageous due to lack of potency, selectivity, and inactivity in cell-based assays. There is a clear need for proteasome stimulators with low toxicity that show selectivity of cyclic, misfolded peptides.

Researchers at Purdue have developed various cyclic proteasome stimulator based upon previously developed predicted natural products (pNPs) that show high selectivity and potency. These developed CyPPS demonstrate incredible efficacy in accelerating the proteasomal degradation of specific malfunctioning proteins while leaving other functioning proteins intact. The CyPPS can be synthesized utilizing well-established techniques, such as solid-phase peptide synthesis. Furthermore, the developed peptides exhibit no toxicity to human cells and hemolysis.

Technology Validation:
- Efficacy of the cyclic peptides was demonstrated through verification of misfolded protein degradation, cell permeability and uptake
- Structure and activity of various proteasomes were confirmed via TAS-1 biochemical assay
- Two-way analysis of variance (ANOVA) analysis was performed comparing the efficacy of various active CyPPS

Advantages:
- Non-hemolytic
- Non-toxic to humans
- High selectivity

Applications:
- Creutzfeldt– Jakob disease
- Alzheimer's disease
- Parkinson's disease
- Amyloidosis
- Huntington's disease

Related Publication:
Discovery and Development of Cyclic Peptide Proteasome Stimulators
https://doi.org/10.1002/cbic.202300671

INTELLECTUAL PROPERTY:

Application Date: September 1, 2023

Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Parkinson, Elizabeth Ivy (Project leader)
Harris, Timothy Jonathan
Nelson, Samantha
Trader, Darci Jones

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Alzheimer's, Biomedical Engineering, Therapeutics

The following section contains non-confidential summaries of infectious disease innovations from Purdue University. These summaries are of the following innovations:

▪ Antibacterial Agents Against Methicillin- and Vancomycin-Resistant Bacteria
2018-SINT-68199 led by Sintim, Herman O
▪ Novel Inhalation Formulation of Antimicrobials
2018-ZHOU-68233 led by Zhou, Qi
▪ Nanoparticles for Intracorporeal Sepsis Treatment
2019-YEO-68355 led by Yeo, Yoon
▪ Antimicrobial Peptides Targeting Intracellular Bacteria
2019-CHMI-68405 led by Chmielewski, Jean Anne (note: *in vivo* data)
▪ Selective Antibiotics for Highly Resistant Enterococcus
2019-FLAH-68419 led by Flaherty, Daniel P
▪ Bactericidal and Bacteriostatic Agents against Drug-Resistant Bacteria
2019-SINT-68535 led by Sintim, Herman O (note: *in vivo* data)
▪ Carbonic Anhydrase Inhibitors as Treatment for Gonorrhea
2020-FLAH-68832 led by Flaherty, Daniel P
▪ Composites with Ivacaftor and Colistin for Cystic Fibrosis and Bacterial Lung Infection Treatment
2020-ZHOU-68954 led by Zhou, Qi
▪ Novel inhalation formulations of polymyxins
2020-ZHOU-68990 led by Zhou, Qi
▪ Low-toxicity Formulations of Polymyxins for Inhaled Treatment of Gram-negative Bacterial Lung Infections
2021-ZHOU-69256 led by Zhou, Qi
▪ Sustained Release Silver Nanoparticulate Compositions for Treating Microbial Infections
2023-RISS-70028 led by Risselada, Marije
▪ Novel Potent and Selective PRMT Inhibitors for Developing Therapeutic Agents
2023-HUAN-70160 led by Huang, Rong
▪ Novel Covalent Protein Inhibitors for Treating Malaria
2023-FLAH-70246 led by Flaherty, Daniel P

ANTIBACTERIAL AGENTS AGAINST METHICILLIN- AND VANCOMYCIN-RESISTANT BACTERIA

TRACK CODE:
2018-SINT-68199

The discovery and development of antibiotics revolutionized health care in such a way that bacterial infections, which were otherwise deadly, could be treated; however, this was met with a rapid development of resistant bacterial strains that rendered many antibiotics ineffective. Consequently, millions of people are infected with drug-resistant bacterial strains yearly resulting in thousands of deaths. Efforts need to be directed towards identifying and developing novel structures as antibacterial agents with possibly novel mechanisms of action.

Researchers at Purdue University have identified compounds with potent antibacterial activities. The most potent compounds inhibited growth of various-resistant Gram-positive bacterial pathogens. Some compounds were active against clinical isolates of methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-intermediate and vancomycin-resistant Staphylococcus aureus (VISA and VRSA respectively), and vancomycin-resistant Enterococcus faecalis (VRE). Through resistance generation experiments it was revealed that MRSA could not develop resistance to one of these compounds.

Advantages:
-Compounds can kill methicillin and vancomycin-resistant bacteria
-No resistance from MRSA
-Potent activity against drug-resistant Gram-positive pathogens

Potential Applications:
-Pharmaceuticals/biotech companies
-Animal medicine
-Bacterial burden in skin wound infections

Related Publications:
Clement Opoku-Temeng et al., N-(1,3,4-oxadiazol-2-yl)benzamide analogs, bacteriostatic agents against methicillin- and vancomycin-resistant bacteria
European Journal of Medicinal Chemistry, 2018
https://doi.org/10.1016/j.ejmech.2018.06.023

INTELLECTUAL PROPERTY:

Application Date: October 12, 2020
Type: NATL-Patent
Country of Filing: Japan
Patent Number: 7357934
Issue Date: September 29, 2023

Application Date: October 12, 2020
Type: NATL-Patent
Country of Filing: United States
Patent Number: 11,731,964

Issue Date: August 22, 2023

Application Date: August 21, 2023
Type: CON-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 29, 2019
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: April 12, 2018
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Sintim, Herman O (Project leader)
Mohammad, Haroon Taj
Naclerio, George
Opoku-Temeng, Clement
Seleem, Mohamed

CATEGORIES:
Biotechnology, Medical/Health

KEYWORDS:
Antibiotic Resistance, Bacteriostatic, Biotechnology, Medical/Health, Multidrug-resistance Bacteria

NOVEL INHALATION FORMULATION OF ANTIMICROBIALS

TRACK CODE:
2018-ZHOU-68233

Antimicrobial therapy via the inhalation route has attracted increasing momentum for the treatment of lower respiratory systems. Inhalation therapy improves drug concentration on airway surfaces with reduced systemic exposure. Typically, the inhaled drug particles produced by the traditional jet-milling approach are highly cohesive and have poor flowability and aerosolization performance. Addition of excipients, such as lactose particles, may improve the aerosolization of cohesive powders; however, for high-dose drugs, like antibiotics, the addition of excipients may increase the inhalation powder mass that needs an excessive number of inhalations to complete the dose and a bulky inhaler to accommodate the large dose.

Researchers at Purdue University have developed a novel inhalation formulation which shows superior antibacterial activity. Incorporation of this formulation is evidenced by an almost two-fold increase in aerosol delivery efficiency expressed as fine particle fraction. The synergistic antimicrobial activities and the increased aerosolization performance from this formulation will not only improve patient compliance by reducing the inhaled powder mass and minimizing local adverse effects, but will also have the potential to achieve superior therapeutic efficacy.

Advantages:
-Enhanced antimicrobial activity
-Reduces inhaled powder mass
-Minimizes local adverse effects

Potential Applications:
-Dry powder inhalers
-Respiratory infections
-Antimicrobial therapy via inhalation

INTELLECTUAL PROPERTY:

Application Date: April 26, 2019
Type: Utility Patent
Country of Filing: United States
Patent Number: 11,278,497
Issue Date: March 22, 2022

Application Date: April 26, 2018
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Zhou, Qi (Project leader)
Mangal, Sharad

CATEGORIES:
Pharmaceuticals, Medical/Health

KEYWORDS:
Aerosol Performance, Antimicrobial Synergy, Colistin, Dry Powder Inhaler, Medical/Health, Meropenem, Pharmaceuticals, Spray Drying

NANOPARTICLES FOR INTRACORPOREAL SEPSIS TREATMENT

TRACK CODE:
2019-YEO-68355

Researchers at Purdue University have developed bio-compatible nanoparticles to treat sepsis systemically. The Centers for Disease Control and Prevention estimate that 33 percent of hospital mortality in the United States is due to sepsis, a disease that occurs when bacterial endotoxins circulate in the bloodstream and trigger the immune system to attack the body. Available treatments largely rely on targeting the bacteria or providing life support, none of which directly clear endotoxins. Others have proposed treatments based on different nanoparticle systems; however, those technologies are not suitable for systemic treatment and would require invasive techniques of extracorporeal blood cleansing. Purdue researchers designed a new solution to sepsis, which can be administered systemically and safely. In mouse models of sepsis, 100 percent of the animals treated with the new nanoparticle system survived while none of the animals in the control group survived. Compared to other exploratory solutions to combat sepsis, the Purdue technology promises a safe and convenient option for both patients and physicians.

Advantages:
-Inactivation of endotoxin
-Prevention of excessive inflammation
-Protection from polymicrobial peritonitis

Potential Applications:
-Sepsis treatment

Publications:
Nanocapsules modify membrane interaction of polymyxin B to enable safe systemic therapy of Gram-negative sepsis
Science Advances; 6 Aug 2021; Vol 7, Issue 32
DOI: 10.1126/sciadv.abj1577

INTELLECTUAL PROPERTY:

Application Date: February 18, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: 11,865,158
Issue Date: January 9, 2024

Application Date: November 1, 2023
Type: CON-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: August 21, 2020
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)

Issue Date: (None)

Application Date: August 21, 2020
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: August 22, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Yuk, Simseok

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Nanoparticles, Pharmaceuticals, Sepsis

ANTIMICROBIAL PEPTIDES TARGETING INTRACELLULAR BACTERIA

TRACK CODE:
2019-CHMI-68405

Researchers at Purdue University developed antimicrobial agents against intracellular human pathogens with improved efficacy compared to the group's previous-generation compounds. Drug resistant bacteria are an increasing worldwide threat, especially in the healthcare environment. Compounding the threat, many bacterial species localize within human cells. Designing and formulating drugs to reach inside host cells without damaging those cells is a key challenge in treating bacterial infection. The Purdue team employs cell-penetrating peptides to meet this challenge. Their newest generation of peptide-based compounds compares well to vancomycin and gentamicin, in some cases outperforming the established antibiotics in cell culture. The Purdue peptides also demonstrate excellent cell penetrating ability and safety against human cells.

Advantages:
-Penetrates human cells to target intracellular pathogens
-Effective alone or as a covalent conjugate with other antibiotics
-Avoids use of delivery vehicles

Potential Applications:
-Antibiotic therapeutic
-Pharmaceuticals

Technology is validated: In vitro testing (patent)

INTELLECTUAL PROPERTY:

Application Date: November 13, 2019
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,875,895
Issue Date: December 29, 2020

Application Date: November 12, 2019
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: October 16, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: December 4, 2018
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)

Issue Date: (None)

PEOPLE:
Chmielewski, Jean Anne (Project leader)
Seleem, Mohamed

CATEGORIES:
Chemistry and Chemical Analysis

KEYWORDS:
Antibacterial, Antibiotic, Bacterial Pathogens, Drug Delivery, Drug Development, Drug Resistance, Immune System, Medicinal Chemistry, Patient Care, Peptides, Pharmaceuticals

SELECTIVE ANTIBIOTICS FOR HIGHLY RESISTANT ENTEROCOCCUS

TRACK CODE:
2019-FLAH-68419

Vancomycin-resistant enterococcus (VRE) is a leading cause of hospital-acquired infections in the US. There is an unmet need for new treatments of VRE, as infected patients frequently exhaust treatment options when fighting bacterial resistance.

Researchers at Purdue University have developed small molecules to combat drug-resistant enterococcus. These acetazolamide analogs demonstrated a 2 to 4-log reduction in VRE gastrointestinal colonization in mice and were superior to linezolid, the current standard of care, in clearing VRE in internal organs. Additionally, they were shown to selectively target VRE without harming the normal gut microbiota. The application for these compounds is for the treatment of drug-resistant enterococcus.

Advantages:
-Improved potency against VRE
-High selectivity for VRE

Potential Applications:
-VRE treatment

INTELLECTUAL PROPERTY:

Application Date: June 18, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: December 18, 2019
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: December 19, 2018
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Flaherty, Daniel P (Project leader)
Seleem, Mohamed

CATEGORIES:

Pharmaceuticals

KEYWORDS:
Antibiotic, Antibiotic Resistance, Drug Development, small molecules, VRE

BACTERICIDAL AND BACTERIOSTATIC AGENTS AGAINST DRUG-RESISTANT BACTERIA

TRACK CODE:
2019-SINT-68535

Researchers at Purdue University have developed novel antimicrobial agents to solve the continued problem of drug-resistant bacterial strains; approximately 20,000 people die in the US every year from drug-resistant infections. These antimicrobial agents potently inhibit bacterial growth in several species, including drug-resistant strains, at concentrations as low as 0.0675 micrograms per milliliter. This family of compounds contains both bactericidal and bacteriostatic agents.

Advantages:
-Inhibits drug resistant bacteria strains
-Kills bacteria at low concentration

Potential Applications:
-Antimicrobial Agent

Related Publications:
Ultrapotent Inhibitor of Clostridioides difficile Growth, Which Suppresses Recurrence In Vivo
Journal of medicinal chemistry 63.20 (2020): 11934-11944.
https://doi.org/10.1021/acs.jmedchem.0c01198

Potent trifluoromethoxy, trifluoromethylsulfonyl, trifluoromethylthio and pentafluorosulfanyl containing (1,3,4-oxadiazol-2-yl)benzamides against drug-resistant Gram-positive bacteria
RSC Med. Chem., 2020,11, 102-110
DOI: 10.1039/C9MD00391F

INTELLECTUAL PROPERTY:

Application Date: November 22, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: October 26, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: April 24, 2020
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: April 26, 2019

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Sintim, Herman O (Project leader)
Naclerio, George

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Antibacteria, Antibiotic, Antibiotic Resistance, Bactericidal, Bacteriostatic, E. faecalis, Enterococcus, L. monocytogenes, Listeria, MRSA, Pharmaceuticals, S. aureus, Staphylococcus, VRE

CARBONIC ANHYDRASE INHIBITORS AS TREATMENT FOR GONORRHEA

TRACK CODE:
2020-FLAH-68832

Researchers at Purdue University have developed a new treatment for the drug resistant pathogen Neisseria gonorrhoeae. CDC has reported a 67% increase in gonorrhoea cases, a sexually transmitted disease, between 2013 and 2017. Pathogenic strains of gonorrhea are notorious for rapidly developing resistance to the current line of antibiotic treatments rendering them futile. The new treatment developed at Purdue leverages FDA approved carbonic anhydrase inhibitors (CAIs) to develop novel analogs that are potent with a narrow spectrum of action to treat gonorrhea. These analogs target the enzyme, carbonic anhydrase in the bacteria, which is crucial for the bacteria to maintain CO2 and pH homeostasis. They do not target other commensal bacteria that are required to maintain healthy microbiome. Most importantly, their mechanism of action prevents the development of rapid antibiotic resistance.

Advantages:
-Selectively targets N. gonorrhea
-Does not target gut and/or vaginal microbiota
-Prevents rapid resistance development
-Works synergistically with approved antibiotics

Potential Applications:
-Treatment of Gonorrhea and treating medical conditions related to antibiotic resistant strains of N.gonorrhoeae.

INTELLECTUAL PROPERTY:

Application Date: December 16, 2021
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 1, 2021
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 16, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Flaherty, Daniel P (Project leader)
Seleem, Mohamed

CATEGORIES:
Pharmaceuticals, Medical/Health

KEYWORDS:
Antibiotic Resistance, Gonorrhea, Pharmaceuticals, STDs, Superbugs

COMPOSITES WITH IVACAFTOR AND COLISTIN FOR CYSTIC FIBROSIS AND BACTERIAL LUNG INFECTION TREATMENT

TRACK CODE:
2020-ZHOU-68954

Intravenous and oral antibiotics are not always effective for lung infections due to limited drug exposure at the infection site and bacterial resistance.

Researchers at Purdue University have developed a novel combination therapy of polymyxins for treating bacterial lung infections. Polymyxins have often been used as the last-line resort for infections caused by multi-drug resistant Gram-negative 'superbugs'; but Inhaled polymyxins can cause toxicity in the lungs. The novel formulation developed by Purdue researchers creates a powerful therapeutic option with better antibacterial killing and much-reduced toxicity than the polymyxins alone. The Purdue dry powder formulation shows promise as an inhaled therapy, with satisfactory stability and high aerosolization performance. This innovative inhalation formulation promises a life-saving option for patients suffering from bacterial lung infections, including people infected by multidrug-resistant Pseudomonas aeruginosa, Acinetobacter baumannii and Enterobacterales.

Advantages:
-Enhanced efficacy
-Decreased drug resistance
-Decreased toxicity

Potential Applications:
-Pharmaceuticals
-Biomedical
-Medicine

Related Publication:
Inhalable Nanocomposite Microparticles with Enhanced Dissolution and Superior Aerosol Performance
Mol. Pharmaceutics, Published online July 24, 2020
https://doi.org/10.1021/acs.molpharmaceut.0c00390

INTELLECTUAL PROPERTY:

Application Date: August 31, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 5, 2021
Type: PCT-Patent
Country of Filing: WO

Patent Number: (None)
Issue Date: (None)

Application Date: March 11, 2020
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Zhou, Qi (Project leader)
Zhu, Chune

CATEGORIES:
Pharmaceuticals, Micro & Nanotechnologies

KEYWORDS:
Aerosol Performance, Bactericidal, Cystic Fibrosis, Dry Powder, Formulation, freeze drying, Gram-Negative, Inhaler, Medicine, Micro & Nanotechnologies, Pharmaceuticals

NOVEL INHALATION FORMULATIONS OF POLYMYXINS

TRACK CODE:
2020-ZHOU-68990

Intravenous and oral antibiotics are not always effective for lung infections due to limited drug exposure at the infection site and bacterial resistance.

Researchers at Purdue University have developed a novel combination therapy of polymyxins for treating bacterial lung infections. Polymyxins have often been used as the last-line resort for infections caused by multi-drug resistant Gram-negative 'superbugs'; but inhaled polymyxins can cause toxicity in the lungs. The novel formulations developed by Purdue researchers create a powerful therapeutic option with better antibacterial killing and much-reduced toxicity than the currently used inhaled polymyxin B and colistin. Furthermore, the Purdue dry powder formulation shows promise as an inhaled therapy, with satisfactory stability and high aerosolization performance. These innovative inhalation formulations promise a life-saving option for patients suffering from bacterial lung infections, including people infected by multidrug-resistant Pseudomonas aeruginosa, Acinetobacter baumannii and Enterobacterales.

Advantages:
-Enhanced efficacy
-Decreased drug resistance
-Improved safety

Potential Applications:
-Pharmaceuticals
-Biomedical
-Medicine

INTELLECTUAL PROPERTY:

Application Date: December 16, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: May 3, 2021
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: May 3, 2021
Type: NATL-Patent
Country of Filing: China
Patent Number: (None)
Issue Date: (None)

Application Date: July 2, 2020

Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Zhou, Qi (Project leader)
Ahmed, Maizbha Uddin
Azad, Mohammad Abul Kalam
Li, Jian

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Acinetobacter baumannii, Aerosol Performance, Antibacterial, bioaerosols, Biopharmaceutical Manufacturing, Cell Biology, Cell Targeting, cell therapy, Chemistry and Chemical Analysis, Colistin, Cystic Fibrosis, Drug Development, Drug Manufacturing, Drug Resistance, Dry Powder Inhaler, Industrial Crystallization, Klebsiella pneumonia, Lung Infection, Medicinal Chemistry, Multi-drug Resistant Bacteria, Patient Care, Pharmaceutical Analysis, Pharmaceuticals, Pharmacology, Polymyxin, Pseudomonas aeruginosa, Pulmonary, Respiratory Infection

LOW-TOXICITY FORMULATIONS OF POLYMYXINS FOR INHALED TREATMENT OF GRAM-NEGATIVE BACTERIAL LUNG INFECTIONS

TRACK CODE:
2021-ZHOU-69256

Researchers at Purdue University have developed an antibiotic drug formulation that reduces the toxicity of polymyxins, drugs of last resort for treating Gram-negative bacterial infections. Polymyxins administered by inhalation in high doses can cause pulmonary eosinophilia and hypersensitivity pneumonitis. The Purdue antibiotic formulation combines polymyxins (i.e. polymyxin B, colistin or colistimethate) with a nontoxic and water-soluble polymer. Upon treatment with the combination of polymyxin B and the polymer, about twice the human lung epithelial cells remained viable after 24 hours compared to treatment with polymyxin B alone, and the combination proved safe to mouse lungs. The formulation prepared by the researchers falls in the ideal size range for dry powder inhalers.

Technology Validation: The Purdue formulations are safer to human lung cells and mouse lungs compared to polymyxins alone. Their particle size falls in the ideal size range for use in dry powder inhalers.

Advantages:
-Safer
-Less toxic
-Ideal inhalable size

Applications:
-Inhaled Antibiotic
-Drug Delivery
-Dry Powder Inhaler

INTELLECTUAL PROPERTY:

Application Date: June 30, 2023
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: October 27, 2021
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: October 27, 2021
Type: NATL-Patent
Country of Filing: China

Patent Number: (None)
Issue Date: (None)

Application Date: October 27, 2021
Type: Foreign, Non-PCT
Country of Filing: Hong Kong
Patent Number: (None)
Issue Date: (None)

Application Date: January 1, 2021
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Zhou, Qi (Project leader)
Ahmed, Maizbha Uddin
Azad, Mohammad Abul Kalam
Li, Jian

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Antibiotic, Dry Powder Inhaler, Gram-negative Bacteria, Infectious Disease, Inhalation, Pharmaceuticals, Polymyxins, Respiratory Infection, Toxicity

SUSTAINED RELEASE SILVER NANOPARTICULATE COMPOSITIONS FOR TREATING MICROBIAL INFECTIONS

TRACK CODE:
2023-RISS-70028

Silver nanoparticles (AgNPs) have emerged as a potent antimicrobial agent to combat a broad range of microbial infections. The unique characteristics of AgNPs, such as their extensive surface area and silver's capacity to disrupt essential biological activities in microbes, contribute to their high effectiveness. Currently, there are silver coated implants and silver impregnated wound dressings that are utilized due to silver's antimicrobial properties. However, there are no treatment options using implantable sustained release nanoparticulate silver for deep seated, organ, and body cavity infections.

