PEPTIDOGLYCAN-BASED BIOMIMETIC NANOMATERIALS REVEAL LECTIN RECOGNITION IN DAP-TYPE BACTERIA: TOWARD RATIONAL DESIGN OF ANTIMICROBIAL THERAPEUTICS

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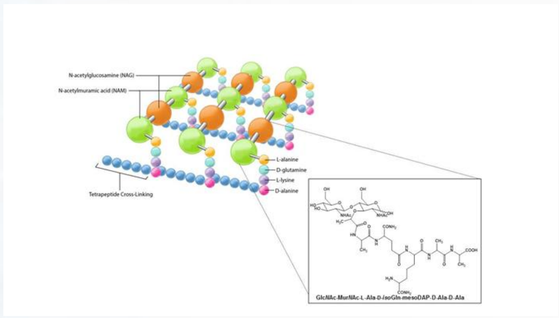
INTRODUCTION

Biomimetic nanomaterials mimic biological systems and offer versatile platforms for biomedical applications, including targeted drug delivery and personalized medicine. Peptidoglycan (PG), an essential component of bacterial cell walls, supports bacterial viability and activates host innate immunity. Building on the known recognition of PG fragments by WGA, this study quantitatively and mechanistically links soluble PGM binding and peptide-stem contributions with the effects of multivalent presentation. We designed PGM-functionalized biomimetic nanomaterials and investigated their interactions with selected lectins to elucidate glycan recognition relevant to host–pathogen interactions.

BACKGROUND & OBJECTIVE

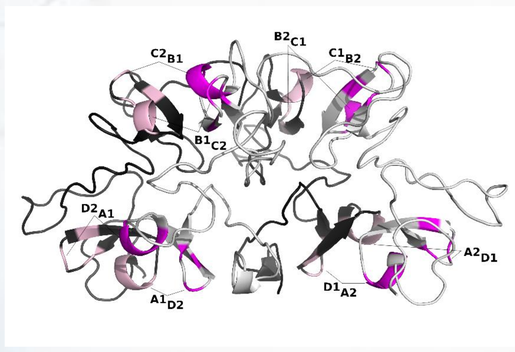
PGM is a chemically defined minimal fragment of DAP-type bacterial cell walls that combines a GlcNAc–MurNAc recognition motif with a native peptide stem.

This study investigates how WGA recognizes soluble PGM and how multivalent presentation influences binding.



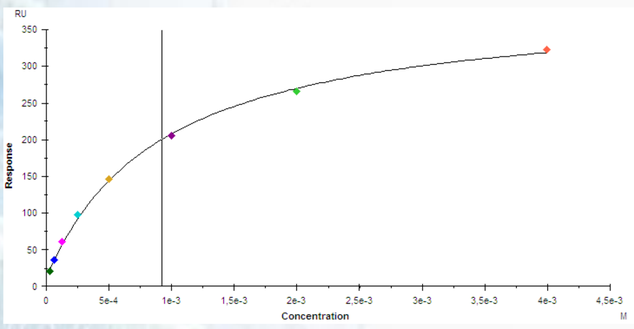
MULTISCALE APPROACH

SPR • ITC • fluorescence spectroscopy
Molecular modelling & 1 µs MD simulations
PGM-functionalized AuNPs and liposomes
DLS and TEM agglutination readouts



Multiple WGA binding sites enable molecular recognition and multivalent crosslinking.

MOLECULAR BINDING

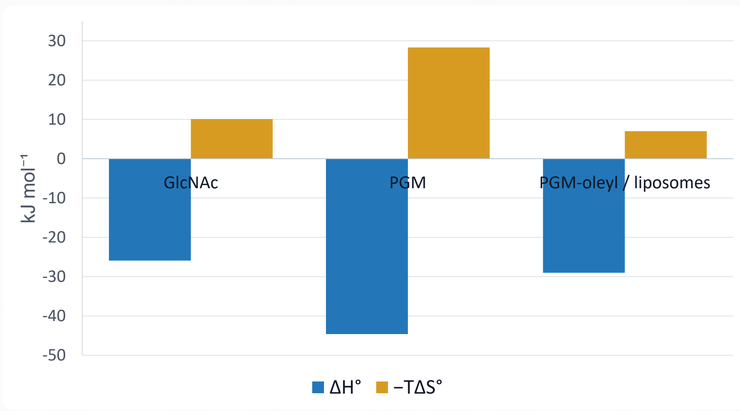


SPR apparent K$_D$ **9.3×10^{-4} M**

Rapid association/dissociation; equilibrium response fitted with a 1:1 steady-state model.

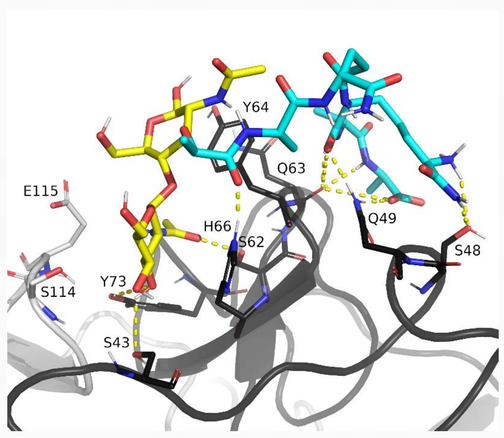
THERMODYNAMIC SIGNATURE

PGM and GlcNAc show similar millimolar affinity, but PGM binding is more exothermic and carries a larger entropic penalty.



