The Young Innovators Program
at the Eshelman Institute for Innovation
Description for Intern Candidates
January 12, 2017

What is the Young Innovators Program (YIP)?

YIP is a direct programmatic offering of the Eshelman Institute for Innovation for high school students interested in career paths in STEM and, specifically, the pharmaceutical sciences and pharmacy practice. As such, the purpose of YIP is to immerse top tier high school students in research laboratories (where they pursue real research projects), expose them to the clinical environments of pharmacy practice, and provide them intensive mentoring support aimed at enhancing their scientific knowledge, growing their interest in STEM, and challenging them to think creatively and critically as they solve real and urgent healthcare problems.

What do YIP Interns do during the 8 week summer program?

- Pursue mentored laboratory projects provided by hosting faculty at the UNC Eshelman School of Pharmacy, UNC Department of Chemistry, and Lineberger Comprehensive Cancer Center.
- Attend and present data at their laboratory's regularly scheduled meetings.
- Participate in panel discussions where interns can interact with undergraduate researchers, graduate and professional students, postdoctoral researchers, biotech industry professionals, and representatives of UNC Undergraduate Admissions.
- Engage in the Innovation Challenge workshop series, which will discuss the practice of pharmacy. The series will challenge groups of interns to consider the future of pharmacy practice, identify current limitations, and develop potential solutions to those limitations.
- Directly observe industrial research at local biotechs, specialized laboratory techniques (e.g. nanofabrication) at UNC core facilities, and clinical environments at UNC Hospitals.
- Write a 2 page final report in the style of an academic paper.
- Present their Innovation Challenge projects as a group at the End-of-Summer Symposium.
- Present their individual research projects in the style of a 10 minute conference talk at the End-of-Summer Symposium.

Where do YIP Interns spend their time at UNC?

Most of your time will be spent in your assigned laboratory, typically located in Marsico Hall or the Genetics Medicine Building (Mason Farm Road). Tours may be located across campus or even off-campus, and assistance will be provided to prevent anyone from getting lost.

Is there a fee for participation in YIP, and will transportation be provided?

There is no fee and the Institute will be providing every intern a one-time stipend of $2500. The Institute will not be providing transportation.

How do I apply to YIP?

Interested intern candidates may submit their applications by accessing the application portal at [http://unceii.org/programs/young-innovators-program/](http://unceii.org/programs/young-innovators-program/). The portal will go live on 1/25. Applications will be accepted from 1/25 to 2/8/17. The application requires the completion of a 1-page essay of interest, a teacher’s letter of recommendation, a transcript (informal or formal), completion of forms for Human Resources, and a short demographic questionnaire. Interviews of selected applicants will be requested within 2 weeks of the closure of the application portal. Final acceptance decisions will be made by March 15.

Please direct all questions to Dr. Adam Friedman at friedmad@email.unc.edu.
Project Descriptions

Preceptor: Jian Liu, PhD

Research in the Jian Liu group is focused on glycobiology and glycobiocchemistry, an emerging field that emphasizes the biological functions of carbohydrates. We are particularly interested in understanding the biosynthetic mechanism of sulfated polysaccharides known as heparan sulfate and heparin. Heparan sulfate is found on the cell surface and in the extracellular matrix in large quantities. Heparan sulfate is involved in a wide range of biological functions, including regulating blood coagulation, controlling embryonic development, and resisting viral infections. We also study the biosynthesis of heparin, a polysaccharide that has similar structure to heparan sulfate. Heparin is a widely used anticoagulant drug with more than $4 billion dollars in worldwide annual sales. In addition to understanding the biosynthesis of heparan sulfate, we are also in the process of developing an enzyme- or chemoenzyme-based method to synthesize heparin. Heparin is currently isolated from animal sources, and its supply chain can be vulnerable to contamination. The chemoenzymatic method should significantly simplify the preparation of heparin and ultra-low molecular weight heparin. This method has great potential to synthesize a cheaper, cleaner, and safer heparin drug. The research group, consisting of postdoctoral fellows, graduate students, and pharmacy students, is actively pursuing different aspects of the biochemistry of heparin and heparan sulfate.