Researchers at Purdue University have developed three distinct implantable and absorbable sustained-release silver nanoparticle (AgNP) compositions for treating microbial infections in animals and humans. These compositions consist of an antimicrobial calcium sulfate hemihydrate (CSH) bead (AgNP–CSH bead), a poloxamer 407 gel (AgNP–gel), and a compressed absorbable gelatin sponge (AgNP–sponge). Each of these formulations encapsulates AgNPs and facilitates their prolonged dispersion. These compositions enable the delivery of high concentrations of antimicrobials at the site of infection, thereby inhibiting localized bacterial growth.

The researchers first demonstrated AgNP release from all three carrier media. Each carrier exhibited an initial burst of AgNP release, which was then sustained for at least 72 hours. The choice of carrier media offers flexibility in the release timing of AgNPs, thereby providing options for an immediate, high-concentration release or alternatively a steady, long-term release. Silver nanoparticles contained within gel and sponge exhibited antibacterial properties in vitro, with AgNP-gel having a bactericidal effect at the concentrations tested for a G- (E coli) and multidrug resistant G+ microbe (Staphylococcus pseudintermedius).

The innovation described here allows for immediate and localized treatment of wounds and surgical site infections. It also provides another treatment option for multidrug-resistant infections. Further, through choice of delivery mode and its corresponding rate of AgNP release, this innovation creates new avenues for personalizing antimicrobial treatment strategies based on specific patient needs and infection types.

Technology Validation:
- Release rate of the AgNPs were studied with the AgNP–gel constructs releasing 98.84% of the total initial AgNPs, AgNP–sponge constructs releasing 17.69%, and AgNP–CSH bead constructs releasing 1.03%
- Both AgNP carried by sponge and beads were effective against 102 CFU/ml E. coli while AgNP carried by gel was against 102-104 CFU/ml E. coli (MSRP results)

Advantages:
- Sustained released of AgNPs compared to traditional methods
- Depending on the distinct carrier construct, a range of release profiles is possible from the AgNP–gel's rapid burst release to the AgNP–sponge's steady, longer-term release
- Enhanced efficacy due to the AgNP–gel's high initial release of AgNPs

Applications:
- Localized treatment of wound infections by directly injecting the AgNP composite into tissue at wound sites.
- Wound healing and prevention of infections
- Treatment of multi-drug resistant (MDR) infections in veterinary and human medicine
- Drug delivery

Webpage for Additional Information:
For additional information on Dr. Marije Risselada, please visit her Purdue website:
https://vet.purdue.edu/directory/person.php?id=1077

INTELLECTUAL PROPERTY:

Application Date: October 6, 2023
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: October 5, 2023
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: October 6, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Risselada, Marije (Project leader)
Bates, Miriam Grace
Hendrix, Gena Kenitra
Pena Hernandez, Daniela Cecilia
Peterson-Levitt, Jennifer Lauren

CATEGORIES:

Biotechnology, Pharmaceuticals

KEYWORDS:

Antibacterial, Biomedical Engineering, Medical/Health, Silver nanoparticles

NOVEL POTENT AND SELECTIVE PRMT INHIBITORS FOR DEVELOPING THERAPEUTIC AGENTS

TRACK CODE:
2023-HUAN-70160

Researchers at Purdue University have developed a novel potent and selective protein arginine methyltransferase (PRMT) inhibitor. Cancer, cardiovascular diseases, inflammatory diseases, and diabetes have been linked to abnormal expression or activity of PRMTs. PRMTs share a highly conserved active, imposing challenges on developing potent and selective inhibitors. S-adenosyl-L-homocysteine (SAH) has a high affinity to PRMTs making SAH mimics an attractive strategy for developing therapeutic agents.

Purdue researchers have developed a focused library of SAH surrogate and profiled the active site of PRMTs. SAH Analog Library Unveils Ligand Preferences for each PRMT, serving as a rational guide to develop isoform-selective inhibitors. Additionally, a unique and novel binding pocket was discovered by a noncanonical but less polar SAH surrogate. This discovery leads to an opportunity for a new class of PRMT inhibitors to be developed.

Notably, there are a few exciting discoveries. 1. New, potent and selective inhibitors of type I PRMTs exhibit inhibitory activity less than 5 nanomolar. 2. Selective and potent inhibitor for PRMT1 exhibits over 7-fold selectivity over other type I PRMTs, which is the most selective inhibitor to date. 3. Potent and selective PRMT4 inhibitors demonstrate picomolar inhibitory activity and over 1,000-fold selectivity to other PRMTs. The prodrug also displayed efficacy in cellular, organoid, and animal models.

Technology Validation: This technology has been validated using SAHH-coupled assay, thermal shift assay, and co-crystallization. These methods demonstrated that these novel compounds selectively inhibit PRMT and do so in a unique and novel binding pocket.

Advantages:
-Novel mechanism of action
-Potent
-Selective

Applications:
-Cancer
-Inflammatory Diseases
-Diabetes

INTELLECTUAL PROPERTY:

Application Date: May 3, 2024
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: May 3, 2023

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Huang, Rong (Project leader)
Deng, Youchao

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Cancer, Diabetes, PRMT

NOVEL COVALENT PROTEIN INHIBITORS FOR TREATING MALARIA

TRACK CODE:
2023-FLAH-70246

Researchers at Purdue have discovered several small molecule drugs that significantly inhibit the growth of the asexual blood stage and the sporozoite hepatocyte stage of the Malaria parasite, Plasmodium falciparum. Recently, resistance to common anti-malaria medications has developed in Asia, South America, and Africa, necessitating the need to develop therapeutics to combat this rise in resistance.

The researchers selected an essential protein to the function of the malaria parasite to target with novel small molecule inhibitors. The selected protein has few known inhibitors and has key differences from the human ortholog. This key difference can be exploited to allow for stronger selection for only the malarial protein, reducing the potential of side effects. The researchers used a known covalent fragment library and were able to identify 6 molecules that showed significant inhibition in vitro at the low to mid micromolar level against three strains of P. falciparum, two of which are multi-drug resistant. Furthermore, these molecules showed high selectivity for the target enzyme in the malaria parasite over the human ortholog.

Technology Validation:
- Inhibitory activity of hit molecules tested in vitro against 3D7, CAM3.II K13 WT, and CAM3.II K13 C580Y malaria strains by exposing each one to a range of concentrations (0.5 – 500 μM) of each molecule and assessing the parasite viability 72 hours later.
- Selectivity of hit molecules for target enzyme over human ortholog assessed by exposing both to varying concentrations of each molecule and measuring the absorbance of the solution over time after initiation with a fluorescent substrate for the enzymes of study.

Advantages:
- Molecules show significant anti-malarial activity to multi-drug resistant strains
- High selectivity for malarial enzyme over human ortholog

Applications:
- Anti-malaria medications
- Medical diagnostics

Webpage for Additional Information:
Dr. Daniel Flaherty is an Associate Professor in the Department of Medicinal Chemistry and Molecular Pharmacology at Purdue University. Dr. Flaherty received his Ph.D. in pharmaceutical sciences from the University of Nebraska Medical Center. Following this, he became a post-doctoral researcher under the direction of Dr. Jeffrey Aubé at the University of Kansas. He has been awarded the Chaney Family Early Faculty Scholar Award in 2023, and the Best Oral Presentation at the 4th International Symposium on Frontiers in Molecular Science in 2022. Dr. Flaherty's lab is particularly interested in developing small molecule drugs for under-explored targets of therapeutic interest.
For further information, visit Dr. Daniel Flaherty's lab website:
https://www.flahertylab.com/

INTELLECTUAL PROPERTY:

Application Date: May 30, 2024

Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 2, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Flaherty, Daniel P (Project leader)
Imhoff, Ryan Dean
Ng, Caroline

CATEGORIES:
(No categories found)

KEYWORDS:
Inhibitor, Malaria

The following section contains non-confidential summaries of drug delivery innovations from Purdue University. These summaries are of the following innovations:

▪ Carrier-Free Nanoparticle Formulation with Good Circulation Stability
2016-YEO-67581 led by Yeo, Yoon (note: *in vivo* data)
▪ Improved Nanoparticle Based Targeted Drug Delivery to Cancerous Cells and Tissues
2017-YEO-67767 led by Yeo, Yoon
▪ Radiation-Controlled Release of Drugs for Chemo-Radiotherapy
2018-WON-68028 led by Won, You-Yeon
▪ Liposomal Carriers with High Drug Loading Capacity
2019-YEO-68485 led by Yeo, Yoon
▪ Nanoparticle Chemotherapeutic Delivery System that Aids in Development of Antitumor Immunity
2020-YEO-68760 led by Yeo, Yoon
▪ Soft, Flexible Non-Cationic Nanocapsules for Systemic Delivery of Nucleic Acids
2020-YEO-68868 led by Yeo, Yoon (note: *in vivo* data)
▪ Cancer Therapy Using an Immunoactive Nanocarrier of Immunogenic Cell Death Inducers
2022-YEO-69546 led by Yeo, Yoon (note: *in vivo* data)
▪ Novel Nanoparticles applied to Pancreatic Adenocarcinoma Treatment
2023-HAN-70164 led by Han, Bumsoo
▪ Nanopuff: A New Class RNA Therapeutic Carrier
2023-YEO-70458 led by Yeo, Yoon

CARRIER-FREE NANOPARTICLE FORMULATION WITH GOOD CIRCULATION STABILITY

TRACK CODE:
2016-YEO-67581

Researchers at Purdue University have developed a method to produce pharmaceutical nanocrystals comprised of more than 85 percent of their respective active ingredients. These nanocrystals are coated with albumin to prevent the immune response and allow the nanocrystals to target cancerous cells unhindered. These nanocrystals have the potential to increase the effectiveness of a wide range of drugs as they contain a much greater percentage of active ingredients, allow for increased bioavailability, and avoid immune recognition.

Advantages:
-Increases bioavailability of insoluble drugs
-Fewer adverse effects
-Avoids immune recognition

Potential Applications:
-Drug formulation

Related Publications:
J. Park, et al., Albumin-coated nanocrystals for carrier-free delivery of paclitaxel. Journal of Controlled Release (2016). http://dx.doi.org/10.1016/j.jconrel.2016.12.040

Enhancing Docetaxel Delivery to Multidrug-Resistant Cancer Cells with Albumin-Coated Nanocrystals
Sheryhan F. Gad, Joonyoung Park, Ji Eun Park, Gihan N. Fetih, Sozan S. Tous, Wooin Lee, and Yoon Yeo
Molecular Pharmaceutics 2018 15 (3), 871-881
DOI: 10.1021/acs.molpharmaceut.7b00783
https://pubs.acs.org/doi/10.1021/acs.molpharmaceut.7b00783

A Comparative In Vivo Study of Albumin-Coated Paclitaxel Nanocrystals and Abraxane
Joonyoung Park, Ji Eun Park, Victoria E. Hedrick, Karl V. Wood, Connie Bonham, Wooin Lee, Yoon Yeo,
First published: 23 March 2018
https://doi.org/10.1002/smll.201703670

Expanding therapeutic utility of carfilzomib for breast cancer therapy by novel albumin-coated nanocrystal formulation,
Journal of Controlled Release,
Ji Eun Park, Joonyoung Park, Yearin Jun, Yunseok Oh, Gongmi Ryoo, Yoo-Seong Jeong, Hytham H. Gadalla, Jee Sun Min, Jung Hwan Jo, Myung Geun Song, Keon Wook Kang, Soo Kyung Bae, Yoon Yeo, Wooin Lee,
Volume 302, 2019,
Pages 148-159,
ISSN 0168-3659,
https://doi.org/10.1016/j.jconrel.2019.04.006.

(https://www.sciencedirect.com/science/article/pii/S0168365919301981)

INTELLECTUAL PROPERTY:

Application Date: June 15, 2017
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,398,651
Issue Date: September 3, 2019

Application Date: June 16, 2016
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Yeo, Yoon (Project leader)
Park, Joonyoung
Sun, Bo

CATEGORIES:

Biotechnology, Pharmaceuticals

KEYWORDS:

Biotechnology, Drug Delivery, Medical/Health, Micro & Nanotechnologies, Pharmaceuticals

IMPROVED NANOPARTICLE BASED TARGETED DRUG DELIVERY TO CANCEROUS CELLS AND TISSUES

TRACK CODE:
2017-YEO-67767

Cancer is a group of diseases involving abnormal cell growth. Currently there are more than 100 types of identified cancer that affect human beings as well as animals. In 2016, there were an estimated 1,685,210 new human cancer cases diagnosed and 595,690 cancer deaths in the United States alone (Cancer Statistics 2016 - American Cancer Society, Inc.). Nanoparticles (NPs) have been considered a promising carrier of chemotherapeutic drugs, but are limited in delivery to tumors due to the diverse nature of the disease. There currently exists the need to leverage the enhanced permeability and retention effect to deliver NPs beyond the current levels possible.

Researchers at Purdue University have developed a method for preparing polyol-modified nanoparticles for targeted delivery to cancerous cells and tissues via transcytosis across the peritumoral endothelium. This method does not depend on the leakiness of the vasculature like traditional nanoparticle formulations, but actively interacts with the vascular lining to enter tumors.

Advantages:
-Increases the amount of drugs deliver to solid tumors
-Reduces the required dose and related side effects
-Does not depend on long-term circulation and passive extravasation

Potential Applications:
-Cancer treatment
-Drug delivery

Related Publication:
Quinic Acid-Conjugated Nanoparticles Enhance Drug Delivery to Solid Tumors via Interactions with Endothelial Selectins
Small 14 (50), 1803601
DOI: https://onlinelibrary.wiley.com/doi/full/10.1002/smll.201803601

INTELLECTUAL PROPERTY:

Application Date: May 8, 2018
Type: NATL-Patent
Country of Filing: Japan
Patent Number: 7164205
Issue Date: October 24, 2022

Application Date: May 8, 2018
Type: NATL-Patent
Country of Filing: India
Patent Number: 398404
Issue Date: June 2, 2022

Application Date: May 8, 2018
Type: NATL-Patent
Country of Filing: Canada
Patent Number: 3,062,624
Issue Date: March 29, 2022

Application Date: November 8, 2019
Type: NATL-Patent
Country of Filing: United States
Patent Number: 11,154,514
Issue Date: October 26, 2021

Application Date: January 8, 2020
Type: NATL-Patent
Country of Filing: China
Patent Number: (None)
Issue Date: (None)

Application Date: December 8, 2019
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: May 8, 2018
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: May 8, 2017
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Xu, Jun

CATEGORIES:
Pharmaceuticals, Medical/Health

KEYWORDS:
Cancer, Cancer Therapy, Drug Delivery, Medical/Health, Nanoparticles, Pharmaceuticals

RADIATION-CONTROLLED RELEASE OF DRUGS FOR CHEMO-RADIOTHERAPY

TRACK CODE:
2018-WON-68028

Over 60,000 new cases of head and neck cancer were diagnosed within the US in 2016, with 20 percent of these cases resulting in death. The current treatment of advanced head and neck cancer involves surgery followed by radiation, i.e. concurrent radiation, systemic chemotherapy, induction chemotherapy, or radiation alone. However, the surgeries are difficult, and radiation therapy afterwards is beneficial only for a few months. Conventional chemotherapy involves administering drugs through veins into the bloodstream, which involves high levels of toxicity and specific eligibility requirements. In addition, only 5 percent of the drug actually reaches the tumor site. There is need of a method for treating locally advanced tumors more effectively.

Researchers at Purdue University have developed a radiation-controlled drug release formulation. The formulation allows toxicity and side effects associated with radiation from chemotherapy to be minimized by co-encapsulating the drug within protective capsules and injecting the solution into the patient's tumor before receiving normal radiotherapy. The release rate of the drug is controlled by radiation dose and frequency, allowing maintained drug concentration within the therapeutic level and toxic threshold over an extended period of time. This technology would be used to help medical/surgical/radiation/interventional oncologists who want to apply chemo-radiotherapy to cancer patients with tumors safely and effectively without compromising their quality of life.

Advantages:
-Controlled drug release
-Minimized toxicity
-Effectiveness
-Longer lifespan

Potential Applications:
-Chemo-radiotherapy

Related Publication:
Radioluminescent nanoparticles for radiation-controlled release of drugs
https://doi.org/10.1016/j.jconrel.2019.04.033

INTELLECTUAL PROPERTY:

Application Date: March 2, 2020
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: February 18, 2020
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: February 11, 2020
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: September 7, 2018
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: September 8, 2017
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Won, You-Yeon (Project leader)
Lee, Jaewon
Misra, Rahul

CATEGORIES:
Chemical Engineering, Medical/Health

KEYWORDS:
Cancer, Cancer Therapy, Chemical Engineering, Chemotherapy, Drug Delivery, Medical/Health, Radiation

LIPOSOMAL CARRIERS WITH HIGH DRUG LOADING CAPACITY

TRACK CODE:
2019-YEO-68485

Researchers at Purdue University have developed a method for encapsulating drugs in liposomes with higher efficiency than competing methods. Liposomal encapsulation of chemotherapeutic agents is widely used to reduce nonspecific side effects, because liposomes will preferentially target the tumor's leaky vasculature. Liposomes are typically loaded with drugs using pH gradients. However, some drugs, such as gemcitabine, a first-line treatment for pancreatic cancer, have proven difficult to load into liposomes with reasonable efficiency. In a proof-of-concept study using this new method, gemcitabine had a loading efficiency of 9.4 - 10.3 wt% compared to 0.14 - 3.8 wt% by conventional methods. Applications for this technology include in the development of novel drug formulations for the treatment of cancer.

Advantages:
-Higher drug loading efficiency
-Good stability and sustained release of drug

Potential Applications:
-Pharmaceutical formulations

Publications:
Development of Liposomal Gemcitabine with High Drug Loading Capacity
Hassan Tamam, Jinho Park, Hytham H. Gadalla, Andrea R. Masters, Jelan A. Abdel-Aleem, Sayed I. Abdelrahman, Aly A. Abdelrahman, L. Tiffany Lyle, and Yoon Yeo
Molecular Pharmaceutics 2019 16 (7), 2858-2871
DOI: 10.1021/acs.molpharmaceut.8b01284

INTELLECTUAL PROPERTY:

Application Date: July 16, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 16, 2020
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: January 16, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Yeo, Yoon (Project leader)
Tamam, Hassan

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Cancer, Drug Delivery, drugs, formulations, Liposomes, loading, Pharmaceuticals

NANOPARTICLE CHEMOTHERAPEUTIC DELIVERY SYSTEM THAT AIDS IN DEVELOPMENT OF ANTITUMOR IMMUNITY

TRACK CODE:
2020-YEO-68760

Researchers at Purdue University have developed a nanoparticle-based system for sustained release of chemotherapeutic drugs at low doses that leaves antitumor immune cells with full functionality. Chemotherapy has been a mainstay in cancer treatment because of the anti-proliferative effects it imposes on tumor cells. Several chemotherapeutic treatment options result in generation of cancer antigens that aid in the activation of the host's antitumor immune response. Paradoxically, these treatment options also damage immune cells, diminishing their antitumor effect. In response to this shortcoming of traditional chemotherapies, Purdue's researchers developed a system to deliver chemotherapeutics and keep immune cells healthy. Their nanoparticle delivery system also elicits an enhanced immunogenic response compared to other chemotherapeutic delivery options along with increasing the metabolic stability and tumor retention of chemotherapeutic drugs. The chemotherapeutic, carfilzomib, formulated with this delivery system showed consistently greater antitumor effects against two tumor types in a mouse model compared to the cyclodextrin-solubilized drug.

Advantages
-Sustained Release of Chemotherapeutic Drug
-Enhanced Immune Response
-Increased Drug Metabolic Stability

Potential Applications
-Chemotherapy
-Cancer Treatment

Related Publication:
Sustained Delivery of Carfilzomib by Tannic Acid-Based Nanocapsules Helps Develop Antitumor Immunity
Nano Lett. 2019, 19, 11, 8333-8341
DOI: 10.1021/acs.nanolett.9b04147
Domain: Pharmaceuticals

INTELLECTUAL PROPERTY:

Application Date: March 8, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: September 11, 2020
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)

Issue Date: (None)

Application Date: September 13, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Taha, Maie

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Cancer, Cancer Drug, Cancer Immunotherapy, Chemotherapy, Drug Delivery, Drug Development, Drug Formulation, immunotherapy, Nanoparticle, Oncology, Pharmaceuticals

SOFT, FLEXIBLE NON-CATIONIC NANOCAPSULES FOR SYSTEMIC DELIVERY OF NUCLEIC ACIDS

TRACK CODE:
2020-YEO-68868

Researchers at Purdue University have developed a soft, flexible non-cationic nanocapsule for systemic delivery of RNA therapeutics. Compared to non-viral vectors, typically based on cationic lipids or polymers, the Purdue technology, dubbed "Nanosac", performs well in the anionic environment prevalent in the body. Nanosac showed efficient cellular uptake in cancer cells. Nanosac was taken up less by macrophages and penetrated more into tumor tissues than hard nanoparticle counterparts. Nanosac was also non-toxic to cells. In a mouse colon cancer model using CT26 cells, siRNA targeting the PD-1/PD-L1 immune checkpoint interaction was delivered via Nanosac systemically, and the treated group showed a significant attenuation in tumor growth.

Advantages:
-Enables systemic delivery of RNA therapeutics
-Avoids toxicity and nonspecific protein adsorption
-Enhanced transvascular and interstitial delivery
-Improved intratumoral penetration
-Safer, more scalable, less heterogeneous, and less immunogenic than cell-derived vesicles

Potential Applications:
-Delivery of RNA-based Gene Therapy

Technology Validation: Cellular uptake and toxicity were evaluated in cell culture, and efficacy of a therapeutic delivered by Nanosac was validated in a mouse model.

