

DBAASP: A COMPREHENSIVE REPOSITORY OF NATURAL MULTIFUNCTIONAL CYCLIC ANTIMICROBIAL PEPTIDES



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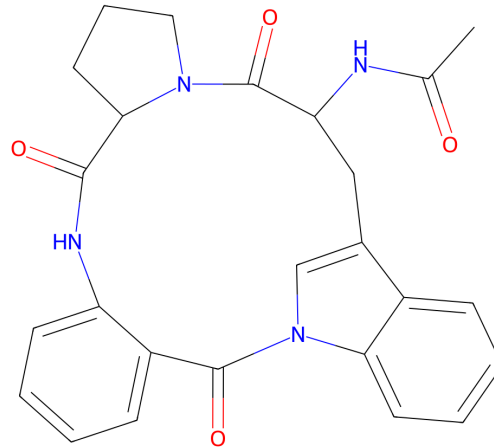
18/09/2023

Cyclic peptides

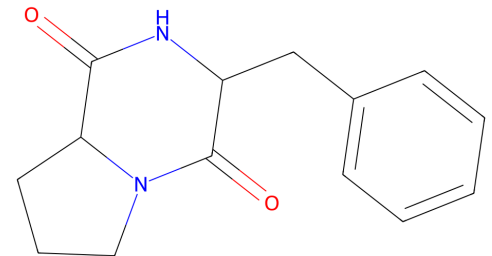
Why Cyclic peptides ?

Macrocyclization improves the pharmacological properties and bioactivity of peptides.

- High metabolic stability
- Oral availability
- Selective affinity for receptors
- Low cytotoxicity



DBAASPN_18738



DBAASPN_6742

DBAASP is a repository of data on antimicrobial/cytotoxic activity and structure of more than 21000 peptides

<https://dbaasp.org/home>



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DBAASP peptides with reported activities against: [SARS-CoV-2](#)

DBAASP peptides with reported activities against enveloped positive-sense RNA viruses: [HIV](#), [HCV](#), [Coronaviruses](#), [PRRSV](#)

Database of Antimicrobial Activity and Structure of Peptides

[SEE ALL MD MODELS](#)



Monomer
20345

Multimer
302

Multi Peptide
229

Records with the Data on Synergistic Activities
658

Overview

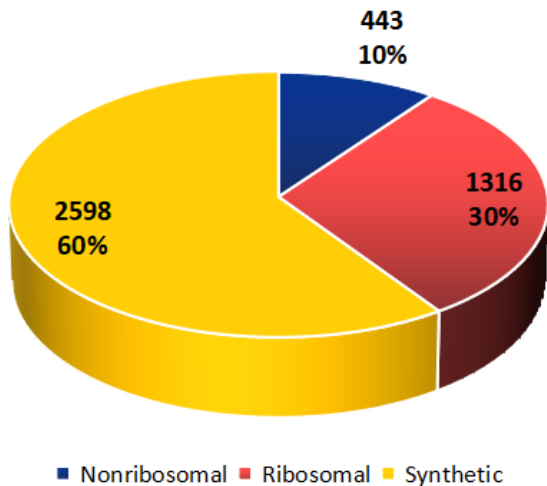
Database of Antimicrobial Activity and Structure of Peptides (DBAASP) is the manually-curated database. It has been developed to provide the scientific community with the information and analytical resources for designing antimicrobial compounds with a high therapeutic index.

Activate Windows
Go to PC settings to activate Windows.

