

Investigating the activity of Antimicrobial Peptides (AMPs) of Myxobacteria against *Neisseria gonorrhoeae*

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Aims

The aim of the present study is to investigate the uses of Antimicrobial Peptides (AMPs) from Myxobacteria as a novel treatment for *Neisseria gonorrhoeae*.

Background

- Antimicrobial resistance in *N. gonorrhoeae* has been rapidly increasing in recent years, posing a threat of untreatable infections
- Untreated *N. gonorrhoeae* infections can lead to serious health implications in both men and women, as well as financial burden on healthcare industries, warranting the need for alternative therapeutic agents
- AMPs are small peptides produced by mammals, insects, plants, amphibians and microorganisms, with a wide range of antimicrobial activity
- Myxobacteria are soil dwelling predatory bacteria that exhibit killing activity against a wide range of bacteria and fungi. In silico studies have shown that they produce AMPs with potent antimicrobial activities
- In this study we investigated the activity of a Myxobacterial AMP Stig_370a using vitro assay susceptibility assays

1: Susceptibility testing of Stig_370a

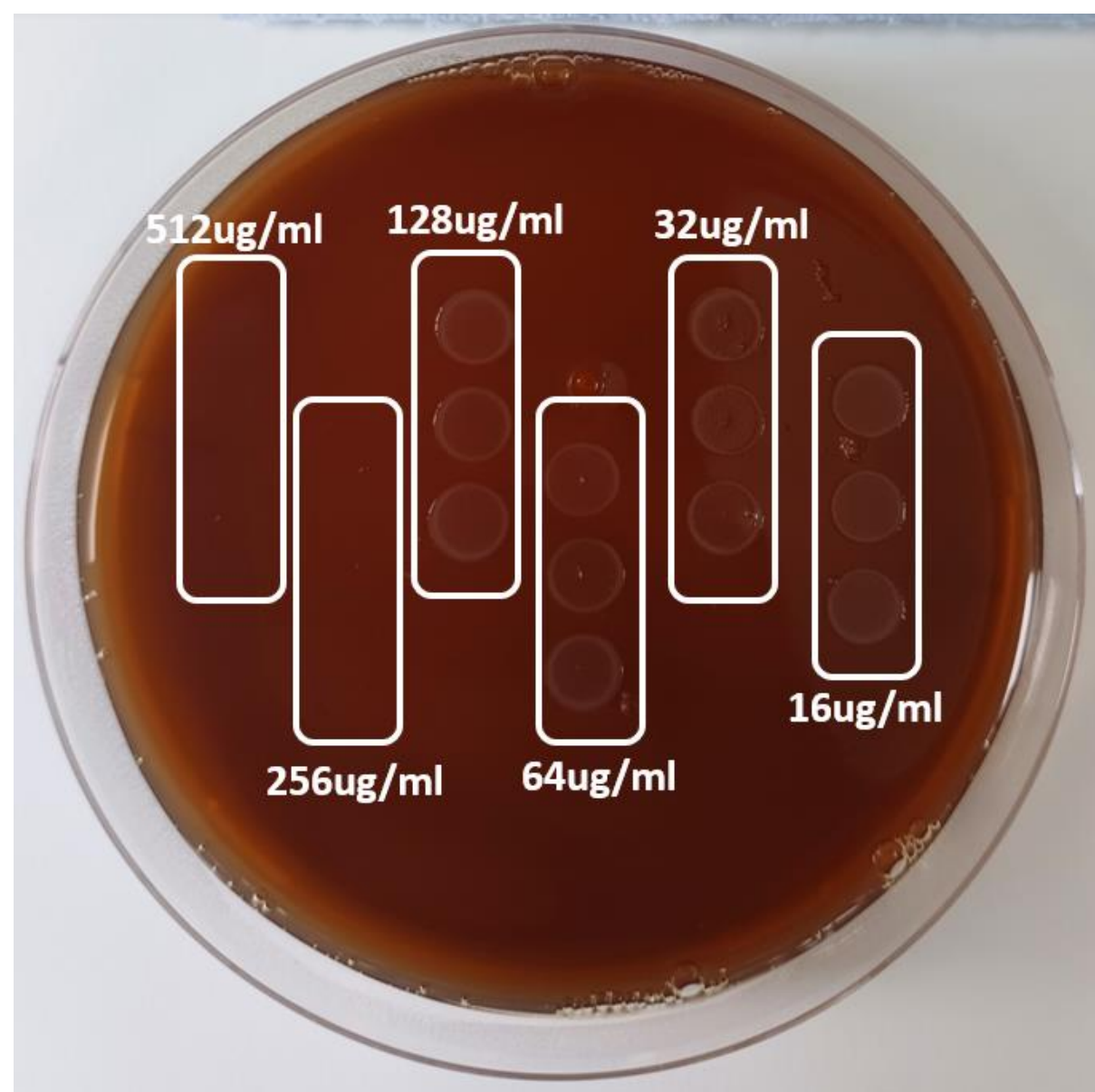


Figure 1. MBCs of Stig370a against strain 8375

A broth microdilution was used to determine the minimum bactericidal concentration (MBC) against 5 *N. gonorrhoeae* strains; a two-fold dilution series of 512ug/ml to 0ug/ml AMP was prepared in 96-well plates using Mueller-Hinton broth with 5% lysed defibrinated sheep blood.

10ul of each well was spotted onto Brain Heart Infusion chocolate agar and incubated at 37°C, 5% CO₂.

The MBC was then taken as the lowest concentration of AMP that showed no visible growth.

<i>Neisseria gonorrhoeae</i> strain					
	WHOF	WHOV	WHOZ	WHOX	8375
MBC (µg/ml) against Stig370a	32	128	128	256	256

