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Liberty, WV, 26074. **High throughput screening in an in vitro infection model of
tularemia to identify novel antibiotics and immunotherapeutics.**

Francisella tularensis is a pathogenic coccobacillus endemic to North America and is classified by the United States government as a Tier 1 bioterrorism agent. The intentional release of antibiotic-resistant strains of *F. tularensis* could be disastrous. Since a vaccine against *F. tularensis* licensed for human use does not exist, we are substantially vulnerable to this pathogen. However, the development of new therapeutics that target tularemia will make our nation safer against a potential terror attack and naturally resistant *F. tularensis*. Here, we investigated a library of natural extracts to identify novel therapies that are effective against *F. tularensis* infections. We have previously engineered *F. tularensis* to express a red fluorescent protein (LVS/ pTC3D) during intracellular infection. LVS/pTC3D was used to infect THP-1 cells (a monocyte line) seeded into a 96-well plate. To identify novel antibiotics and immunomodulatory therapies, each well was treated with an extract from a cataloged natural product library. Several extracts that led to a reduction in fluorescence over time were selected for further investigation. Current investigations seek to determine whether library extracts directly inhibit bacterial growth in rich culture media (no host cells) or decrease replication in THP-1 cells through immunomodulation. Any extract that inhibited growth in both scenarios would likely be a traditional small molecule antibiotic. Extracts that ONLY inhibit intracellular bacterial growth within the THP-1 cells would likely be doing so by augmenting the host immune responses. Because these act on the host cells and not the bacterium, the potential for the development of antimicrobial resistance is eliminated.