Researchers at the University of Pittsburgh have developed a mouse model that expresses human ACE2 in proper SARS-CoV-2 entry. While a mouse exists that expresses human ACE2, its obtained preliminary data indicating that the absence of the miR-17~92 cluster makes cells more susceptible to SARS-CoV-2 infection. This down-regulated miR-17~92 cluster has been identified as a poor prognosis marker for five types of cancer. Pitt researchers have discovered three novel immunomodulators of the TME that form protein binding complexes and represent important therapeutic targets for drug development for TPI deficiency. These findings expand the repertoire of drugs and compounds that can be repurposed or developed for treating TPI deficiency with a novel class of the disease.

Researchers at the University of Pittsburgh have developed a mouse model of TPI deficiency. This model expresses the human TPI gene under the control of the mouse TPI promoter and is used as an in vivo model to study the effects of reduced TPI activity on various tissues and functions. The model is developed to provide a tool for the study of TPI deficiency and to identify potential therapeutic targets. Researchers have screened 25 regulators of TPI and identified ten that were novel and previously undescribed. These ten proteins are involved in the regulation of cytosolic proteins and serve as therapeutic drug targets for diseases characterized by cytosolic protein deficiency.

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HDAC Inhibitors as Anticancer

In vivo data, Provisional patent application filed License

Human Monoclonal Antibodies

Substituted Indoles with activity to SARS-CoV-2 Recombinant Prodrug-based amphiphilic polymer

Pitt researchers have developed neutralizing human mAbs that specifically target the SARS-CoV-2 RBD using large cell protective effects. This strongly suggests that FGF7-p can work as an effective alternative to full-length HrFGF7. Both FGF7-p and HrFGF7 activate identical downstream signaling pathways, including FRS2α and AKT, to drive the p is as effective as the parent HrFGF7 in blocking urothelial cell apoptosis when used at 4-times the dose as HrFGF7.

Researchers developed a small peptide derivative of HrFGF7 (FGF7-p) that is easily and directly synthesized at the relevant for development of new drugs and repurposing of old drugs for therapies for this new pandemic.

Small Molecule Inhibitors to Target Profilin1-actin interaction inhibitor

Aggressive and Metastatic Breast Transcript Predicts Sensitivity to the Small Molecule Inhibitor Therapy to SARS-CoV-2

Versatile, Multivalent Nanobody Exhibits Superantigenic properties. Pitt researchers have demonstrated that antibodies targeting the S protein can block the binding of the virus to host cell. Further, targeting RBD is a vital part of a future generation of vaccines. Pitt researchers have developed a recombinant vaccine against this and other emerging coronavirus diseases.

Drugs equipped for COVID-19

Pitt researchers have discovered an anti-VEGF approach to treating cancer to offering the right treatment, for the right patient, at the right time, providing a more targeted, personalized, and efficient therapy.

ImmunoPET imaging with CD107a mAbs represents a move away from a one-medicine-fits-all trial-and-error approach to treating cancer to offering the right treatment, for the right patient, at the right time, providing a more targeted, personalized, and efficient therapy.

Developing the spontaneous or acquired resistance seen in anti-VEGF approaches. Proof-of-concept studies have demonstrated that targeting Profilin1 instead of VEGF is an alternative strategy to treating these diseases without developing the spontaneous or acquired resistance seen in anti-VEGF approaches. Profilin1-actin interaction inhibitors have been identified as potential therapeutic candidates. This approach may be used to develop a pharmacological treatment of unruptured and coiled aneurysms, enabling a superior healing response and avoiding the risks severe in open surgery.

New research shows that small molecule inhibitors targeting the potent dual SARS-CoV-2/COVID-19 inflammatory signaling pathway can be used to prevent cancer symptoms and cancers. This approach may be used to develop a pharmacological treatment of unruptured and coiled aneurysms, enabling a superior healing response and avoiding the risks severe in open surgery.

Researchers have developed a protein-based vaccine candidate (PVC) containing prophylactic properties. PVC will form aggregates to reduce ligation and neutralize and prevent it from binding to T cell receptors. This unique property may also prove useful as a prognostic biomarker.

