Immunoinformatics approach for developing a multi-epitope vaccine against *Pseudomonas aeruginosa* infection

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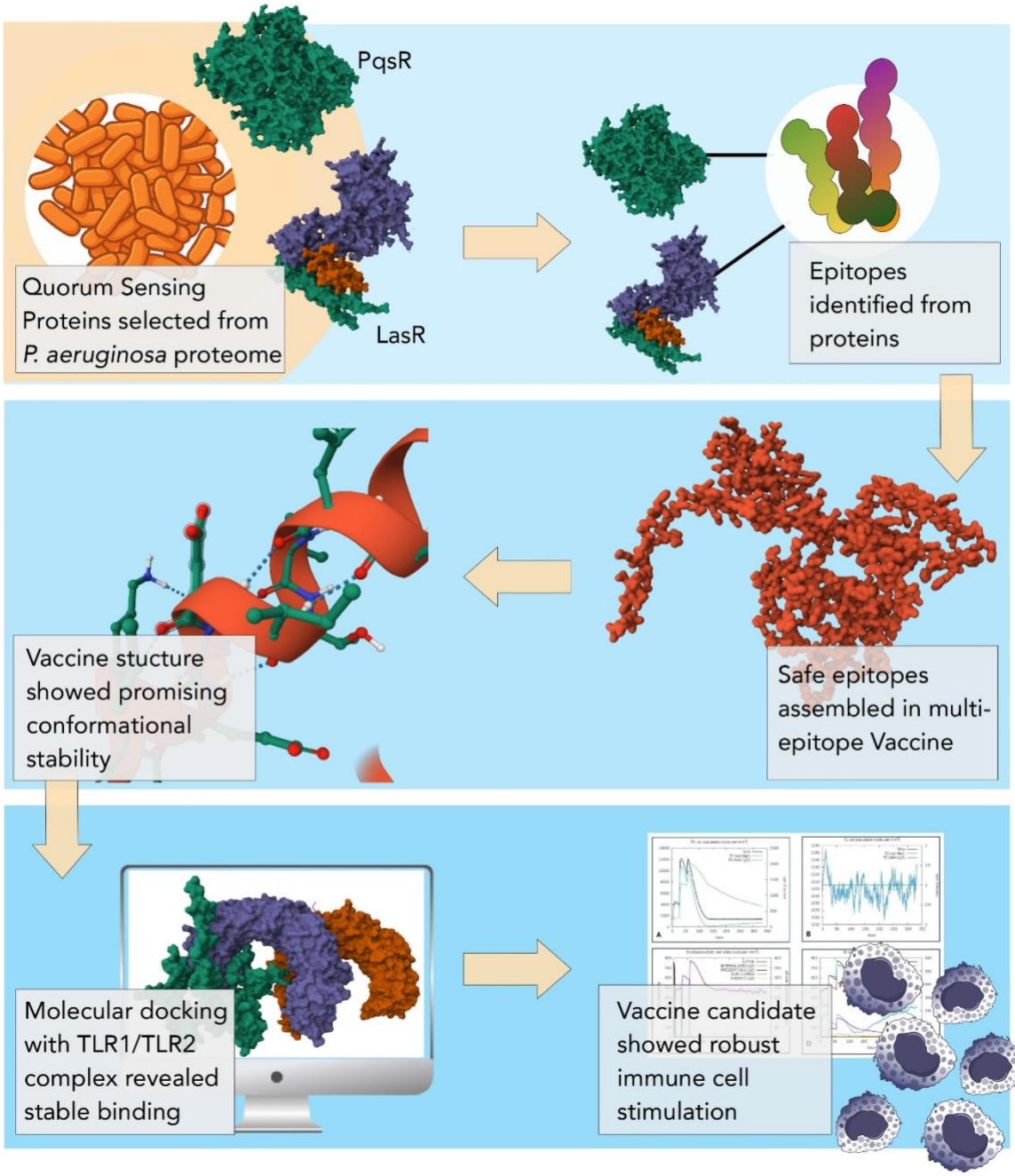
Graphical Abstract



Abstract

The rising threat of multidrug-resistant *Pseudomonas aeruginosa* has intensified the need for alternative therapeutic strategies, particularly vaccines that target virulence rather than viability. Quorum sensing (QS) regulators LasR and PqsR drive the pathogen's ability to coordinate infection, evade immune responses, and persist within host environments, yet remain underexploited as vaccine targets. This study presents a computationally designed multi-epitope subunit vaccine aimed at disarming *P. aeruginosa* through immune recognition of its QS machinery. Using immunoinformatics, machine learning-based epitope prediction, and reverse vaccinology approaches, immunodominant B-cell, MHC-I, and MHC-II epitopes were identified from the regulatory proteins. Six vaccine constructs were assembled with varied epitope arrangements, linked to a human β-defensin-3 adjuvant and TAT peptide for enhanced delivery and immunogenicity. Structural modeling, molecular docking with bacterial QS proteins, as well as Toll-like receptors (TLR1/2), and immune simulations, were used to assess vaccine performance. The top construct exhibited favorable physicochemical properties, strong structural integrity, and potent *in silico* immunogenicity, including predicted induction of IFN-γ, memory T and B cells, and high-affinity interactions with both target proteins and immune receptors. The study presents a promising computational vaccine candidate with novel potential to interfere with *P. aeruginosa*'s virulence strategies and support future translational development. This warrants subsequent in vitro and in vivo validation.