Preceptor: Ken Pearce, PhD

The dynamic control of chromatin architecture is a key process for controlling gene expression. The addition, recognition, and removal of post-translational modifications (PTMs) on histone proteins by various enzymes and binding proteins regulates this process. One of these recognition events is binding of methylated lysine residues on histone tails by methyl-lysine (Kme) binding proteins. Histone Kme binding by these reader proteins has been shown to play a fundamental role in control of DNA integrity, gene expression, and certain disease states such as cancer. A key activity in the Center for Integrative Chemical Biology and Drug Discovery is development of potent and specific chemical probes for Kme reader proteins. Ongoing projects include characterizing chemical probes with biochemical, biophysical, and cellular assays.

Preceptor: Jeff Aubé, PhD

The development of new drugs for therapy or, for that matter, small molecules that can be used as probes of biological function, requires access to a versatile and effective toolbox of chemical reactions. Our laboratory is interested in both the development of new chemical reactions for synthetic medicinal chemistry as well as the specific applications of this chemistry toward directed biological problems. In the first category, we have recently introduced a novel variant of the venerable Friedel–Crafts reaction that permits the synthesis of heterocyclic molecules under very mild conditions. Currently active biological problems in our group include the search for agents active against non-replicating Mycobacterium tuberculosis, inhibitors of RNA–protein interactions as potential anticancer agents, and the study of novel opioids capable of functional selectivity (the ability to selectively activate particular intracellular pathways upon binding to a surface receptor). Potential projects will be offered in each of these areas to interested students.
Preceptor: Qisheng Zhang, PhD

Most antibacterial and anti-viral therapeutics target the pathogens directly in an attempt to clear infection. However, such a strategy most often leads to mutations resulting in drug resistance. Targeting host specific pathways can potentially prevent infection, virulence, replication, and/or proliferation while avoiding development of drug resistance, and consequently a better approach for drug discovery. We recently identified one family of small molecule drugs that block the growth of Francisella and Listeria in host cells but do not have effects on hosts or pathogens alone. In another discovery, we found new anti-malaria drugs that retain effectiveness against resistant parasites. This project is designed to further optimize these drugs through organic synthesis and understand their mechanism of actions through cutting edge technologies such as proteomics and microarray.

Preceptor: Alex Tropsha, PhD

Protein kinases are enzymes that chemically modify other proteins by adding phosphate groups to them. Kinases, thus, regulate cellular pathways, particularly those involved in signal transduction. Deregulation of kinase activity can lead to aberrations in cell growth, motility, and death, thereby causing diseases such as cancer. Drugs that inhibit deregulated kinases, therefore, are sought after as treatments for various diseases. Using an approach called Quantitative Structure-Activity Relationship (QSAR) modeling, a statistical relationship between the chemical structure of compounds and their associated kinase inhibition can be derived computationally. These QSAR models can then be used to prioritize new hits (compounds) with desired kinase inhibition profiles. The most promising computational hits will be tested and confirmed experimentally in Structural Genomics Consortium. The Tropsha lab at UNC-CH seeks a volunteer interested in computational modeling and drug discovery to work on QSAR modeling of a particular kinase in the hopes of identifying an inhibitor and potential drug candidate.

Preceptor: Robert McGinty, MD, PhD

Despite every cell in the human body having a nearly identical genetic sequence, divergent patterns of gene expression lead to the development of diverse cell types and functions. These patterns are established through epigenetic changes to the composition and structure of chromatin, the physiologic state of the genome. By displaying diverse combinations of post-translational modifications, chromatin serves as an active signaling hub in the regulation of gene expression and when misregulated is correlated with many human diseases, especially cancer. The McGinty Laboratory studies mechanisms governing epigenetic signaling through visualization at atomic resolution. Projects include cloning, purification, biochemistry, and structural biology of important chromatin regulators.

Preceptor: Tim Wiltshire, PhD

Determining the right dose of a drug, or the right drug, for a patient, based on their genetic information is now becoming part of what is termed Precision Medicine, or Personalized Medicine. We have developed a test, called PGx, that is used to determine the genetic information for 18 genes that are important pharmacogens; that is they will provide the genetic information associated with over 100 prescribed...
drugs. Our PGx test is a new approach that uses next-generation sequencing: generating a lot of DNA sequence data. Projects would involve aspects of development of this test, analysis of DNA sequence data and how to report back the outcomes, or results.