Table 1. MBCs of all strains tested against Stig_370a

2: In silico AMP modifications

Stig_370a

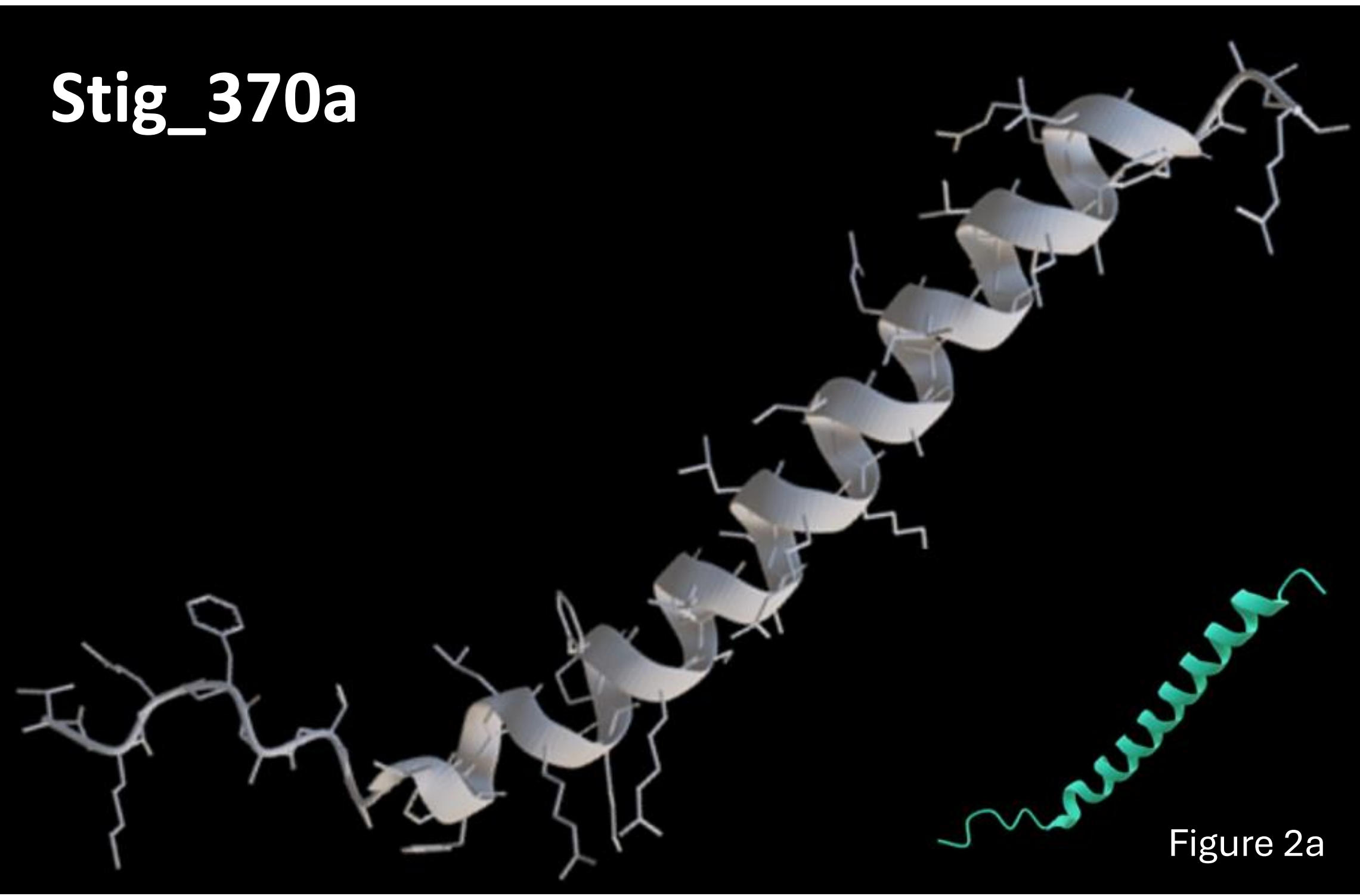


Figure 2a

Modified Stig_370a



Figure 2b

Stig370a (Figure 2a) was modified In silico in an attempt to increase the antimicrobial activity further.

The addition of several serine and threonine residues throughout the structure increases the likelihood of the peptide forming disulphide and thioether bridges between side chains (Figure 2b).

This makes it less likely to undergo proteolytic degradation, as well as enhanced selectivity and stability.