Related Publications:
Nanosac, a Noncationic and Soft Polyphenol Nanocapsule, Enables Systemic Delivery of siRNA to Solid Tumors
ACS Nano 2021, 15, 3, 4576–4593
https://doi.org/10.1021/acsnano.0c08694

INTELLECTUAL PROPERTY:

Application Date: May 31, 2023
Type: NATL-Patent
Country of Filing: Republic of Korea
Patent Number: (None)
Issue Date: (None)

Application Date: May 2, 2023
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: October 27, 2021
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: October 27, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: October 27, 2021
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: November 6, 2020
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Kim, Hyungjun

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Cancer, Drug Delivery, Gene Therapy, Immune Checkpoint Blockade, Nanocapsule, Oncology, Pharmaceuticals, RNA, Solid Tumor

CANCER THERAPY USING AN IMMUNOACTIVE NANOCARRIER OF IMMUNOGENIC CELL DEATH INDUCERS

TRACK CODE:
2022-YEO-69546

Purdue University researchers have developed a nanoparticle delivery system to enhance the efficacy of immunogenic cell death (ICD) inducing cancer drugs. ICD inducers are being used to improve the scope of immune checkpoint blockade therapy, which is effective in as few as 20 percent of patients for some cancer types. Unfortunately, traditional ICD inducers are limited by their immunotoxicity and insufficient adjuvanticity. The Purdue researchers designed a nanoparticle drug carrier to address these shortcomings. This technology encapsulates ICD inducers in functionalized nanoparticles. The nanoparticles are s designed to release the ICD inducers in a sustained manner, and the nanoparticles are functionalized with a chemoattractive agent to recruit immune cells and prevent an immunosuppressive microenvironment. The nanoparticle's chemoattractive properties were validated in an in vitro cell migration assay and in vivo anti-tumor immune responses. Tumors grew slower in mice treated with paclitaxel encapsulated in the functionalized nanoparticle than those treated with paclitaxel in non-functionalized nanoparticles or with a mixture of paclitaxel in non-functionalized nanoparticles and the chemoattractive agent in its free form.

Technology Validation: The functionalized nanoparticle attracts immune cells in a cell migration assay and slows tumor growth in a mouse xenograft model.

Advantages

-Less toxic
-Improves anti-tumor immune response
-Promises to expand the scope of immune checkpoint blockade therapy

Applications:
-Cancer Treatment

Related Publications:
Systemic delivery of paclitaxel by find-me nanoparticles activates anti-tumor immunity and eliminates tumors. ACS Nano. (2024) 18: 3681–3698. doi: 10.1021/acsnano.3c11445

INTELLECTUAL PROPERTY:

Application Date: January 19, 2024
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: July 20, 2022
Type: PCT-Gov. Funding

Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: July 20, 2022
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: July 20, 2022
Type: NATL-Patent
Country of Filing: Japan
Patent Number: (None)
Issue Date: (None)

Application Date: July 20, 2022
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: July 21, 2021
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Kwon, Soonbum

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
ATP, Cancer, Chemoattractant, Combination Therapy, Drug Delivery, Immune Checkpoint Blockage, Immunofuctional, Immunogenic Cell Death, immunotherapy, Oncology, Pharmaceuticals, Polymeric Nanoparticles, Sustained Release

NOVEL NANOPARTICLES APPLIED TO PANCREATIC ADENOCARCINOMA TREATMENT

TRACK CODE:
2023-HAN-70164

Researchers at Purdue have developed a novel nanoparticle formulation from common reagents that can deliver the FDA approved drug Vorapaxar (VPX) to cells for the potential treatment of pancreatic adenocarcinoma (PDAC) tumors. Currently, VPX is used as a treatment to reduce the chance of cardiovascular issues such as strokes and myocardial accidents. Its potential as an anti-cancer drug targeting the PAR1 cell-membrane protein has been studied, however there has been difficulty in delivering the free VPX to the protein-of-interest, due to unique geometry of PAR1 protein configuration. The Purdue invention uses a microfluidic apparatus to both synthesize the nanoparticles and to encapsulate the free VPX within them in order to enhance the cell membrane permeability.

Technology Validation:
The cytotoxicity of the VPX-NPs was tested by treating PANC-1 and CAF19 pancreatic cancer cell lines with VPX-NPs. It was found that the VPX-NPs reduced the viability of the PANC-1 cells by 25% and the CAF19 cells by 50%. The encapsulation efficiency was found to be 75% and 70% for the VPX-NPs synthesized at 20.5 and 205 mL/hr, respectively. Finally, the drug loading efficiency was 55% and 50% for the 20.5 mL/hr and 205 mL/hr samples, respectively.

Advantages:
- Reduce the cell viability of the two tested pancreatic cancer cell lines by 25% and 50 % at 20 uM VPX.
- Can be synthesized at high flow rates within the microfluidic cell - Low polydispersity index (between 0.1 – 0.2) from lowest to highest flow rates.
- Materials to produce NPs are common and inexpensive.

Applications:
- Pancreatic Cancer treatment
- Medical diagnostics
- Biological investigation of PAR1 protein

INTELLECTUAL PROPERTY:

Application Date: April 18, 2024
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 18, 2024
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: April 18, 2023
Type: Provisional-Gov. Funding

Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Han, Bumsoo (Project leader)
Shen, Yingnan
Yeo, Yoon

CATEGORIES:
Pharmaceuticals, Medical/Health

KEYWORDS:
Anti-cancer, Medical/Health, Microfluidics, Pharmaceuticals

NANOPUFF: A NEW CLASS RNA THERAPEUTIC CARRIER

TRACK CODE:
2023-YEO-70458

Researchers at Purdue University have developed an effective carrier system for RNA drugs. Labeled "Nanopuff," this technology helps deliver RNA therapeutics to target cells via systemic administration to treat cancers, infectious diseases, and neurological disorders. Currently lipid and cationic nanoparticles are used as delivery systems for RNA, but their weaknesses are the limited control of biodistribution and the potential toxicity due to the positive charge. They also require complex preparation procedures.

Unlike the lipid and cationic nanoparticles, Nanopuff is made of polydopamine, which brings no positive charges. Nanopuff promotes ease of preparation and fulfills the unmet need for efficient RNA delivery. The technology alleviates safety concerns attributed to traditional cationic carriers and protects RNA from its harsh physiological environment. Nanopuff also enhances cellular uptake and avoids toxicity. It can be implemented as a simple, efficacious pharmacological treatment in a variety of areas, ranging from infectious diseases to cancer.

Technology Validation:
The optimal condition for siRNA binding to polydopamine was determined. The optimized form of Nanopuff showed a slightly negative charge and a z-average of 100 nm and protected siRNA from the RNase.

Advantages:
-Ease of use
-Enhanced safety profile
-Versatile

Applications:
-Pharmacology
-Infectious disease
-Neurological and cancer treatments

INTELLECTUAL PROPERTY:

Application Date: October 16, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Yeo, Yoon (Project leader)
Kim, Woojun

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:
Nanoparticles, nanopuff, polydopamine, polyphenol, RNA delivery, siRNA

The following section contains non-confidential summaries of excipient innovations from Purdue University. These summaries are of the following innovations:

▪ Sustained Release Formulation of Griseofulvin for Treatment of Wet Macular Degeneration
2020-YEO-69132 led by Yeo, Yoon
▪ Sequence-Controlled Polymers for Sustained Release of Pharmaceutical Ingredients
2022-WON-69547 led by Won, You-Yeon
▪ Nanoparticle-based Opioid Abuse Deterrent Formulations
2022-YEO-69643 led by Yeo, Yoon
▪ Method for Excipient-free Lyophilization of Drugs for Respiratory Treatment
2023-WON-69925 led by Won, You-Yeon
▪ Innovative Polymeric Excipients for Enhancing Stability and Shelf-Life of Protein Therapeutics
2024-WON-70668 led by Won, You-Yeon

SUSTAINED RELEASE FORMULATION OF GRISEOFULVIN FOR TREATMENT OF WET MACULAR DEGENERATION

TRACK CODE:
2020-YEO-69132

Researchers at Purdue University have developed a formulation that allows sustained release of drugs for treatment of wet age-related macular degeneration (AMD). Currently, treatment for wet AMD involves intravitreal injections of anti-VEGF agents. However, around 40% of patients do not respond to anti-VEGF therapy. Individuals that do respond often incur adverse effects, such as increased intraocular pressure or endophthalmitis, because of repeated intravitreal injections. To address these pitfalls, Purdue researchers have developed a polymeric nanoparticle formulation for long term ocular delivery of griseofulvin (GRF), an antifungal drug repurposed for antiangiogenesis, as an alternative wet AMD therapy. The particle size and nanoparticle component molecular weights were optimized to limit burst release of GRF. Release studies of nanoparticle-encapsulated GRF displayed 5.6% release in 1 hour and ~75% release over the course of 30 days. Cell based proliferation assays with human retinal endothelial cells demonstrate the efficacy of this sustained release formulation. GRF-loaded nanoparticles inhibited the proliferation of human retinal endothelial cells about half as much as free GRF over 48 hours at a concentration equivalent to 100 micromolar GRF, as expected for a slow-release formulation. This technology could prove to be a safer and more effective treatment option against wet AMD upon further development.

Advantages
-Novel Age-Related Macular Degeneration Target
-Reduce Frequency of Ocular Injections
-Less Expensive than Existing Formulations for AMD

Applications
-Wet Age-Related Macular Degeneration
-Sustained Drug Release

Technology Validation:
Dynamic light scattering displayed homogenous size distribution of GRF-encapsulated nanoparticles. Burst release was reduced by optimizing particle size and molecular weight of encapsulating polymers. Scanning electron microscopy showed spherical particles with smooth surfaces. Cell based proliferation assays show comparable activity of GRF-loaded nanoparticles to free GRF.

INTELLECTUAL PROPERTY:

Application Date: December 22, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2021
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)

Issue Date: (None)

Application Date: June 24, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2021
Type: NATL-Patent
Country of Filing: India
Patent Number: (None)
Issue Date: (None)

Application Date: June 24, 2021
Type: NATL-Patent
Country of Filing: China
Patent Number: (None)
Issue Date: (None)

Application Date: June 26, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Chobisa, Dhawal
Corson, Timothy

CATEGORIES:
Pharmaceuticals

KEYWORDS:
Age Related Macular Degeneration, AMD, Griseofulvin, Intraocular Injection, Pharmaceuticals, PLGA microparticles, PLGA Nanoparticles, Sustained Release, Wet macular degeneration

SEQUENCE-CONTROLLED POLYMERS FOR SUSTAINED RELEASE OF PHARMACEUTICAL INGREDIENTS

TRACK CODE:
2022-WON-69547

Purdue University researchers have produced sequence-controlled polymers for pharmaceutical formulations with superior sustained release properties. Poly-(lactic-co-glycolic acid) (PLGA) is a common material used in controlled drug delivery systems, but limitations in its manufacturing process result in an uncontrollable initial release of the intended active pharmaceutical ingredient (API). Seeking to alleviate this problem, researchers at Purdue University have developed a method for manufacturing PLGA that results in a microstructure capable of housing a uniform distribution of the API, reducing hard to predict initial bursts and allowing for slower, more sustained release behavior. This first-in-class method stands as a proof of concept and paves the way for a significant improvement in the controllability of drug delivery.

Related Publication:
Strategy for Synthesis of Statistically Sequence-Controlled Uniform PLGA and Effects of Sequence Distribution on Interaction and Drug Release Properties
ACS Macro Lett. 2021, 10, 12, 1510–1516
https://doi.org/10.1021/acsmacrolett.1c00637

Advantages:
-More homogeneous PLGA microstructure
-Facilitates sustained release of API
-Significantly reduces the initial burst release of API

Applications:
-Pharmaceuticals
-Drug delivery systems
-Non-clinical PLGA products

Technology Validation:
This technology has been validated through the laboratory testing and kinetics analysis of prototypes. Molecular weight and sequence properties were determined from NMR. Polymer physical properties were analyzed by dynamic light scattering, transmission electron microscopy, and scanning electron microscopy. Drug release kinetics were demonstrated with paclitaxel in buffer.

INTELLECTUAL PROPERTY:

Application Date: January 4, 2024
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: May 10, 2022
Type: PCT-Gov. Funding
Country of Filing: WO

Patent Number: (None)
Issue Date: (None)

Application Date: May 10, 2022
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: July 13, 2021
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Won, You-Yeon (Project leader)
Yoo, Jin

CATEGORIES:
Pharmaceuticals, Materials and Manufacturing

KEYWORDS:
biopharmaceutical, Biopharmaceutical Manufacturing, Biopharmaceuticals, Drug Delivery, Drug Formulation, Drug Manufacturing, paclitaxel, Pharmaceuticals, PLGA, Sustained Release

NANOPARTICLE-BASED OPIOID ABUSE DETERRENT FORMULATIONS

TRACK CODE:
2022-YEO-69643

NCS: Researchers at Purdue University have developed a new method to deter opioid tampering. Drug abusers may tamper with opioids to experience the analgesic effects as quickly as possible. Tampering methods include pulverizing the drugs or extracting them with common household solvents such as ethanol or vinegar. Abuse deterrent formulations (ADFs) are used to limit the physical and chemical tampering of drugs without compromising their therapeutic effects. However, there are publicized methods to circumvent ADFs. The Purdue researchers' method to prevent opioid tampering uses nanoparticles along with ADFs. The researchers encapsulated opioid compounds in nanoparticles resistant to household solvents to prevent solvent extraction. The nanoparticle-based ADF is also resistant to pulverization because they are too small to crush. What's more, if injected, nanoparticles preferentially accumulate in the liver, where they are converted to inactive forms. The nanoparticle ADFs used by the researchers also prevent physical manipulation by gelling when subjected to liquids.

Technology Validation: When thebaine, a model opioid drug, was encapsulated in nanoparticles and mixed with excipients, all the drug remained in the powder, unextracted after subjection to common solvents like ethanol, acetone or sodium bicarbonate solution for 1 h. Tablets made with nanoencapsulated thebaine and the excipients formed a gel that cannot be injected when added to aqueous solvents and did not release thebaine upon crushing followed by extraction.

Advantages
-Prevents organic solvent extraction
-Resistant to physical crushing or gelling

Applications
-Preventing opioid tampering

INTELLECTUAL PROPERTY:

Application Date: April 18, 2024
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: October 17, 2022
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: October 17, 2022
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)

Issue Date: (None)

Application Date: October 18, 2021
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Yeo, Yoon (Project leader)
Gad, Sheryhan F

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Abuse deterrent formulation, Drug abuse, Nanoparticles, Opioid, Pharmaceuticals

METHOD FOR EXCIPIENT-FREE LYOPHILIZATION OF DRUGS FOR RESPIRATORY TREATMENT

TRACK CODE:
2023-WON-69925

Researchers at Purdue University have developed an excipient (cryoprotectants)-free method of lyophilization of aqueous polymer micelle suspensions. Lyophilization is a pharmaceutical manufacturing method that provides drugs with improved shelf lives and reconstitution characteristics. Excipients like binders and glidants are typically added to the active pharmaceutical ingredient to improve formulation or release properties of the drug, and cryoprotectants may be added for lyophilized drug forms. However, excipients can be determinantal to the pharmacological properties of a drug formulation in certain cases. In a formulation of polymer lung surfactants (PLS), excipients negatively impact the air-water surface-mechanical properties of the formulation. The Purdue researchers' method allows excipient-free production of a PLS comprised of poly(ethylene glycol) (PEG)-based block copolymer micelles, which can be used to treat acute respiratory distress syndrome (ARDS) and other respiratory problems. The Purdue researchers' method allows use of lyophilization for production of PLS, providing shelf-stable, easily reconstituted, and effective drugs.

Technology Validation: In vivo therapeutic efficacy of a lung surfactant (in improving the compliance of injured lungs) correlates with the high-surface-pressure-generating (surface-tension-reducing) capability of the surfactant. For this reason, the initial screening of candidate lung surfactant materials can be conveniently accomplished with in vitro evaluation of the surface pressure-area (p-A) isotherms of the materials. The researchers have confirmed that the surface pressure and also nanostructural characteristics of PLS are unchanged after the lyophilization treatment.

Related Publications: Seyoung Kim, Daniel J. Fesenmeier, Sungwan Park, Sandra E. Torregrosa-Allen, Bennett D. Elzey, and You-Yeon Won. "Pulmonary Pharmacokinetics of Polymer Lung Surfactants Following Pharyngeal Administration in Mice", Biomacromolecules 23(6), 2471-2484, 2022 (DOI: 10.1021/acs.biomac.2c00221).

H. C. Kim, M. V. Suresh, V. V. Singh, D. Q. Arick, D. A. Machado-Aranda, K. Raghavendran, Y.-Y. Won, "Polymer Lung Surfactants", ACS Applied Bio Materials 1(3), 581-592, 2018 (DOI: 10.1021/acsabm.8b00061).

Advantages:
-Drug can be administered as dry powder or liquid formulation for aerosolized delivery
-High shelf-life
-Low surface tension at the air-water interface that helps maintain the surfactant property of PLS
-Low/no toxicity

Applications:
-Manufacturing of drugs for treating acute respiratory distress syndrome (ARDS)
-Possible treatment for acute lung injury (ALI) and neonatal respiratory distress syndrome (NRDS)

INTELLECTUAL PROPERTY:

Application Date: October 4, 2023
Type: PCT-Patent

Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: October 5, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Won, You-Yeon (Project leader)
Fesenmeier, Daniel James
Kim, Seyoung
Park, Sungwan

CATEGORIES:
Pharmaceuticals, Chemical Engineering

KEYWORDS:
Excipient, Excipient-free, Lyophilization, Micelle, Pharmaceuticals, Polymer lung surfactants

INNOVATIVE POLYMERIC EXCIPIENTS FOR ENHANCING STABILITY AND SHELF-LIFE OF PROTEIN THERAPEUTICS

TRACK CODE:
2024-WON-70668

Researchers at Purdue University have engineered novel polymeric excipients that enhance the stability of protein biologics. Monoclonal antibody-based therapies are increasingly being developed to treat cancer, autoimmune, and degenerative diseases. However, antibodies can be susceptible to denaturation and aggregation, and thus present challenges for manufacturing and storage. To combat these pitfalls, surfactants are used to mitigate protein aggregation, but are notoriously limited in polydispersity, purity, and stability. Improving therapeutic protein formulations is therefore crucial for reducing patient health risks and minimizing the economic burden on the healthcare industry.

Researchers at Purdue University have developed polymer excipients to help scientists and pharmaceutical companies bolster the stability of protein therapeutics by suppressing protein aggregation and denaturation. Not only are these alternative compositions based on FDA-approved and biocompatible chemistries, but the excipients also offer tailored thermodynamic properties. The engineered formulations will be monumental in advancing formulations, storage conditions, and product purity of therapeutic antibody solutions.

Technology Validation:
Accelerated dynamic light scattering experiments highlighted the excipient's exceptional efficacy in preserving antibody protein stability, surpassing conventional excipients such as polysorbates under high-temperature conditions. Complementary circular dichroism spectroscopy results revealed conformational alterations associated with aggregation, with the new polymer excipients consistently demonstrating a significant protective effect by mitigating negative shifts at the 220 nm wavelength, indicative of changes in secondary structure.

Advantages:
-Applicable to a wide range of protein biologics
-Reduces health risks for patients
-Minimizes economic losses for pharmaceutical companies and healthcare systems
-Improves drug stability and lengthens shelf-life of antibody therapeutics

Applications:
-Poloxamers (a.k.a., pluronics)
-Surfactants, notably polysorbates
-Protein biologics products

INTELLECTUAL PROPERTY:

Application Date: April 16, 2024
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Won, You-Yeon (Project leader)
Jun, Taesuk

CATEGORIES:
Pharmaceuticals, Medical/Health

KEYWORDS:
air-water interface, Antibodies, excipients, Medical/Health, Pharmaceuticals, protein denaturation, Stability

The following section contains non-confidential summaries of diagnostic innovations from Purdue University. These summaries are of the following innovations:

▪ Diagnostic Panel of Modified Proteins for Breast Cancer
2017-TAO-67681 led by Tao, Weiguo Andy
▪ Liquid Biopsy for Determining Breast Cancer Subtypes
2019-TAO-68555 led by Tao, Weiguo Andy
▪ Assessing In Vivo Efficacy of Drug Therapeutics by Monitoring Proteins from Extracellular Vesicles
2020-TAO-69103 led by Tao, Weiguo Andy
▪ Direct Isolation of Exosome and Other Extracellular Vesicle Particles for Chemotherapeutic Outcomes Assessment, Disease Diagnosis, and Monitoring Disease Progression
2022-TAO-69815 led by Tao, Weiguo Andy

DIAGNOSTIC PANEL OF MODIFIED PROTEINS FOR BREAST CANCER

TRACK CODE:
2017-TAO-67681

Breast cancer is the most frequently diagnosed cancer in women in the U.S. and Europe and the second leading cause of cancer deaths in American women. Early intervention and treatment will produce healthier, more successful outcomes for patients. Diagnostic markers are important for prognosis, diagnosis, and monitoring disease and changes in health status. Diagnostic markers are important for predicting and monitoring response to treatment and selecting appropriate treatment. Identifying these health issues accurately is extremely important for correct treatment. Improved diagnostics would greatly improve the health of these women. Unfortunately, there are currently no effective biomarkers reported that can differentiate between a benign or malignant breast lesion or tumor that has been visually detected by an imaging method.

Researchers at Purdue University have developed a diagnostic panel of modified proteins for breast cancer. The breast cancer diagnosis may be a determination of whether a breast tissue lesion or tumor is benign or malignant. The diagnostic breast cancer panel provides a method for diagnosing a malignant tumor based on a blood test. Using this diagnostic method as a screening test is a promising advancement for people who are susceptible to developing breast cancer, need periodic monitoring after surgery, or possess a high genetic risk for the disease. Early diagnosis and identification of the disease and changes in health status may permit earlier intervention and treatment that will produce healthier, more successful outcomes for patients.