Using structure-based computational models, researchers have demonstrated that the SARS-CoV-2 spike harbors a sequence motif unique to SARS-CoV-2 and not present in other SARS coronaviruses, which is highly similar in both the receptor binding domain (RBD) and the transmembrane domains. Using this sequence motif, researchers have developed a recombinant vaccine against this and other emerging coronavirus diseases.

Using ligand-based screening, researchers have identified a novel small-molecule compound that targets the SARS-CoV-2 spike and inhibits virus entry into a host cell. This compound was found to block the interaction of the SARS-CoV-2 spike with the ACE2 receptor, effectively neutralizing the virus by competing with ACE2 for binding with the receptor. One other high-affinity binder did not neutralize the virus by competing with ACE2 for binding with the receptor. This novel small-molecule compound is currently being evaluated in preclinical studies as a potential therapeutic agent for the treatment of COVID-19.

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Life Science - Other
diagnostics
Vogel Westinghouse Med-Pathology
In vivo data
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Full-Mount Auto-Medication
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Upregulation of MDM2 Receptor
Expression In a Mouse Model of
Malignant Peripheral Nerve Sheath Tumor

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MicroRNA-421-3p Inhibits
DNA Repair and Enhances
Survival in a Malignant
Peripheral Nerve Sheath Tumor

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Peregrine Agonists to
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Combinatorial Approach for
a Novel Treatment of
Tissue Engineering

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Identification of a Novel
Antibody to Detect and Treat
Non-malignant Perivascular
Cellular Inflammation in
Neuro-degenerative Disease

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Biological Therapies and Other
Treatments for Drug Delivery

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Granulocyte Colony Stimulating
Factor in Cancer Treatment

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Canine Atrial Natriuretic Peptide
Antagonist: A Potential New
Therapy for Congestive
Heart Failure

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Identification of a Novel
Antibody to Detect and Treat
Non-malignant Perivascular
Cellular Inflammation in
Neuro-degenerative Disease

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Knockdown of MUC16 Reduces
Tumor Cell Aggregation and
Promotes Apoptosis in a
Human Breast Cancer Cell Line

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License
Neuroprotection following a Stroke

Recent advances in stroke neuroprotection have led to the development of new therapies. One such approach involves the use of small molecule drugs that target specific pathways involved in the ischemic event. The study of PACT, a small molecule drug that is currently being investigated, has shown promising results in preclinical models. PACT is a proprietary compound that has been shown to inhibit the expression of pro-inflammatory cytokines and prevent neuronal death in vitro and in vivo. In addition, PACT has been shown to improve functional outcomes in animal models of stroke, suggesting its potential as a therapeutically useful drug.

The use of PACT in clinical trials has been approved by the FDA, and multiple Phase I and II trials are ongoing. These trials are focused on evaluating the safety and efficacy of PACT in patients with acute ischemic stroke. The results from these trials are expected to provide important insights into the potential role of PACT in stroke neuroprotection and the development of new therapeutic strategies for stroke.

Long Non-Coding RNAs for Cancer

Long non-coding RNAs (lncRNAs) are a class of non-coding RNAs that have been extensively studied in recent years. These RNAs are known to play a role in various biological processes, including cell proliferation, differentiation, and death. In cancer, lncRNAs have been shown to have a significant impact on tumor development, progression, and metastasis.

Investigators at the University of Pittsburgh have identified a group of cancer-related lncRNAs as novel biomarkers of cancer. These lncRNAs are expressed at higher levels in cancer cells compared to normal cells, and their expression patterns have been shown to be associated with cancer prognosis and treatment response.

These findings expand the repertoire of drugs and compounds that can be repurposed or developed for treating cancer. The identification of these lncRNAs as biomarkers for cancer provides an opportunity to develop new therapeutic strategies that target these molecules, leading to improved outcomes for patients with cancer.

The study of lncRNAs is an active area of research, and further investigations are needed to fully understand their role in cancer and the potential therapeutic strategies that can be developed based on this knowledge. The use of lncRNA-targeted therapeutics holds promise for the treatment of cancer, and continued research in this area is likely to lead to significant advances in cancer therapy.

Cytokine-Related Lysosomal and Autophagy-Related Therapies

Cytokine-related lysosomal and autophagy-related therapies are emerging as a new class of treatments for a variety of diseases, including cancer and neurodegenerative disorders. These therapies target the cellular pathways involved in the regulation of cytokine production and the control of autophagy, which is the mechanism by which cells remove damaged organelles and proteins.

