Research Interests and Ongoing Projects

Antibiotic Drug Discovery

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Research interests:

- **Antibiotics** My overall research focus is on the discovery and development of therapeutics for infectious diseases. The projects utilizes medicinal chemistry and microbiology to evaluate novel compounds as antibacterial and anti-biofilm agents.

- **Drug Discovery** My research interest in antibiotic drug discovery is in the chemical design and screening of novel compounds as treatments for infection. Current projects focus on identifying substance that effectively penetrate biofilms and inhibit biofilm formation or bacterial growth.

- **Medicinal Chemistry** My research in antibiotic drug discovery employs synthetic organic chemistry to construct novel compounds of interest. Data obtained from susceptibility testing (e.g. MIC) is used to guide future drug designs once a "hit" compound that effectively penetrates the biofilm and inhibits the test bacteria is identified.

Clinical interests and applications of research:

- **Clinical/Therapeutic Interests** The development of new antibiotics and strategies to treat and prevent infection in at risk patients are my primary clinical interests.

Research opportunities for students:

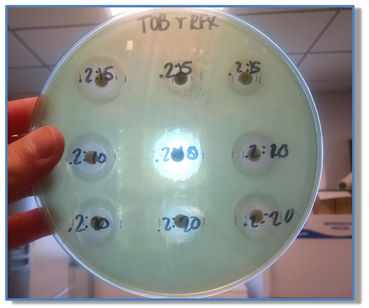
- **Antibiotic Drug Discovery & Development**

  Students will have the opportunity learn about antibiotic drug design, medicinal chemistry and microbiology. The research experience affords students a chance to design and synthesize their own antibiotics, test them against pathogenic bacteria, and assess their physicochemical and *in vitro* ADME properties. For more information, please contact me at longt@marshall.edu.

Expertise:

- **Synthetic Organic Chemistry** The techniques used in the lab are those common to an organic chemistry lab such as recrystallization, extraction, and chromatography. Once a pure compound, the molecular structure is determined by spectroscopy. NMR and mass spectroscopy are the most common methods to determine atom arrangement. Other methods such as HPLC are used to determine purity.

- **Susceptibility Testing** Once synthesized and purity is confirmed, the compounds are tested for antibacterial activity against CDC ESKAPE pathogens (*Enterococcus, Staphylococcus*, *Klebsiella*, *Acinetobacter, Pseudomonas, Enterobacter* spp.) and for efficacy to penetrate biofilms. Active compounds will be further assessed for cytotoxicity using mammalian cells.



- **Physicochemical and ADME Analysis** Hit compounds with low cytotoxicity will be evaluated for acid stability, whole blood and plasma binding, and microsomal stability prior to testing as "lead" compounds in mice .

Summary of ongoing projects:

- **Anionic Antibacterials** Mucin and biofilms are comprised of negatively charged constituents. Most antibiotics possess either a positive or neutral (zwiterionic) charge at physiological pH that may be hinder biofilm penetration to the underlying bacteria. In this project, we are examining the antibacterial activity of anionic derivatives of fluoroquinolones and rifamycins and their ability to transverse *Pseudomonas* biofilms.

- **Polycationic Antimicrobial Peptides** Polycationic peptides are effective treatments for infections by ESKAPE species; however toxicity, metabolic stability, and slow eradication rates have limited their use in treatment. In this project, we are examining strategies to enhance the pharmacological properties of cationic antimicrobial peptides using unnatural amino acids.