## ABSTRACT

TALIB, A. ALBOSLEMY, Ph.D., May 2018 BIOMEDICAL SCIENCES

Kruppel-like factor 2: A regulator of macrophage-mediated innate immune response against *Staphylococcus aureus* biofilm (122 pp.)

Dissertation Advisor: Min-Ho Kim

Complications arising from cutaneous and soft tissue infections with *Staphylococcus aureus* (*S. aureus*) are a major clinical problem due to the high incidence of these infections and the widespread emergence of antibiotic-resistant bacterial strains. In particular, *S. aureus* infection involving the formation of biofilm is clinically challenging due to antibiotic resistance and immune evasive characteristics of biofilm-associated infection. Accumulating evidences support that macrophages associated with *S. aureus* biofilms have decreased secretion of cytokines and chemokines, which might have contributed to the impaired bactericidal activity. A series of recent studies have demonstrated that *S. aureus* biofilms skew macrophage polarization towards an anti-inflammatory phenotype that persists bacterial survival. However, the detailed mechanism underlying the evasion of macrophage-mediated innate immune response against *S. aureus* biofilm is poorly understood. The central hypothesis of this study is that *S. aureus* biofilm environment skews macrophage polarization toward the anti-inflammatory phenotype by interfering with a pattern recognition receptor (PRR)-dependent positive regulatory mechanism or aberrantly amplifying a negative regulatory mechanism of NF-kB activation.

In this study, using an in vitro model of murine macrophages exposed to the secreted factors from *S. aureus* biofilm, we have determined the impact of the *S. aureus* biofilms on macrophage-mediated innate immune response and elucidated its associated signaling mechanism. The major finding of this study is that *S. aureus* biofilm environment associated