SUPPLEMENTARY FIGURE LEGENDS

Figure S1. Analysis of labelling pattern distribution of metabolites of the central carbon metabolism after MRSA infection. HeLa cells were infected with USA300 (MOI 100) for 6 hours and labelling distribution were obtained by GC-MS. This figure illustrates the labelling pattern of each metabolite in cells infected with USA300 strain. The area of the filled circle depicts the fraction of label for each isolate, where blue represents carbon coming from glucose-labelled, red is carbon coming from glutamine-labelled and the black line is 100% of labelling.

Figure S2. Differences in the pool sizes of metabolites of the central carbon metabolism after *S. aureus* NCTC 13626 infection of HeLa cells. HeLa cells were lysed after vancomycin-protection assays with NCTC 13626 (MOI 100) for 6 hours and metabolites were detected by GC-MS. Graphs show absolute levels of each metabolite in uninfected cells (white bars) and cells infected with NCTC 13626 strain (shredded bars). This figure shows means ± standard error of two independent experiments performed in triplicates. Statistical differences were tested using Student´s t-test against uninfected cells. p-value ≤0.05 (*); ≤0.01 (**); ≤0.001 (***). Y-axis scale units are arbitrary units (x1,000).

Figure S3. Differences in the pool sizes of metabolites of the central carbon metabolism after *S. aureus* NCTC 13626 infection of BALB/c Mouse Bone Marrow macrophages. Bone marrow macrophages were lysed after vancomycin-protection assays with NCTC 13626 (MOI 100) for 6 hours and metabolites were detected by GC-MS. Graphs show absolute levels of each metabolite in uninfected cells (white bars) and cells infected with NCTC 13626 strain (shredded bars). This figure shows means ± standard error of two independent experiments

performed in triplicates. Statistical differences were tested using Student´s t-test against uninfected cells. p-value ≤0.05 (*); ≤0.01 (**); ≤0.001 (***). Y-axis scale units are arbitrary units (x1,000).

Figure S4. Co-localization assay of USA300-GFP and mCherry-CWT by confocal microscopy. (A) HeLa cells expressing the fluorescent escape marker mCherry-CWT were infected with USA300-GFP strain (MOI 100; 6h); DAPI was employed for nucleus staining. The recruitment of mCherry-CWT (red) to the bacterial cell wall of USA300-GFP (green) identifies cytosolic bacterial cells. (B) Quantification of percentage of USA300-GFP cells labelled with mCherry-CWT. Data are expressed as means ± standard errors of three different experiments. SA= *S. aureus*-infected cells.

Figure S5. Dorsomorphin does not have a direct effect on *S. aureus* growth. MRSA USA300 was grown in 96-wells plates in the presence of DMSO (Mock), Dorsomorphin at different concentrations ranging from 1-10 µM, or gentamicin. Absorbance (OD_{600nm}) was measured at 2, 4, 6 and 24 hours to produce the growth curves. Data are expressed as means ± standard errors of three different experiments performed in triplicates.

Figure S6. Analysis of host cell viability and intracellular bacterial survival during *S. aureus* USA300 and NCTC 13626 infection assays, and their resistance to gentamycin, vancomycin and lysostaphin. A) Quantification of host cell viability at different time points of infection, measured by flow cytometry using double annexin V-FITC and PI staining. B) Intracellular survival of USA300 and NCTC13626 at different time points; HeLa cells were infected with *S. aureus* and lysed in 0.1% Triton X-100 for CFU evaluation. C) Bacterial

growth levels at 6 hours in NB medium supplemented with gentamycin (100 µg/ml), vancomycin (5 µg/ml) and lysostaphin (5 µg/ml). Graphs display means ± standard error of three independent experiments. Statistical significance was analysed by one-way ANOVA and *post hoc* Tukey's multiple comparison tests. p-value ≤0.05 (*); ≤0.01 (**); ≤0.001 (***).