RES-269

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Molecular Dynamics Simulation of the Interaction between Penicillin and PBP2X Mutants from *Streptococcus pneumoniae* Isolates in Indonesia

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Background

Alterations in PBP2X have been linked to reduced susceptibility to β-lactam antibiotics in *Streptococcus pneumoniae*

Genomic analysis of Indonesian isolates showed that penicillin resistance was predominantly associated with serotype 19F

Structural and dynamic implications during antibiotic binding remain poorly elucidated.

Methods

Sample collection
522 *S. pneumoniae*-positive samples were collected between 2012–2024 from hospital- and community-based sources across 11 sites in Indonesia

Whole-genome sequencing

Antibiotic Susceptibility Testing
Subset of isolates tested

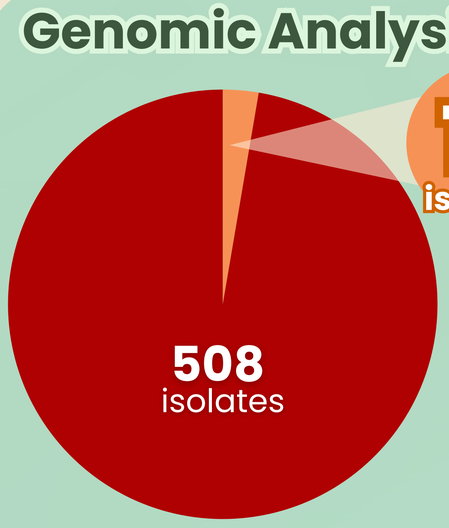
Structural Modelling (PBP2X)
FoldX in YASARA View (version 25.1.13), PDB ID: 5OIZ

Molecular Docking
PyRx v0.8

Molecular Dynamics Simulation
100 ns MD (GROMACS 2025)
Analysis of RMSD & RMSF

Results

Genomic Analysis



14 isolates predicted penicillin-intermediate/resistant

13 of which belonged to serotype 19F.

