

Important Mutations for Phenotype Difference in *Staphylococcus Aureus* 6850

Abstract

Staphylococcus aureus and *Pseudomonas aeruginosa* often occur together in polymicrobial diseases [1] such as in cystic fibrosis [2] and their interactions cause an increase in β -lactam antibiotic resistance [3] which can severely complicate the treatment. To better understand the adaptations of the submissive *S. aureus* we investigated correlations between data for the 6850 strain, obtained by Niggli et al. (2023) [4]. We used RStudio [5] in combination with ChatGPT [6], which was exclusively used for code generation and debugging. We then performed Linear regression on the phenotype data of 44 *S. aureus* 6850 clones and no correlation with an R-squared over 0.1 was found. To further investigate the interaction, a principal component analysis (PCA) was performed, which yielded a good separation depending on the presence or absence of *P. aeruginosa* supernatant and between low and high growers. Hierarchical clustering was performed on this data to identify patterns. Additionally a PCA was done for the genotype data, and we found the best separation between evolution conditions to be along PC2 and PC6. Translating the established phenotype clusters we obtained similar clusters in the genotype data. We further inspected the loadings of the genotype PCs and selected significant mutations in proteins that cause this separation and related their functions to the loadings of the phenotype PCA. Some of the selected mutations possibly contribute to the increased antibiotic resistance. Through better understanding the interaction between *S. aureus* and *P. aeruginosa* treatments for these polymicrobial diseases could be improved and help over 150.000 people [7] that are affected world wide.

1 References

- [1] Kim A Brogden, Janet M Guthmiller, and Christopher E Taylor. Human polymicrobial infections. *Lancet (London, England)*, 365(9455):253, 1 2005. ISSN 01406736. doi: 10.1016/S0140-6736(05)17745-9. URL [/pmc/articles/PMC7119324//pmc/articles/PMC7119324/?report=abstracthttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC7119324/](https://pubmed.ncbi.nlm.nih.gov/pmc/articles/PMC7119324/).
- [2] G. B. Rogers, C. A. Hart, J. R. Mason, M. Hughes, M. J. Walshaw, and K. D. Bruce. Bacterial Diversity in Cases of Lung Infection in Cystic Fibrosis Patients: 16S Ribosomal DNA (rDNA) Length Heterogeneity PCR and 16S rDNA Terminal Restriction Fragment Length Polymorphism Profiling. *Journal of Clinical Microbiology*, 41(8):3548, 8 2003. ISSN 00951137. doi: 10.1128/JCM.41.8.3548-3558.2003. URL [/pmc/articles/PMC179861//pmc/articles/PMC179861/?report=abstracthttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC179861/](https://pubmed.ncbi.nlm.nih.gov/pmc/articles/PMC179861/).
- [3] Irena Pastar, Aron G. Nusbaum, Joel Gil, Shailee B. Patel, Juan Chen, Jose Valdes, Olivera Stojadinovic, Lisa R. Plano, Marjana Tomic-Canic, and Stephen C. Davis. Interactions of methicillin resistant *Staphylococcus aureus* USA300 and *Pseudomonas aeruginosa* in polymicrobial wound infection. *PloS one*, 8(2), 2 2013. ISSN 1932-6203. doi: 10.1371/JOURNAL.PONE.0056846. URL <https://pubmed.ncbi.nlm.nih.gov/23451098/>.
- [4] Selina Niggli, Lukas Schwyter, Lucy Poveda, Jonas Grossmann, Rolf Kümmerli, Dominique H Limoli, and Jennifer M Bomberger. Rapid and strain-specific resistance evolution of *Staphylococcus aureus* against inhibitory molecules secreted by *Pseudomonas aeruginosa*. *mBio*, 14(5), 10 2023. ISSN 21507511. doi: 10.1128/MBIO.03153-22. URL <https://journals.asm.org/journal/mbio>.
- [5] RStudio Team. RStudio: Integrated Development Environment for R, 2021. URL <http://www.rstudio.com/>.
- [6] ChatGPT. URL <https://chat.openai.com/>.
- [7] Jonathan Guo, Anna Garratt, and Andrew Hill. Worldwide rates of diagnosis and effective treatment for cystic fibrosis. *Journal of Cystic Fibrosis*, 21:456–462, 2022. doi: 10.1016/j.jcf.2022.01.009. URL <https://doi.org/10.1016/j.jcf.2022.01.009>.