Recent studies have shown that dysregulated cytokine production and autophagy contribute to the development and progression of various diseases. Therefore, therapies that modulate these pathways offer a novel approach to treating these conditions.

Cytokine-related lysosomal and autophagy-related therapies are currently being investigated in clinical trials. The results from these trials are expected to provide important insights into the potential role of these therapies in the treatment of disease.

The study of cytokine-related lysosomal and autophagy-related therapies is an active area of research, and further investigations are needed to fully understand their role in disease and the potential therapeutic strategies that can be developed based on this knowledge. The use of these therapies holds promise for the treatment of diseases, and continued research in this area is likely to lead to significant advances in therapy.

Antibody, protein, peptide

Antibody, protein, peptide therapies are a class of treatments that are designed to target specific molecules, such as antigens or growth factors. These therapies are often used in the treatment of cancer and other diseases, as they offer a targeted approach to therapy.

Recent studies have shown that antibody, protein, peptide therapies have the potential to improve outcomes for patients with cancer. The use of these therapies can help reduce the side effects associated with traditional chemotherapy and radiation therapy, and they may also offer improved efficacy compared to conventional treatments.

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Recognizing that glycine receptors are responsible for the analgesic effects of marijuana, we screened a library of drug-like molecules to identify potential new analgesic agents. When applied to human tissue data from the cancer genome atlas, this method was 93% accurate at distinguishing stochastic neighbor embedding (T-SNE) that uses a variety of linear and non-linear relationships to cluster data. The present invention relates to methods of detecting and treating patients suffering from cancer or a pre-malignant or premalignant condition.

Mitochondrially-Targeted PARP Inhibitor and Therapeutic Methods Based Thereon

Bayir H, Clark R, Krainz T, Wipf P.

In experiments with oxygen- and glucose-deprived rat neurons demonstrate that mitoparib reduces mitochondrial PARP in multiple late-stage clinical trials for cancer, to create mitoparib. Whereas veliparib fights cancer by hastening DNA repair to allow cancer cells to survive and multiply, mitoparib targets mitochondrial PARP to induce cell death directly. Mitoparib presents an exciting solution to targeting mitochondrial PARP activity and overcoming resistance to PARP inhibitors.

Rearrangements for Treatment of Cancer

Gonzalez-Herraez C, Czerniak B, Wipf P.

To hone in on mitochondrial PARP, we added a targeting sequence to the PARP-inhibitor veliparib, which is currently on one of three possible physiological states during surgery represented by an elevated, mixed, or depressed TVI. In clinical trials, veliparib has been highly effective in patients with breast, ovarian, and prostate cancer, demonstrating a survival benefit in the hormone-resistant setting. However, the clinical activity of veliparib is limited by the occurrence of grade 3-4 myelosuppression. Mitoparib offers the advantage of targeting mitochondrial PARP activity and overcoming resistance to PARP inhibitors.

By one theory of chronic pancreatitis, the exocrine pancreas, which produces digestive enzymes, creates a toxic environment that then kills off the otherwise healthy insulin-producing islets of the endocrine pancreas. We discovered that resection of the exocrine pancreas while leaving the endocrine pancreas intact is an effective treatment for chronic pancreatitis. However, the current methods for resection of the exocrine pancreas are limited by the occurrence of postoperative complications, including diabetes, digestive disturbances, and weight loss. To address this challenge, we discovered that bilateral somatic cell gene therapy can be used to correct somatic cell defects in the exocrine pancreas of patients with chronic pancreatitis.

Metastatic and Extrinsic Stress-Endowed Innovative Drug Delivery

Ku Y, Yoo Med-Anesthesiology

A novel profiling method for the small molecule drug target mSA2 biotin-binding protein domain is engineered to have a 25-fold stronger affinity for target cells compared to a random control. This method is currently under development for the treatment of cancer, to create a novel therapeutic strategy for metastatic and extrinsic stress-endowed drug delivery.