Advantages:
-Breast cancer diagnostic markers
-Distinguishes between benign or malignant tumors and skin lesions
-Early diagnosis may permit earlier intervention and treatment

Potential Applications:
-Breast cancer screening test
-Breast cancer diagnostic test
-Monitor treatment effectiveness

Related Publications:
Chen, I-Hsuan, et al. Phosphoproteins in Extracellular Vesicles as Candidate Markers for Breast Cancer. Proceedings of the National Academy of Sciences of the United States of America. 2017, 114 (12), pp 3175-3180. DOI10.1073/pnas.1618088114.

INTELLECTUAL PROPERTY:

Application Date: January 8, 2018
Type: Utility Patent
Country of Filing: United States
Patent Number: 11,480,573
Issue Date: October 25, 2022

Application Date: January 6, 2017
Type: Provisional-Patent
Country of Filing: United States

Patent Number: (None)
Issue Date: (None)

PEOPLE:
Tao, Weiguo Andy (Project leader)
Andaluz, Hillary
Chen, I-Hsuan
Ilyuk (Iliuk), Anton B.
Pan, Li

CATEGORIES:
Medical/Health, Chemistry and Chemical Analysis

KEYWORDS:
Breast Cancer, Cancer, Cancer Screening, Chemistry and Chemical Analysis, Diagnostics, Medical Diagnostics, Medical/Health

LIQUID BIOPSY FOR DETERMINING BREAST CANCER SUBTYPES

TRACK CODE:
2019-TAO-68555

Researchers at Purdue University have developed a method that can differentiate cancer subtypes and aid in early detection for breast cancer. Early diagnosis and identification of the disease may permit earlier intervention and treatment and more successful outcomes for patients. Blood testing aka "liquid biopsy" for early diagnosis and monitoring of cancer is highly attractive; however, the number and complexity of various proteins in the blood makes the identification of appropriate diagnostic markers a serious challenge. This innovation reduces the complexity of the liquid biopsy samples. Extracellular vesicles, membrane encapsulated particles whose contents are protected from enzymes in the blood, are isolated from the blood and used as a source of biomarkers. This technology isolates extracellular vesicles from a patient sample and analyzes their contents to differentiate breast cancer subtypes. With knowledge of the specific breast cancer subtype, doctors can better tailor treatment for the patient.

Advantages:
-Differentiate cancer subtypes
-Allows for tailored treatment

Potential Applications:
-Breast cancer diagnosis
-Subtype identification

INTELLECTUAL PROPERTY:

Application Date: September 3, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 3, 2020
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 3, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Tao, Weiguo Andy (Project leader)
Andaluz, Hillary
Chen, I-Hsuan

CATEGORIES:
Biotechnology, Chemistry and Chemical Analysis

KEYWORDS:
Biotechnology, Breast Cancer, Cancer, Chemistry and Chemical Analysis, Diagnostics, Disease Detection, Extracellular Vesicle, Liquid Biopsy

ASSESSING IN VIVO EFFICACY OF DRUG THERAPEUTICS BY MONITORING PROTEINS FROM EXTRACELLULAR VESICLES

TRACK CODE:
2020-TAO-69103

Researchers at Purdue University have developed a new method for monitoring absorption, distribution, metabolism, and excretion (ADME) of new drug therapeutics by quickly and noninvasively measuring proteins from extracellular vesicles (EVs), a class of biological entities released by cells that includes microvesicles and exosomes and that is present in fluids such as urine or blood. Current ADME studies are invasive and slow as researchers collect tissue samples from patients in clinical drug trials and use centrifugation to extract cytochrome P450 (CYP) and UDP-glucuronosyltransferase enzymes responsible for metabolizing over 90% of drugs. Purdue researchers introduce a new biochemical assay to assess ADME properties of therapeutics by quantifying enzymes extracted from EVs. Using their previously described EVtrap method to isolate EVs, extracting proteins, and analyzing with mass spectrometry Purdue researchers identified multiple CYP family enzymes from cell culture media. They also quantified induction of the enzyme, CYP 34A, in hepatocyte lysate in response to two drug treatments and quantified the same enzyme in human plasma.

Advantages:
-Able to Detect More Peptides and Proteins Than Current Technology
-Non-Invasive
-High Throughput

Potential Applications:
-Pharmaceutical Research
-Clinical Studies

Technology Validation:
The abundance of peptides from the ADME protein, CYP3A4, was measured in extracellular vesicles extracted from hepatocyte lysates and from human plasma.

INTELLECTUAL PROPERTY:

Application Date: June 1, 2021
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: June 1, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Tao, Weiguo Andy (Project leader)

Wu, Xiaofeng

CATEGORIES:
Biotechnology, Pharmaceuticals

KEYWORDS:
Biotechnology, Cancer Research, Drug Development, Extracellular Vesicle, Medicinal Chemistry, Metabolomics, Patient Care, Peptides, Pharmaceutical Development, Pharmaceutical Research, Pharmaceuticals, Proteins

DIRECT ISOLATION OF EXOSOME AND OTHER EXTRACELLULAR VESICLE PARTICLES FOR CHEMOTHERAPEUTIC OUTCOMES ASSESSMENT, DISEASE DIAGNOSIS, AND MONITORING DISEASE PROGRESSION

TRACK CODE:
2022-TAO-69815

Researchers at Purdue have developed an Extracellular Vesicle to phosphoprotein (EVTOP) strategy which benefits chemotherapeutic outcome assessment, disease diagnosis, and disease progression monitoring. This EVTOP strategy uses a dual affinity magnetic probe to directly circulating extracellular vesicles (EVs) from capture cerebrospinal fluid (CSF), plasma, urine, or saliva, and enrich their iphosphopeptides for the phosphoproteomic assessment. This technology utilize the properties of octa-arginine and titanium (IV) to enable efficient isolation of circulating EVs and enhanced identification of signaling molecules that are critical in many diseases.

The researchers were able to demonstrate the EVTOP strategy for analyses of clinical primary central nervous system lymphoma (PCNSL) samples in comparison with controls. This led them to identify 18 phosphoproteins that demonstrated a significant reduction in intensity among at least eight PCNSL patients post-chemotherapy. The identified phosphoproteins include SPP1, TRH, SCG2, TNC, and SELENOP and are known to be associated with neurological diseases. The use of this EVTOP strategy allowed researchers to identify the listed phosphoproteins as biomarkers for evaluating the chemotherapeutic performance in PCNSL patients due to the enriched presence of signaling pathways such as PI3K-Akt, PI3K-Akt-mTOR, and oncogenic MAPK, all of which are related to PCNSL development. This novel technology allows for more efficient and accurate biofluid phosphoproteomics, reduces the required volume of samples, and shortens the time for sample processing.

Technology Validation:
- Enrichment efficiency of EVTOP was tested using synthetic phosphopeptides with known sequences. Results showed the method could recover an average of 84.36% of the synthetic phosphopeptides added in the lysis, and approximately 36.5% of the synthetic phosphopeptides were recovered from cerebrospinal fluid (CSF) extracellular vesicle (EV) samples
- EVTOP method was applied to 21 primary central nervous system lymphoma (PCNSL) patient samples and 21 non-PCNSL control samples for differential phosphoproteomics analysis, leading to the identification of upregulated phosphoproteins in PCNSL samples.
- Parallel reaction monitoring and parallel accumulation-serial fragmentation (prm-PASEF) were used to monitor the intensity changes of these upregulated phosphoproteins before and after chemotherapy in PCNSL patients. This helped to validate identified phosphoproteins as potential biomarkers for evaluating chemotherapeutic performance.

Advantages:
- More efficient isolation and identification process compared to the traditional centrifugation method of circulating extracellular vesicles (EVs) and their phosphopeptides; only microliters of biofluids such as plasma are needed to monitor the change of signaling molecules
- More accurate results due to enriched phosphopeptides

Applications:

- Disease monitoring
- Disease screening
- PCNSL chemotherapeutic outcomes assessment

Publications:
Profiling Phosphoproteome Landscape in Circulating Extracellular Vesicles from Microliters of Biofluids through Functionally Tunable Paramagnetic Separation
doi: https://doi.org/10.1002/anie.202305668

INTELLECTUAL PROPERTY:

Application Date: March 6, 2024
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 6, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Tao, Weiguo Andy (Project leader)

CATEGORIES:

Biotechnology, Pharmaceuticals

KEYWORDS:

Cancer, Medical Health, Medicinal Chemistry, Pharmacology

The following section contains non-confidential summaries of pharmaceutical manufacturing innovations from Purdue University. These summaries are of the following innovations:

▪ Completely Continuous Plug Flow Crystallization Process of Pharmaceutical Production
2016-KOSW-67539 led by Nagy, Zoltan Kalman
▪ Micro-scale Powder Process for Drug Particle Filled Capsules
2018-REKL-68230 led by Reklaitis, Gintaras "Rex" V
▪ Crystallization Method to Reduce Filtration Time of Agrochemical Products
2020-NAGY-69085 led by Nagy, Zoltan Kalman
▪ Mixed Solvent Micelle Formation Procedure
2020-WON-69093 led by Won, You-Yeon
▪ Polymer Salts for Improved Drug Delivery from Amorphous Solid Dispersions
2022-TAYL-69671 led by Taylor, Lynne S
▪ Precision 3D Printing Method for Customizable Pharmaceutical Mini-Tablets
2023-SUND-70094 led by Sundarkumar, Varun

COMPLETELY CONTINUOUS PLUG FLOW CRYSTALLIZATION PROCESS OF PHARMACEUTICAL PRODUCTION

TRACK CODE:
2016-KOSW-67539

Using a traditional plug flow crystallization method for the manufacture of an active pharmaceutical ingredient creates encrustation in the system, causing inefficient production. This encrustation blocks flow through the reactor resulting in an inconsistent product and necessitating frequent cleaning. Most importantly, the resulting pharmaceutical product will have inferior properties, resulting in inconsistent dosage in the patient. However, a perfected method of plug flow crystallization has the potential to increase manufacturing productivity and product quality.

Researchers from Purdue University have developed a reactor system that eliminates encrustation in plug flow crystallization platforms used in pharmaceutical manufacturing. This system eliminates down time for reactor cleaning, increases product yield, and yields a more consistent product. The more consistent active pharmaceutical ingredients produced using this plug flow system will ultimately provide an optimum dose for the patient's best means of recovery.

Advantages:
-Efficient manufacturing
-Higher production yield
-Allows for continuous pharmaceutical manufacturing

Potential Applications:
-Drug manufacturing

INTELLECTUAL PROPERTY:

Application Date: April 25, 2017
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,766,014
Issue Date: September 8, 2020

Application Date: April 29, 2016
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Nagy, Zoltan Kalman (Project leader)
Koswara, Andy

CATEGORIES:

Pharmaceuticals, Chemical Engineering

KEYWORDS:

Algorithm, Chemical Engineering, Crystallization, Drug Development, Drug Manufacturing, Pharmaceuticals, Software

MICRO-SCALE POWDER PROCESS FOR DRUG PARTICLE FILLED CAPSULES

TRACK CODE:
2018-REKL-68230

Oral solid doses constitute approximately 60% of drug products. Oral solid dose manufacturing must deal with challenges associated with powder rheology; this is problematic for micronized powders which are cohesive. Poorly water-soluble compounds constitute 40% of currently marketed compounds. Particle size reduction is used to improve drug bioavailability, but causes rheological problems in manufacturing. The lack of constitutive equations leads to a demand for an effective precision dosing process.

Researchers at Purdue University have developed a new micron-scale powder process. This process enables accuracy dosing of drug mass and low product relative standard deviation; additionally, the method allows for specification of particle size distribution in a product by choice of source material, as experiments have demonstrated that particle size is preserved through the printing process.

Advantages:
-Versatile processing of fine particles
-Low relative standard deviation
-Enables production of high-dose pharmaceuticals

Potential Applications:
-Compounding pharmacy
-Slurry printing

INTELLECTUAL PROPERTY:

PEOPLE:

Reklaitis, Gintaras "Rex" V (Project leader)
Giridhar, Arun V
Nagy, Zoltan Kalman
Radcliffe, Andrew J
Taylor, Lynne S

CATEGORIES:

Pharmaceuticals, Chemical Engineering

KEYWORDS:

Chemical Engineering, Oral Solid Dose, Pharmaceutical Suspension, Pharmaceuticals, Pharmaceutics

CRYSTALLIZATION METHOD TO REDUCE FILTRATION TIME OF AGROCHEMICAL PRODUCTS

TRACK CODE:
2020-NAGY-69085

Purdue University researchers have developed a crystallization methodology for more efficient purification of agrochemical compounds. Agrochemical companies need to abide by purity standards for the products and compounds they produce. Crystallization is a common technique utilized to refine impure compounds but is rife with challenges including long process and filtration times. To address these problems, Purdue University researchers developed an approach that optimizes the process time of crystallization. The system measures the real-time turbidity of the crystallization process and converges on a temperature to achieve optimum crystal growth. This technology has been used on a proprietary agrochemical compound and displayed three to four times faster filtration after crystallization of 200 grams of material (in 500 milliliter and 2-liter chambers) than traditional filtration methods. Successful implementation of this method not only generates feasible process parameter trajectories of an unknown agrochemical crystallization process with minimal thermodynamic knowledge, but also provides invaluable process and thermodynamic data (solubility, metastable zone width, crystallization kinetics) for future experimental or modeling studies. This technology promises to provide agrochemical companies with a more efficient process for attaining purity standards through crystallization.

Technology Validation: With a proprietary agrochemical compound, the researchers improved filtration times three to four fold over traditionally used filtration methods.

Advantages
-Increased Efficiency of Agrochemical Compound Crystallization
-Significantly Reduces Filtration Time
-Rapid Process Design of Unknown Agrochemical Crystallization Systems

Applications
-Agrochemical Crystallization
-Compound Purification

INTELLECTUAL PROPERTY:

Application Date: November 10, 2021
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: November 11, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Nagy, Zoltan Kalman (Project leader)
Chappelow, Chris
Larsen, Paul
Wu, Wei-Lee

CATEGORIES:
Chemical Engineering, Biotechnology

KEYWORDS:
Agrochemical, Biotechnology, Chemical Engineering, Crystallization, Crystallization Design, Rapid Filtration

MIXED SOLVENT MICELLE FORMATION PROCEDURE

TRACK CODE:
2020-WON-69093

Researchers at Purdue University have developed a new procedure for creating polymer micelle formulations such as polymer lung surfactant therapeutics that are used to treat respiratory distress syndrome (RDS). RDS is a disease of native lung surfactants that causes a severe decrease in blood oxygenation and affects approximately 190,000 patients in the United States each year. Traditional manufacturing methods pose challenges for producing polymer micelles employed in Purdue's efforts to develop an artificial polymer lung surfactant. The equilibrium-nanoprecipitation (ENC) method created by Purdue researchers minimizes variation between batches and pre-treats bulk amphiphilic block copolymers to alleviate mixing nonuniformity. The ENC technique has been tested with three unique batches of RDS therapeutics using dynamic light scattering to verify the composition of each batch.

Advantages:
-Uniformity
-Large-Scale Manufacturing
-Efficiency

Potential Applications:
-Pharmaceuticals
-Nanotechnologies
-Scientific Research
-Drug Discovery

Technology Validation:
The compositions and batch consistency for solvent micelle formations produced using the new procedure developed by Purdue researchers have been verified by dynamic light scattering (DLS).

Recent Publication:
"Polymer Lung Surfactants"
American Chemical Society Journal of Applied Bio Materials
DOI: 10.1021/acsabm.8b00061/

INTELLECTUAL PROPERTY:

Application Date: November 17, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: June 1, 2021
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: June 1, 2021
Type: NATL-Patent
Country of Filing: Canada
Patent Number: (None)
Issue Date: (None)

Application Date: June 1, 2021
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: June 1, 2021
Type: NATL-Patent
Country of Filing: Japan
Patent Number: (None)
Issue Date: (None)

Application Date: June 2, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Won, You-Yeon (Project leader)
Fesenmeier, Daniel James

CATEGORIES:
Pharmaceuticals, Micro & Nanotechnologies

KEYWORDS:
Biopolymer, Drug Formulation, Drug Manufacturing, Micro & Nanotechnologies, Nanoparticles, Nanoscale, Pharmaceutical Analysis, Pharmaceutical Research, Pharmaceuticals, Pharmaceutics, Respiratory Diseases

POLYMER SALTS FOR IMPROVED DRUG DELIVERY FROM AMORPHOUS SOLID DISPERSIONS

TRACK CODE:
2022-TAYL-69671

Researchers at Purdue University have developed polymer salts with high rates of dissolution that improve drug release, particularly for lipophilic drugs, that can account for approximately 90% of developmental or approved drugs . Typically, protonated polymers have been used as enteric coatings to prevent drug release in the stomach. These polymers developed for use as enteric coatings have been used in the formulation of amorphous solid dispersions (ASD), where the drug is molecularly dispersed in a polymer matrix. However, only low amounts of the drugs can be blended with the polymers due to their low rates of dissolution upon reaching their target. The Purdue researchers found that ionizing an enteric polymer into a polymer salt had a higher rate of dissolution in the drug's target area and improved the drug release from ASDs until after the formulation exited the stomach. These polymer salts also have improved solubility in organic solvents, allowing easier processing.

Technology Validation: The drug release profile of an enteric non-ionized polymer was compared with an ionized polymer salt, and it was observed that the rate of drug dissolution and release for the ionized polymer salt was twice that of the non-ionized polymer.

Related Publication: Qingqing Qi, Lynne S. Taylor. Improved dissolution of an enteric polymer and its amorphous solid dispersions by polymer salt formation. International Journal of Pharmaceutics. Volume 622, 2022, 121886, ISSN 0378-5173. https://doi.org/10.1016/j.ijpharm.2022.121886.

Advantages
- Allows for higher drug loading
- Soluble in organic solvents
- Higher drug release performance

Applications
- Pharmaceuticals manufacturing

INTELLECTUAL PROPERTY:

Application Date: January 18, 2023
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: August 18, 2022
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: February 14, 2022

Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Taylor, Lynne S (Project leader)
Qi, Qingqing

CATEGORIES:
Pharmaceuticals, Chemistry and Chemical Analysis

KEYWORDS:
Drug Development, Drug release, Drug solubility, Enteric Polymer, Pharmaceuticals, Polymer salt

PRECISION 3D PRINTING METHOD FOR CUSTOMIZABLE PHARMACEUTICAL MINI-TABLETS

TRACK CODE:
2023-SUND-70094

Traditional manufacturing methods struggle to offer personalized dosages, often following a 'one-dose-fits-all' model which does not suit specific patient groups like children, the elderly, and individuals with unique metabolic or organ functions. The industry's challenge is further compounded in pediatric medication (comprising less than 10% of the overall drug market share). Pediatric patients require flexible, low-dose, and palatable medications due to their distinct physiological responses. Traditional delivery solutions, such as crushed tablets or liquid medicines, are fraught with issues like altered dissolution rates, and dosing inaccuracies, and limited active pharmaceutical ingredient (API) stability respectively. Mini-tablets, which are small-form dosages, have been proposed as a solution. Their production however is hindered by the challenges of direct compression and the temperature-sensitive nature of hot melt extrusion.
Researchers at Purdue have developed a new method for manufacturing mini-tablets that ensures precise doses, content uniformity, and the controllable dissolution behavior. The method uses a drop-on-demand (DoD) three-dimensional (3D) printing system that consists of preparing a drug formulation by mixing an active pharmaceutical ingredient (API) with one or more excipients. The formulation can then be used to obtain either a melt-based suspension or solution, which can then be printed as droplets via the DoD printing system. Each droplet is solidified in an inert solvent bath, and isolated as ready-to-use drug product after washing and drying. This developed method allows for the production of mini-tablets with high content uniformity and customizable release profiles, which meets regulatory requirements on these metrics.

Technology Validation:

-Mini-tablets comprising of different types of polyethylene glycols (polypropyleneglycols, kolliphor® D-a-tocopherol polyethylene glycol succinate (TPGS), gelucire® 44/14, food oil) were developed
-Various formulations of the mini-tablets to ensure uniformity in the distribution of the active pharmaceutical ingredient (API) within each tablet
-Dissolution profiles of the mini-tablets were tested, which determined how quickly and completely the mini-tablets released their medication when exposed to an appropriate solvent
-Ultra-pressure liquid chromatography (UPLC) was used to confirm the amount of API present in each mini-tablet

Advantages:

-Personalized, customizable dosages of mini-tablets
-High degree of uniformity in the active pharmaceutical ingredient (API)
-Customized release profiles, such as fast-release or extended-release

Applications:

-Pharmaceutical tablets

Related Publications:

1.Sundarkumar, V., Wang, W., Nagy, Z., & Reklaitis, G. (2023). Manufacturing pharmaceutical mini-tablets for pediatric patients using drop-on-demand printing. International Journal of Pharmaceutics, 644, 123355.
2.Sundarkumar, V., Wang, W., Mills, M., Oh, S. W., Nagy, Z., & Reklaitis, G. (2023). Developing a Modular Continuous Drug Product Manufacturing System with Real Time Quality Assurance for Producing Pharmaceutical Mini-Tablets. Journal of Pharmaceutical Sciences.

