Identification of Novel Drug Targets in *Xanthomonas citri* pv. *citri* using Subtractive Genomics and Coevolution Analysis

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Abstract

Citrus canker is a devastating bacterial disease of citrus crops caused by *Xanthomonas citri* pv. *citri* (Xcc), a Gram-negative, rod-shaped pathogen possessing a polar flagellum and belonging to the family *Xanthomonadaceae*. Bacterial plant diseases cause significant agricultural losses worldwide, posing serious challenges to food security. The increasing emergence of antibiotic-resistant Xcc strains has further reduced the effectiveness of existing control measures, emphasizing the urgent need for novel therapeutic targets. In this study, a subtractive genomics approach was employed to identify potential drug targets essential for Xcc survival but absent in the citrus host. The complete Xcc proteome was retrieved from the UniProt database, followed by removal of paralogous sequences. Non-homologous proteins were identified using BLASTp against citrus proteins (e-value < 0.005). Essential proteins were screened using the Database of Essential Genes (DEG) with a stringent threshold (e-value < 0.00001), yielding 750 essential, non-host homologous proteins. Subsequent analyses included metabolic pathway mapping, subcellular localization prediction, and druggability assessment. Eight proteins-GlmU, CheA, RmlD, GspE, FleQ, RpoN, Shk, and SecB- were prioritized as promising drug targets, with RpoN, FleQ, and SecB identified as previously unexplored targets in Xcc. Protein–protein interaction analysis using STRING supported their functional importance. Coevolution analysis via the CoeViz server and active site prediction further validated their suitability for structure-based drug design. These findings provide a strong foundation for developing novel antimicrobial strategies to manage citrus canker effectively.

Keywords

Citrus canker, *Xanthomonas citri* pv. *citri*, drug target proteins, subtractive genomics, computational biology.