PBP2X Variants

2 Novel Forms

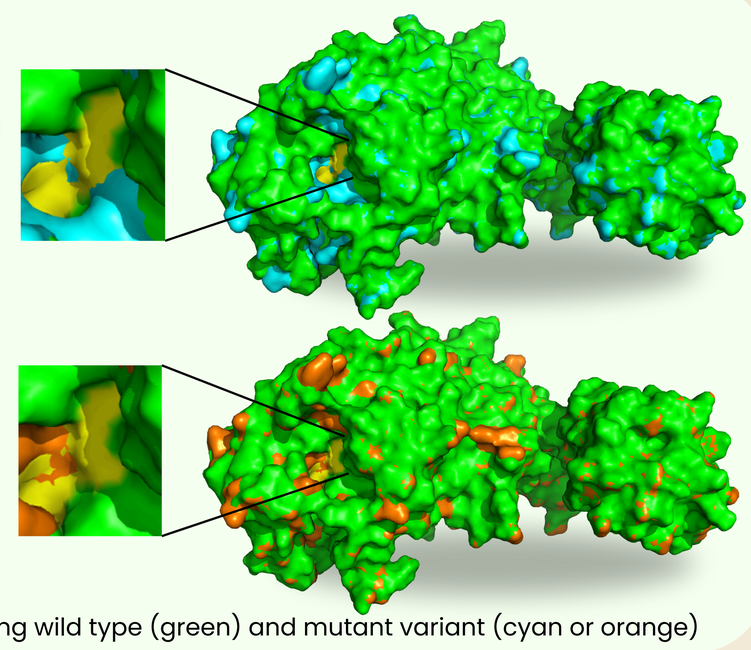
Type 318

Type 20

Type 16

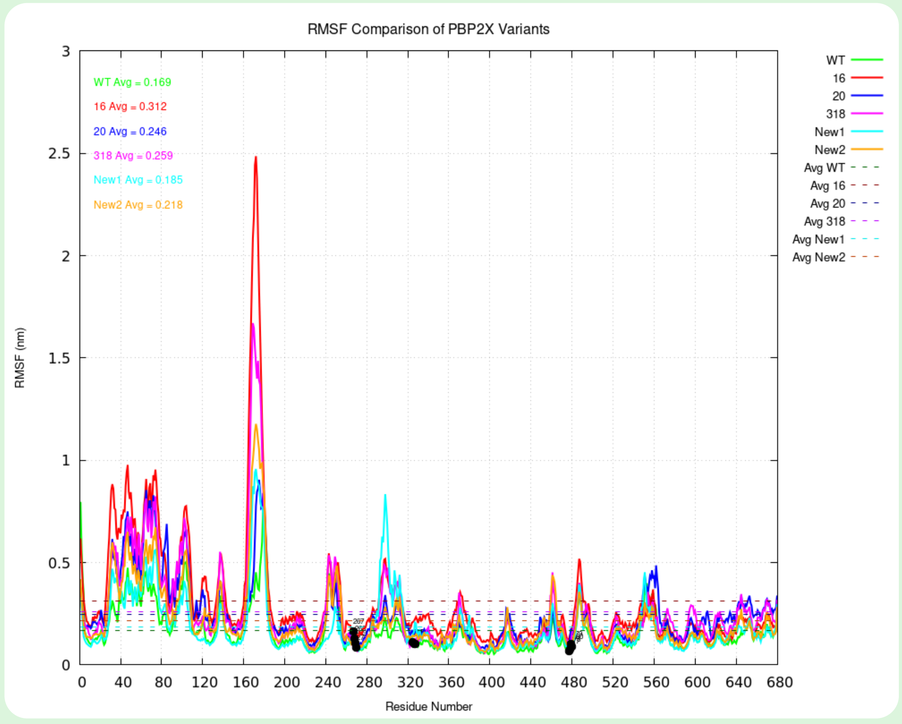
Novel 1: 43 amino acid substitutions in transpeptidase domain (T338A & M339I in conserved motifs)

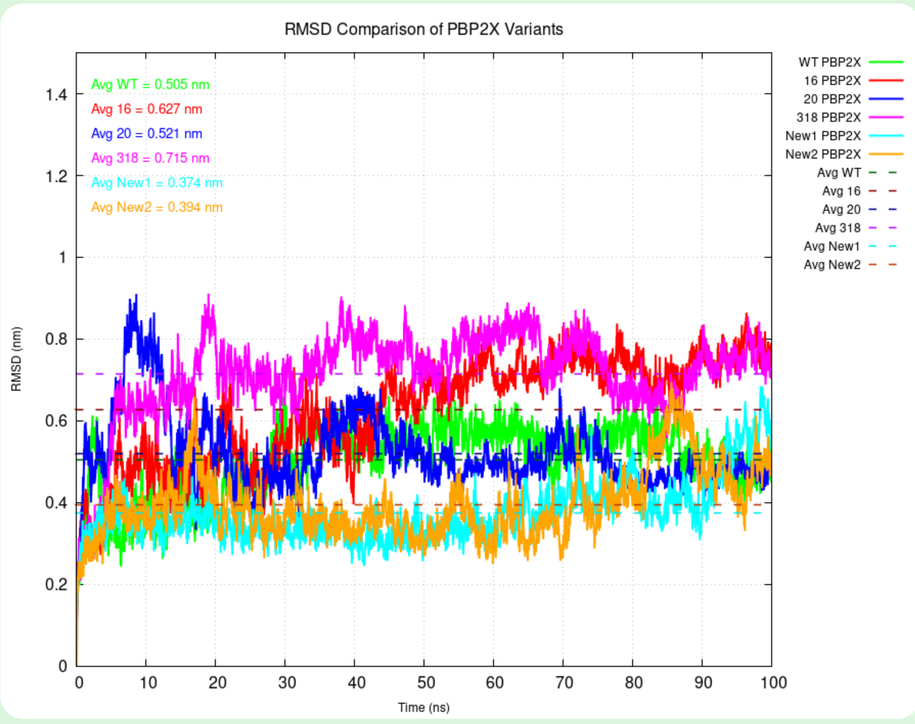
Novel 2: 42 amino acid substitutions in transpeptidase domain (T338A in conserved motifs)



*Overlay of PBP2X protein surfaces showing wild type (green) and mutant variant (cyan or orange)

Molecular Docking & Dynamics





Docking revealed **reduced penicillin binding in type 16** and **novel form 1**, while **RMSD/RMSF** analyses showed decreased stability and increased flexibility, **weakening penicillin binding.**

Conclusion

Molecular dynamics simulation showed that PBP2X mutations alter protein stability and penicillin interaction. These findings support dynamic structural analyses to understand resistance mechanisms and improve genomic surveillance.

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