

- A large collection of daptomycin non-susceptible clinical isolates (n=12) were evaluated for minimum inhibitory concentration values (MIC), stability, and daptomycin population analysis profiles (PAPs).
- All 12 isolates displayed stability on serial passage, MIC values of 2-4 mg/L and area under the curve (AUC) values from 14.01 - 26.85 with variability among isolates with the same MIC value.
- When isolates with the same MIC value were compared in an in vitro pharmacokinetic/pharmacodynamic (PK/PD) model against daptomycin 6 and 10 mg/kg/day for 96 hours, isolates with smaller AUC values (left shift) displayed sustained bactericidal activity versus isolates with larger AUC values (right shift) which displayed a pattern of re-growth.
- Analysis of isolates recovered at 96 hours in the in vitro PK/PD model revealed an increase in the daptomycin AUC on PAP but no increase in MIC in the overall population.
- Analysis of an isolate recovered at 96 h in the in vitro PK/PD model revealed a novel Q326Stop mutation in *mprf*, hypothesized to render the mprF protein non-functional.

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