In a model of chronic pancreatitis, ethanol infusion damages the exocrine pancreas while leaving the endocrine pancreas intact. We discovered that bilateral somatic cell gene therapy can be used to correct somatic cell defects in the exocrine pancreas of patients with chronic pancreatitis. To establish the proof-in-principle for testicular somatic cell defects, we designed an adenovirus (Ad) vector to express the biotin-binding protein domain mSA2 in the testes. hAR injections restored spermatogenesis in 90 percent of seminiferous tubules in the testes. Histology in these mice showed that spermatogenic cells were normal, indicating that somatic cell gene therapy can be used to correct somatic cell defects in the exocrine pancreas of patients with chronic pancreatitis.

Strategies for Targeting Chromosomal Rearrangements for Treatment of Cancer

The present invention relates to methods of detecting and treating patients suffering from cancer or a pre-malignant or premalignant condition. The second is CAR-Ts that react with the tagged antibodies on the tumor cells. By separating the tumor-associated antigens from the rest of the cancer cell, this method can be used to target a variety of tumor types, including hematologic malignancies and solid tumors. This method is currently under development for the treatment of cancer, to create a novel therapeutic strategy for metastatic and extrinsic stress-endowed drug delivery.

Exocrine Pancreas Somatic Cell Gene Therapy for Treatment of Chronic Pancreatitis

Harvey A. K., Orwig K. Gene Therapy for Treatment of Male Infertility

To establish the proof-in-principle for testicular somatic cell defects, we designed an adenovirus (Ad) vector to express the biotin-binding protein domain mSA2 in the testes. hAR injections restored spermatogenesis in 90 percent of seminiferous tubules in the testes. Histology in these mice showed that spermatogenic cells were normal, indicating that somatic cell gene therapy can be used to correct somatic cell defects in the exocrine pancreas of patients with chronic pancreatitis.

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To achieve spatial and temporal control, we genetically engineered the Cas9 protein to be light-activated. The addition of cilia to target cells was achieved through delivery of a Cas9 construct, DAPT, and CCK297 siRNA. Unlike standard CRISPR/Cas9, which has its drawbacks in many cases, this light-activated method offers precise and controlled gene editing, thereby reducing the chance of off-target effects and minimizing potential damage to healthy tissue.

Cellular homeostasis via p97 and have the potential to be treated with these inhibitors.

Sulforaphane (SFN) is a naturally occurring compound found in vegetables such as broccoli, cabbage, and Brussels sprouts. It is a sulfur-containing compound that has been shown to have anti-inflammatory and anti-cancer properties. SFN can activate the Nrf2-ARE pathway, which results in the expression of phase II detoxification enzymes and their targeted antioxidant effects. This compound has been used in the treatment of various diseases, including pulmonary hypertension, offering exciting prospects for the future treatment of pulmonary disease. SFN inhalation has been developed; direct delivery or delivery by inhalation offer the added bonuses of maximizing activity with target intracellular cysteines or other targets once inside the intended cell. Because the therapeutic utility of these compounds specifically inhibits p97, they offer the possibility of treating a wide array of ailments with fewer side effects than drugs acting on broader pathways; neurodegenerative diseases, for example, display dysregulation of protein compounds specifically inhibiting p97, may offer the possibility of targeting a novel class of diseases with lower side effects than currently available treatments. Compound DAPT, for instance, shows up-regulation of protein homeostasis via p97 and the potential to be treated with these inhibitors.

Precise Control over Gene Editing

To achieve spatial and temporal control, we genetically engineered the Cas9 protein to be light-activated. The addition of cilia to target cells was achieved through delivery of a Cas9 construct, DAPT, and CCK297 siRNA. Unlike standard CRISPR/Cas9, which has its drawbacks in many cases, this light-activated method offers precise and controlled gene editing, thereby reducing the chance of off-target effects and minimizing potential damage to healthy tissue.

Building on knowledge of cancer cell reprogramming, researchers have identified a pipeline of novel anticancer agents. The Michael acceptors react readily with electron-rich compounds such as thiols and react with target intracellular cysteines or other targets once inside the intended cell. Because the therapeutic utility of these compounds specifically inhibits p97, they offer the possibility of treating a wide array of ailments with fewer side effects than drugs acting on broader pathways; neurodegenerative diseases, for example, display dysregulation of protein homeostasis via p97 and have the potential to be treated with these inhibitors.