

## **Expanded View Figures**

## Figure EV1. Determination of the stoichiometry of WT to dominantnegative LukED required for protection in human PMNs.

Viability of primary human PMNs in the presence of a LD50 (46.9 nM) of WT LukED and a titration of LukE<sup>mut1</sup>LukD<sup>mut</sup> evaluated using the metabolic dye CellTiter.

## Figure EV2. Evaluation of the activity of dominant-negative toxins in vivo.

- A Experimental scheme to determine "half-life" of prophylactic LukE<sup>mut1</sup>LukD<sup>mut</sup>. Mice were challenged with wild-type LukED at 0 and 5 h post-treatment with the dominant-negative toxins. t, time in hours.
- B Survival of Swiss-Webster mice after treatment with LukE<sup>mut1</sup>LukD<sup>mut</sup> or buffer as indicated in (A). n = 2 for buffer and n = 3 for LukE<sup>mut1</sup>LukD<sup>mut</sup>
- C Experimental scheme to determine "half-life" of prophylactic LukE<sup>mut1</sup>LukD<sup>mut</sup>, after lethal challenge with wild-type LukED 1 and 24 h post-treatment with the dominant-negative toxins. t, time in hours.
- D Survival of Swiss-Webster mice after challenge with wild-type LukED 1 and 24 h post-treatment with LukE<sup>mut1</sup>LukD<sup>mut</sup>, GFP (negative control protein), or buffer, as indicated in (C). n = 3 per condition.
- E Experimental scheme to determine whether the LukE<sup>mut</sup>LukD<sup>mut</sup> dominant-negative toxins protect from *in vivo* infection when injected at 0, 24, and 48 h post-intravenous infection. t, time in hours.
- F Survival of Swiss-Webster mice after simultaneous prophylaxis and infection with LukE<sup>mut1</sup>LukD<sup>mut</sup>, followed by treatment at 24 or 48 h post-infection, as indicated in (E). n = 10 per condition.