

Lukab potentiation of
activity (i.e.,
combination effect)



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LukAB is secreted by *S.*

aureus as a heterodimer, with oligomerization and pore formation occurring on the surface of phagocytes at the time of cellular destruction. Our recent data indicate that neutralizing anti-LukAB human mAbs achieve toxin neutralization by distinct mechanisms. Based on these findings, we hypothesize that an oligoclonal mixture of anti-toxin mAbs with high affinity and distinct properties will have increased potency in the blockage of LukAB-mediated cytotoxicity. To assess this, we propose a series of related experiments: In vitro toxin neutralization with distinct mAb combinations.

We will assess potentiation of activity (i. e., combination effect) in a series of experiments measuring mAb neutralization of LukAB-mediated neutrophil killing. Methods: Anti-LukAB mAb preparations (or isotype controls) will be incubated in the presence of LukAB for 30 minutes, prior to the addition of neutrophil-like HL-60 cells. After a one-hour intoxication, Cell Titer® Aqueous One dye will be added, and neutralization of cytotoxicity will be measured as a function of the percentage of cells that remain alive following intoxication relative to controls. Experiments will be performed in triplicate with cells from independent vials.