

**Supplemental Figure 2**. Mouse genetic background influences priming effects on host protection and pro-inflammatory responses. MRSA SSSI in BALB/c naïve mice resulted in greater bacterial burden in skin abscesses as compared to C57BL/6 naïve mice (**A**). No differences were found in  $rag1^{-/-}$  mice (**B**). P < 0.01 (\*\*) vs. corresponding BALB/c mice (wild-type, N ≥ 16;  $rag1^{-/-}$ , N ≥ 8) using student's t-test. Data are represented as mean ± SD. Immune cell infiltration (**C**-**D**), cytokine expression (**E**-**F**) and host defense peptide (HDP) induction (**G**-**H**) indices of BALB/c versus C57BL/6 were compared during primary and secondary MRSA SSSI. Pro-inflammatory responses were greater in wild-type C57BL/6 mice as compared to BALB/c mice during primary MRSA SSSI. However, BALB/c mice had greater pro-inflammatory responses during recurrent MRSA SSSI as compared to C57BL/6 mice (**C**, **E**, **G**). Pro-inflammatory responses in C57BL/6 mice were absent in the  $rag1^{-/-}$  background. Select host responses in the BALB/c background were induced in the absence of adaptive immunity (**D**, **F**, **H**). P < 0.001 (\*\*\*) versus corresponding BALB/c mice via student's t test (N ≥ 10+ images per sample). Cytokine index was calculated by taking expression levels of samples (% of uninfected control) normalized per 10<sup>6</sup> MRSA CFU in abscesses of corresponding samples as previously described (1). Data are represented as mean index ± SD.