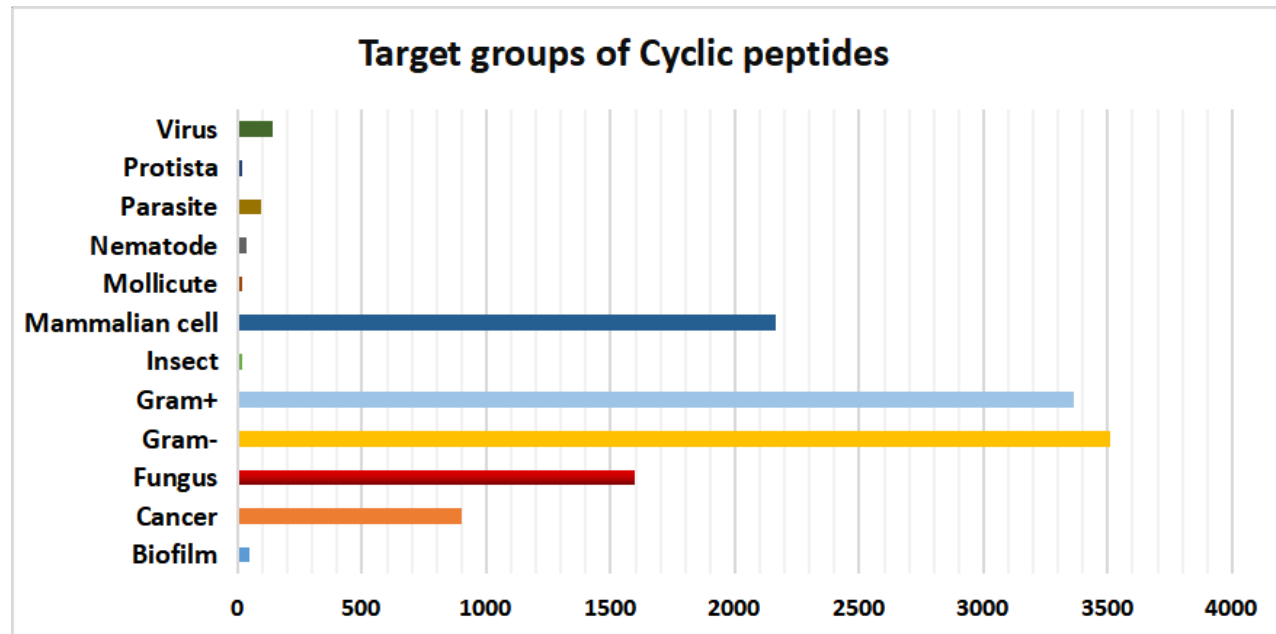
DBAASP stores data on 4357 Cyclic peptides

1759 peptides are natural

DBAASP Cyclic peptides

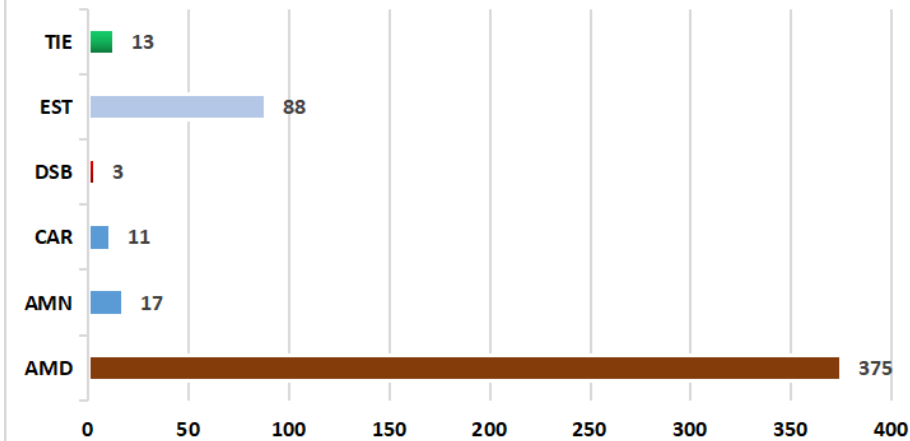


They have various targets



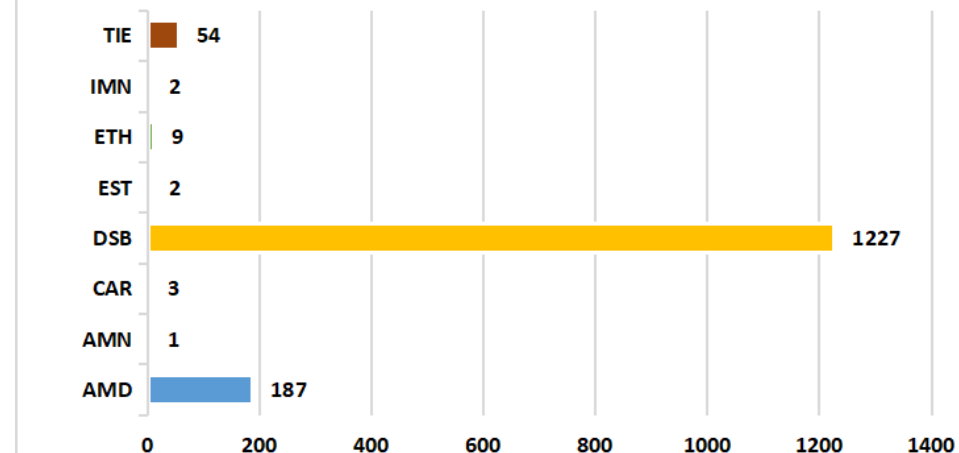
Which bonds are used by nature to cyclize peptides?