Preceptor: Craig Lee, PharmD, PhD

The Craig Lee laboratory aims to develop and optimize therapeutic strategies that improve health by elucidating the mechanisms that underlie inter-individual variability in drug response. A major focus of our work includes investigating how genetics impacts drug metabolism and disease progression in patients with cardiovascular and metabolic disease, and whether implementation of genetic and biomarker-guided strategies can reduce variability in drug response and improve outcomes in patients. Ongoing projects include both mechanistically-driven preclinical studies in the laboratory and observational clinical studies.

Preceptor: Dhiren Thakker, PhD

A major research focus of the Thakker Lab is to develop experimental approaches and models to predict safe and effective doses of medicines for different pediatric populations. As is done for the adult population, safety and efficacy of medicines cannot be evaluated via clinical studies in children. Hence, doses for medicines given to children are often extrapolated (based on weight and body surface area differences) from the doses administered to adult population. This assumes that children are physiologically similar to the adults, which is not a valid assumption. In fact, from the time of birth through age 18 (adult age) the expression of drug metabolizing enzymes, transporters, receptors, etc undergoes significant changes in different age groups (e.g. Newborn, ages 2 through 10, ages 11 through 18). Hence, there are several projects in the Thakker Lab to investigate comparative disposition of drugs used in pediatric population in children and in adults, and to develop physiologically based pharmacokinetic models that account for these differences and predict safe and effective doses in children based on clinically established safe/effective doses in adults. The YIP intern who joins the Thakker Lab will have an opportunity to work on one of these projects under the supervision of senior graduate students who are pursuing this research. The intern will learn various cellular, molecular biology, and analytical techniques and will learn the overall context of how this research can benefit pediatric patients.

Preceptor: Dan Crona, PharmD, PhD

The Crona laboratory in the UNC Center for Pharmacogenomics and Individualized Therapy focuses on how common variations to genes that encode for proteins involved in drug influx, efflux, metabolism, and oncogenic signaling explain interindividual differences in pharmacokinetics (PK) and pharmacodynamics (PD) of targeted therapies used in oncology. Elucidation of the interplay between pharmacogenetic variants and determinants of PK and/or PD will invariably help to personalize treatment paradigms for cancer patients receiving targeted agents so that efficacy (e.g., survival) is maximized and toxicity minimized. Moreover, development of sophisticated PK/PD models (e.g., population PK/PD models), which incorporate genotype information, can help to pinpoint the optimal treatment that patients receive. Finally, the lab’s translational research program focuses on a functional genomics paradigm that helps reveal molecular mechanisms that underlie these genotype-phenotype associations. Ongoing
projects include: laboratory-based preclinical and mechanistic studies, as well as retrospective, observational, and correlative clinical studies.

Preceptor: Yanguang Cao, PhD

Our group is interested in developing system pharmacology platforms (models) integrating pharmacokinetic (PK) /pharmacodynamics (PD) to facilitate drug development and optimize therapeutics for cancers and autoimmune diseases. We specifically work on targeted therapy, including monoclonal antibody, cell-based therapy, and nanoparticle based therapeutics. In our approaches, we integrate knowledge of drug PK and tissue/target exposure, kinetics of target-drug interactions, PD, tumor physiology, immune functions, and immune dynamics to understand treatment failure/resistance, and develop dose/dosing optimization and drug combinations. In our studies, we largely adopt intravital imaging techniques to track therapeutic modalities, lymphocytes migration/trafficking, and biological biomarkers to support model development. These quantitative platforms will be eventually applied to optimize current therapy and support effective drug development strategies.

Preceptor: Amber Frick, PharmD, PhD

The focus of this research involves educational innovations and assessment in pharmacogenomics among healthcare students, clinicians, and members of the public. All projects involve data/desk-based work. Pharmacogenomics has transitioned to clinical implementation. However, resistance by clinicians has been met, partly due to deficiencies in education. We are using innovative methods, including genotyping and educational technology, to reach and educate future healthcare providers in the classroom, practicing clinicians at continuing education events, and the public at local pharmacies. Outcomes measured from these projects include knowledge gained, personal reflections and attitudes, and the feasibility of various pharmacogenomics educational initiatives. This series of projects build upon previously conducted pharmacogenomics educational investigations.