3: Susceptibility testing of modified Stig370a

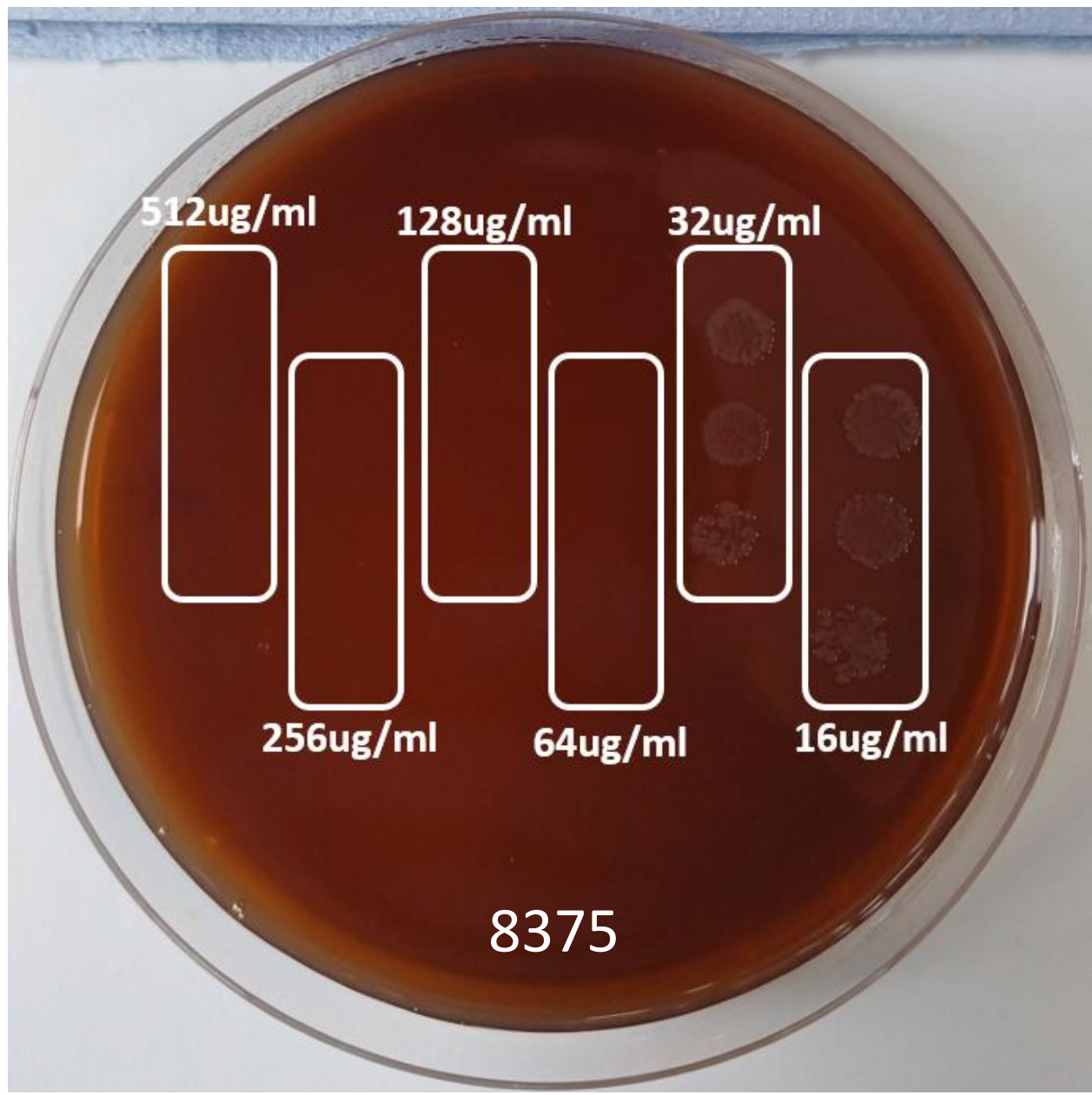


Figure 3. MBC of Modified Stig370a against strain 8375

When testing modified Stig370a, there was a reduction in the MBCs against WHOV and 8375 (green) and increased in WHOF (Red) (Table 2).

<i>Neisseria gonorrhoeae</i> strain					
	WHOF	WHOV	WHOZ	WHOX	8375
Observed MBC (µg/ml) against modified AMP	64	64	128	256	64

Table 2. MBCs of all strains tested against modified Stig_370a

Results & Discussion

- Both Stig370a and modified Stig_370a showed activity against all *N. gonorrhoeae* strains, with varying MBCs
- The modified Stig370a exhibited increased activity against two *N. gonorrhoeae* strains
- The strain WHOV has high level resistance to Azithromycin (>256 µg/ml), an antibiotic commonly used to treat *N. gonorrhoeae* infections. Both the Stig370a (128ug/ml) and modified Stig370a (64ug/ml) exhibited good activity against WHOV
- The results of the current experiments portray In silico modifications of AMPs to be a worthwhile area of exploration in the fight against antibiotic resistance in *N. gonorrhoeae*

Next steps

- Combine AMP and modified AMP with traditional antibiotics to see if there is a synergistic effect
- Combine AMP and modified AMP with live Myxobacteria colonies to see if there is a synergistic effect

References

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