Bonds of Nonribosomal cyclic peptides



TIE = Thioether
IMN = Imine
ETH = Ether
EST = Ester
DSB = Disulfide
CAR = Carbon
AMD = Amide
AMN = Amine

Bonds of Ribosomal cyclic peptide



Small macrocyclic peptides represent more valuable drug candidates

Small Cyclic peptides defined as a peptides with the length 1-25 aa

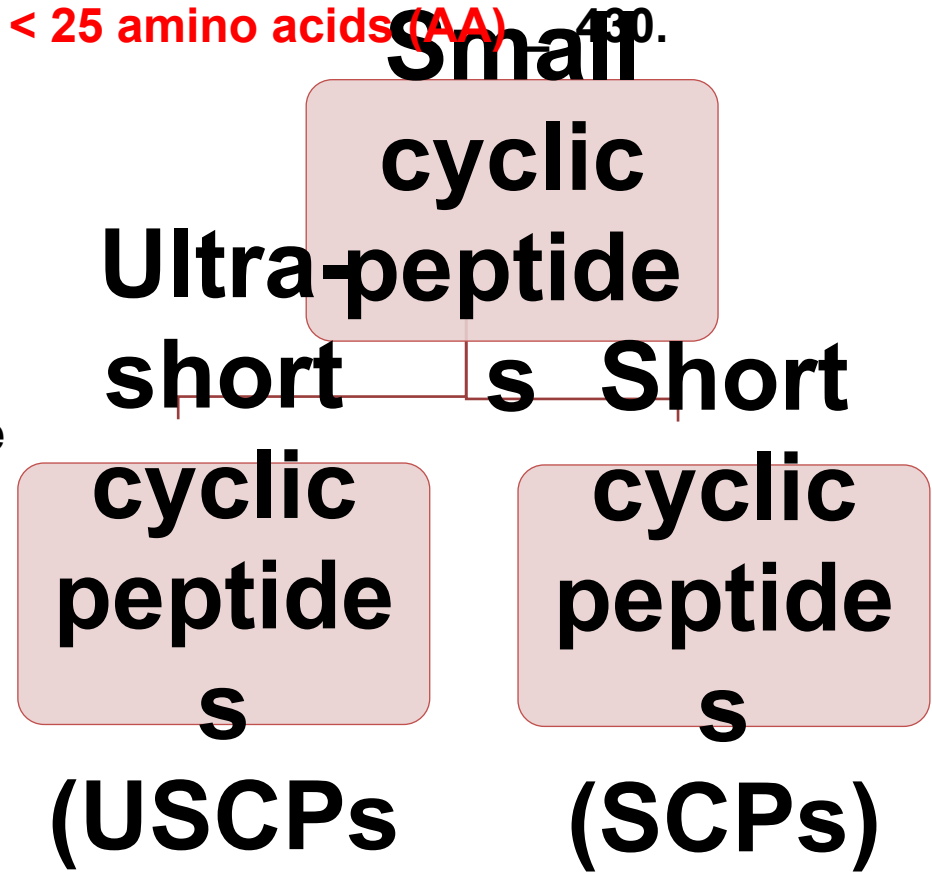
Ribosomal cyclic peptides length <25 AA _ 421.

Non-ribosomal cyclic peptides length < 25 amino acids (AA) ⁴³⁰.

