ETH zürich

Functional Genomics Center Zurich

Important Mutations for Phenotype Difference in Staphylococcus Aureus 6850

Dominik Götz[1], Natalia Zajac[2], Jonas Grossmann [2], Selina Niggli[2], Rolf Kümmerli[2]
[1]Department of Applied Biosciences, ETH Zurich, CH, [2]Functional Genomics Center Zurich, University/ETH Zurich

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 H_2O_2 survival and average growth in pqs.

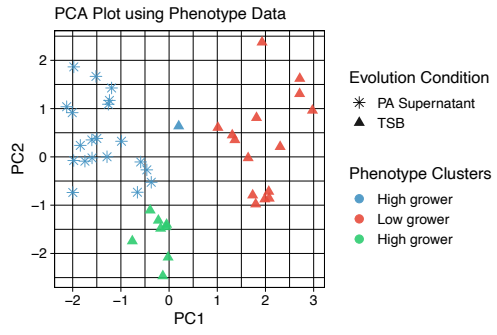

Figure 1: PCA plot of phenotype data, with a cumulative variance of 75%. We get a good separation between low and high growers and evolution condition along PC1 (50% prop. var.) and along PC2 we can further differentiate between the strong growing clones according to their evolution condition.

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.

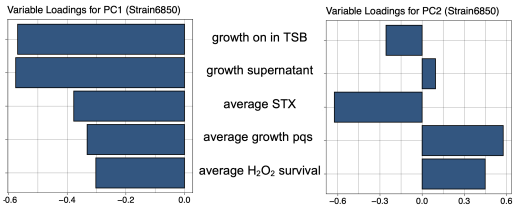

Figure 2: Loadings for the phenotype data PCA. For PC1 growth independent of media is most important. Whereas for PC2 average staphyloxanthin production and average growth in pqs are most important.

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.

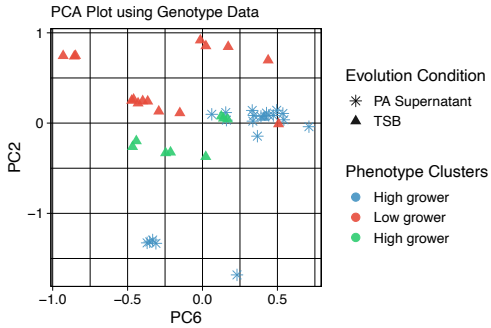

Figure 3: PCA plot of genotype data, with a cumulative variance of 19%. We again see a separation between low and high growers along PC2 (13% prop. var.) We cannot see a separation for the evolution condition that is as clear as in Figure 1, although there is some. Along PC6 (6% prop. var.) we get a looser separation between evolution conditions.

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
alsT	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 alsT 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 al loss of function, since no bacteriolyses [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

References, code and additional images

Contact and digital poster