INTELLECTUAL PROPERTY:

Application Date: February 28, 2024
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: May 24, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Sundarkumar, Varun (Project leader)
Nagy, Zoltan Kalman
Reklaitis, Gintaras "Rex" V

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:

Biomedical Engineering, Pharmaceutical Development, Therapeutics

The following section contains non-confidential summaries of research tool innovations from Purdue University. These summaries are of the following innovations:

▪ Reagent for Measurement of Protein Phosphorylation by Gel Electrophoresis
2014-TAO-66895 led by Tao, Weiguo Andy
▪ Direct Contact Blood Brain Barrier Triculture
2015-KNIP-67191 led by Knipp, Gregory Thomas
▪ Reporter Molecule for 20S Proteasome Stimulators for Parkinson's and Aging
2017-TRAD-67888 led by Trader, Darci Jones
▪ Live Cell Conjugation Chemistry for Imaging, Sensing, Biomanufacturing, and Cell Therapy
2018-CHOP-68209 led by Chopra, Gaurav
▪ Tool to Identify Host Proteins Involved in Viral and Bacterial Pathogenesis
2019-TAO-68397 led by Tao, Weiguo Andy
▪ Selective Fluorescent Probe for the Immunoproteasome
2019-TRAD-68454 led by Trader, Darci Jones
▪ Reporter Molecule for Study of Alzheimer's Disease
2019-CHOP-68541 led by Chopra, Gaurav
▪ In vitro Model for Testing Efficacy and Neurotoxicity of Neurotherapeutic
2020-KNIP-68758 led by Knipp, Gregory Thomas
▪ Activity-Based Probes with Unnatural Amino Acids to Monitor the Proteasome in Living Cells
2020-TRAD-68937 led by Trader, Darci Jones
▪ Fluorescent Probes for Monitoring Serine Ubiquitination by Bacterial Enzymes
2020-DAS-69098 led by Das, Chittaranjan
▪ Peptide crystal formulation for room temperature storage of biopharmaceuticals and other proteins
2021-CHMI-69348 led by Chmielewski, Jean Anne
▪ pH-Activable Fluorescent Probes for Targeting Cell Organelles
2021-CHOP-69413 led by Chopra, Gaurav
▪ A Fluorescence-based Assay Benefitting PROTAC Drug Discovery and Development
2023-DAS-69989 led by Das, Chittaranjan

REAGENT FOR MEASUREMENT OF PROTEIN PHOSPHORYLATION BY GEL ELECTROPHORESIS

TRACK CODE:
2014-TAO-66895

Research and Development labs (R&D) in academia, pharmaceutical, and biotech companies often assess the phosphorylation of a protein or classes of proteins. Currently, large-scale phosphorylation analysis is used to understand how signaling pathways work and how they may be deregulated in disease states. Even though thousands of protein phosphorylation sites can be identified, researchers may only be interested in a small sample of proteins for a signaling pathway. Hence, these large scale analysis techniques are time-consuming and cost-prohibitive. The applicability of gel-based proteomic strategy in phosphoproteomics has been largely limited by the lack of technologies for specific and quantitative detection of phosphoproteins in gels.

To resolve these issues, researchers at Purdue University have developed a novel gel-based process, called Differential Gel Electrophoresis of Phosphoproteome (DiGEP). This process uses metal ions, such as Ti4+, Zr4+, Fe3+, and Ga3+, which are attracted to phosphate groups and attach fluorophores on the phosphoproteins. This ultimately helps visualize phosphorylation changes in different samples on the same gel. DiGEP analyses are advantageous because they enable the visualization of phosphoproteins on a single gel and select only relevant proteins for in-gel digestion and mass spectrometric analysis. It is highly specific, selective, and quantitative and can be used routinely in labs for quantitative phosphorylation measurement, in vitro kinase assay, kinase and phosphatase activity assay, kinase/phosphatase inhibitor screening, and detection of in vivo phosphorylation. Not only will this technology help a general biological laboratory to effectively measure changes in protein phosphorylation, but will also help pharmaceutical and biotech industries to develop effective diagnostic and therapeutic agents relating to kinases.

Advantages:
-Visualization of phosphoproteins
-Selection of proteins for spectrometric analysis
-Effective and quantitative measures

Potential Applications:
-R&D labs
-Disease research

INTELLECTUAL PROPERTY:

Application Date: January 22, 2016
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,060,929
Issue Date: August 28, 2018

Application Date: January 23, 2015
Type: Provisional-Patent

Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Tao, Weiguo Andy (Project leader)
Wang, Linna

CATEGORIES:
Biotechnology

KEYWORDS:
Assays, Biotechnology, Genomics & Proteomics, Kinases, Proteins

DIRECT CONTACT BLOOD BRAIN BARRIER TRICULTURE

TRACK CODE:
2015-KNIP-67191

Neurological disorders have been steadily increasing over the last several decades. While drug discovery and development efforts to mitigate these diseases have concurrently increased to meet the change in prevalence, clinical translation into marketed products have been hindered. One of the main difficulties in creating this translation is the lack of a model that can predict the ability of new chemical entities to permeate through the brain blood barrier (BBB). Current models suffer from leakiness of the in vitro cellular tight junctions and that leakiness leads researchers to overestimate the amount of drug permeation.

Researchers at Purdue University have developed a model that represents a more restrictive, accurate model of the BBB. This model is a direct contact, triculture model containing astrocytes, pericytes, and the brain microvessel endothelial cells (BMEC) configured in a physiologically similar manner to an in vivo BBB. This method allows for direct contact between the pericytes and the astrocytes and measures the transendothelial electrical resistance (TEER) as an indirect measure of cell tightness. Researchers monitor the TEER until they determine a window in which a triculture would be of utility for permeability studies. This model will offer superior selectivity for screening neuroactive or neurotoxicant agents in vitro and help in the rational selection of candidates for advancement into further clinical studies based on its physiological similarity to the in vivo BBB cellular configuration. This model may also be adopted to select compounds that have a lower potential of eliciting a neurotoxicant effect.

Advantages:
-More accurate model representing the BBB
-Allows materials to permeate through it
-Allows for direct contact between the astrocytes and pericytes

Potential Applications:
-Medical/Health
-Pharmaceuticals
-Research & Development
-Drug discovery

Related Publication:

"Design of experiment based optimization of an in vitro direct contact triculture blood brain barrier model for permeability screening"
Pharmacy & Pharmacology International Journal
Volume 9 Issue 4 - 2021

INTELLECTUAL PROPERTY:

Application Date: September 7, 2017
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,877,026

Issue Date: December 29, 2020

Application Date: December 18, 2020
Type: CON-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: September 7, 2016
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Knipp, Gregory Thomas (Project leader)
Kulczar, Christopher Dale
Lavan, Monika
Lubin, Kelsey Eileen
Ngendahimana, Aimable

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Alzheimer's Disease, Autism, Biotechnology, Blood Brain Barrier, Brain, Drug Development, Neurological Disorders, Pharmaceuticals

REPORTER MOLECULE FOR 20S PROTEASOME STIMULATORS FOR PARKINSON'S AND AGING

TRACK CODE:
2017-TRAD-67888

Accumulation of excess protein is linked to aging, Parkinson's disease, and other human diseases. The large enzyme complex known as the proteasome, specifically its subunit the 20S core particle (20S CP), can degrade proteins to then be recycled to make new proteins. Scientists hypothesize that chemically stimulating the 20S CP can degrade the disease-related proteins and serve as a treatment for protein accumulation disorders. The reporter molecule currently available to assay new compounds for 20S CP-stimulating activity produces a high level of background signal in the absence of any stimulators, making discovery of new 20S CP stimulators via high-throughput screening a challenge.

Researchers at Purdue University have designed a new reporter molecule to detect stimulation of the 20S CP that is 3.5 times as sensitive as the current reporter. The sensitivity and effectiveness of this new FRET-based reporter was validated by screening 715 compounds for 20S CP stimulating activity. Four 20S CP stimulators were found in the screen, two of which were missed in a screen using the established reporter molecule.

Related Publications:
Rachel A. Coleman and Darci J. Trader, Developement and Application of a Sensitive Peptide Reporter to DIscover 20S Proteasome Stimulators
ACS Comb. Sci., DOI: 10.1021/acscombsci.7b00193

Advantages:
-More sensitive
-Amenable to high-throughput drug screening

Potential Applications:
-Parkinson's disease drug discovery

INTELLECTUAL PROPERTY:

Application Date: August 13, 2021
Type: DIV-Patent
Country of Filing: United States
Patent Number: 11,808,762
Issue Date: November 7, 2023

Application Date: September 12, 2018
Type: Utility Patent
Country of Filing: United States
Patent Number: 11,092,596
Issue Date: August 17, 2021

Application Date: October 17, 2023
Type: CON-Patent
Country of Filing: United States
Patent Number: (None)

Issue Date: (None)

Application Date: September 15, 2017
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Trader, Darci Jones (Project leader)
Coleman, Rachel Anne

CATEGORIES:
Pharmaceuticals, Chemistry and Chemical Analysis

KEYWORDS:
Aging, Assays, Peptides, Protein Degradation

LIVE CELL CONJUGATION CHEMISTRY FOR IMAGING, SENSING, BIOMANUFACTURING, AND CELL THERAPY

TRACK CODE:
2018-CHOP-68209

Surface modification of live cells has many biomedical and therapeutic applications, such as live cell imaging and cell therapy. The current approaches have limitations including poor stability over time and incompatibility with mammalian cells due to toxicity. There is a need for a new technology that improves surface modification of live cells.

Researchers at Purdue University have developed a new technology that enables surface modification of live mammalian cells. This cell-modification technology has applications in live cell imaging, manufacturing of cell therapies, enhancement of cells for therapeutic applications, cell-drug conjugation for enhanced killing of cancer cells, and drug delivery in a pH dependent manner to sites of inflammation. This technology conjugates small molecules, proteins, fluorophores, and PET tracers to live cells without nanoparticles or other vehicles.

Advantages:
-Conjugation to cell membranes without killing cells
-Functionalizes living cells with components such as small molecules, proteins, fluorophores, and PET tracers
-No use of nanoparticles or other vehicles

Potential Applications:
-Cell membrane imaging
-Enhanced cell therapy
-Production of therapeutic cells

INTELLECTUAL PROPERTY:

Application Date: October 16, 2020
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: April 17, 2019
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: April 17, 2018
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)

Issue Date: (None)

PEOPLE:
Chopra, Gaurav (Project leader)

CATEGORIES:
Biotechnology, Medical/Health

KEYWORDS:
Biotechnology, Drug Conjugates, Drug Delivery, Imaging, Medical/Health

TOOL TO IDENTIFY HOST PROTEINS INVOLVED IN VIRAL AND BACTERIAL PATHOGENESIS

TRACK CODE:
2019-TAO-68397

Purdue researchers have developed a chemical probe to facilitate quantitative proteomic analysis of potential drug targets for infectious diseases, identifying interactions between infectious particles and host proteins. Pathogens rely on their host's cells to proliferate and must bind to host cellular components. The weak and often transient nature of these interactions make capturing these interactions difficult due to harsh measures available to isolate such interactions. To aid in mitigating the high false positive rate brought about by these contemporary methods, Purdue researchers have synthesized chemical probes to label bacteria or virus particles that crosslink with interacting host proteins during infection. The probe contains a modifiable isolation tag to allow for identification of host proteins through mass spectrometry. The researchers have demonstrated this technology by isolating host proteins that directly interact with Salmonella and Zika virus, which might be critical for their pathogenesis. This method could serve as a universal tool to map the entry pathway of other pathogens.

Related Publication:
Tracking Pathogen Infections by Time-Resolved Chemical Proteomics
Angewandte Chemie, Feb 2020, Vol.132(6), pp.2255-2260
DOI: 10.1002/anie.201911078

Advantages:
-Able to identify previously unknown protein interactions
-High throughput

Potential Applications:
-Drug development
-Viral and bacterial pathogenesis research

INTELLECTUAL PROPERTY:

Application Date: April 17, 2020
Type: Utility-Gov. Funding
Country of Filing: United States
Patent Number: 11,480,580
Issue Date: October 25, 2022

Application Date: April 19, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Tao, Weiguo Andy (Project leader)

CATEGORIES:

Chemistry and Chemical Analysis, Biotechnology

KEYWORDS:
Bacterial Identification, Chemical Proteomics, Chemistry and Chemical Analysis, Molecular Biology, Research Tools, Virology, Zika, Zika Virus

SELECTIVE FLUORESCENT PROBE FOR THE IMMUNOPROTEASOME

TRACK CODE:
2019-TRAD-68454

Researchers at Purdue University have developed a fluorescent probe, TBZ, which selectively targets the core particle of the immunoproteasome (iCP) and can be used to monitor its expression in live cells. In an important cellular process that occurs within human and animal cells, proteins are degraded by the proteasome. As part of the molecular machinery of immune cells that have encountered inflammatory signals, a type of proteasome, the immunoproteasome, is a target of interest for autoimmune disease and cancer drug development. Current probes are not selective for iCP; they do not distinguish between this and other forms of the proteasome core particle. This new probe that fluoresces upon cleavage by iCP is efficient, selective, and can be used in live cells. Within 15 minutes of incubating the cell with 31 micromolar TBZ, iCP was detected in Ramos, SK-MEL-2, and A549 cell lines. At 31 micromolar, TBZ retains 3:1 selectivity for iCP versus the standard core particle.

Advantages:
-Selective towards iCP
-Can be used in live cells
-Higher fluorescence signal than commercial probe

Potential Applications:
-Intracellular iCP pathway monitoring
-Investigative protein expression

Tags: Chemistry and Chemical Analysis, Pharmaceuticals, Fluorescent Dyes, Reagents, Research Tools, Proteasome, Immune, Drug Discovery

INTELLECTUAL PROPERTY:

Application Date: August 5, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 29, 2020
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: February 5, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Trader, Darci Jones (Project leader)
Zerfas, Breanna

CATEGORIES:
Chemistry and Chemical Analysis, Pharmaceuticals

KEYWORDS:
chemestry, Chemistry and Chemical Analysis, Fluorescent Dyes, Immune, Pharmaceuticals, Proteasome, Reagents, Research Tools

REPORTER MOLECULE FOR STUDY OF ALZHEIMER'S DISEASE

TRACK CODE:
2019-CHOP-68541

Researchers at Purdue University have developed pH-dependent fluorogenic amyloid-beta reporters for the study of Alzheimer's disease (AD). Microglial phagocytosis of amyloid-beta peptides is a critical step in the regulation of brain homeostasis during the initiation and progression of AD. Unlike common methods to study this phenomenon, this technology is specific for amyloid-beta and functions in live cells. The reporter, an isoform of human amyloid-beta tagged with a pH-dependent fluorogenic moiety, fluoresces only upon phagocytosis in the acidic intracellular phagosomes. It clearly differentiates between phagocytic and non-phagocytic cells within live human and nonhuman microglial cells. This technology promises to aid in the discovery of new therapeutics for AD.

Advantages:
-Facilitates live cell tracking of microglial phagocytosis
-Differentiates between phagocytic and non-phagocytic microglial cells

Potential Applications:
-Development of Alzheimer's Therapeutics

Publication: Monitoring phagocytic uptake of amyloid into glial cell lysosomes in real time.
doi: https://doi.org/10.1101/2020.03.29.002857

INTELLECTUAL PROPERTY:

Application Date: September 27, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 27, 2020
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 29, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Chopra, Gaurav (Project leader)
Jethava, Krupal P.
Prakash, Priya

CATEGORIES:
Biotechnology, Pharmaceuticals

KEYWORDS:
Alzheimer's Disease, Amyloid-beta, Biotechnology, Pharmaceuticals, Reagent, Reporter, Research Tools

IN VITRO MODEL FOR TESTING EFFICACY AND NEUROTOXICITY OF NEUROTHERAPEUTIC

TRACK CODE:
2020-KNIP-68758

Researchers at Purdue University have developed a physiologically relevant in vitro screening tool combining blood-brain barrier (BBB) permeability testing with subsequent neuronal response to evaluate the effects of permeation on observed neuroactivity in one assay. Clinical translation of neurotheraputics significantly lags behind the rapid increase in neurological disorders seen worldwide. One of the primary hurdles to neurotherapeutic development is the blood brain barrier (BBB). Others have developed in vitro assays to emulate the BBB; however, the result of these assays does not translate to real efficacy, because the assays do not incorporate downstream neuroactivity or associated neurotoxicity as the Purdue technology does. Preliminary tests of the Purdue technology revealed it correctly rank-orders compounds compared to known parameters. The technology is versatile and can be adapted to utilize multiple cell types. The technology promises to reduce the resources needed for ranking hit and lead candidate compounds in the development of new neurotheraputic agents.

Advantages

-Promises to reduce time and cost associated with pharmaceutical development
-Flexible system: adaptable to multiple cell types
-Increased translational efficiency

Potential Applications

-Neurotherapeutic drug development
-Drug Discovery and Development

INTELLECTUAL PROPERTY:

Application Date: August 30, 2019
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Knipp, Gregory Thomas (Project leader)
Lubin, Kelsey Eileen

CATEGORIES:

Biotechnology, Pharmaceuticals

KEYWORDS:

Biotechnology, Blood Brain Barrier, Drug Development, In Vitro Screening, Neurite Inhibition, Neurite Outgrowth, Neuron Viability, Neurotherapeutic, Neurotoxicant, neurovascular unit, Pharmaceuticals, Toxicity

ACTIVITY-BASED PROBES WITH UNNATURAL AMINO ACIDS TO MONITOR THE PROTEASOME IN LIVING CELLS

TRACK CODE:
2020-TRAD-68937

Researchers at Purdue University have developed a set of activity-based probes which have shown improved fluorescence properties and selectivity towards the proteasome compared to other cellular proteases. They have included unnatural amino acids and have found probes which can be utilized in various applications, including monitoring the effects of small molecule stimulators of the proteasome in live cells and comparing the relative proteasome activity across different cancer cell types.

Advantages:
-Improved Proteasome Sensitivity
-Cell-Based Assay Compatibility

Potential Applications:
-High throughput assays
-Finding Proteasome Stimulators and Inhibitors

INTELLECTUAL PROPERTY:

Application Date: September 8, 2022
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 11, 2021
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 11, 2020
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Trader, Darci Jones (Project leader)
Salazar-Chaparro, Andres
Zerfas, Breanna

CATEGORIES:

Pharmaceuticals, Biotechnology

KEYWORDS:
Activity Based Probe, Pharmaceuticals, Proteasome

FLUORESCENT PROBES FOR MONITORING SERINE UBIQUITINATION BY BACTERIAL ENZYMES

TRACK CODE:
2020-DAS-69098

Purdue University researchers have developed a fluorometric assay for real-time monitoring of ubiquitination events catalyzed by bacterial SidE enzymes in Legionella infections. The assay is well suited for high-throughput identification of Legionella infection inhibitors. The enzymes of the Legionella SidE family catalyze host protein ubiquitination events via a recently discovered mechanism distinct from ubiquitination by eukaryotic enzymes and are required for optimal Legionella infection. Contemporary methods to investigate the ubiquitination activity of SidEs include mass spectrometry and SDS-PAGE gel shift assays. These current techniques are not continuous, only measuring the end point of the reaction, and are not amenable to high throughput formats. Purdue researchers synthesized a fluorescently labelled synthetic substrate peptide for SdeA, a member of the SidE family, that displays a change in fluorescence polarization when ubiquitinated by the enzyme. This technology is amendable to high throughput screening and will assist in discovery of inhibitors for Legionella infection as well as identifying and characterizing SidE-like enzymes in other bacterial species.

Advantages:
-Real-Time SidE Ubiquitination Analysis
-Amenable to High Throughput Screening

Potential Applications:
-Legionella Research
-Investigating Ubiquitination Events
-Fluorescence Polarization

Related Publication:

Fluorescent Probes for Monitoring Serine Ubiquitination
Biochemistry 2020, 59, 13, 1309–1313
?https://doi.org/10.1021/acs.biochem.0c00067

INTELLECTUAL PROPERTY:

Application Date: June 18, 2021
Type: Utility-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: June 18, 2020
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Das, Chittaranjan (Project leader)
Chmielewski, Jean Anne
Curtis, Ryan William
Kinzer-Ursem, Tamara Lea
Puvar, Kedar
Saleh, Aya M

CATEGORIES:
Biotechnology

KEYWORDS:
Assay, Biotechnology, Fluorescence Polarization, Fluorescent Peptide, High-Throughput Screening, Legionella, SidE, Ubiquitin, Ubiquitination

PEPTIDE CRYSTAL FORMULATION FOR ROOM TEMPERATURE STORAGE OF BIOPHARMACEUTICALS AND OTHER PROTEINS

TRACK CODE:
2021-CHMI-69348

Researchers at Purdue University have developed a platform technology comprising a nano-delivery system that stabilizes protein cargoes to prevent aggregation during storage at room or elevated temperature with retention of protein bioactivity. Current formulations of protein biopharmaceuticals in solution require specialized low-temperature equipment and careful handling to avoid stability changes and subsequent degradation that renders them inactive. Purdue researchers designed a trimeric coiled coil peptide nano-crystal that can stably incorporate His-tagged protein cargoes, limiting protein deterioration while preserving tertiary structure and stability of the protein cargo. The researchers incorporated green fluorescent protein (GFP) and red fluorescent protein (RFP) at one to two percent of the total crystal volume. This technology will facilitate room temperature storage of protein drugs and other proteins of commercial interest, allowing availability in locations that do not have cold storage facilities.

Technology Validation: Trimeric coiled coil peptide crystals containing His8-tagged GFP were subjected to elevated temperatures and compared to protein solutions of His8-GFP without the coiled coil peptide nano crystal. Crystals containing His8-GFP displayed fluorescence even after being heated to 100 degrees Celsius for 1 hour, whereas solutions of His8-GFP alone were no longer fluorescent after 1 minute, indicating that the 3D crystal assembly is required to maintain functionality and protein stability at elevated temperatures.

Advantages
-Improves stability of proteins including protein-based drugs
-No need for cold storage

Applications
-Improves shelf life of biopharmaceuticals
-Isolation of proteins in a crystal matrix

Publications:

Jorgensen, M. D.; Chmielewski, J. "Co-assembled Coiled-Coil Peptide Nanotubes with Enhanced Stability and Metal-Dependent Cargo Loading" ACS Omega. 2022, 7, 24, 20945–20951.

Curtis, R. W.; Scrudders, K. L.; Ulcickas, J. R. W.; Simpson, G. J.; Low-Nam, S. T.; Chmielewski, J. "Supramolecular Assembly of His-Tagged Fluorescent Protein Guests within Coiled-Coil Peptide Crystal Hosts: Three-Dimensional Ordering and Protein Thermal Stability" ACS Biomater. Sci. Eng. 2022, 8, 5, 1860–1866.