Ultra-short length _ 2-5aa and short length 6 _ 25aa

Ultra-short peptides(USP) satisfy Rule of 5 (Ro5)

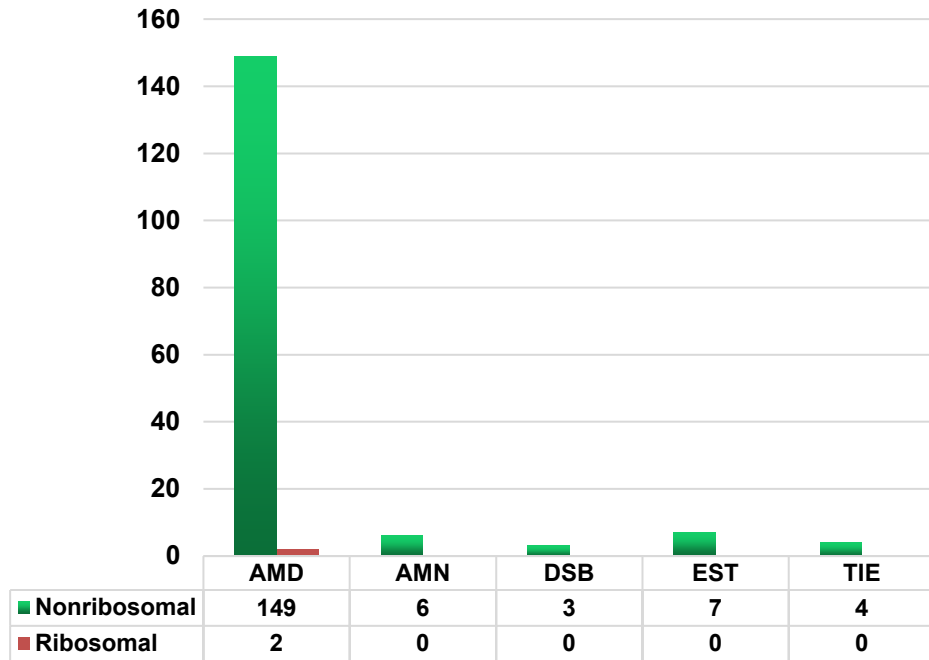
Short peptides (SP) does not. They have beyond Ro5 (bRo5) targets



Natural USCP

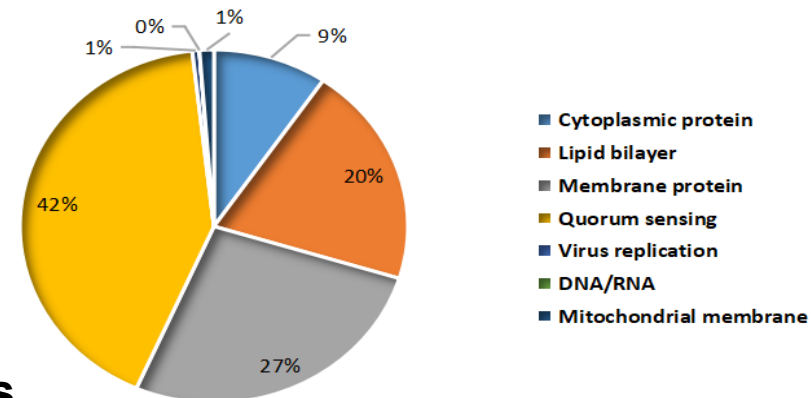
Total number of natural USPs in DBAASP is 197, comprising 7 ribosomal and 190 non-ribosomal peptides. Among non-ribosomal 145 are cyclic. Among ribosomal only 2 are cyclized.

