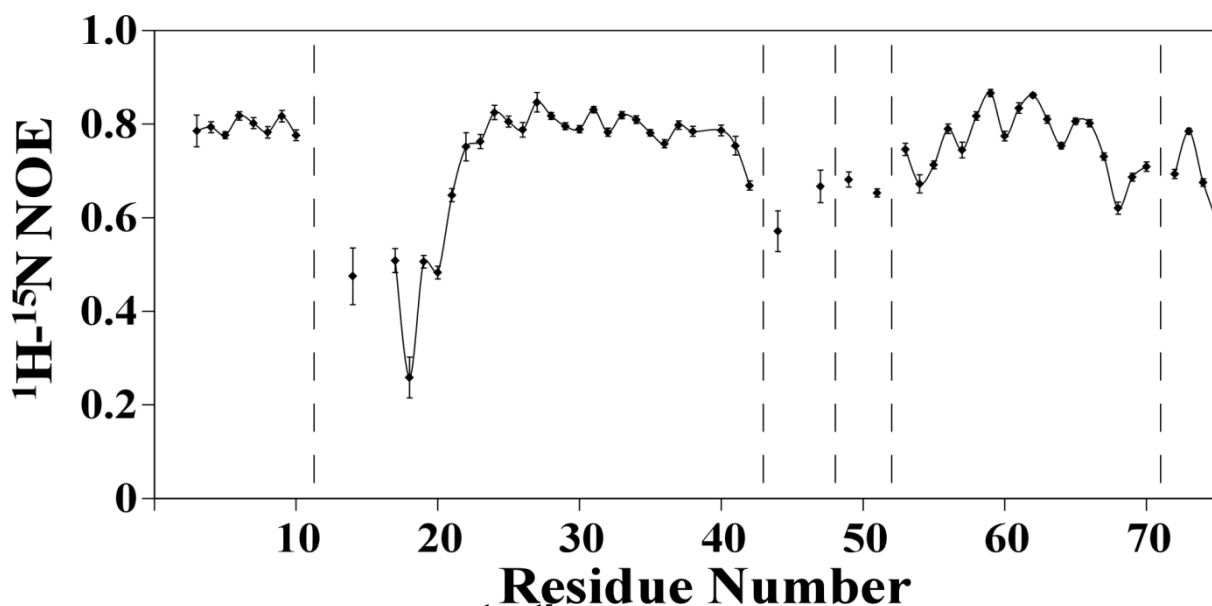


Supplementary table S1. Summary of the observed disulfide-connected peptide fragments of theromacin and neuromacin after proteolytic cleavage. Peptides with oxidized cysteines were proteolytically cleaved by different proteases. The resulting peptides were separated by RP-HPLC and analyzed by nanoESI-orbitrap MS/MS. C1 to C8 label four covalent cysteine-residue bonds conserved in all macins according to their relative position in the primary structure, whereas C31-C73 labels an additional fifth cysteine-residue bond in theromacin according to their absolute position in the primary structure. All corresponding cysteine residues are colored yellow. TM, theromacin; NM, neuromacin.

	Observed Peptide Fragments	Molecular Weight, Da		Observed Ions
		theoretical	experimental	
TM	GC1FE.D A.DSPSLNC6PHR.L	1576.64	1576.68	789.34 ²⁺ /526.56 ³⁺ / 395.17 ⁴⁺
	R.C2SPSTASATGVLWR.S K.ADRGEC5Y.D	2244.99	2245.02	749.34 ³⁺ /562.26 ⁴⁺
	R.LPNNKQC7R C8INAR.T R.SC3DSY C4KVC31FKA.D K.DNRNPT C73WA	3968.74	3968.80	993.20 ⁴⁺ /794.76 ⁵⁺ / 662.47 ⁶⁺ /567.98 ⁷⁺
	R.C5VDSPSK.H R.C2TPGTSFLTGILWKDC3HSR.C K.NNKQC7HC8Y R.C4KELGHR.G	4699.11	4699.10	1175.79 ⁴⁺ /940.83 ⁵⁺ / 784.19 ⁶⁺ /672.3 ⁷⁺
NM	DC1YEDWSR.C R.C5VDSPSKHC6PGVLK.N R.C2TPGTSFLTGILWK.D	4059.86	4059.90	1015.98 ⁴⁺ /812.98 ⁵⁺ / 677.65 ⁶⁺



Supplementary Figure SF1. Plot of (^1H)- ^{15}N heteronuclear (het) NOEs relaxation ratios at 600 MHz against residue number of theromacin. Since the NOE transfer rate for directly bonded nuclei depends on the dynamics of the bond vector reorientation, the (^1H)- ^{15}N hetNOE characterizes flexible residues by low hetNOE values. Generally, (^1H)- ^{15}N hetNOE values in the range of 0.8 indicate that the N-H vector is rigid with respect to the rest of the protein, whereas smaller values are due to increased backbone mobility. Strong reductions in the hetNOE ratios were observed for residues 12-21, 42-55, and 68-75, suggesting flexibility of these regions, whereas the residues that form secondary structures are more or less constant. Residue numbers without shown NOE values either belong to prolines 11, 43, 48, 52, and 71 (dashed lines), or the corresponding NOE intensities were below the minimum intensity necessary for a significant signal/noise ratio.