Role of NOD2 Receptor in Immune Response to Staphylococcus Aureus

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INTRODUCTION

Staphylococcus aureus, a gram-positive, commensal bacterium, causes several opportunistic diseases and infections in humans. Furthermore, some strains of *S.aureus* have developed resistance to antibiotics such as methicillin and pose a health risk. Pattern Recognition Receptors (PRRs) on host immune cells recognize specific components of *S.aureus* cell wall and mount an immune response against the bacteria. One such PRR is the Nuclear Oligomerization Domain 2 (NOD2) receptor which is present in the cytosol of host immune cells. NOD2 recognizes Muramyl-Dipeptide (MDP), a component of the peptidoglycan cell wall of several bacteria including *S. aureus*. The binding of MDP to NOD2 allows the activation of host immune response by secretion of pro-inflammatory cytokines and antimicrobial compounds. The exact mechanism of binding of bacterial components to the NOD2 receptor is unknown. This study aims to utilize a *S.aureus* mutant library to screen for bacterial mutants that either fail to bind to NOD2 or show higher binding to NOD2 when compared to wild type bacteria. Commercially available Human Embryonic Kidney cells transfected with a mouse NOD2 gene (HEK-BLUE mNOD2) will be treated with wild type or mutant bacterial components from the *S.aureus* mutant library. Binding of bacterial components to NOD2 will be detected using a colorimetric assay and quantified by absorbance at 650nm. This screen will enable us to determine the bacterial components that are essential to NOD2 binding and may also shed light on ways by which *S.aureus* evades host immune responses.

Background

- *S. aureus* is a commensal bacterium found on the nasal cavity of 30% of healthy individuals
- *S. aureus* causes diseases such as endocarditis, skin infections, and pneumonia
- NOD2 is a cytosolic receptor in immune cells
- NOD2 binds to a breakdown product of bacterial peptidoglycan, MDP
- Binding of *S. aureus* to NOD2 causes an innate immune response
- Exactly how bacteria bind to NOD2 is unknown
- Nebraska Transposon Mutant Library has 1,920 *S. aureus* mutants that all have a single gene mutation

METHODS

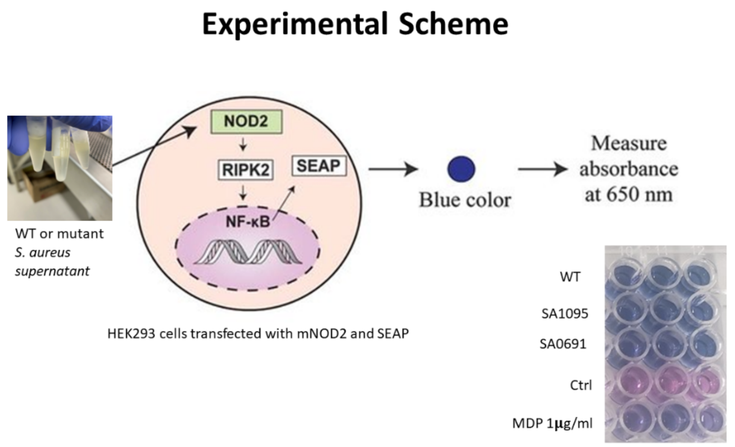

Figure 1: Experimental Scheme.

RESULTS

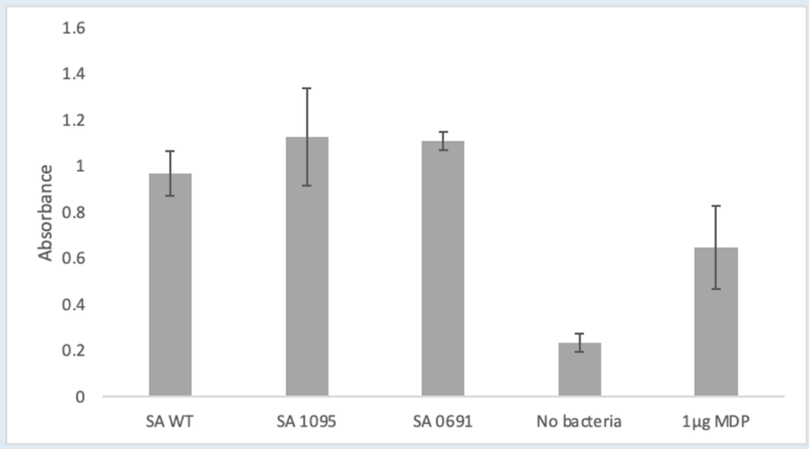

Figure 2: Best optimization results so far. *S. aureus* wild type and two mutant strains from the Nebraska Transposon Mutant Library binding to mNOD2. The positive control is MDP by itself and the negative control is no bacteria. Both mutant strains had a higher amount of MDP binding to NOD2 compared to the wild type.

Next Steps

Once optimization is complete, we will begin running a screening of the library to look for mutants that bind differently than the wild type *S. aureus*.

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