Bonds of short cyclic peptides



AMD = Amide
 AMN = Amine
 DSB = Disulfide
 EST = Ester
 TIE = Thioether

Nonribosomal USCPs target objects

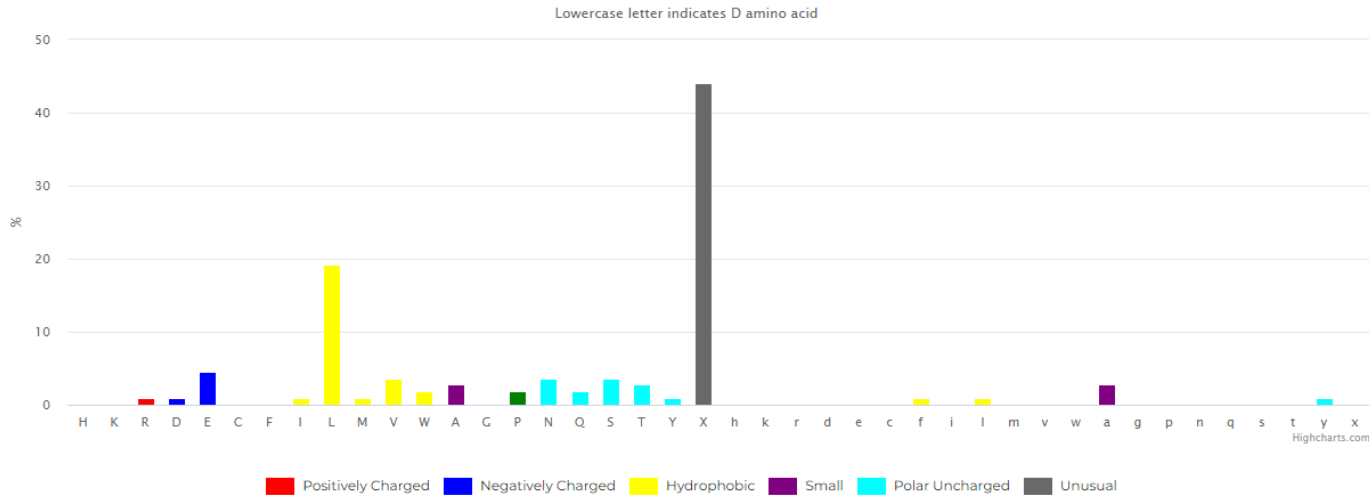


Majority of USCPs are cyclized by amide bonds

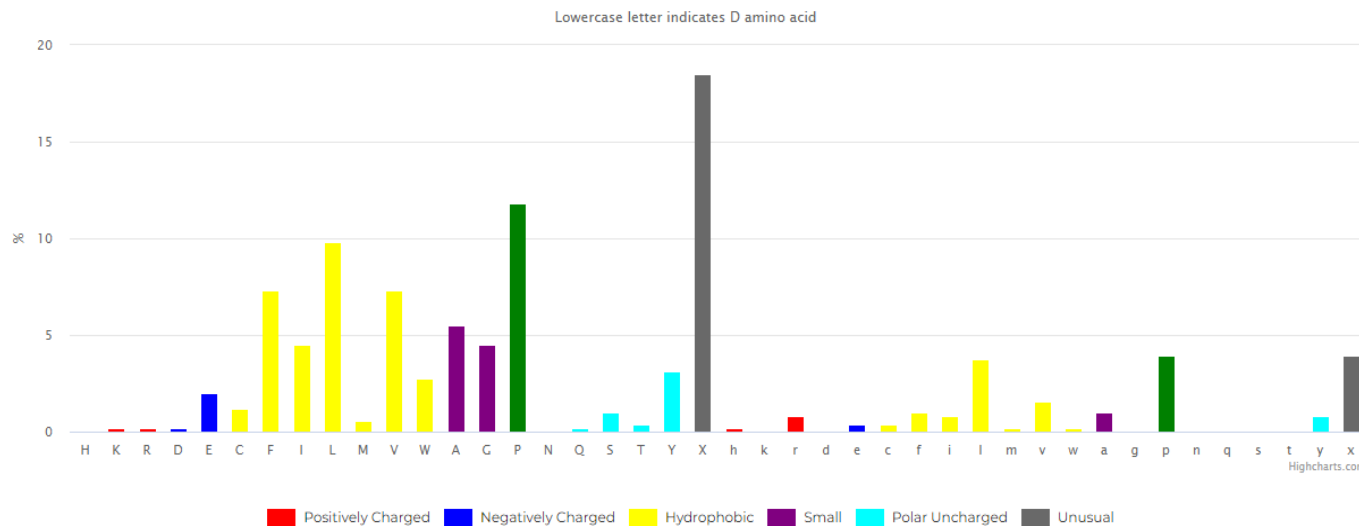
Cyclic types of Natural USCP bonds

Type of bond	Type of Cycle formed by:	Nonribosomal AMPs	Ribosomal AMPs
Amide 	LAC-Lactam NCB(head to tail cyclized) DKP (2,5 diketopiperazine)	+ + +	 +
Amine 	LAC	+	
Disulfide 		+	
Ester 	LCN-Lactone 	+	
Thioether 	THZD (Thiazolidine) 	+	

Pro is abundant in the natural USCPs



Amino acid composition of nonribosomal **linear** peptides length of 1-5 (USPs). Total 29 entries.

