Database Analysis of Antimicrobial Peptides for Use in a Nanoparticle Antibiotic

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INTRODUCTION

Bacterial infections that are managed with antibiotic treatments are becoming a thing of the past: Marked by the CDC there are 18 species of antibiotic resistant bacteria and counting with three million people a year becoming infected.[1] Antimicrobial Peptides (AMPs) look to be a novel solution to these growing concerns.

AMPs are a diverse class of peptides apart of the innate immune system. A specific class of AMPs, known as cationic antimicrobial peptides have been shown to have antibacterial properties.

Figure 1. Image of Cathelicidin LL-37. One of many cationic AMPs with an α helix.[3]

AMPs experience a narrower mutation window when used against bacteria.[2] This is due to their:

- ➢ Non specific Mechanisms of Action
- ➢ Physiochemical Diversity
- ➢ Time-Kill dynamics

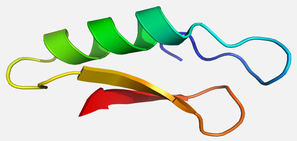


Figure 2. Image of Plectasin. An AMP with both a β sheet and α helix.[3]

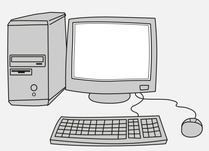
To harness the the antibiotic qualities of AMPs, these peptides will be encapsulated in synthetic polymers to create nanocomplexes for targeted delivery into the lung tissues of patients with Cystic Fibrosis. This work compiles a list of AMP candidates the polymer-AMP nanocomplex.

METHODOLOGY

Selecting Primary Databases
Various AMP databases were reviewed and compared. Three main databases were selected:

APD3
dbAMP
ADAM

1



Compile a List
General search for AMPs using database search features. Created an excel sheet to track selections.

Physicochemical Properties
Antibacterial Activity
Toxicity

2

Cluster and Compare Peptides
Grouped similar AMPs together. Reviewed list and selected 8 AMPs to move forward with testing.

Source
Effectiveness
Synergy

3

To be able to select AMPs for antibiotic use, we used a multi-step literature and database-guided review to compile a list. This list was then subjected to further research and comparison to obtain the final product.

RESULTS

Name	Source	Amino Acid Sequence	Structure	Charge	Effectiveness			Boman Index (kcal/mol)
					G-	G+	*Pseudomonas* spp.	
Myxindin	*Myxine glutinosa*	GIHDILKYGKPS	α-helix	+1	√	√	**MIC:** >16 ug/ml	0.94
Paracentrin 1	Synthetic	EVASFDKSKLK	Unk.	+1	√		**MIC:** 1.5 ug/ml	2.29
Coprisin	*Copris tripartitus*	VTCDVLSFEAKGIAVNHSACALHCIALRKKGGSCQNGV CVCRN	Complex	+3	√	√	**MIC:** 2 ug/ml	0.96
LL-37	*Homo sapiens*	LLGDFFRKSKEKIGKEFKRIVQRIKDFLRNLVPRTES	α-helix	+6	√	√	**MIC:** 0.05 ug/ml	2.99
Polymyxin B	*Bacillus polymyxa*	KTKKKFLKKT	Unk.	+6	√	√	**MIC:** 1.0 ug/ml	3.05
Protegrin 1	*Sus scrofa*	RGGRLCYCRRRFCVCVGR	β-sheet	+7		√	**MIC:** 0.5 ug/ml	3.65
Tachyplesin III	*Tachypleus gigas*	KWCFRVCYRGICYRKCR	β-sheet	+7	√	√	**MIC:** 2.0 ug/ml	2.98
SMAP-29	*Ovis aries*	RGLRRLGRKIAHGVKKYGPTVLRIIRIAG	α-helix	+9	√	√	**MIC:** 4.0 ug/ml	2.16

CONCLUSION

From the 3,000 AMPs available, we were able to identify 61 with antibacterial properties. By clustering and comparing the data, we created a final list with 8 contenders. The AMPs on this list show:

- ➢ Optimized activity against pathogenic bacteria known to reside in the lungs
- ➢ Moderate to High protein binding efficiencies (Boman Index)

FUTURE DIRECTIONS

Future projects include:

- ➢ formulating selected AMPs with polymers to assess whether nanoparticles can be formed and enable sustained release
- ➢ testings against planktonic and biofilm cultures of *Pseudomonas spp.*

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