INTELLECTUAL PROPERTY:

Application Date: July 12, 2023
Type: NATL-Patent
Country of Filing: United States

Patent Number: (None)
Issue Date: (None)

Application Date: January 13, 2022
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: January 13, 2022
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: January 13, 2021
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Chmielewski, Jean Anne (Project leader)
Curtis, Ryan William

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biopharmaceuticals, Biopolymers, Biotechnology, Chemistry and Chemical Analysis, Micro & Nanotechnologies, Pharmaceuticals

PH-ACTIVABLE FLUORESCENT PROBES FOR TARGETING CELL ORGANELLES

TRACK CODE:
2021-CHOP-69413

Researchers at Purdue University have developed new pH-activable fluorescent probes for targeting cell organelles in live cells. Unlike traditional multi-step probes for live-cell organelle imaging, this technology requires the use of a common intermediate probe only. In addition, currently, only a few sensing and imaging technologies are commercially available that are responsive to pH; and activation or deactivation by pH can be used to improve targeting to specific cells and organelles. The robust probes created by Purdue researchers emit high fluorescence at the acidic pH of the organelle and negligible fluorescence at cytosolic neutral pH. The probes are soluble, cell-permeable, and readily taken up by target organelles. This platform uses a single molecular scaffold that can be implemented in a variety of applications in drug discovery and other investigations of cellular biology. The researchers have designed three probes using this platform that localize to the lysosome, mitochondria, or nucleus, respectively, and are activated upon uptake by the organelles. These probes were tested in live BV2 microglial cells and had little effect on cellular metabolism. Using primary microglial cells and BV2 cells, the cellular localization was confirmed with confocal microscopy, and the technology was demonstrated to be compatible with cell sorting by flow cytometry.

Advantages:
-pH Sensitive
-Can Improve Drug Targeting

Potential Applications:
-Drug Discovery and Development
-Bioconjugation Reaction Synthesis

Technology Validation:
The new pH-activable fluorescent probes have been used to measure A-beta(I-42) peptide activity, studying microglial uptake in specific cells and organelles.

INTELLECTUAL PROPERTY:

Application Date: September 8, 2023
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 8, 2022
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 12, 2021
Type: Provisional-Patent
Country of Filing: United States

Patent Number: (None)
Issue Date: (None)

PEOPLE:
Chopra, Gaurav (Project leader)
Arora, Harshit
Jethava, Krupal P.
Manchanda, Palak
Prakash, Priya

CATEGORIES:
Biotechnology, Chemistry and Chemical Analysis

KEYWORDS:
Biotechnology, Cell Biology, Cell Targeting, Chemistry and Chemical Analysis, Drug Conjugates, Medicinal Chemistry, Pharmaceutical Development, Pharmaceutical Research, Probe

A FLUORESCENCE-BASED ASSAY BENEFITTING PROTAC DRUG DISCOVERY AND DEVELOPMENT

TRACK CODE:
2023-DAS-69989

Researchers at Purdue University have developed a fluorescence polarization (FP)-based activity assay to monitor tight binders to the substrate recognition domain of a family of E3 ligases. The design of proteolysis targeting chimeras (PROTACs) has so far relied on a limited amount of well-characterized E3 ligases. Most of these ligases are either cytosolic or nuclear in their cellular distribution.

By targeting membrane-bound proteins for their assay, researchers at Purdue University have opened new paths to the discovery and development of therapeutics. This assay can be used to screen for binders, which would open new avenues in the PROTAC field (i.e., utilization of novel E3 ligases). The FP-based assay is reproducible, and specific. Further, the assay may have other uses such as deubiquitinating enzyme (DUB) identification. The identification of DUBs in and of itself, presents new targets for drug discovery and development.

Technology Validation: Fluorescence Polarization was used to monitor ubiquitination of the peptide. Ubiquitination was confirmed via SDS-PAGE. Upon the addition of DUB, deubiquitination occurred, as shown by decreased FP. Deubiquitination was also confirmed by SDS-PAGE.

Advantages:
-Screen binders of novel E3 ligases
-Reproducible and selective
-Assay can also be used to screen for DUBs

Applications:
- Drug development
- Drug discovery

INTELLECTUAL PROPERTY:

Application Date: December 15, 2023
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: December 16, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Das, Chittaranjan (Project leader)
Kenny, Sebastian

CATEGORIES:
Pharmaceuticals, Biotechnology

KEYWORDS:
Biotechnology, Chemistry and Chemical Analysis, Drug Development, Pharmaceutical Development

The following section contains non-confidential summaries of software research tool innovations from Purdue University. These summaries are of the following innovations:

▪ Patch-Surfer 2.0: A Protein-Ligand Modeling and Prediction Tool
2015-KIHA-67110 led by Kihara, Daisuke
▪ PatchSurfer: Software for Exploring Protein-Ligand Interactions
2015-KIHA-67111 led by Kihara, Daisuke
▪ IDP-LZerD, a Software that Models Disordered Protein Assembly
2021-KIHA-69433 led by Kihara, Daisuke
▪ LZerD, a Computational Method for Modeling Protein Pairwise Assembly
2021-KIHA-69434 led by Kihara, Daisuke
▪ Computational Method for Modeling Protein Assembly with More Than Two Protein Subunits
2021-KIHA-69437 led by Kihara, Daisuke
▪ Accurate Software-Assisted Laser Scanning Imaging and Optical Manipulation System for Biological and Pharmacological Samples
2024-ZHAN-70384 led by Zhang, Chi

PATCH-SURFER 2.0: A PROTEIN-LIGAND MODELING AND PREDICTION TOOL

TRACK CODE:
2015-KIHA-67110

Researchers at Purdue have developed a software tool called "Patch-Surfer 2.0" that can take an enzyme binding pocket as an input, and compares the queried binding pocket to known ligand binding pockets in its database. From there, the software predicts ligands that could bind strongly to the input binding pocket. Other binding pocket-ligand modeling software's primarily identify possible ligands for a given binding pocket by analyzing the whole protein structure, and determining what ligands could fit in the binding pocket. These other approaches have difficulty with proteins that have very different global structures but bind to the same ligand molecules.

The researchers devised an updated protein-ligand binding interaction system, which avoids this issue and improves on the previous version of the program. To get around the issue of being unable to predict different structured molecules binding to the same ligand, the researchers took a more local approach, and split up the binding pockets into a set of small, local "patches" which are subsequently evaluated for their geometric shape, surface electrostatic potential, hydrophobicity, and concavity. These patches are then compared to a database of patches with known ligand binding geometries to generate a ranked list of ligands that would bind optimally to the queried binding pocket.

Technology Validation:
The software's ability to predict possible ligands that could bind to a queried binding pocket was verified by comparing its performance to other ligand-binding modeling software systems such as APoc and eF-Seek. Fifteen ligands were chosen, and the area-under-the-curve (AUC) was calculated for each ligand, using each software. It was found that Patch-Surfer 2.0 showed a higher relative partial AUC than eF-Seek for all but one ligand, and Patch-Surfer 2.0 showed a higher AUC for 13 of the ligands as compared to the APoc software.

Advantages:
- Improved ligand searching ability
- Better results than similar programs

Applications:
- Pharmaceuticals development
- Modeling Ligand-Protein interactions

INTELLECTUAL PROPERTY:

PEOPLE:

Kihara, Daisuke (Project leader)
Lee, Sael
Zhu, Xiaolei

CATEGORIES:

Biotechnology, Computer Technology

KEYWORDS:

Biotechnology, Computer Technology, Ligand, Protein-Ligand Modeling

PATCHSURFER: SOFTWARE FOR EXPLORING PROTEIN-LIGAND INTERACTIONS

TRACK CODE:
2015-KIHA-67111

Interactions with small ligand molecules are essential aspects of proteins and there is an urgent need for computational methods for function prediction. A major drawback of current approaches is the dependency on the chemical features present in the known actives.

Researchers at Purdue University have addressed this major drawback by developing an alignment free, surface-based, pocket comparison program called PatchSurfer. PatchSurfer represents a binding pocket as a combination of segmented surface patches, with each patch characterized by its geometrical shape, the electrostatic potential, the hydrophobicity, and the concaveness. The device searches a database of known pockets and finds similar ones based on the surface patch similarity. Because each surface patch characterizes geometrical and physicochemical properties of a protein pocket and ligand on a continuous surface, the surface representation is less sensitive to subtle changes on the pocket and ligand conformation. This aspect helps to quickly allow a better understanding of protein-ligand interactions, and ultimately, can help to enhance the design of new ligands for a wide array of drug targets.

Advantages:
-Less sensitive to subtle changes on the pocket/ligand conformation
-Faster search speed
-New ligands for a wide array of drug targets

Potential Applications:
-Ligand design
-Virtual screening
-Pharmaceuticals
-Drug targets

INTELLECTUAL PROPERTY:

Application Date: January 5, 2016
Type: Copyright
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Kihara, Daisuke (Project leader)
Hu, Bingjie
Shin, Woong-Hee
Zhu, Xiaolei

CATEGORIES:

Biotechnology, Computer Technology

KEYWORDS:

Assays, Computer Technology, Computing Methods, Drug Development, Ligands, Medical/Health, Pharmaceuticals, Proteins

IDP-LZERD, A SOFTWARE THAT MODELS DISORDERED PROTEIN ASSEMBLY

TRACK CODE:
2021-KIHA-69433

Purdue University researchers have developed a computational docking method for modeling the structure of disordered protein-protein interactions (PPIs) dubbed IDP-LZerD. Protein-protein docking is extensively utilized in the biotechnology, pharmaceutical, and biomedical industries to model the three-dimensional structure of protein complexes. Current docking methods are predominantly optimized to model the complex formation of ordered protein partners, whose three-dimensional structure is assumed to remain constant upon binding. However, intrinsically disordered proteins (IDPs) do not adopt a single three-dimensional structure, and current docking strategies do not reliably model IDP-involved PPIs. IDPs serve critical roles in the regulation of PPIs across various biological pathways, but current tools cannot accurately model these interactions. IDP-LZerD is a first-of-its-kind method that utilizes biophysical principles to reliably model the conformation of the disordered protein in PPIs involving long IDPs up to 69 amino acids. IDP-LZerD performs than existing methods in producing docking models with correct bound conformations. Notably, IDP-LZerD was able to correctly model longer IDPs when compared to two other methods. These results highlight the utility of IDP-LZerD for structural modeling of disordered protein interactions.

Advantages
-Accurate modeling of protein-protein interactions with long intrinsically disordered proteins (IDPs)
-Novel computational method that follows the known biophysical mechanisms of IDPs

Applications
-Computational Protein Modeling
-Modeling 3D structures of disordered ligand-receptor pairs
-Drug discovery
-Biotechnology

Technology Validation:
-Produced docking models with correct bound conformations with better performance than existing methods
-Correctly modeled longer IDPs when compared to two other methods

Related Publications :

Modeling disordered protein interactions from biophysical principles
PLoS Computational Biology
DOI: 10.1371/journal.pcbi.1005485

IDP-LZerD: Software for Modeling Disordered Protein Interactions
Methods in Molecular Biology
DOI: 10.1007/978-1-0716-0708-4_13

INTELLECTUAL PROPERTY:

Application Date: May 10, 2021
Type: Copyright
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Kihara, Daisuke (Project leader)
Christoffer, Charles W.
Peterson, Lenna

CATEGORIES:

Biotechnology

KEYWORDS:

Bioinformatics, Biotechnology, Chemistry and Chemical Analysis, Computer Technology, Disordered Protein, Protein-Protein Interaction

LZERD, A COMPUTATIONAL METHOD FOR MODELING PROTEIN PAIRWISE ASSEMBLY

TRACK CODE:
2021-KIHA-69434

Researchers at Purdue University have developed a model for predicting protein-protein interactions called LZerD. Protein-protein interactions mediate many biological processes, and deciphering the protein interactome can help elucidate signaling pathways and drive drug design. Researchers have developed various methods for protein interactome predictions governed by different interaction parameters. The Purdue researchers' method searches the scientific literature for protein-protein interface information and predicts the most likely docking structures based on ranking of statistical scoring performance. The top scoring structures are then relaxed by a molecular dynamics simulation to resolve atom clashes and improve side-chain conformations. In rounds 38-46 of the Critical Assessment of Prediction of Interactions (CAPRI), a protein interactome prediction competition, the Purdue researchers' model was a top performer in the server group. Evaluation of the server group relies on the performance of the automatic model itself, with no post-prediction manual refinement by research teams. The researchers have also expanded their work with the development of Multi-LZerD technology, software that can predict the interactome of more than two protein subunits.

Related Publication: Performance and enhancement of the LZerD protein assembly pipeline in CAPRI 38-46. Proteins. 2020 Aug;88(8):948-961. DOI: 10.1002/prot.25850.

Technology Validation: In rounds 38-45 of the CAPRI competition, the researchers' model predicted the structure of the protein-protein interface at an acceptable or higher level in 15/22 cases (68.2%).

Advantages:
- Automatic
- Accurate -- award-winning accuracy in CAPRI
- Able to consider experimental constraints

Applications:
- Protein interactome predictions

INTELLECTUAL PROPERTY:

Application Date: (None)
Type: Copyright
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Kihara, Daisuke (Project leader)
Christoffer, Charles W.
Venkatraman, Viswesh

CATEGORIES:

Biotechnology, Computer Technology

KEYWORDS:
Biotechnology, CAPRI, Interactome, LZerD, Protein assembly, protein docking, protein structure prediction, protein-protein interactions, Proteins

COMPUTATIONAL METHOD FOR MODELING PROTEIN ASSEMBLY WITH MORE THAN TWO PROTEIN SUBUNITS

TRACK CODE:
2021-KIHA-69437

Researchers at Purdue University have developed a model for predicting protein-protein docking. Software previously developed for predicting protein-protein interactions includes CombDock. The Purdue software, called Multi-LZerD, uses a more rigorous physics-based approach to model the interactions. The model also uses the 3D Zernike descriptor (3DZD) to allow a level of soft-docking to influence the docking prediction. The Multi-LZerD software is an improvement on the researchers' previous work; it allows more than two protein-protein interaction predictions among many proteins. For final selection of the most-favorable docking, a small translation and rotation is applied to each of the most-favorable protein-protein pairs .

Technology Validation: Multi-LZerD outperformed CombDock for 8 out of 10 tested unbound docking cases with more than two subunits and had slightly worse performance for the 10 bound docking cases with more than two subunits.

Advantages:
•Better performance than CombDock for unbound docking cases

Applications:
•Predicting protein-protein interactions for more than two subunits

Related Publication: Multi-LZerD: multiple protein docking for asymmetric complexes. Esquivel-Rodríguez J, Yang YD, Kihara D. Proteins. 2012 Jul;80(7):1818-33. doi: 10.1002/prot.24079.

INTELLECTUAL PROPERTY:

Application Date: May 10, 2021
Type: Copyright
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Kihara, Daisuke (Project leader)
Christoffer, Charles W.
Esquivel Rodríguez, Juan Manuel

CATEGORIES:

Biotechnology, Computer Technology

KEYWORDS:

Biotechnology, Bound, Docking, Interactions, Proteins, Unbound

ACCURATE SOFTWARE-ASSISTED LASER SCANNING IMAGING AND OPTICAL MANIPULATION SYSTEM FOR BIOLOGICAL AND PHARMACOLOGICAL SAMPLES

TRACK CODE:
2024-ZHAN-70384

Researchers at Purdue University have developed a software-assisted laser-scanning imaging and optical manipulation system. This technology allows users to manually or automatically select a desired region of interest (ROI) and the system then controls the selected laser beams to the ROI during laser scanning. Related technologies use light patterning based on spatial light modulators or digital micromirror devices for spatial light control. However, these techniques possess laser speckles and can affect unwanted locations. Current confocal fluorescence microscopes can scan a manually selected pattern but cannot select targets based on optical signals. No system currently exists that provides as much flexibility and freedom for optical manipulation as this technology.

This technology helps biologists and pharmaceutical scientists by producing high spatiotemporal accuracy of ROIs. The system is tailored to precisely control intracellular molecular activities and provide a diffraction-limited resolution. This technology works with lasers ranging from IR to UV wavelengths, and from continuous wave to femtosecond pulse durations. The system is chemically selective and minimizes phototoxicity and perturbation. Applications include selective activation of photosensitive targets, flexible FLIP and FRAP, induction of reactive oxygen species at gated areas on samples, and controlling cell behaviors and fate.

Technology Validation:
Photobleaching and reactive oxygen species were induced in cells using a 405 nm laser at selected locations. Different cellular responses in protein dynamics were observed during and after laser interactions. Control of cell division was shown by selectively disrupting centrosomes using the 405 nm laser.

Advantages:
High spatial precision and free of laser speckles
Separate or in tandem manual automatic target selection
Simultaneous control of multiple laser wavelengths
Compatible with all laser-scanning platforms such as two-photon excitation fluorescence microscopy

Applications:
Pharmaceutical R&D
National labs
University and college facilities

INTELLECTUAL PROPERTY:

Application Date: November 2, 2023
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Zhang, Chi (Project leader)
Dong, Bin
Everly, Robert Michael

CATEGORIES:
Chemistry and Chemical Analysis, Biotechnology

KEYWORDS:
Biotechnology, cell molecular activity, Chemistry and Chemical Analysis, confocal fluorescence microscopy, flexible FRAP/FLIP, laser-scanning, optical manipulation, Reactive Oxygen Species, ROI imaging

The following section contains non-confidential summaries of MedTech innovations from Purdue University. These summaries are of the following innovations:

▪ Surgical Tool for Minimally Invasive Lumbar Discectomy
2015-CAPP-67213 led by Cappelleri, David John
▪ Wearable Biometric to Predict and Prevent Preeclampsia and Hypertension
2018-GOER-68042 led by Goergen, Craig Jonathan
▪ Strain Gauge Integrated Magnetic Microactuator for Smart Self-Clearing Catheter
2019-LEE-68342 led by Lee, Hyowon
▪ Novel Robotic Cannula for Minimally Invasive Lumbar Discectomy Surgery
2020-CAPP-68748 led by Cappelleri, David John
▪ Bioresorbable Materials for Unobtrusive, Sustained Topical Delivery of Therapeutics
2020-LEE-68893 led by Lee, Chi Hwan
▪ Resorbable Surgical Mesh Impregnated with Calcium Peroxide
2020-RAHI-68984 led by Rahimi, Rahim
▪ Wearable Ozone Generating System for Treatment of Infected Dermal Wounds
2020-RAHI-69057 led by Rahimi, Rahim
▪ A Wireless Implantable Passive Intra-Abdominal Pressure Sensing Scheme via Ultrasonic Imaging of a Microfluidic Device
2021-RAHI-69409 led by Rahimi, Rahim
▪ Microneedle Patch for Wound Oxygenation and Biofilm Eradication
2021-RAHI-69535 led by Rahimi, Rahim
▪ Device for Ocular Drug Delivery
2022-LEE-69581 led by Lee, Chi Hwan
▪ Low-cost, Wireless Radiation Sensor
2022-RAHI-69718 led by Rahimi, Rahim
▪ Titanium Implants with Enhanced Cell Integration and Antimicrobial Properties
2022-RAHI-69768 led by Rahimi, Rahim
▪ Image Recognition Integrated Service (IRIS) Prosthetic Arm
2023-WEIB-69953 led by Weibel, Justin A
▪ Remote Sensing Platform to Monitor Urine Bags in a Medical Environment
2023-RAHI-70178 led by Rahimi, Rahim
▪ Design for a Portable, Low-Cost, Magnetic Microrobot Control and Imaging System for Medical Use on Humans and Large Animals
2024-CAPP-70412 led by Cappelleri, David John

SURGICAL TOOL FOR MINIMALLY INVASIVE LUMBAR DISCECTOMY

TRACK CODE:
2015-CAPP-67213

Discectomy is the surgery to remove the herniated disc material that is pressing on a nerve root or spinal cord. The surgical workspace is very small and surgeons have to navigate through channels as small as 3mm. Current surgical instruments consist of rigid probes with tips that manipulate and remove the patient's tissue; surgeons are limited to using just one at a time. The rigid structure of surgical tools increases the risk of inadvertent damage to spinal nerves, as well as other potential risks that can leave the patient paralyzed or require further surgery.

Researchers at Purdue University have developed a surgical master-slave manipulator for use in minimally invasive lumbar discectomies. This technology increases the extended range of motion by allowing wrist-like movements of various robotic manipulators that are controlled simultaneously from a single controller. This technology is MRI compatible, disposable, and made using 3D printing, allowing it to be mass-produced in large quantities at a very low cost.

Advantages:
-Increased ease of use and mobility of surgical tools used in discectomies
-Disposable
-MRI compatible
-Inexpensive

Potential Application:
-Surgical tools
-Lumbar discectomies

INTELLECTUAL PROPERTY:

Application Date: January 15, 2018
Type: CIP-Patent
Country of Filing: United States
Patent Number: 10,806,489
Issue Date: October 20, 2020

Application Date: July 29, 2016
Type: Utility Patent
Country of Filing: United States
Patent Number: 10,709,324
Issue Date: July 14, 2020

Application Date: July 31, 2015
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Cappelleri, David John (Project leader)
Cole, Brian Anthony
Johnson, Benjamin Varughese

CATEGORIES:
Biomedical Engineering, Micro & Nanotechnologies

KEYWORDS:
Biomedical Engineering, Micro & Nanotechnologies, Orthopedics, Surgical Tools

WEARABLE BIOMETRIC TO PREDICT AND PREVENT PREECLAMPSIA AND HYPERTENSION

TRACK CODE:
2018-GOER-68042

Preeclampsia (or pregnancy related hypertension) is the most common complication to occur during pregnancy. It accounts for over $2.18 billion of U.S. health care expenditures in the first 12 months after birth. Of the 131 million pregnancies per year (4 million in the United States), approximately 10 percent are complicated by hypertension, leading to 3 million premature births. New insights suggest compromised blood flow through the kidneys plays a fundamental role in the development of preeclampsia. Researchers at Purdue University are refining a wearable biometric intended to screen for compromised kidney blood flow in 100 percent of pregnant women with the goal of predicting and preventing preeclampsia.