Preceptor: Kim Brouwer, PharmD, PhD

The liver plays a key role in the metabolism and elimination of many chemicals, including drugs and toxins, as well as naturally occurring compounds in the body, such as bile acids. Bile acids, which are synthesized in the liver, are important signaling molecules that affect numerous physiological functions. Transporters are membrane proteins that function as “gatekeepers” to facilitate the cellular uptake and excretion of many drugs and bile acids in the liver. These transport proteins are influential in determining beneficial or harmful effects of medications. For example, impaired function of bile acid transporters in the liver is one mechanism responsible for drug-induced liver injury, which is the most common cause of acute liver failure (>50% of cases in the U.S.). The main research focus of the Brouwer lab is to elucidate the mechanisms responsible for altered transport protein function in the liver. These studies will provide new mechanistic information and predictive tools to address how disease, genetic variation, and drugs can cause changes that impact the handling of medications by the liver. Projects will include transport experiments with cells overexpressing specific drug transport proteins, cloning, staining, and analysis of drug interactions. This research will contribute to timely, more cost-effective development of safer medications with improved therapeutic outcomes.
HIV is the sixth leading cause of death in the world and the third leading cause of death as a communicable disease. Despite decades of research, globally ~37 million people are living with HIV and ~2.0 million people were newly infected with the virus in 2014. Oral pre-exposure prophylaxis (PrEP) with Truvada® is an effective prevention intervention for HIV acquisition, in particular when adherence is high. However, poor adherence renders this therapy ineffective. Innovations recently introduced into the field of systemic PrEP are long-acting (LA) formulations of antiretrovirals (ARVs) that stably release drugs over many weeks as nano-formulations and have activity in animal models of prevention. The ultimate goal of this project is to develop an injectable polymer-based delivery system for LA PrEP that offers durable and sustained protection from HIV transmission, high efficacy of HIV inhibition, increased user compliance, and the ability to be removed in case of unanticipated adverse events or when considering discontinuation from the LA PrEP. We will achieve this goal by developing a liquid ARV formulation utilizing excipients that form a biodegradable depot after subcutaneous injection (in-situ forming implant (ISFI)).

This is an ongoing project that was recently funded by the NIH-KL2 CTSA program. It is a laboratory-based project that will be completed using in vitro release studies, ISFI characterization (DSC analysis, accelerated stability studies, electron microscopy, viscosity analysis), HPLC analysis, drug solubility analysis. The high school intern student working on this project will work closely with members of the Benhabbour lab (research technicians, PharmD students, and/or undergraduate students).

Bacteriophages are highly abundant bacterial viruses, nature’s vehicle for delivery of genetic materials into bacteria. Nearly all bacteriophage engineering efforts to date have focused on lytic phages, in particular the use of lytic phages to kill antibiotic-resistant bacteria. In contrast, far fewer studies investigate the use of so-called temperate phages, which can integrate their genetic material into the host bacterial genome without killing the bacteria. Through customization of the integrated genetic material, lysogenic bacteriophage can be engineered to precisely insert or silence specific genetic elements in the host. The Lai Lab is developing temperate phages that can induce vaginal commensal bacteria (i.e. bacteria that are pre-existing in the vagina) to produce antiviral peptides against HIV, as a strategy for blocking vaginal HIV transmission. Students will assist with bacteriophage engineering through DNA cloning and bacteria cultures as well as development of antiviral peptide detection assays.

Engineered tumor-homing neural stem cells (tNSCs) are a promising therapy for the highly aggressive brain cancer Glioblastoma (GBM). The unique tumor-homing capacity of tNSCs allows the cells to seek out and deliver anti-cancer gene products directly into local and invasive GBM foci. We recently discovered that polymeric scaffolds significantly increase the transplant and survival of therapeutic stem cells in the GBM resection cavity. Initial versions of the scaffold were modified to remain permissive to stem cell tumorotropic homing and allow robust drug release to dramatically suppress GBM recurrence. Yet, limitations to scaffold design are likely to prevent the effective application of scaffold/tNSC therapy.
in a clinical setting. Additionally, the matrix properties that regulate tNSC therapy are unknown. In the current project, students will seek to develop new scaffold materials with the goal of creating the optimal matrix for tNSC therapy. Working as part of a diverse team comprised of engineers and biologists, students will use the newest technology in stem cell generation, scaffold fabrication, animal models of surgery, and non-invasive molecular imaging to advance tNSC therapy towards human patient testing. Ultimately, this work seeks to create a new approach to treating GBM and providing hope to patients suffering from this devastating disease.