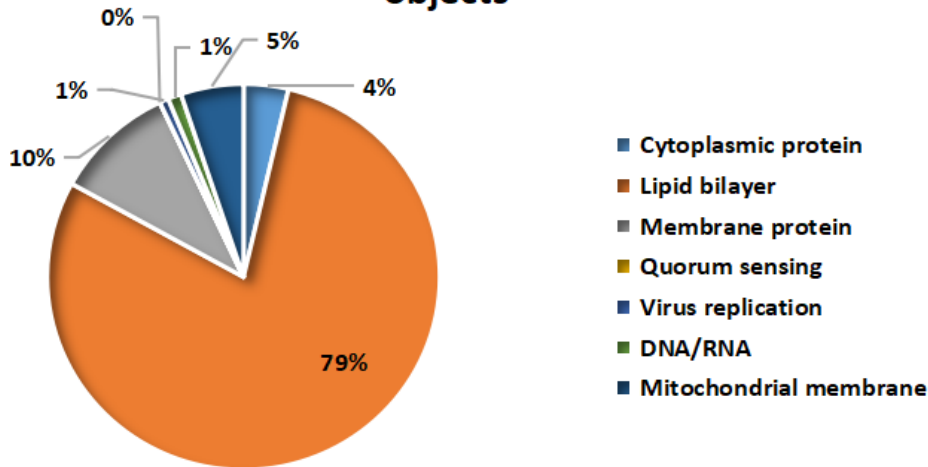


Amino acid composition of nonribosomal **cyclic** peptides length of 1-5 (USCPs). Total 145 entries.

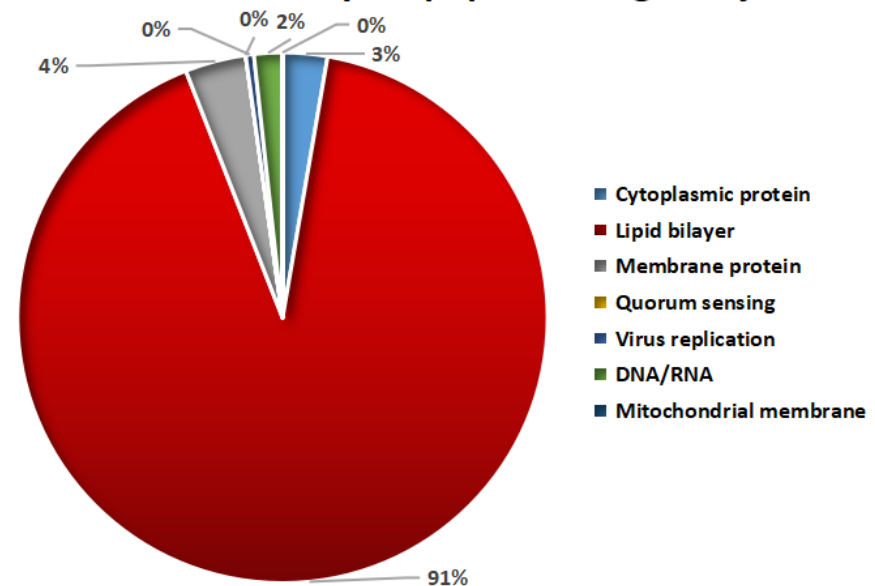
Natural SCPs of DBAASP

DBAASP stores data on 1482 ribosomal and 355 nonribosomal SPs of length in the interval of 6-25 aa. Among Ribosomal SP, 419 are cyclic. Among nonribosomal SP cyclized 295 peptides.

