

Important Mutations for Phenotype Difference in *Staphylococcus Aureus* 6850

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1 Introduction

The interaction between *Pseudomonas aeruginosa* and *Staphylococcus aureus* causes rapid evolution of *S. aureus* [1] leading to increased antibiotic resistance [2] in *S. aureus*.

2 Method Overview

- i) Linear regression was performed to find correlations between traits in the *S. aureus* 6850 phenotype data.
- ii) To investigate patterns in the phenotype data a PCA was performed (Fig. 1). The data we subsequently clustered using a hierarchical algorithm.
- iii) Additionally, a PCA for the genotype data was done and the clusters found in II were transferred (Fig. 3).
- iv) With a threshold of 0.25 we selected the most important mutations and investigated the proteins they occurred in and connected them to the previously found separation in phenotype. Further, we categorized mutations according to PMBEC score [3].

3 Results and Discussion

- i) We found no correlation between all combinations of the following variables with an R² over 0.1: average STX, average H₂O₂ survival and average growth in pqS.

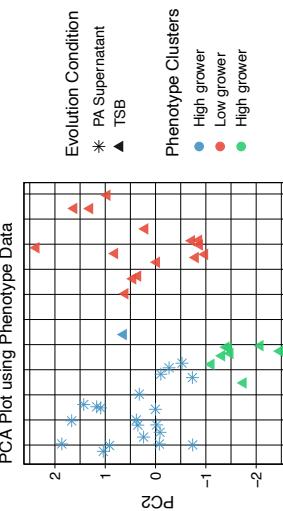


Figure 1: PCA plot of phenotype data, with a cumulative variance of 75%. We get a good separation between low and high growers are evolution condition along PC1 (50% prop. var.) and along PC2 we can further differentiate between the strong growing clones according to their evolution condition.

- ii) By looking at the loadings of the PCs (Figure 2) we see that PC1 (50% prop. var.) separates the data into low (red) and high (blue and green) growers. PC1 also yields a good separations between the evolution conditions except for two populations of TSB clones. Along PC2 (25% prop. var.) we can differentiate between strong growing *P. aeruginosa* (PA) supernatant and TSB grown clones.

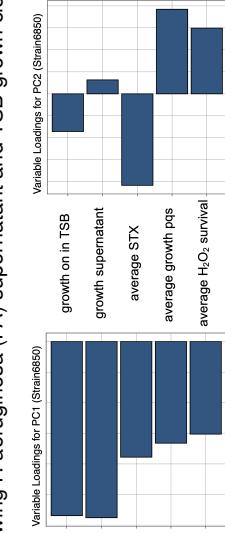


Figure 2: Loadings for the phenotype data PCA. For PC1 growth independent of media is most important. Whereas for PC2 average staphyloxanthin production and average growth in pqS are most important.

3 Results and Discussion

- iii) The phenotype clusters are preserved in this PCA (Fig. 3, 19% cumulative var.) except for some supernatant clones. Along PC2 (13% prop. var.) we again get a separation between growing strength. PC6 (6% prop. var.) gives some separation between evolution condition.

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- iv) Selected Proteins form genotype loading (github) only if in a protein coding gene

Table 1: Important genes names, function, evolution condition of clone and PC of origin.

Protein	Function	Condition	PC
Q2G2T6	c-di-AMP phosphodiesterase	TSB	2 & 6
aisT	Na:ala symporter	PA sup.	2 & 6
walk	Sensor protein kinase	TSB	6
lyrA	Lysostaphin resistance	TSB	6
Q2G2N1	Aromatic acid exporter family	PA sup.	2

4 Conclusion

- Phenotype is partly driven by genetic adaptation.
- c-di-AMP is linked to antibiotic resistance and over all cell function [4] and aisT is linked to staphyloxanthin production [5]. This is important because virulence is impacted by antibiotic resistance [6].
- walk is involved in growth [7], and the observed mutation might increase its function.
- lyrA only drastic mutation, could lead to all loss of function, since no bacteriolyse [8] resistance is needed in TSB.
- We would investigate all genes but Q2G2N1 in a knockout experiment to further with subsequent analysis of the observed mutations.

References

