Supplementary Figures For 'Global Network Analysis of Drug Tolerance, Mode of Action and Virulence in MRSA'

Table of Contents

Supplementary Figures

Figure S1 Network Degree Distribution 2
Figure S2 Network Clustering Coefficient Distribution 3
Figure S3 Disruption of vraR and tcaA confers ranalexin sensitivity 4
Figure S4 Raw Network Blind Test Datasets 5
Figure S5 F-measure for Edge Threshold Determination 6
Figure S6 Network Module Size Distribution 7
Figure S1. Network Degree Distribution. The red line shows a power law that has been fitted to the network degree distribution (correlation = 0.818). The function $y = 1320x^{-1.35}$ describes the scaling of the degree, which is a characteristic feature of hierarchical (and scale-free) networks (Yamada & Bork 2009). This figure was generated with NetworkAnalyzer (Assenov et al. 2008), a plugin to Cytoscape (Shannon et al. 2008).
Figure S2. Network Clustering Coefficient Distribution. The red line shows a power law that has been fitted to the network clustering coefficient distribution (correlation = 0.663). The scaling of the clustering coefficient can be described by the function $y = 0.6x - 0.24$, and is consistent with hierarchical modularity (Yamada & Bork 2009). This figure was generated with NetworkAnalyser (Assenov et al. 2008), a plugin to Cytoscape (Shannon et al. 2008).
Figure S3. - Disruption of vraR and tcaA confers ranalexin sensitivity.

a) Growth, measured by change in optical density (600nm), of the parent strain RN4220 (◇) and a vraR mutant (○) in the absence of ranalexin, or in the presence of 60µg ml⁻¹ ranalexin (□, △) respectively. Time is indicated in hours: minutes: seconds. A representative result of triplicate experiments is shown. The effect on viability of exposing RN4220 (filled symbols) and the vraR mutant (open symbols) to ranalexin: b) the effect of exposure to increasing ranalexin concentration (0-160µg ml⁻¹ in TSB) for 1 h; c) the effect of increasing duration of exposure (0-120 min) to 120µg ml⁻¹ ranalexin in TSB. In each case, representative results from duplicate experiments are shown. d) Growth of RN4220 (◇) and a tcaA mutant (○); in the absence of ranalexin, or in the presence of 60µg ml⁻¹ ranalexin (□, △) respectively. A representative result of triplicate experiments is shown.
**Figure S4. Predictive Power Over Unthresholded Network** Receiver Operator Characteristic Plots are shown for blind test datasets TEST-N (real-world distribution of non-interacting and interacting genes) and TEST-B (balanced distribution). Neither TEST-N nor TEST-B was used in any part of the network development process. Areas under the curve are given at the bottom right of the figure (TEST-N 0.791, TEST-B 0.792). This figure was generated in R (R Development Core Team 2010).
Figure S5. F-measure for Edge Threshold Determination. The F-measure (van Rijsbergen 1979) is shown over TRAIN-N. The edge threshold was determined by reference to the F-measure, FPR and number of edges over TRAIN-N in order to generate the high-confidence network. A threshold value of 0.75 was determined, corresponding to the left side of the ‘plateau’ with values of F-measure >0.37. This threshold value was chosen to maximise the number of network edges while maintaining high F-measure and low false positive rate. This figure was generated in R (R Development Core Team 2010).
**Figure S6. Network Module Size Distribution.** The above figure outlines the distribution of 597 clusters (size 2 or more) identified by MCL. One module of size 52 was identified, but there were no modules with size 19-51. This figure was generated in R (R Development Core Team 2010).