Comparing the virulence of *S. aureus* Mu50Ω1 and Mu50Ω2 in a *C. elegans* model

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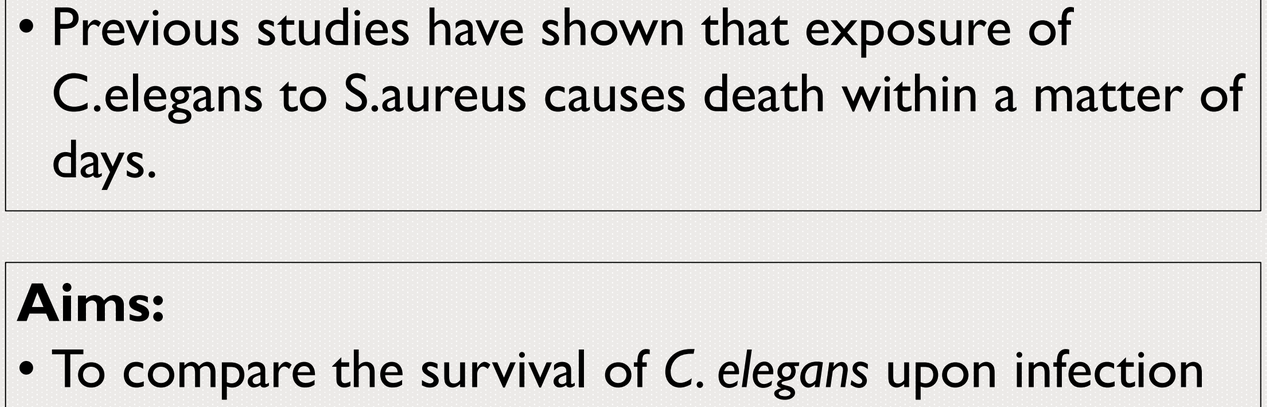
Introduction:

- *Staphylococcus aureus* causes a multitude of infections in humans although it is part of commensal flora. [1]
- Methicillin is used against penicillin-resistant strains and in turn vancomycin is used against methicillin-resistant *S. aureus* (MRSA).
- Increasing antibiotic-resistant strains and a lack of a vaccine for *S. aureus* place a burden on modern medicine and society that requires urgent intervention.
- Vancomycin-susceptible MRSA Mu50Ω strains are believed to be derivatives of the vancomycin-intermediate Mu50 *S. aureus* strain.[1][2]
- *C. elegans* is a popular model choice because it has over 60% genetic homology with humans, its small size (1mm) makes it examinable microscopically and its maintenance affordable; and one worm can produce 1000 eggs/day.
- *E. coli* is a natural food source for *C. elegans* growth and maintenance.
- Previous studies have shown that exposure of C.elegans to S.aureus causes death within a matter of days.

Aims:

- To compare the survival of *C. elegans* upon infection by Mu50Ω1 and Mu50Ω2 as food sources.
- The survival of worms reflects the virulence of S. aureus strains.

Methodology:



Transfer 30 6-day old worms from maintenance plates (Fig 1.1) onto assay plates seeded with *E. coli* OP50 (Fig 1.2), S. aureus Ω1 (Fig1.3) and Ω2 (Fig 1.4). The number of alive and dead worms was scored after certain interval of infection until all the worms were dead.

Results (continued):

	Mean survival time for C.elegans (hours)	
E.coli OP50 (Control)	312.0	
S.aureus Mu50Ω1	196.4	*
S.aureus Mu50Ω2	246.7	*

Table 1.1 (left) shows the mean time of survival of *C. elegans* upon infection by *S. aureus* strains. The uninfected worms fed on *E. coli* OP50 serves as a control. (* $p<0.0001$)

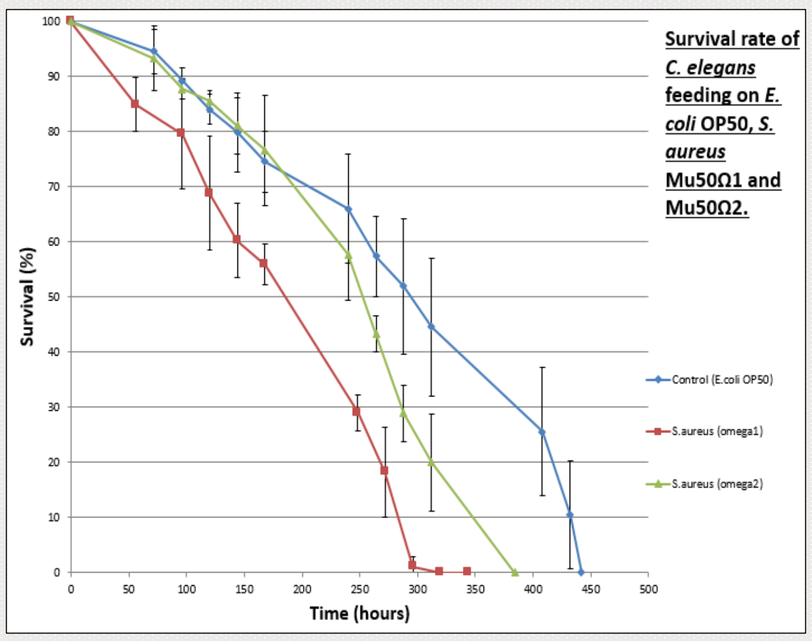


Fig 2.1 (above) shows a graph of the mean rates at which the number of *C .elegans* declined in the assay plates containing E.coli OP50, S.aureus Mu50Ω1 and Mu50Ω2. The rate of decline for the C.elegans feeding on Mu50Ω1 is faster than that of Mu50Ω2.

Discussion and conclusion:

- A wide gap in research into Mu50 Ω strains exists.
- A report was made that Mu50 Ω1 is more susceptible to beta-lactams than Mu50 Ω2.[2]
- Based on Table 1.1, *C. elegans* has a a shorter mean survival time was noted when Mu50Ω1 was fed to the worms compared to use of Mu50 Ω 2 or *E. coli* OP50.
- Therefore Mu50 Ω 1 is more virulence in term of killing *C. elegans* and potentially humans than Mu50 Ω2.
- $P<0.0001$ (Table 1.1) indicates significant difference in mean survival time between control vs. Mu50 Ω1and control vs Mu50 Ω2.
- Molecular mechanisms responsible for this difference need to be elucidated through further biochemical tests such as virulence factors analysis as well as transcriptomic and protemic analysis.
- The virulence of these two MRSA strains can be tested further in higher model organisms.
- Studies to compare the mean survival time for C.elegans using other S.aureus strains could be carried out as well.

References:
1. Cui L, Neoh H, Shoji M, Hiramatsu K. Contribution of *vraSR* and *graSR* Point Mutations to Vancomycin Resistance in Vancomycin-Intermediate *Staphylococcus aureus* . *Antimicrobial Agents and Chemotherapy*. 2009;53(3):1231-1234.
2. Cui L, Neoh H, Iwamoto A, Hiramatsu K. Coordinated phenotype switching with large-scale chromosome flip-flop inversion observed in bacteria. *Proceedings of the National Academy of Sciences of the United States of America*. 2012;109(25):E1647-E1656. doi:10.1073/pnas.1204307109.