



National Institute of  
General Medical Sciences



## Training Interdisciplinary Pharmacology Scientists (TIPS)

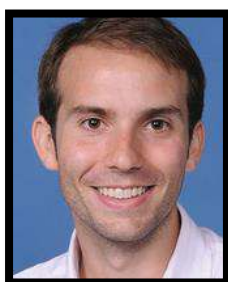
Program Director: **Carmen Dessauer**, PhD, Professor, Integrative Biology and Pharmacology,  
The University of Texas Health Science Center at Houston

Program Co-Director: **Timothy Palzkill**, PhD, Professor and Chair  
Pharmacology, Baylor College of Medicine

<http://www.gulfcoastconsortia.org/home/training/pharmacological-science-tps/>

### Meet the Trainees

**Cohort 1**, Appointed December 1, 2016 – November 30, 2017



**Cameron Brown**

Pharmacology, Baylor College of Medicine

**Primary Mentor**: Timothy Palzkill, Pharmacology (BCM)

**Secondary Mentor**: Martin Matzuk, Pathology & Immunology (BCM)

***Characterizing mutations of CTX-M-14 found in clinical isolates and designing small molecules to inhibit antibiotic resistance.***

$\beta$ -lactam are the most prescribed class of antibiotics, and the most common mechanism of resistance is through the production of  $\beta$ -lactamase enzymes. One class of  $\beta$ -lactamases, CTX-M, confers high levels of resistance to cephalosporins, and there are more than 140 variants isolated

in the clinics. My project aims to characterize many of the naturally occurring mutation found in these variants, as well as use DNA-encoded libraries and fragment based drug discovery to identify inhibitors.



**Elizabeth Campbell**

Biochemistry and Molecular Biology, Baylor College of Medicine

**Primary Mentor**: Trey Westbrook, Molecular & Human Genetics (BCM)

**Secondary Mentor**: Damian Young, Pharmacology (BCM); Adjunct in Chemistry (Rice Univ)

***Developing Spliceosome Inhibitors as a New Therapeutic Class for Myc-Driven Cancers***

Our lab has discovered that Myc-driven TNBCs are sensitive to partial inhibition of RNA processing machinery including the spliceosome while normal cells are not. Small molecules targeting the spliceosome have entered clinical trials, opening this avenue of therapy to further development.

My project is aimed at furthering the utilization of spliceosome inhibition as a targeted therapy for TNBCs. I will identify genes that control the response of cancers to spliceosome inhibition in order to nominate predictors of patient response and delineate pathways of resistance. I will also identify additional molecules that inhibit the activity of the spliceosome that can be developed into therapeutics. Successful completion of this work will further spliceosome inhibition as a therapeutic strategy against TNBCs and other cancers.



**Nicholas Hummell**

BioSciences, Rice University

**Primary Mentor**: Natasha Kirienko, BioSciences (Rice Univ)

**Secondary Mentor**: Damian Young, Pharmacology (BCM); Adjunct in Chemistry (Rice Univ)

**Tertiary Mentor**: Laura Segatori, Chemical & Biomolecular Engineering, BioSciences (Rice Univ)

***Characterization of Protein Aggregate Inhibitor LK16***

Neurodegenerative diseases pose a huge problem upon aging populations in developed countries.

Many of these diseases share a common characteristic of abnormal protein aggregation which is hypothesized to be linked to their pathogenesis. We have discovered an uncharacterized small molecule, LK16, which

aids in the prevention of heat induced protein aggregates. My project is focused on finding a mechanism of action for this aggregate prevention as well as determining its efficacy in preventing neurodegenerative related phenotypes using *C. elegans* as a model.



**Daniel Konecki**

Structural & Computational Biology & Molec Biophysics (SCBMB), Baylor College of Medicine

**Primary Mentor:** Olivier Lichtarge, Molecular & Human Genetics (BCM)

**Secondary Mentor:** Devika Subramanian, Computer Science; Electrical Engineering (Rice U)

***Drug Repurposing Based On Multi-modal Biological Networks: Whole Exome Sequencing for Prediction of Personalized Chemotherapy***

A major barrier to the development of precision medicine for the treatment of cancer, and many other diseases, is the slow process for developing drugs and bringing them to market. This project seeks to address this issue by automating the process of drug repurposing, treating a disease using drugs which are already approved to treat another disease, which could drastically increase the number of drugs available to treat diseases in a much shorter time frame. In pursuit of this goal we are constructing multimodal networks of associations between proteins, drugs, and diseases, to which we can apply reasoning algorithms to predict drugs based on a patients diagnosis and available genetic data. To develop this method we will use the mutations present in cell lines stored in the Cancer Cell Line Encyclopedia and evaluate the drugs predicted to treat them using screening data stored in the Genomics of Drug Sensitivity in Cancer database. Using standard of care drugs and successful drug predictions, we will generate multi-drug combinations to target as many affected cellular functions as possible, in an effort to treat cancer cell lines most effectively.



**Doris Taylor**

Biochemistry and Molecular Biology, Baylor College of Medicine

**Primary Mentor:** Timothy Palzkill, Pharmacology (BCM)

**Secondary Mentor:** BVV Prasad, Biochemistry & Molecular Biology (BCM)

***Mechanistic Characterization of OXA-48  $\beta$ -lactamase Mediated Hydrolysis of Antibiotics and Discovery of Inhibitors***

$\beta$ -lactam antibiotics are the most prescribed worldwide and have revolutionized treatment of bacterial infection, but they are susceptible to hydrolysis by bacterial enzymes called  $\beta$ -lactamases. OXA-48 is a  $\beta$ -lactamase that confers resistance to carbapenems, the last resort  $\beta$ -lactam antibiotics, and has dispersed globally.

To better characterize the mechanism by which OXA-48 hydrolyzes different  $\beta$ -lactam antibiotics, I will create individual alanine mutants of residues implicated in catalysis, study their ability to hydrolyze various antibiotics and their structure to understand how substitution of a given residue affects the enzyme's function and structure. This will help elucidate the role of each of these residues in catalysis. To potentially find an inhibitor for OXA-48, I will be performing drug discovery using DNA-encoded library technology to screen for potential inhibitors that could block the action of OXA-48 and thus restore effectiveness to antibiotics that OXA-48 would typically hydrolyze.

The TIPS program is Administered by the:



[www.gulfcoastconsortia.org](http://www.gulfcoastconsortia.org)

Questions: Contact Vanessa Herrera

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The GCC is a collaboration of:

Rice University

Baylor College of Medicine

University of Houston

University of Texas Health Science Center at Houston

University of Texas Medical Branch at Galveston

University of Texas MD Anderson Cancer Center

Institute of Biosciences & Technology at Texas A&M Health Science Center