Preceptor: Delesha Carpenter, PhD, MSPH

Our lab recently conducted a survey of school nurses in NC and SC to determine whether there are issues related to opioid use and abuse. Most nurses believed students would benefit from a short educational video that discussed appropriate use of opioids. We would like your help developing these videos. Ideally, we’d like to develop separate videos for elementary, middle, and high school students. You would assist with developing the scripts for the videos, recruiting students to act in the videos (you are welcome to act in the video as well), and recording the videos. Your perspective as a high school student would help us ensure that our video is relevant to students, and also not perceived as “lame.” You would be working with Dr. Carpenter under the direct supervision of her project manager, Courtney Roberts.

Preceptor: Gang Fang, PharmD, PhD

The U.S. is facing great challenges in sustaining its 3 trillion-dollar-cost health-care system, which ranked the highest in spending among all the developed countries, and with its continued annual increases in costs yet unclear improvements in care outcomes. A suggested solution for the challenge is to build an efficient health care with improved quality of care and reduced waste. To improve the efficiency of health care, research and innovation is needed to investigate whether health-care resources has been overused or underused and assess the performance of healthcare providers based on health outcomes. The research program of Dr. Fang and his team is focusing on the innovative solutions. Projects include analysis on geospatial access to pharmacy, primary care physicians, and other healthcare providers, intensity of healthcare market competition, and characterization of pharmacies based on their services.

The projects will require prior experience and skills in using database (Microsoft Access) and advanced training in mathematics (having high grades in AP Calculus BC or equivalent).

Preceptor: Robert Hubal, PhD

This research project will support the Carolina virtual patient initiative. The virtual patient is being developed to provide immersive, varied educational experiences to students in healthcare professions (medicine, nursing, pharmacy) to increase their confidence and competence, better preparing them for actual patient engagement. The virtual patient has a number of components, including one that drives its physiology, another that monitors social cues and controls emotional responses, and another that manages the reasoning and decision making behind the patient’s actions. This work will involve literature searches and summarization, observational research, and exploration of the range of situations that a healthcare professional may encounter. Through this work, the student will develop an ability to summarize findings and translate them into detailed rules.
Preceptor: Jerry Heneghan, MBA

The UNC Center for Innovation in Pharmacy Simulation (CIPS) advances professional excellence and patient safety through the research, development, validation, and integration of emerging technologies into the UNC Eshelman School of Pharmacy curriculum. Our team specializes in providing research and development capabilities for faculty, staff, and collaborators interested in applying new technologies to improve teaching and learning. We stay on the forefront of current educational technologies and teaching modalities, including researching and developing: simulations, educational games, ebooks, medical animations, illustrations, mobile applications, interactive web content, multimedia, video capture, 360 video capture, virtual, augmented, mixed realities, and more. This work will involve software quality assurance testing and reporting. Through this work, the student will develop an ability to identify deviations from specified performance parameters and will work closely with our development team.

Preceptor: Roy Zwahlen, JD

Each university researcher is surrounded by a large supporting cast to ensure that ground-breaking science is funded, executed, and delivered to the world. The intern pursuing this project will work directly with Roy Zwahlen, Assistant Dean for Strategy and Innovation, where they will study the entrepreneurial ecosystem of offices and processes surrounding our faculty. The intern will learn about academic management strategies and skills necessary for bringing an idea from inception to patient impact. This experience will involve shadowing to gain a broad understanding of technology commercialization, entrepreneurial development in the university setting, and matters of conflict of interest (COI), grant management, and related activities. The intern will complete an independent project based on his/her strengths and interests; potential projects include market research, development of technology marketing materials, technology assessment, intellectual property review, and/or web-based resource development.