

POSTDOCTORAL RESEARCHER RECRUITMENT LETTER

Dear Prospective Postdoctoral Candidates,

We are excited to invite applications for three Postdoctoral Researcher positions in the Department of Chemistry and Biochemistry at Florida State University, focused on utilizing cutting-edge **droplet microfluidics and multi-omics** to accelerate the discovery of new antibiotics and combat the growing global threat of Antimicrobial Resistance (AMR).

Our work leverages droplet-based microfluidics—a transformative platform enabling massively parallel, compartmentalized analysis at the single-cell level using picoliter to nanoliter droplets. We seek three highly motivated researchers to drive forward key areas of this research pipeline. All positions are one year and can be extended.

Position 1: Microfluidic-Based Antimicrobial Discovery and High-Throughput Screening

This position will focus on breaking the bottlenecks associated with cultivation and compound identification. Key responsibilities include:

1. **Microbial Dark Matters (MDMs) Cultivation:** You will utilize droplet microfluidics for high-throughput cultivation to access **MDMs**, which represent an immense, untapped source of novel bioactive compounds. Droplet cultivation has shown significant promise in enhancing microbial richness and diversity, enabling the recovery of rare and previously unculturable taxa.
2. **Dissecting Microbial Interactions and Activating Cryptic BGCs:** You will design and execute scalable co-culture and interaction studies using modular droplet systems. This work aims to reveal higher-order dependencies and emergent microbial behaviors that can activate silent Biosynthetic Gene Clusters (BGCs).
3. **High-Throughput Phenotypic Assays:** You will develop and implement massively parallel, high-resolution screens. This includes utilizing **Fluorescence-Activated Droplet Sorting (FADS)** to selectively enrich for strains that exhibit specific desired phenotypes, such as antibiotic production or resistance/metabolic activity.

Position 2: Droplet Mass Spectrometry and Chemical Dereplication

This position focuses on accelerating the identification of chemically mediated inhibition and preventing the frequent rediscovery of known compounds by integrating microfluidics with mass spectrometry.

1. **Accelerating Chemical Dereplication:** You will integrate droplets directly with Mass Spectrometry (MS) tools to obtain rapid chemical fingerprints of individual droplets, thereby streamlining the discovery pipeline.
2. **Enhancing Detection Sensitivity:** You will explore and implement strategies to enhance dereplication efficiency and sensitivity for detecting low-concentration compounds at the picoliter scale. This may involve using high-resolution MS, such as Fourier Transform Ion Cyclotron Resonance MS (FT-ICR MS), which offers exceptional mass accuracy and resolving power (This may involve collaboration with The National High Magnetic Field Laboratory in Tallahassee).
3. **Computational Data Analysis and Database Integration:** You will be responsible for developing robust data analysis pipelines necessary to efficiently process the high-throughput mass spectrometry data and streamline the dereplication process.

Position 3: Single-Cell Genomics and Mechanisms of Resistance/Persistence

This position focuses on high-resolution, single-cell techniques to understand how resistance genes emerge and spread, and to investigate the mechanisms underlying antibiotic persistence.

1. **High-Throughput Single-Cell Sequencing:** You will utilize and advance microbial single-cell sequencing techniques (e.g., EASi-seq) to recover whole genomic content from individual cells. This

approach overcomes limitations of bulk metagenomics by preserving cell-specific context and linking genomic information to individual cells, allowing high-resolution genomic analysis.

2. Mapping Antibiotic Resistance Genes (ARGs) to Hosts: You will employ single cell targeted amplicon sequencing methods. This technique leverages droplet microfluidics to enable the simultaneous tracking of taxonomic associations for multiple ARGs, plasmid replication genes, and taxonomic markers within complex microbial communities, addressing a critical gap in traditional ARG identification.

3. Investigating Antibiotic Persistence: You will apply single microbial RNA sequencing (transcriptome sequencing) to resolve gene expression heterogeneity in bacterial populations following antibiotic treatment. This is crucial for studying persister cells—a subpopulation that enters a transient, dormant state to survive treatment, leading to recurrent infections.

Required Qualifications and Environment

Candidates should possess a Ph.D. in Chemistry, Pharmacy, Biochemistry, Microbiology, Bioengineering, or a related interdisciplinary field. Expertise in at least one of the following is highly desirable: droplet microfluidics, high-throughput screening, single-cell multi-omics (genomics, transcriptomics), advanced mass spectrometry, microbial ecology, or complex data analysis pipelines specific to single-cell genomics.

We are committed to continuous technological development to address existing challenges, such as improving single-cell genomic coverage, enhancing detection sensitivity for low-concentration bioactive compounds (a known limitation for ESI-MS), and achieving the feasibility of integrated multi-omics within a single droplet.

This work is essential for revitalizing the antibiotic discovery pipeline with speed, precision, and innovation, positioning droplet microfluidics as a powerful engine against AMR.

For questions regarding this research, please contact Dr. Xiangpeng Li at xli@chem.fsu.edu. More info can be found at li-lab.us.