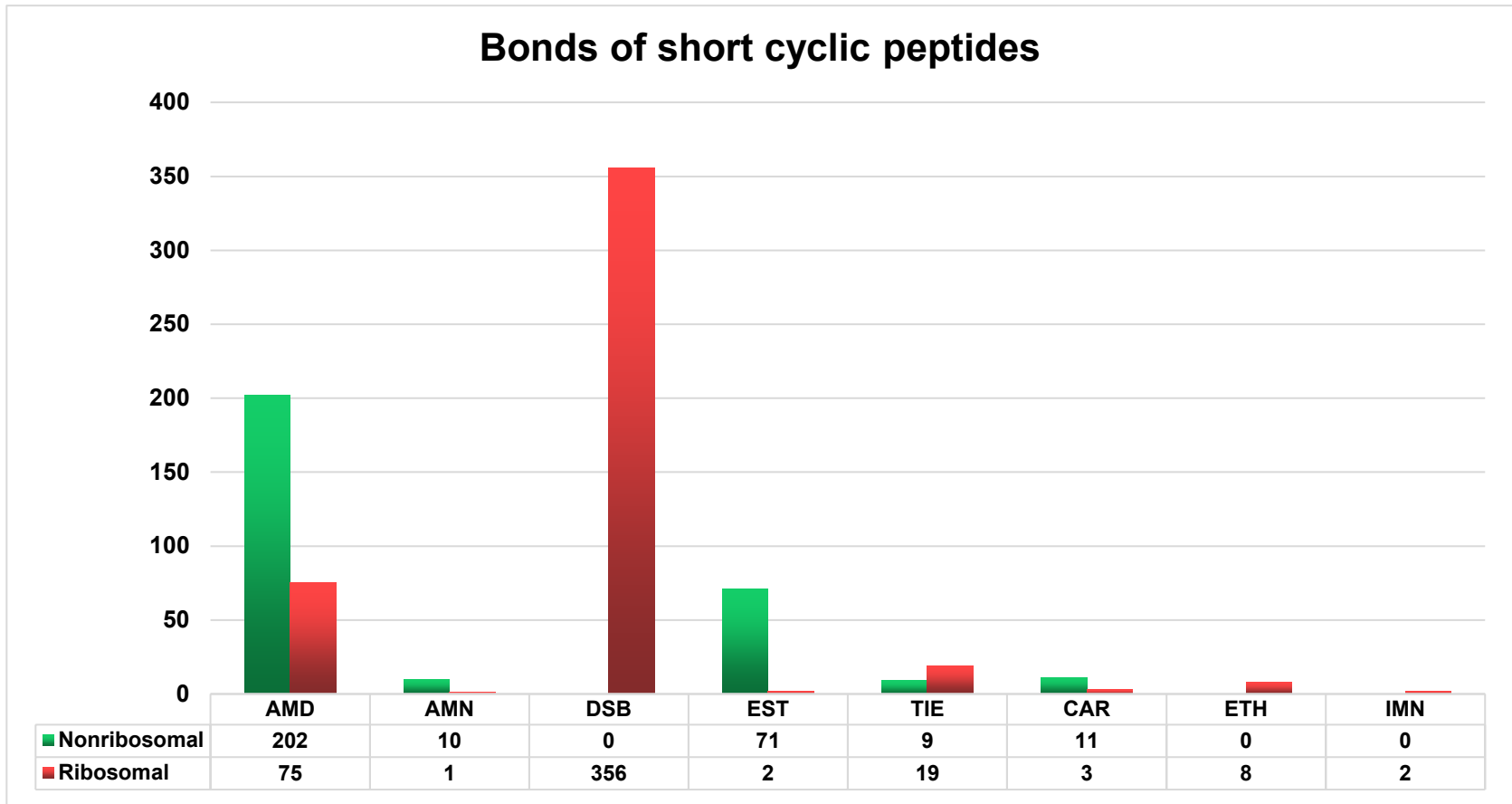
Short nonribosomal cyclic peptides target objects



Short ribosomal cyclic peptides target objects



Bonds used for cyclization of Natural SCPs



AMD = Amide **AMN** = Amine **DSB** = Disulfide **EST** = Ester **TIE** = Thioether **CAR** = Carbon **ETH** = Ether **IMN** = Imine

Majority of ribosomal SCPs are cyclized by disulfide bonds, while in nonribosomales such bonds are not appeared.

