INTRODUCTION

Each year in the United States, more than 1.6 million people are diagnosed with cancer and more than half a million die from this terrible disease. And each year, our researchers spend thousands of hours in their laboratories looking for cures.

The fight against cancer doesn’t start in the doctor’s office. It begins in places like the Purdue University Center for Cancer Research, where world-renowned scientists search inside cells for the origins of cancer.

Using the combined expertise of scientists from disciplines as varied as engineering and veterinary medicine, biology and chemistry, the Center for Cancer Research promotes discovery into how cancers develop, progress, and respond to treatment. Our work leads to the advancement of new medicines, early detection and diagnostic methods, more effective treatments and highly efficient drug delivery systems – all with the hope of seeing fewer cases and more survivors each year.

Tim’s Twigs is a strategic research initiative in which individuals or foundations have the opportunity to make a genuine impact on innovative research. This funding spearheads new research projects that otherwise may not get off the ground. With start-up funding for these strategic initiatives, the projects are likely to attract larger grants in the future, thus moving discoveries from the research laboratory to the clinic faster to save lives. Learn more inside and join with us in saving lives.

PREVIOUSLY FUNDED PROJECTS

- Prostate Cancer Research - Adult Prostate Stem Cells
- Super Computing for Cancer
- Canine Bladder Cancer and its Relationship to Human Cancer
- Human Clinical Trial of Combo-therapy in Pancreatic Cancer
- Novel Biosensor Platform in Pancreatic Cancer Diagnostics
Development and Testing of a MicroRNA Sponge Inhibitor for Liver Cancer

There are 250 million people in the world that are chronically infected by Hepatitis B virus (HBV) who are at very high risk of developing liver cancer in the next 20 years. Although an HBV vaccine is available, the vaccine will not work for people who are already infected. More disturbing, is the fact that children born from HBV infected mothers become chronic carriers of the virus, destined to develop liver cancer in early adulthood. Sadly, liver cancer is incurable. A drug (sorafenib) that is used now with liver cancer patients, only extends life by two-three months. Thus, we are in great need of new drugs that target and inhibit key molecules in the liver to block and cure the disease.

The Andrisani laboratory has now identified a way to prevent the destruction of a protein (PRC2 complex) that happens during infection by the virus. These are ongoing studies and have not yet been published. They have found a group of genetic material, called microRNAs, which block the production of a key component of the PRC2 complex. In experiments using cells grown in the petri dish, they used an inhibitor that blocks these microRNAs from acting, called a “microRNA sponge” because it soaks up specific microRNAs.

The next step in this innovative research is to show that this "microRNA sponge" will work in suppressing formation and growth of tumors. The study of this and the mechanisms discovered will help researchers understand its functions in liver and other types of human cancers, including prostate and pancreatic cancers.

Funding Needed: $15,000                Dr. Ourania Andrisani
A Revolutionary Model for the Treatment of Metastatic Liver Tumors with Radiotherapy

Primary and metastatic liver tumors are a major source of mortality. The liver is a primary target for metastatic gastrointestinal, genitourinary, and breast cancers. Ninety percent of such tumors cannot be surgically removed, leaving limited treatment options (mostly aggressive chemotherapy and, to a limited extent, radiotherapy). This project aims to design a new liver-on-a-chip model (mimics the architecture and physiology of the human liver) to be used to test engineering-based therapies for liver metastasis.

The urgent need for this model is to assess a microablator system (high-energy radio waves for treatment) that might revolutionize the management of patients with liver metastasis, a frequent consequence of major types of cancers usually associated with very poor outcomes. Once the liver-on-a-chip for metastasis study is built and validated, it will become a precious research and preclinical tool for researchers to design, test and validate new therapies of metastases from any cancer type that disseminates to the liver. We strive to perform enough work to have the preliminary results necessary to apply for a translational extramural grant.

Funding needed: $15,000

Dr. Sophie A. Lelièvre
Dr. Babak Ziaie

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Microfluidic Tumor Platform (MTP): New Platform for Evaluating Drug Screening and Drug Delivery

The Han laboratory research aims to develop a new tumor model, using microfluidics and tissue engineering technology, capable of re-creating the tumor environment. To achieve the research objective, the Han laboratory needs to design and fabricate the Microfluidic Tumor Platform (MTP) and test them using tumor and tumor stem cells.

The structure of the platform, named tumor-microenvironment-on-chip (T-MOC), is used to mechanically simulate the environment of a tumor. The chip recreates a fluid and tissue environment that would naturally be present. This T-MOC has channels and these channels simulate the exchange of drug into and throughout the tumor; similar to what occurs in the tumor’s capillary blood vessels. The fabrication was validated through wet laboratory techniques and cell culture. The goal was to utilize advanced modeling and quantitative measures to show a difference with or without drug treatment. The results suggest that the T-MOC platform is capable of providing detailed information to test and improve new drugs and drug delivery systems. We aim to put this T-MOC into practice to solve the pancreatic cancer problem.

