Exploring the metabolic profile of A. baumannii for antimicrobial development using genome-scale modeling

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Abstract

With the emergence of multidrug-resistant bacteria, the World Health Organization published a catalog of microorganisms urgently needing new antibiotics, with the carbapenem-resistant Acinetobacter baumannii designated as “critical”. Such isolates, frequently detected in healthcare settings, pose a global pandemic threat. One way to facilitate a systemic view of bacterial metabolism and allow the development of new therapeutics is to apply constraint-based modeling. Here, we developed a versatile workflow to build high-quality and simulation-ready genome-scale metabolic models. We applied our workflow to create a metabolic model for A. baumannii and validated its predictive capabilities using experimental nutrient utilization and gene essentiality data. Our analysis showed that our model iACB23LX could recapitulate cellular metabolic phenotypes observed during in vitro experiments, while positive biomass production rates were observed and experimentally validated in various growth media. We further defined a minimal set of compounds that increase A. baumannii’s cellular biomass and identified putative essential genes with no human counterparts, offering new candidates for future antimicrobial development. Finally, we assembled and curated the first collection of metabolic reconstructions for distinct A. baumannii strains and analyzed their growth characteristics. The presented models are in a standardized and well-curated format, enhancing their usability for multi-strain network reconstruction.