Intrinsic K$_D$ (ITC)
GlcNAc 1.68 mM • PGM 1.44 mM

STRUCTURAL INTERPRETATION



The GlcNAc–MurNAc head group remains anchored in canonical WGA sites. The peptide stem samples multiple orientations and forms transient protein contacts.

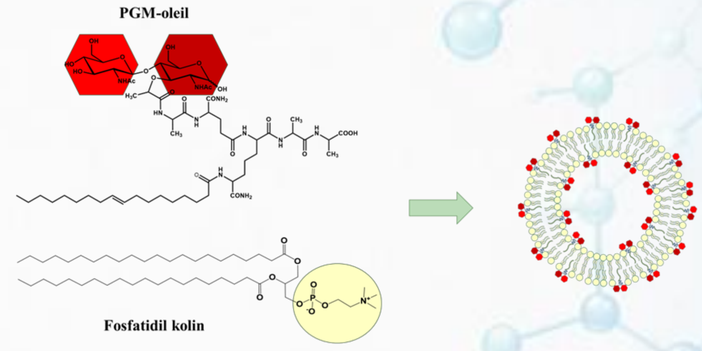
MECHANISTIC INSIGHT

The peptide stem modulates the energetic and conformational signature—without substantially increasing monovalent affinity.

LECTIN SELECTIVITY

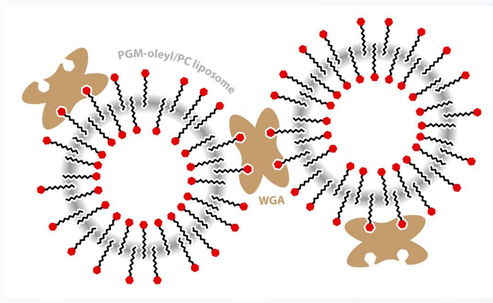
WGA showed reproducible PGM recognition. UEA-II and GS-II did not show comparable SPR responses: GlcNAc content alone does not predict PGM binding.

MULTIVALENT AMPLIFICATION ON BIOMIMETIC NANOSYSTEMS

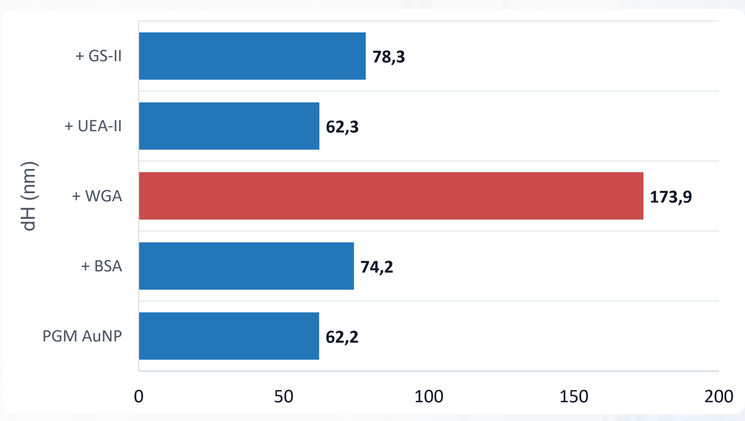


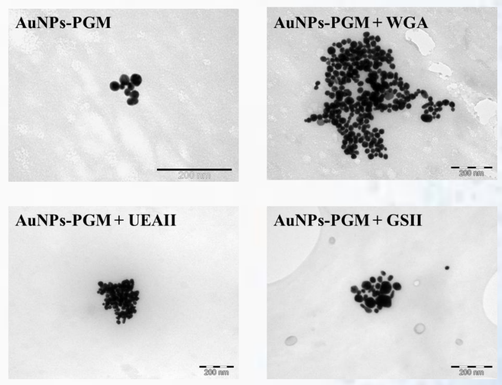
~10× higher apparent affinity
K$_D$ = 0.14 mM for PGM-oleyl/PC liposomes

Surface preorganization lowers the entropic cost and enables WGA-mediated bridging between lipid assemblies.



WGA DRIVES AuNP–PGM AGGREGATION





DLS and TEM confirm pronounced, time-dependent aggregation in the WGA–AuNP–PGM system.

CONCLUSIONS

- WGA primarily recognizes the GlcNAc–MurNAc head group, while the peptide stem forms heterogeneous, transient contacts that modulate the bound state.
- Peptide-stem interactions provide favorable enthalpy but impose an entropic penalty, resulting in an affinity comparable to GlcNAc yet a distinct thermodynamic and conformational response.
- Multivalent PGM presentation on liposomes and gold nanoparticles enhances functional avidity, crosslinking and agglutination.
- These findings provide a mechanistic bridge between molecular binding and recognition at complex biological interfaces and establish a foundation for the rational design of glyco-biomimetic materials and more biologically relevant models of lectin–bacterial cell-wall interactions.

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