Pancreatic cancer, specifically pancreatic ductal adenocarcinoma (PDAC), is one of the deadliest cancers. In 2016, about 53,000 new cases and 42,000 deaths are estimated to occur in the United States. Although the five-year survival rates of other cancers have been improved, the survival rate of PDAC remains at dismal 7% and hasn't been improved significantly from 3.0% in 1975. This is attributed to the difficulty of early diagnosis, the short relapse time, frequent metastases, failure to achieve effective intra-tumor drug delivery, and intrinsic drug resistance of the cancer cells. Most PDAC patients with an inoperable tumor, which is approximately 80% of patient population, are currently treated with various chemotherapeutic drugs.
Most often, these chemotherapeutic regimens prolong life by only a few months. Consequently, treatment outcomes are still significantly limited so that overall median survival is a dismal 8-12 months in patients with localized disease, and 4-6 months in patients with metastatic disease. This limited treatment outcome is primarily due to poor delivery of drugs to cancer cells, which is thought to be associated with one of the most notable characteristics of PDAC; its desmoplasia, a growth situation that creates a unique environment to understand. Understanding how drugs interact and are delivered is important because the environment significantly hinders treatment and poses a significant barrier to successful delivery of drugs to kill pancreatic cancer cells. There is a dire need for novel therapeutic approaches to identify promising drug candidates and improve the delivery of currently available drugs, as well as develop new drug candidates.

**Funding needed: $15,000**

Dr. Bumsoo Han

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**Targeting PRMT5 as a Novel Treatment for Neuroendocrine Prostate Cancer**

Prostate cancer remains the second leading cause of cancer death among American men according to American Cancer Society. The vast majority of prostate cancer death is due to the development of castration resistant prostate cancer (CRPC), a lethal and end stage of the disease. Despite multiple mechanisms that may underlie the development of CRPC; neuroendocrine differentiation (NED), a process by which prostate cancer cells change into neuroendocrine prostate cancer (NEPC), represents an emerging and important mechanism. NEPC is highly aggressive and tends to metastasize to internal organs with an average survival of less than one year. The Hu laboratory is working on developing an effective treatment for NEPC that will provide an urgently needed option to manage this deadly disease.

**cont. p.5**
OPPORTUNITIES FOR FUNDING (continued p.5)

During the course of this research, the lab identified a protein called protein arginine methyltransferase 5 (PRMT5), which is key to genetic regulation. Although we have made some progress, we are still in need of two pieces of critical preliminary data. First, we need to determine genes that are regulated by PRMT5 in NEPC. Second, we need to acquire several NEPC tumors from prostate cancer patients. These tumors are available and used to create patient-derived models for studying cancer. Completion of the proposed mechanistic and preclinical studies with a novel PRMT5 inhibitor will provide preclinical evidence that targeting PRMT5 is a novel and effective treatment for NEPC, so patients with this type of disease have a treatment option.

Funding needed: $15,000

Dr. Chang-Deng Hu

Synergistic Combinations that Overcome Therapy-Resistant Tumors, using Nanomedicines

Gold nanoparticles in tumor tissues can synergize with various anti-tumor therapies by introducing localized heat to enhance drug action. These synergies are critical for eliminating tumor cells that are resistant to chemotherapy or radiotherapy. Combining gold nanoparticles with drugs and biologics is a powerful strategy for defeating chemo-resistance in tumor tissues without increasing toxic side effects.

There is exciting progress in the development of therapeutic approaches against cancer, many of which have reached the clinic. To be effective, drugs and radiation therapy are administered at their maximum tolerated doses, in the hopes of killing cancer cells without greatly compromising the patient’s quality of life. However, cancer cells often become resistant to these treatments. This is especially problematic with recurrent cancers, which are evolved from a small population of surviving cancer cells that have acquired a greater ability to resist the killing effects of drugs or radiation. To overcome these resistant cancers, we need combination therapies that can knock out resistance factors and re-sensitize tumor cells to chemotherapy.
Nanomedicines based on the unique properties of gold nanoparticles offer a promising approach to enhance cancer therapies. Gold nanoparticles (NPs) are not toxic on their own, but can absorb energy from laser pulses and x-ray beams to produce various anti-tumor effects. When properly timed, these effects can boost the potency of chemo or radiotherapy against recurrent tumors that are resistant to standard treatments. For example, we have shown that gold NPs can produce heat inside of tumors that enhances cisplatin therapy (a long used cancer therapy for bladder, cervical, ovarian, lung, gastric, breast, and head and neck cancers, along with malignant mesothelioma and some less-common tumors; first approved in 1978). Local heating helps cisplatin get inside of tumor cells, and also causes DNA to unravel which increases its exposure to cisplatin.

Unfortunately, heat is not enough to completely overcome tumor resistance to cisplatin therapy. Tumor cells have multiple ways to combat drug action, such as by repairing DNA damaged by cisplatin or by producing enzymes that allow tumor cells to change into other forms with greater chemo-resistance. Simply increasing cisplatin is not the answer, as too much will cause severe side effects. This means implementing new strategies that can defeat these resistance factors.

We are developing a two-pronged approach to create synergy with nanoparticle-based systems. The first prong involves the design of gold NP carriers for targeted delivery of agents (RNA molecules) that can “knock down” resistance factors inside of tumor cells, while also producing localized heat. The second prong involves the production of “nano-capsules” for delivering potent anti-cancer drugs to where they are needed—while keeping them out of areas in the body where they might cause harm. These can be used together in ways that bring out the maximum benefit of each type of therapy.

**Funding needed: $15,000**

Dr. Alexander Wei