Symptoms of preeclampsia can include high blood pressure, protein in the urine, swelling, and seizures. After the 20th week of pregnancy, the mass of the pregnant abdomen is well known to affect kidney blood flow, especially when a woman lies on her back. In women with a vulnerable anatomy, this compromised blood flow leads to high blood pressure. Previously published work has shown that an acute elevation in blood pressure associated with a pregnant woman shifting from her side to her back predicts approximately 90% of preeclampsia. The procedure is known as the supine pressure test (SPT). Furthermore, when detected early, rest in a therapeutic position, on one's side for example, has been shown to prevent preeclampsia.

Purdue University researchers have developed a wearable biometric intended to both predict preeclampsia and better manage those women identified to be at risk. The technology couples a blood pressure measuring device with a body position sensor to ensure meticulous execution of the SPT. The device transmits via smartphone the changes in blood pressure and calculated predictive risk to a remote medical location. Sequential testing is intended to optimize test sensitivity. For those women identified to be at risk, the wearable device is also programmed to monitor a pregnant woman's resting position and communicate with her as needed to optimize position. The goal is to better predict and prevent preeclampsia and to allow expecting mothers to monitor their own health without frequent travel to a clinic.

Advantages:
-Predicts, manages, or prevents preeclampsia
-Testing performed in the comfort of home
-Results transmit to remote medical professionals
-Affordable
-Portable

Potential Applications:
-Early detection and prevention of preeclampsia
-Reduce the number of premature births resulting from preeclampsia
-Allow expecting mothers to monitor their own blood pressure without traveling to a clinic for frequent monitoring
-Similar application available for those with obesity-related hypertension, since physiology has been shown to be similar. U.S. hypertensive population is 76 million.

INTELLECTUAL PROPERTY:

Application Date: February 13, 2020
Type: NATL-Patent
Country of Filing: United States
Patent Number: 11,559,214
Issue Date: January 24, 2023

Application Date: January 21, 2020
Type: NATL-Patent
Country of Filing: Europe
Patent Number: (None)
Issue Date: (None)

Application Date: August 29, 2018
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: September 5, 2017
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Goergen, Craig Jonathan (Project leader)
Foster, Kirk Solon
Reuter, David
Wodicka, George R

CATEGORIES:

Biomedical Engineering, Medical/Health

KEYWORDS:

Biomedical Engineering, Blood Pressure, Medical Devices, Medical Diagnostics, Medical/Health, Mobile Apps, Preeclampsia, Sensors, Smartphones, Testing, Wearable Electronics

STRAIN GAUGE INTEGRATED MAGNETIC MICROACTUATOR FOR SMART SELF-CLEARING CATHETER

TRACK CODE:
2019-LEE-68342

Hydrocephalus is a neurological disease characterized by an excessive accumulation of cerebral spinal fluid (CSF) in the ventricles of the brain. Treatment requires the implantation of shunts through which CSF can be drained from the brain. However, the failure rate of these systems remain high, especially among children. According to the Journal of Neurosurgery, a study conducted from April 2008 to December 2011 reported that 33% out of 1036 patients experienced shunt failure. Common causes of failure include obstruction, over-drainage, and loculated ventricles.

Researchers at Purdue University have developed an implantable catheter capable of obstruction detection and removal, device alignment, and flow rate measurement. Previously, Purdue researchers introduced a fully integrated self-clearing implantable catheter that was able to clear obstructions, but found that once the device was implanted it was impossible to determine whether the device was oriented properly or actuating as expected. With new additions, in real-time the catheter can detect obstructions, confirm device alignment, and measure the CSF flow-rate on top of the existing biofouling-removal capabilities of the microactuator in the catheter. This device has demonstrated the ability to solve one of the largest challenges that clinicians encounter with chronically implanted catheters.

Advantages:
-Obstruction Detection
-Device Alignment
-Flow Rate Measurement
-Self-Clearing
-Ease of Fabrication

Potential Applications:
-Hydrocephalus Treatment

INTELLECTUAL PROPERTY:

Application Date: November 20, 2019
Type: Utility Patent
Country of Filing: United States
Patent Number: 11,534,584
Issue Date: December 27, 2022

Application Date: November 20, 2018
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Lee, Hyowon (Project leader)
Yang, Qi

CATEGORIES:
Biomedical Engineering, Medical/Health

KEYWORDS:
Biomedical Engineering, Hydrocephalus, Implantable Devices, Medical/Health, Obstruction Detection, Piezoresistor, Strain Gauge

NOVEL ROBOTIC CANNULA FOR MINIMALLY INVASIVE LUMBAR DISCECTOMY SURGERY

TRACK CODE:
2020-CAPP-68748

Researches at Purdue University have developed a robotic cannula system that can be easily integrated and deployed with existing technology already in use. This new system removes the need for human interaction once it is in place. This robotic system will improve the efficiency of the surgical tool use. The robotic cannula system allows the tools to be used together, coupling all of their back and forth movement. This will free up some of the responsibility of the doctors performing surgery and let them focus on the more important aspects.

Advantages:
-Improves efficiency of surgical tool use
-Decreases possibility of human error
-Decreased responsibility during surgery

Potential Applications:
-Surgery
-Robotics

INTELLECTUAL PROPERTY:

Application Date: December 16, 2019
Type: Utility Patent
Country of Filing: United States
Patent Number: 11,642,185
Issue Date: May 9, 2023

PEOPLE:

Cappelleri, David John (Project leader)
Ding, Yang
Johnson, Benjamin Varughese

CATEGORIES:

Biomedical Engineering, Mechanical Engineering

KEYWORDS:

Mechanical Engineering, Medical Devices, Medical/Health, Robotics, Surgical Tools

BIORESORBABLE MATERIALS FOR UNOBTRUSIVE, SUSTAINED TOPICAL DELIVERY OF THERAPEUTICS

TRACK CODE:
2020-LEE-68893

Researchers at Purdue University have developed new bioresorbable materials for improving efficacy of unobtrusive, topical delivery of therapeutics. Currently, cancer therapies such as chemotherapy and radiation create cell toxicity as well as undesired side effects, and often require repeated treatments to be fully effective. Another technology, polymeric microneedles, is less invasive and improves drug targeting; however, these are not well adapted to delivery cancer drugs or for other skin diseases, which require lasting release times. In addition, these polymer-based needles cannot be used in many sensitive target areas such as corneas in ocular cancers. Purdue researchers introduce a small, thin, flexible, water-soluble medical film that can be interfaced amicably with the soft, curvilinear surface of the skin as inserted by porous silicon needles dissolving completely in just one minute. These needles are designed to degrade through a simple hydrolysis process which initiates drug release over the course of a couple days. Minimal side effects were observed in mice after using this method for chemotherapy delivery and no signs of muscle inflammation at the site of injection were observed. This technique also showed less relapse in melanoma in mice. An in vitro analysis was also conducted on human fibroblast cells, and cell viability remained at 99.3% over the course of three days of treatment.

Advantages:
-Minimally-invasive Sustained Drug Release
-Improves Patient Care

Potential Applications:
-Drug Delivery
-Biomedical
-Topical Cancer Therapy

Technology Validation:
This invention was tested in vivo in mice, reducing relapse in melanoma as well as in vitro with human fibroblast cells showing excellent cell viability over time.

Recent Publication:
"Wearable patch may provide new treatment option for skin cancer"
Purdue University Research Foundation News

https://www.purdue.edu/newsroom/releases/2020/Q2/wearable-patch-may-provide-new-treatment-option-for-

INTELLECTUAL PROPERTY:

Application Date: June 10, 2021
Type: Utility-Gov. Funding
Country of Filing: United States
Patent Number: 11,793,982
Issue Date: October 24, 2023

Application Date: June 10, 2020
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Lee, Chi Hwan (Project leader)
Kim, Dong Rip
Yeo, Yoon

CATEGORIES:
Biomedical Engineering, Biotechnology

KEYWORDS:
Biomedical Engineering, Biotechnology, Cancer, Cancer Therapy, Drug Delivery, Ligand-Targeted Therapeutics, Patient Care, Targeted Therapeutic

RESORBABLE SURGICAL MESH IMPREGNATED WITH CALCIUM PEROXIDE

TRACK CODE:
2020-RAHI-68984

Researchers at Purdue University have developed a new resorbable surgical mesh that is impregnated with calcium peroxide for regeneration of tissue at dermal wound sites. Surgical mesh is used to prevent bacteria and carry oxygen, especially for surgical wound sites however, current mesh technologies are often expensive and can lead to long-term post-surgical complications such as adverse bodily response to a foreign object. Purdue researchers introduce a new solvent-free, cost-efficient, scalable process for making strong, flexible, biodegradable surgical mesh. This approach has been tested with various compositions of calcium peroxide on polymer fibers to develop a mesh with optimal porosity, verified by scanning electron microscopy (SEM), which allows for excellent oxygen permeability. The new mesh was cultured with HMS-32 skin cells in vitro, exhibiting 90-92% cell viability as well as having ability to prevent necrosis by reducing hypoxia-induced cell death within six days.

Advantages:
-Biodegradable
-Strong
-Flexible
-Reduced Hypoxia Induced Cell Death
-High Cell Viability

Potential Applications:
-Surgical Mesh
-Hernia Surgical Mesh
-Stress Incontinence-Urologic/Gynecologic Applications

Technology Validation:
In vitro skin cell culture with new mesh, tested in lab to determine best manufacturing technique, and shows 90-92% cell viability as well as higher oxygen permeability and less hypoxia induced cell death at surgical wound sites.

Recent Publication:
"Wearable, portable invention offers options for treating antibiotic-resistant infections, wounds"
Purdue Research Foundation News

https://www.purdue.edu/newsroom/releases/2020/Q3/wearable,-portable-invention-offers-options-for-treating

INTELLECTUAL PROPERTY:

Application Date: May 11, 2021
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: May 13, 2020

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Rahimi, Rahim (Project leader)
Woodhouse, Ian B
Zareei, Amin

CATEGORIES:
Biotechnology, Biomedical Engineering

KEYWORDS:
Antibacterial, Biomedical Engineering, Biotechnology, Tissue Engineering, Tissue Swelling, Wound Dressing

WEARABLE OZONE GENERATING SYSTEM FOR TREATMENT OF INFECTED DERMAL WOUNDS

TRACK CODE:
2020-RAHI-69057

Dermal wounds are common in an aging population, diabetic patients, and persons with obesity to name a few, and many bacterial infections are gaining resistance to currently available antibiotic treatments. Recent scientific discovery indicates that ozone can not only topically treat wounds but also signal tissue regeneration and repair. Researchers at Purdue University have developed a new wearable ozone generating system for treatment of infected dermal wounds. They have created fine-tuned materials to fabricate disposable semipermeable wound dressings and have connected these through a flexible tube to a portable generator that produces about 90-130 ppm of ozone. Technology has been validated In in vitro by testing for cytotoxicity on human fibroblast cells; no signs of adverse reaction were observed and the device was effective in treating both Pseudomonas aeruginosa and Staphylococcus, two of the most common types of bacteria found in wound sites.

Advantages:
-Accurate
-Reliable
-Fast Acting
-Antibacterial

Potential Applications:
-Wound Treatment
-Infection Treatment

Technology Validation:
In vitro cytoxicity testing with two common types of bacteria.

Recent Publication:
"Wearable and Flexible Ozone Generating System for Treatment of Infected Dermal Wounds"
Frontiers in Bioengineering and Biotechnology
DOI: 10.3389/fbioe.2020.00458

INTELLECTUAL PROPERTY:

Application Date: January 20, 2023
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: July 23, 2021
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: July 23, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Rahimi, Rahim (Project leader)
Roth, Alexander G
Ziaie, Babak

CATEGORIES:
Biotechnology, Materials and Manufacturing

KEYWORDS:
Antibacterial, Antibiotic Resistance, Biomedical Engineering, Biotechnology, Electrical Engineering, Materials and Manufacturing, Multi-drug Resistant Bacteria, Wound Dressing, Wounds

A WIRELESS IMPLANTABLE PASSIVE INTRA-ABDOMINAL PRESSURE SENSING SCHEME VIA ULTRASONIC IMAGING OF A MICROFLUIDIC DEVICE

TRACK CODE:
2021-RAHI-69409

In order to help patients of abdominal compartment syndrome (ACS), researchers at Purdue University have developed a method for wirelessly measuring intra-abdominal pressure via the ultrasonic imaging of a passive implantable device. This implantable device enables noninvasive measurement of pressure data that can be used by health professionals to diagnose and treat ACS in a more informed and responsive manner. By helping better inform decisions, this technology could be used to reduce morbidity and increase overall survival in patients with risk of ACS. This technology has applications in the medical device space to measure in-vivo pressures via ultrasound in order to help patient outcomes.

Advantages:
- Wireless measurement of pressure via ultrasound
- Gives doctors easier access to patient conditions
- Non-invasive monitoring of patient, once device is implanted

Applications:
- Monitoring of abdominal compartment syndrome
- In vivo pressure monitoring
- Implantable Medical Devices
- Biotechnology

Technology Validation: this technology has been validated through ex vivo demonstration of 600 cycles at pressures up to 55 kPa over the course of 2 days.

Related Publications: H. Jiang et al., "A Wireless Implantable Passive Intra-Abdominal Pressure Sensing Scheme via Ultrasonic Imaging of a Microfluidic Device," in IEEE Transactions on Biomedical Engineering, vol. 68, no. 3, pp. 747-758, March 2021, doi: 10.1109/TBME.2020.3015485.

INTELLECTUAL PROPERTY:

Application Date: April 29, 2022
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: April 30, 2021
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Rahimi, Rahim (Project leader)

CATEGORIES:
Biomedical Engineering, Medical/Health

KEYWORDS:
Biomedical Engineering, Electrical Engineering, Medical/Health, Ultrasound

MICRONEEDLE PATCH FOR WOUND OXYGENATION AND BIOFILM ERADICATION

TRACK CODE:
2021-RAHI-69535

Purdue University researchers have developed a flexible microneedle array on a polyethylene terephthalate (PET) support that can puncture biofilms and provide oxygen and antibiotics to the wound site. Biofilms are strong, bacterial films that form on open wounds, causing hypoxia and inflammation of the wound site, leading to complications or even interruption of the healing process. Additionally, removing biofilms can be ineffective and very painful for the patient. The microneedle array developed by Purdue researchers dissolves upon contact with the wound's biological fluid, avoiding the pain associated with removing biofilms or using hypodermic needles. The microneedle array is also effective for decontamination and increasing the healing process of wounds. Specifically, it increased the wound's oxygen content by 50 percent, killed all gram-positive bacteria within 24 hours, and killed all gram-negative bacteria within 12 hours. Finally, the array is nontoxic; it preserved 90 percent of skin cells over six days of testing. The novel microneedle array developed by Purdue researchers paves the way for a better wound treatment and patient care, along with reducing complications during the wound healing process.

Technology Validation: The microneedle array developed by Purdue researchers dissolves upon contact with the wound's biological fluid, avoiding the pain associated with removing biofilms or using hypodermic needles. The microneedle array is also effective; when tested, it increased the wound's oxygen content by 50 percent, killed all gram-positive bacteria within 24 hours, and killed all gram-negative bacteria within 12 hours. Finally, the array is nontoxic; it preserved 90 percent of skin cells over 6 days of testing.

Advantages
- Nontoxic
- Better patient care (Less Painful)
- Versatile applications
- Effective for wound treatments

Applications
- Human or animal wound treatment

INTELLECTUAL PROPERTY:

Application Date: March 12, 2024
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: September 14, 2022
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: September 14, 2021

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Rahimi, Rahim (Project leader)

CATEGORIES:
Biomedical Engineering, Medical/Health

KEYWORDS:
Biofilms, Biomedical Engineering, Medical/Health, Wound Treatment, Wounds

DEVICE FOR OCULAR DRUG DELIVERY

TRACK CODE:
2022-LEE-69581

Ocular drug delivery is very challenging due to the complex and sensitive structure of the eye. Researchers at Purdue University have developed a minimally invasive and effective ocular drug delivery platform. This method enables long term sustained release of therapeutic ocular drugs via a tear-soluble contact lens that leaves behind biodegradable silicon nanoneedles. The tear-soluble contact lens provides an optimal curvature to fit the cornea and it is degraded in less than a minute, enabling initial short-term release of anti-inflammatory drugs and long-term release of therapeutic drugs. This technology directly benefits patients undergoing treatment for chronic diseases or injuries, including glaucoma, cataract, and graft rejection.

Advantages

Minimally invasive

- Long term sustained release
- Initial burst release of anti-inflammatory
- Long-term release of therapeutic drugs
- Demonstrated biosafety and efficacy in lab testing

Applications

- Ocular drug delivery
- Treatments for glaucoma, cataract, and graft rejection

Technology Validation:
This technology has been validated for efficacy and safety through successful in vivo testing in a rabbit corneal neovascularization (CNV) model.

INTELLECTUAL PROPERTY:

Application Date: April 8, 2024
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: October 10, 2022
Type: PCT-Gov. Funding
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: October 8, 2021
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Lee, Chi Hwan (Project leader)
Kim, Dong Rip
Paulus, Yannis Mantas

CATEGORIES:
Medical/Health, Biomedical Engineering

KEYWORDS:
Biomedical Engineering, Drug Delivery, Glaucoma, Intraocular Injection, ocular

LOW-COST, WIRELESS RADIATION SENSOR

TRACK CODE:
2022-RAHI-69718

Researchers at Purdue University have developed a printable, wireless device (dosimeter) for detecting radiation. Sterilization via radiation is the preferred technique for sterilization of health instruments like masks, gloves, and syringes, medical devices, and pharmaceutical packaging. There is demand for measurement of radiation dosage due to the deleterious effects of both under- and over-exposure of materials to gamma radiation. The Purdue researchers' device is made of PEDOT : PSS/PU polymer composite. This is a low-cost material; the device need not be recovered after use. The composite deforms when exposed to gamma radiation, which is interpreted as an increase in impedance. A vector network analyzer (VNA) emits a signal toward a sensor adhered to the composite; the backscattered signal is detected as impedance by an antenna connected to the VNA. The impedance value can then be transferred to any Wi-Fi connected device and used to evaluate the sterilization process.

Technology Validation: The researchers' device responded to radiation exposure of 40 kGy with an impedance increase of 375%.

Advantages:
- Wireless, radiofrequency signal transmission
- Printable reference and sensing tags
- Real-time
- Detection of radiation exposure up to 40 kGy
- Low-cost

Applications:
- Evaluation of radiation sterilization used to disinfect health instruments, medical devices, and pharmaceutical packaging

INTELLECTUAL PROPERTY:

Application Date: July 21, 2023
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: July 21, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Rahimi, Rahim (Project leader)

CATEGORIES:

Biomedical Engineering, Materials and Manufacturing

KEYWORDS:
Biomedical Engineering, Gamma radiation, Printable, Radiation, Sterilization, Wireless

TITANIUM IMPLANTS WITH ENHANCED CELL INTEGRATION AND ANTIMICROBIAL PROPERTIES

TRACK CODE:
2022-RAHI-69768

Researchers at Purdue University have developed a new method to manufacture antimicrobial, cell-integrated implants. Despite the great advancement and wide use of titanium (Ti) and Ti-based alloys in different orthopedic implants, device-related infections remain the major complication in orthopedic and trauma surgery. Most of these infections are often caused by both poor antibacterial and osteoinductive properties of the implant surface. The Purdue researchers' process is a two-step laser nanotexturing (LN) and immobilization (LI) method of coating silver onto titanium implants. LN increases cell integration, and LI reduces the toxicity of silver nanoparticles to surrounding cells. Use of this method causes implants to better-integrate into the body and be toxic to bacteria but not cells, and ultimately reduce chances of bacterial infection.

Technology Validation: The researchers' nanotexturing method caused a 2.5-fold increase in osseointegration compared to pristine Ti surface. In testing with gram-positive and gram-negative bacteria, the LN-Ti/LI-Ag surface was observed to have efficient and stable antimicrobial properties for over six days yet has similar cytotoxicity to LN-Ti.

Advantages:
- Increases cell integration compared to pristine Ti implants- Antimicrobial properties
- Not toxic for animal cells

Applications:
- Titanium implants

INTELLECTUAL PROPERTY:

Application Date: December 31, 2022
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: February 25, 2022
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Rahimi, Rahim (Project leader)
Selvamani, Vidhya

CATEGORIES:

Biomedical Engineering

KEYWORDS:
Biomedical Engineering, Nanotexturing, Osteoinductive, Silver nanoparticles

IMAGE RECOGNITION INTEGRATED SERVICE (IRIS) PROSTHETIC ARM

TRACK CODE:
2023-WEIB-69953

Researchers at Purdue University have developed an image recognition integrated service (IRIS) robotic prosthetic arm targeted to help children aged 7-14 adjust to disabilities early to enhance quality of life in adulthood. By using an embedded camera for object recognition, the system can identify objects in the environment and determine their distance from the camera. This is used to control the prosthetic's 5 functional fingers, palm, and optional 4 degree of freedom wrist. This enables the prosthetic to grasp, apply force to, or lift everyday objects in a manner appropriate to the object.

Technology Validation: This technology has been validated through the fabrication and testing of a prototype. The prosthetic hand was capable of object recognition-based actuation.