Cyclic types of Natural SCP bonds

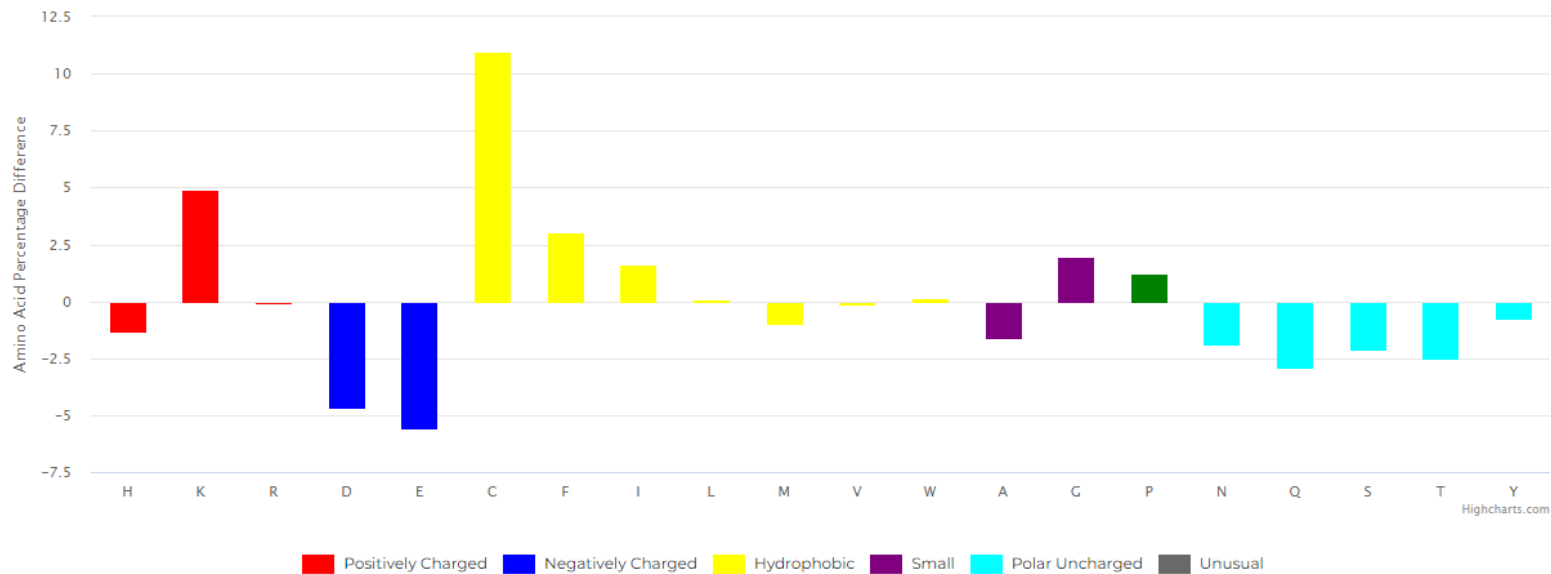
Type of bond	Type of Cycle formed by:	Nonribosomal AMPs	Ribosomal AMPs	Type of bond	Type of Cycle formed by:	Nonribosomal AMPs	Ribosomal AMPs
<p>Amide</p>	<p>Macrolactams</p> <p>NCB(head to tail cyclized)</p>	+	+	<p>Thioether</p>	<p>THZD (Thiazolidine)</p> <p>THZ(Thiazoline)</p>	+	+
<p>Amine</p>	<p>Macrolactams</p>	+	+	<p>LNT(Lanthionine)</p>	+	+	
<p>Disulfide</p>	<p>CST(Cystine)</p>		+	<p>Carbon</p>	+	+	
<p>Ester</p>	<p>LCN-Lactone</p>	+	+	<p>Ether</p>	<p>OXZ (Oxazoline)</p>		+
				<p>Imine</p>	<p>THZ (Thiazoline)</p> <p>OXZ (Oxazoline)</p>	+	+

NCB, Macrolactams, Lactones, Thiazolines Thiazolidines are presented in both ribosomal and nonribosomal SCPs.

Oxazolines, Lanthionines and Cystines _in ribosomal SCPs.

Natural short cyclic peptides amino acid composition relative to UniProt

Ribosomal short cyclic peptides Amino acid composition relative to 'average protein'



RSCPs contain more hydrophobic (with a higher abundance of phenylalanine, isoleucine, leucine, and tryptophan) and more basic (due to higher abundance of lysine) amino acids compared to the 'average protein'.

Conclusion

- **Bonds used to cyclize structure in both ribosomal and nonribosomal peptides are : amide, ether, ester, thioether, amine.**
- **Disulfide bonds are formed mostly in ribosomal peptides.**
- **Thiazoline, Thiazolidine and Lactams and Lactones have been appeared in both, ribosomal and nonribosomal peptides.**
- **Different system of synthesis creates similar rings , the proteins engaged in these systems are not homologous, and consequently can be supposed, that have arisen through convergent evolution.**

Thanks for attention!