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SHORTENED AURELIN-DERIVED PEPTIDES

The Role of Derivatization in Modulating Antimicrobial Efficacy

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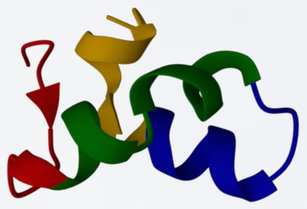
01 FROM AURELIN TO SHORTENED FRAGMENTS

Aurelin is 40 aa **cationic antimicrobial peptide** isolated **from jellyfish *Aurelia Aurita*** that exhibits activity against both Gram-positive and Gram-negative bacteria.
Four distinct fragments were selected as promising scaffolds for further optimization.

Full length sequence:
AACSDRAHGHICESFKSFCKDSGRNGVKLRANCKKTCGLC



Aurelia Aurita



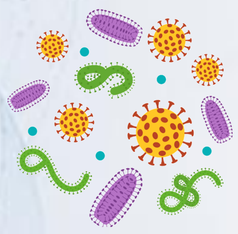
Aurelin 40 aa

Selected shortened fragments

AACSDRAHGH
ICESFKSFCK
DSGRNGVKLR
ANCKKTCGLC

02 WHY REDISIGN THEM?

Initial antimicrobial screening

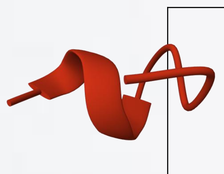
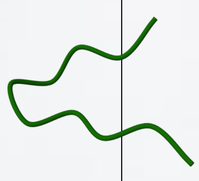
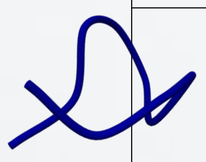


NO DETECTABLE ACTIVITY against *E.coli* and *S.epidermidis (>1.2 mM)*
-for all parent fragments - most likely due to low cationicity



RATIONAL REDESIGN to enhance cationic character and modulate activity

03 DESIGN STRATEGY

	PARENT FRAGMENTS	MODIFIED FRAGMENTS Cys to Arg	CYCLIC ANALOGUES
	AACSDRAHGH ~ 0	AARSDRAHGH +2	
	ICESFKSFCK +1	IRESFKSFRK +4	ICESFKSFCK +1
	DSGRNGVKLR +1		
	ANCKKTCGLC +1	ANRKKTRGLR +7	ANCKKTCGLR +3

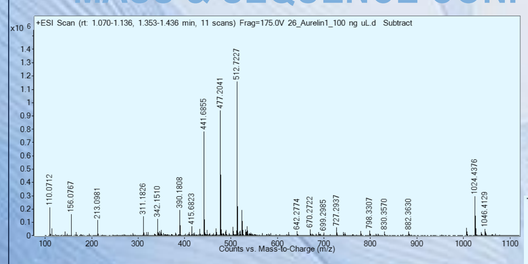
04 SYNTHESIS & CHARACTERIZATION

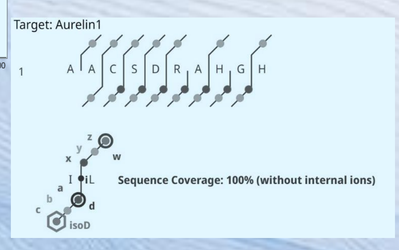


Automated SPPS — SYNTHESIS → **Preparative RP-HPLC** — PURIFICATION → **Analytical RP-HPLC** — PURITY CHECK

HR MS

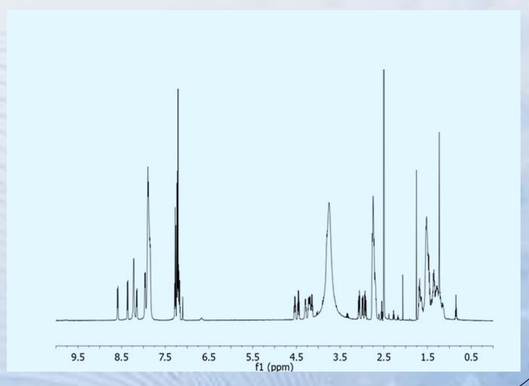
MASS & SEQUENCE CONFIRMATION





NMR

STRUCTURAL CHARACTERIZATION



05 DOES REDISIGN CHANGE ACTIVITY?

Antimicrobial activity, MIC

PARENT FRAGMENTS
NO DETECTABLE ACTIVITY

MODIFIED & CYCLIC FRAGMENTS
?

REFERENCES

1.Ovchinnikova T., et al. (2006) Aurelin, a novel antimicrobial peptide from jellyfish Aurelia aurita with structural features of defensins and channel-blocking toxins, *Biochem. Biophys. Res. Commun*. 348 (2): 514-523
2. Berger, I.; Loewy, Z.G. (2024) Antimicrobial Resistance and Novel Alternative Approaches to Conventional Antibiotics. *Bacteria* , 3, 171-182.
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TAKE-HOME MESSAGE: Loss of activity upon aurelin shortening guided the rational design of new derivatized and cyclic peptide candidates.

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