Advantages
-Aimed to help children aged 7-14
-Low cost, minimized form factor
-Object and distance identification
-Semi-autonomous manipulation of everyday objects

Applications
-Prosthetic limbs for children
-Image recognition in real world AI
-Robotics

INTELLECTUAL PROPERTY:

Application Date: February 16, 2024
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: February 18, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Weibel, Justin A (Project leader)
Bandyopadhyay, Soumya

CATEGORIES:

Medical/Health, Mechanical Engineering

KEYWORDS:

Assistive Technology, Biomedical Engineering, disability, image recognition, Mechanical Engineering,

REMOTE SENSING PLATFORM TO MONITOR URINE BAGS IN A MEDICAL ENVIRONMENT

TRACK CODE:
2023-RAHI-70178

Researchers at Purdue University have developed a remote sensing platform to continuously monitor urine bags in medical environments. Current solutions require visual monitoring from staff to assess when bags need to be replaced, and direct contact is often required to analyze for onset of urinary tract infections (UTIs). Purdue's Sticker Type Antenna for Remote Sensing (STARS) technology enables wireless measurement of conductivity and volume of fluid in the urine bag and can alert hospital staff when intervention is required. This simultaneously offers patients the continuous monitoring needed to lead to better outcomes while reducing the burden on care providers. This technology has applications in both medical and senior living environments.

Technology Validation: This technology has been validated through a proof-of-concept demonstration where the STARS system was used to detect filling and electrical conductivity of a urine bag.

Advantages:
- Continuously monitored care for patients
- Enables healthcare workers to be more effective
- Improves operational efficiency and patient outcomes

Applications:
- Patient status monitoring
- Healthcare
- Medical technology

INTELLECTUAL PROPERTY:

Application Date: April 10, 2024
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: April 10, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Rahimi, Rahim (Project leader)
Gopalakrishnan, Sarath

CATEGORIES:

Biomedical Engineering, Medical/Health

KEYWORDS:

(No keywords found)

DESIGN FOR A PORTABLE, LOW-COST, MAGNETIC MICROROBOT CONTROL AND IMAGING SYSTEM FOR MEDICAL USE ON HUMANS AND LARGE ANIMALS

TRACK CODE:
2024-CAPP-70412

Researchers at Purdue have designed an integrated, low-cost, microrobot control and imaging system for patients undergoing treatment with magnetically controlled microrobots. Current systems for magnetic microrobot control require either large robotic arms, high current electrical coils and cooling systems, or extremely large permanent magnets. These systems can be prohibitively expensive, and are large and bulky, requiring a dedicated operating room for use. Ideally, a magnetic microrobot control system should be low-cost, easy to implement in hospital environments, and should be able to carry out many different end-use applications.

The researchers designed a portable, gantry-style, microrobot control system affixed to a metal frame large enough to accommodate humans and large animals. The control system can maneuver in the X and Y dimensions and has two arms that can move in the Z-dimension (towards vs away from the patient). Attached to one Z-axis control is a high-frequency ultrasound imaging system and a directed ultrasound probe for local heating. Attached to the other Z-axis control is a rotating permanent magnet with two degrees of freedom to control the movement of the microrobot.

Technology Validation:
The researchers plan to validate the design for the microrobot control system through several tests. First, the researchers will test the functionality of the ultrasound imaging system and heating probe in a biologically relevant fluid bath to calibrate the required heating settings. Next, they plan to optimize the ultrasound imaging system settings with a microrobot being actuated at different magnetic control frequencies. The functionality of the design will be verified initially by navigating the microrobot through a 5-10 mm diameter agarose tunnel immersed in biological fluid, with further tests including navigation through a anatomically-accurate phantom, and finally in an ex vivo pig model.

Advantages:
- Low cost
- Portable
- Versatile use-cases

Applications:
- Targeted drug delivery
- Directed sample collection
- Internal microrobot surgery

INTELLECTUAL PROPERTY:

Application Date: September 27, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Cappelleri, David John (Project leader)

CATEGORIES:
Medical/Health, Micro & Nanotechnologies

KEYWORDS:
Micro & Nanotechnologies, Microtechnology

The following section contains non-confidential summaries of MedTech research tool innovations from Purdue University. These summaries are of the following innovations:

▪ Cellular Model of Parkinson's Disease
2016-ROCH-67263 led by Rochet, Jean-Christophe
▪ Method of Thin Flexible Electrode Insertion for Deep Brain Neural Recording and the Design of Electrode Insertion Device
2018-IRAZ-68150 led by Irazoqui, Pedro P.
▪ Ultrasensitive Biosensor
2019-ZUO-68465 led by Zuo, Fan
▪ High-performance Platinum Neurostimulation Electrode with 97% Reduction in Corrosion
2019-LEE-68525 led by Lee, Hyowon
▪ Artificial Retina Based on Photon-Assisted Electrochemical Doping
2022-MEI-69888 led by Mei, Jianguo
▪ Light Pipe Microscope for large-scale dynamic imaging
2023-CUI-69962 led by Cui, Meng
▪ Novel Patient-Specific Method to Predict Prostate Cancer Relapse after Radiation Therapy
2023-DIAZ-70044 led by Gomez Diaz, Hector
▪ Photonic-organic Electrochemical Transistor
2023-MEI-70196 led by Mei, Jianguo
▪ Formulation for Novel, Blood Catalyzed Conductive Polymer for use in Bioelectronics, Bioimaging, and Biosensors
2024-MEI-70435 led by Mei, Jianguo

CELLULAR MODEL OF PARKINSON'S DISEASE

TRACK CODE:
2016-ROCH-67263

Alpha-synuclein (aSyn) is central in Parkinson's disease pathogenesis. Converging evidence suggests that the level of aSyn expression plays a critical role in both familial and sporadic Parkinson's disease. The study of aSyn toxicity remains critical because the manner in which aberrant aSyn leads to neuronal degeneration is not yet understood. Current methods of monitoring aSyn toxicity levels in cell culture require inducing cellular differentiation, a process that is time-consuming, costly, and highly susceptible to variations in experimental conditions from one lab to another. Additionally, the current cellular model is insensitive to the toxic effects of aSyn, making it very difficult to monitor the effect of treatment on aSyn toxicity.

Purdue University researchers have developed an assay to address these challenges that uses an undifferentiated immortalized cell line that expresses aSyn at high levels. Importantly, aSyn is thought to carry out its neurotoxic effect in part by disrupting mitochondrial function; the new assay takes advantage of cell culture conditions to ensure that cells retain functional mitochondria. As a result, this assay displays pronounced aSyn toxicity enabling more robust measurement of a treatment's effect on toxicity. Because this assay does not require differentiation of the cell line, it is also more reproducible and less time-consuming.

Advantages:
-Less costly
-Faster
-Less susceptible to variation

Potential Applications:
-Screening assay for Parkinson's disease drug discovery
-Interrogation of Parkinson's disease biology

INTELLECTUAL PROPERTY:

Application Date: July 22, 2016
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Rochet, Jean-Christophe (Project leader)
Mishra, Vartika
Ysselstein, Daniel

CATEGORIES:

Pharmaceuticals, Chemistry and Chemical Analysis

KEYWORDS:

Assays, Chemistry and Chemical Analysis, Medical/Health, Neurodegenerative Disease, Parkinson's Disease, Pharmaceuticals

METHOD OF THIN FLEXIBLE ELECTRODE INSERTION FOR DEEP BRAIN NEURAL RECORDING AND THE DESIGN OF ELECTRODE INSERTION DEVICE

TRACK CODE:
2018-IRAZ-68150

Inserting a device to record deep brain activity is not a new technology. However, the current technology is not as efficient as it could be. Some of the problems with the current technology include leaving a flexible electrode behind after completion of the recording, coating with biodegradable materials to increase stiffness, and using a magnetic field to obtain necessary energy to penetrate the brain. All of these issues are very invasive to the brain that is being recorded and could potentially cause health issues for the individual. There is a need for a less invasive way to record deep brain activity.

Researchers at Purdue University have developed a new technology that allows for less invasive recording of deep brain activity. This new technology allows for insertion of 25 um platinum electrode in the deep brain. This electrode does not need any supporting tube, cannula, or biodegradable material to assist it in the recording of the deep brain. This means it is much less invasive and cause minimal neuronal damage. This new technology could open the door for recording deep brain activity.

Advantages:
-No support needed
-Less invasive
-Causes minimal neuronal damage

Potential Applications:
-Neurological studies
-Brain surgery

INTELLECTUAL PROPERTY:

PEOPLE:

Irazoqui, Pedro P. (Project leader)
Arafat, Muhammad Abdullah
Jefferys, John Gordon

CATEGORIES:

Biomedical Engineering, Medical/Health

KEYWORDS:

Biomedical Engineering, Medical Devices, Medical/Health, Neuroscience, Surgical Tools

ULTRASENSITIVE BIOSENSOR

TRACK CODE:
2019-ZUO-68465

Researchers at Purdue University have developed a biosensor that can detect ultralow concentrations of biomolecules. The biosensor successfully detected glucose and dopamine and could be used to detect other molecules which are difficult to detect using conventional methods. This biosensor detects biomolecules that release protons during enzymatic reactions unlike commercially available devices which rely on electron detection. The biosensor also has the capability to detect different biomolecules simultaneously. Dopamine and glucose were detected in water with a limit of detection of 50 and 500 attomolar concentration respectively. The biosensor is compact and can easily be integrated into wearable and implantable devices.

Advantages:
-Low limit of detection of biomolecules:
-100 million times more sensitive than conventional glucose monitor
-10,000x more sensitive than glucose transistor device
-10x more sensitive than glucose electrochemical sensor
-Capable of being integrated in implantable and wearable devices:
-Compact size
-Does not require external energy input
-Works at room temperature

Potential Applications:
-Glucose sensors
-Biomolecule sensors

Related Publication:
Perovskite nickelates as bio-electronic interfaces
Nature Communications 10, Article number: 1651 (2019)
DOI: 10.1038/s41467-019-09660-6

INTELLECTUAL PROPERTY:

Application Date: June 8, 2021
Type: NATL-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: December 10, 2019
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: December 19, 2018

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Zuo, Fan (Project leader)
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Li, Feiran
Ramanathan, Shriram
Zhang, HaiTian

CATEGORIES:
Chemistry and Chemical Analysis, Biomedical Engineering

KEYWORDS:
Biomarkers, Biomedical Engineering, Chemistry and Chemical Analysis, Diabetes, Diagnostics, Dopamine, Glucose, Medical Devices, wearable

HIGH-PERFORMANCE PLATINUM NEUROSTIMULATION ELECTRODE WITH 97% REDUCTION IN CORROSION

TRACK CODE:
2019-LEE-68525

Researchers at Purdue University have developed neurostimulation microelectrodes that solve the current concerns of safety and reliability, while still maintaining high performance. Platinum (Pt) is one of the most commonly used materials for neurostimulation devices due to its excellent biocompatibility and good charge transfer characteristics. Although Pt is regarded as safe, it commonly goes through irreversible electrochemical corrosion during neurostimulation which leaves cytotoxic byproducts. To combat these issues, Purdue Researchers micro-fabricated graphene-coated Pt microelectrodes with circular and fractal designs to show that graphene can significantly suppress Pt corrosion while maintaining excellent performance. In fact, over a 10 hour testing time, the graphene layer reduced Pt corrosion by 97 percent for fractal microelectrodes and 88 percent for circular microelectrodes all while retaining superior charge transfer characteristics.

Advantages:
-Decreased Corrosion
-Safe
-Reliable

Potential Applications:
-Neurostimulation devices

INTELLECTUAL PROPERTY:

Application Date: February 14, 2024
Type: CON-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 7, 2021
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: January 8, 2020
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Lee, Hyowon (Project leader)
Chen, Zhihong

Park, Hyunsu

CATEGORIES:
Biomedical Engineering, Electrical Engineering

KEYWORDS:
Biomedical Engineering, Corrosion, Electrical Engineering, Graphene, Materials and Manufacturing, Neurostimulation, Platinum Electrode

ARTIFICIAL RETINA BASED ON PHOTON-ASSISTED ELECTROCHEMICAL DOPING

TRACK CODE:
2022-MEI-69888

Researchers at Purdue University have developed an artificial retina based on a photonic-organic electrochemical transistor (related: 2023-MEI-70196). The device is capable of emulating typical synapse behaviors, including paired-pulse facilitation (PPF), short-term plasticity (STP), and long-term plasticity (LTP). This is achieved by means of electrochemical doping facilitated by captured light. When the light source is turned off, some electrons remain separated from holes resulting in nonvolatile memory. Additional advantages include a low writing voltage (< 1 V), and a high light responsiveness. By leveraging the functions of light sensitivity, data processing, and memory, a single layer synapse array was used for facial recognition with high efficiency. Broader applications include computer vision and high bandwidth computing based on electronics mimicking biological functions (brain synapses, iris, etc). Devices made from this technology are ideal for interfacing biosystems.

Advantages:
- Low writing voltages (< 1 V)
- Emulation of synapse behaviors
- High light responsiveness
- Interfacing with biosystem

Applications:
- Computer vision
- High bandwidth computing
- Photonics
- Facial recognition

Technology Validation:
This technology has been validated through fabrication of a prototype system which was tested in facial recognition applications.

Related Publications:
Ke Chen et al, Organic optoelectronic synapse based on photon-modulated electrochemical doping, Nature Photonics (2023). DOI: 10.1038/s41566-023-01232-x

https://techxplore.com/news/2023-11-human-eye-boost-vision-efficiency.html

INTELLECTUAL PROPERTY:

Application Date: March 7, 2024
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 9, 2023

Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Mei, Jianguo (Project leader)
Chen, Ke

CATEGORIES:
Electrical Engineering, Biomedical Engineering

KEYWORDS:
biological, Computer Vision, Electrochemical, facial recognition, machine vision, Photonic, Photonic Devices, Photons, Photovoltaics, retina, synapse, Transistors

LIGHT PIPE MICROSCOPE FOR LARGE-SCALE DYNAMIC IMAGING

TRACK CODE:
2023-CUI-69962

Researchers at Purdue University have developed a method for better understanding the animal brain and neurological disorders. This method involves a redesign of the microscope for more detailed imaging along with capturing signals that are sent through the brain. The light pipe microscope can take images on a centimeter scale instead of the current millimeter scale along with multiple larger regions simultaneously instead of one region at a time. This large region imaging allows imaging of the entire brain with high resolution. This technology can be used to observe various types of cells noninvasively across the entire brain which can benefit neuroscience research and possibly be used in the medical field on humans in the future.

Technology Validation:
This technology has been validated using a prototype light pipe microscope. This prototype successfully enabled in vivo deep-tissue calcium imaging.

Advantages:
- Large-scale and high-resolution images of the brain
- Efficient deep tissue imaging
- Detail understanding of animal brain functions.

Applications:

- Simultaneously image the entire brain of animals for neuroscience research.
- Large region imaging for intraoperative fluorescence imaging.
- High-performance miniature microscope for head-mounted systems.

INTELLECTUAL PROPERTY:

Application Date: August 30, 2023
Type: Utility-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: August 30, 2022
Type: Provisional-Gov. Funding
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Cui, Meng (Project leader)

CATEGORIES:

Biomedical Engineering, Medical/Health

KEYWORDS:
Biomedical Engineering, deep-tissue, Imaging, light pipe, Medical/Health, Microscope, Neurological Disorders, Neuroscience

NOVEL PATIENT-SPECIFIC METHOD TO PREDICT PROSTATE CANCER RELAPSE AFTER RADIATION THERAPY

TRACK CODE:
2023-DIAZ-70044

Researchers at Purdue University, Universita degli Studi di Pavia, and Universidad de Castilla la Mancha have developed a biomechanistic model that provides personalized predictions of prostate-specific antigen (PSA) dynamics for patients after external radiotherapy. Detection of prostate cancer recurrence depends on measuring the sustained rise of serum PSA in patients, but this biochemical relapse is variable and unpredictable. Therefore, identifying patients with relapsing prostate cancer through radiation therapy usually occurs too late. Current observational metrics of PSA dynamics offer a limited representation of underlying tumor development, which delays diagnosis and treatment of tumor recurrence.

This method helps oncologists and doctors treating patients with prostate cancer identify tumor recurrence earlier than conventional methods after external radiotherapy. The model predicts the occurrence of biochemical relapse to facilitate an earlier diagnosis, maximizing the chances of tumor control. This method is an excellent tool for prostate cancer personalized medicine, as it is patient-specific and provides the opportunity to implement treatment more quickly.

Technology Validation:
The model-based predictors of release identified relapsing patients a median of 14.8 months earlier than the current clinical practice.

Advantages:
-Earlier detection of tumor reoccurrence for prostate cancer patients
-Accurately predicts PSA dynamics
-Personalized and patient-specific

Applications:
-Personalized medicine companies
-Doctors using radiation therapy to treat patients with prostate cancer

INTELLECTUAL PROPERTY:

Application Date: March 7, 2024
Type: Utility Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

Application Date: March 7, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Gomez Diaz, Hector (Project leader)
Lorenzo, Guillermo
Perez Garcia, Victor
Reali, Alessandro

CATEGORIES:
Medical/Health, Biotechnology

KEYWORDS:
Biotechnology, Medical/Health, personalized medicine, prediction, Prostate Cancer, relapse

PHOTONIC-ORGANIC ELECTROCHEMICAL TRANSISTOR

TRACK CODE:
2023-MEI-70196

Researchers at Purdue University have developed a photonic-organic electrochemical transistor (POECT). This device uses the 3-terminal layout of a conventional transistor (source, drain, gate), but uses light rather than electricity as the means of signal transmission enabling significantly faster transmission while mitigating crosstalk. Test results from a prototype POECT demonstrated continuously programmable conductance states and low writing energy. Applications of this technology will allow for the creation of systems that emulate biological synapse functions or artificial retinas.

Advantages:
- Ultra-fast signal transmission
- Limited crosstalk between transistors
- Continuously programmable conductance states
- Low writing energy

Applications:
- Biosensors
- Synaptic devices for biological applications
- Neuromorphic computing
- Emulation of biological elements (artificial retina)

Technology Validation:
This technology has been validated with lab-scale fabrication and testing of the proposed device.

Related Publications:
Ke Chen et al, Organic optoelectronic synapse based on photon-modulated electrochemical doping, Nature Photonics (2023). DOI: 10.1038/s41566-023-01232-x

https://techxplore.com/news/2023-11-human-eye-boost-vision-efficiency.html

INTELLECTUAL PROPERTY:

Application Date: March 7, 2024
Type: PCT-Patent
Country of Filing: WO
Patent Number: (None)
Issue Date: (None)

Application Date: March 9, 2023
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:

Mei, Jianguo (Project leader)

Chen, Ke

CATEGORIES:
Chemistry and Chemical Analysis, Electrical Engineering

KEYWORDS:
biological, Electrochemical, Photonic, Photonic Devices, Photons, Photovoltaics, Transistors

FORMULATION FOR NOVEL, BLOOD CATALYZED CONDUCTIVE POLYMER FOR USE IN BIOELECTRONICS, BIOIMAGING, AND BIOSENSORS

TRACK CODE:
2024-MEI-70435

Researchers at Purdue have synthesized a blood catalyzed, electrically conductive n-doped polymer (dubbed n-PBDF) through in vivo polymerization in a zebra fish embryo. Conductive polymers (CP) have gained attention for their possible use in biomedical applications such as bioimaging, biosensors, neural interfaces, and drug delivery for charged drug molecules, with zebrafish embryos emerging as a potential platform for biomedical applications due to their high throughput and cost-effective breeding and screening, ease of genetic manipulation, and relevance for human applications. However, current CP formulations for biomedical applications require injection of pre-polymerized CPs into living tissue, increasing complexity and causing possible plugging of vasculature or aggregation around neurons for neural stimulation applications. Other methods involve genetic modification of living systems to produce enzymes for in vivo polymerization of the CP monomers, which is not ideal for human applications.

The researchers discovered that whole human blood effectively acted as a catalyst to produce n-PBDF CPs. Additionally, the researchers verified the ability to produce n-PBDF CPs in vivo, in a zebra fish embryo, with low toxicity observed.

Technology Validation:
The formation of n-PBDF conductive polymer was verified in vitro by conducting a kinetics study in which 25 mM BDF (the monomer) is dissolved in RPMI-1640 media with 10% FBS and 0.1 mol% Hb and measuring the spectrogram of the solution for 360 minutes in UV-Vis-NIR. The overall absorbance of the solution increased with time, especially in the Vis-NIR region, indicating polymerization of BDF to n-PBDF. The conductivity of the polymer was improved when using RPMI media with 10% FBS as the solvent, as compared to PBS with Hb, giving a maximum conductivity of 1.6 S/cm at 0.5 mol% Hb. By observing the reaction kinetics under UV-Vis-NIR spectroscopy, the researchers discovered that whole human blood acted as a more efficient catalyst for polymerization than isolated red blood cells, and that the minimum concentration of the monomer necessary for polymerization using this method was 5 mM BDF.

The ability to polymerize BDF monomers in vivo was tested by injecting zebrafish embryos with 1 mM – 15 mM BDF monomer with 1% w/v TPGS in PBS and incubating at 34 ?C for 24 hours. Polymerization was verified in vivo by measuring the absorbance of the control and experimental zebrafish embryos, with strong peaks observed at 960 nm in the experimental group, indicating successful polymerization of the monomer. All embryos injected with 5 mM BDF and above were observed to darken the yolk with the n-PBDF. Additionally, at least 80% of the BDF-treated embryos survived the full 24 hours of incubation and showed similar movement to the control embryos, indicating low toxicity of the polymer. When tested against A549 lung-cancer cells, the researchers found the n-PBDF polymer to be non-toxic, with viability remaining near 100% regardless of the polymer concentration. When incubated with the monomer however, the cancer cell viability dropped to 75% and 10% for monomer concentrations of 5 ug/mL and 0.167 mg/mL, respectively, in a 72-hour assay.

Advantages:
- Blood catalyzed; minimal reactants introduced to living system
- Low toxicity in zebra fish embryo and A549 lung-cancer cell model
- Relevant for human applications

Applications:
- Bioimaging
- Biosensors
- Bioelectronics
- Neural interfaces
- Drug delivery

INTELLECTUAL PROPERTY:
Application Date: January 29, 2024
Type: Provisional-Patent
Country of Filing: United States
Patent Number: (None)
Issue Date: (None)

PEOPLE:
Mei, Jianguo (Project leader)
Samal, Sanket

CATEGORIES:
Biomedical Engineering, Biotechnology

KEYWORDS:
Bioelectronics, Bioimaging, Biomedical Engineering, Biotechnology, Conducting Polymer