Stanford

Sumin Lee

Postdoctoral Research Fellow, Pathology

NIH Biosketch available Online

Curriculum Vitae available Online

Bio

BIO

Chemical biology research scientist with 8 years of experience in Chemistry/Bioinorganic Chemistry and with 8 publications in high-visibility journals, such as JACS, Angewante Chemie, Chem Sci, Inorg Chem. among others over 350 total citations to date.

Strong track record of managing collaborations with researchers from Universities and research institutes.

PROFESSIONAL EDUCATION

- Master of Science, Ewha Women's University (2012)
- Bachelor of Science, Ewha Women's University (2018)
- Doctor of Philosophy, University of California Berkeley (2018)

STANFORD ADVISORS

- Matthew Bogyo, Postdoctoral Faculty Sponsor

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Staphylococcus aureus is a commensal human pathogen that is a major cause of infections worldwide. It is the causative agent of life threatening disease over the past two decades including skin and soft tissue, pleuropulmonary, device related infections, osteomyelitis, infective endocarditis, and prosthetic joint infection. The most common methods to monitor infection progress involve the blood cultures, histology, or PCR. These approaches are sensitive, but none allow for noninvasive imaging to determine the precise site or extent infection. Thus, new methods for visualizing the site of infection and subsequent response to treatment would greatly improve current clinical management of S. aureus infection.

I aim to develop imaging tool to monitor infection in vivo that make use of small molecule activity-based probes (ABPs) that specifically target a family of serine hydrolases enzymes in S. aureus. Recently, our group has reported a small molecule that covalently modifies an enzyme found on the S. aureus bacterial cell surface. Subsequent screening of a library of serine hydrolase inhibitors identified JCP251, that selectively targets one of the serine hydrolases on the bacterial surface, named as FphB, through covalent bond formation. Surface-exposed serine hydrolases like FphB are ideal targets for both anti-virulence and imaging agents. My goal is to develop red-shifted fluorescent imaging probes and ultrasound contrast agents based on the selective targeting of JCP251 toward FphB, which will serve as non-invasive probes to visualize sites of infection. Mice infected with S. aureus fphB transposon mutant had much lower bacterial loads in liver and heart tissues, suggesting that FphB is important for and expressed during infection.

I synthesized the red-shifted fluorescent probes through the conjugation of CY5 fluorophore onto JCP251 via click chemistry. SDS–PAGE analysis revealed that JCP251-CY5 labeled FphB enzyme in S. aureus, which is confirmed by comparison with the fphB transposon mutant strain. Confocal fluorescence microscopy experiments with wild-type and and fphB transposon mutant cells revealed that JCP251-CY5 is specific for FphB. To evaluate this probe as a diagnostic agent, I will use a mouse model of S. aureus infection. Mice will be systemically infected via intravenous tail-vein injection or be continually exposed to S. aureus through drinking water. By comparison with the fphB transposon mutant strain infection, the probe will allow the direct imaging of the changes in overall bacterial burden in various tissues (heart, liver, kidney) related to FphB.

Microbubbles (MB), which are gas-filled particles with stabilizing shell, have been reported as an emerging ultrasound contrast agent. Upon injection, MBs remain within the vascular compartment because of their micrometer size, so they are particularly well suited for detecting and monitoring vascular disease. MBs are readily functionalized with appropriate ligands, therefore I hypothesize that JCP251-conjugated MBs will have selective affinity toward S. aureus biofilms and will allow for ultrasound detection of infection.

I conjugated JCP251 to the outer shell in order to generate targeted MBs. Ultrasound imaging will be performed in collaboration with Jeremy Dahl’s lab in Stanford. To test for FphB-dependent accumulation, I will compare the affinities of targeted MBs toward biofilms grown on glass slides from wild-type or fphB mutant S. aureus and then I will use a mouse model of S. aureus infection. S. aureus is the most common cause for endocarditis, therefore, targeted MBs will be especially useful for imaging FphB’s involvement in endocarditis development.

Additionally, antibiotic drugs such as Vancomycin could be loaded on the microbubbles, for release after accumulation at the site of infection. Therefore, targeted MB contrast agents can be used both to diagnose S. aureus infection and to guide decision making for treatment strategies.

LAB AFFILIATIONS

- Matthew Bogyo, Matt bogyo (9/3/2018)