

James Schaller, MD (Research)

Peptide certified

Not standard of care

Tables from: Luo Y, Song Y. Mechanism of Antimicrobial Peptides: Antimicrobial, Anti-Inflammatory and Antibiofilm Activities. Int J Mol Sci. 2021 Oct 22;22(21):11401. doi: 10.3390/ijms222111401. PMID: 34768832; PMCID: PMC8584040.

Table 2. Summary of the targets, typical AMPs, and specific action modes of AMPs.

Specific Mechanism of Action	AMPs	Action Site	References
Induce degradation of genomic DNA and total RNA	TO17	Nucleic acid	[96]
Bind with nucleic acids and finally inhibit the synthesis of DNA, RNA, and proteins	Buforin-2 and indolicidin	Nucleic acid	[100,101]
Bind with nucleic acids	A series of derived peptides, such as HPA3NT3-A2, MBP-1, IARR-Anal10, and KW4	Nucleic acid	[40,94,102,103]
Bind to RNA polymerase and inhibit the activity of RNA polymerase	Microcin J25 and capistruin	Nucleic acid synthetases	[95]

Act on the termination process of translation. Inhibit protein synthesis by capturing the release factor on the 70S ribosome after hydrolysis of the new polypeptide chain	Apidaecin 1b and Api137	Ribosome	[39]
Transfer of aa-tRNA from EF-Tu to ribosome; a site blocked to inhibit protein synthesis	Bac7, Onc112, pyrrocoricin, and metalnikowin	Ribosome	[39]
Inhibit the protein synthesis of 70S ribosome and interact with DnaK to inhibit the necessary ATPase activity or protein folding activity	Bac7	Molecular chaperone DnaK	[77]
Inhibit DnaK activity	Abaecin	Molecular chaperone DnaK	[97]
Affect cell cycle, inhibit DNA synthesis, and prevent cell division	Indolicidin	Nucleic acid; cell division	[101]
Affect cell cycle and inhibit cell division	HD5ox	Cell division	[98]
Destruct organelles and inhibit mitochondrial respiration to destroy mitochondria	His-rich AMPs	Mitochondria	[42]
Inhibit the activity of energy metabolism proteins to affect energy metabolism	Magainin 1	Energy metabolism protein	[99]

Table 3. AMPs with antibiofilm activity, including the strains and modes of action.

AMPs	Microorganisms	Mechanism of Action	References
LL-37	<i>Pseudomonas aeruginosa</i>	Inhibit bacterial adhesion; disruption of cell signaling system	[126]
DJK5 and DJK6	<i>Pseudomonas aeruginosa</i>	Suppress the alarm system	[131,132]
1081	A series of G+ and G–(<i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , etc.)	Suppress the alarm system; eradication of mature biofilms	[130]
Human β -defensin 3	<i>Staphylococcus epidermidis</i>	Downregulate the expression of binding protein transport genes responsible for biofilm formation	[133,134]
1037	<i>Pseudomonas aeruginosa</i>	Downregulate the expression of binding protein transport genes responsible for biofilm formation	[135]
Nisin A	MRSA	Interfere with the bacterial membrane potential in the biofilm	[125]
Esculentin (1–21)	<i>Pseudomonas aeruginosa</i>	Interfere with the bacterial membrane potential in the biofilm	[137]
G3	<i>Streptococcus mutans</i>	Inhibit bacterial adhesion; degrade EPSs	[141]
P1	<i>Streptococcus mutans</i>	Degrade EPSs	[138]

References

39. Graf, M.; Wilson, D.N. Intracellular Antimicrobial Peptides Targeting the Protein Synthesis Machinery. *Adv. Exp. Med. Biol.* **2019**, 1117, 73–89. [CrossRef]
40. Park, J.; Kang, H.K.; Choi, M.C.; Chae, J.D.; Son, B.K.; Chong, Y.P.; Seo, C.H.; Park, Y. Antibacterial activity and mechanism of action of analogues derived from the antimicrobial peptide mBjAMP1 isolated from *Branchiostoma japonicum*. *J. Antimicrob. Chemother.* **2018**, 73, 2054–2063. [CrossRef]
42. Lei, J.; Sun, L.; Huang, S.; Zhu, C.; Li, P.; He, J.; Mackey, V.; Coy, D.H.; He, Q. The antimicrobial peptides and their potential clinical applications. *Am. J. Transl. Res.* **2019**, 11, 3919–3931.
77. Cardoso, M.H.; Meneguetti, B.T.; Costa, B.O.; Buccini, D.F.; Oshiro, K.G.N.; Preza, S.L.E.; Carvalho, C.M.E.; Migliolo, L.; Franco, O.L. Non-Lytic Antibacterial Peptides That Translocate Through Bacterial Membranes to Act on Intracellular Targets. *Int. J. Mol. Sci.* **2019**, 20, 4877. [CrossRef] [PubMed]
94. Ramamourthy, G.; Park, J.; Seo, C.H.; Vogel, H.J.; Park, Y. Antifungal and Antibiofilm Activities and the Mechanism of Action of Repeating Lysine-Tryptophan Peptides against *Candida albicans*. *Microorganisms* **2020**, 8, 758. [CrossRef]
95. Braffman, N.R.; Piscotta, F.J.; Hauver, J.; Campbell, E.A.; Link, A.J.; Darst, S.A. Structural mechanism of transcription inhibition by lasso peptides microcin J25 and capistruin. *Proc. Natl. Acad. Sci. USA* **2019**, 116, 1273–1278. [CrossRef] [PubMed]
96. He, S.W.; Wang, G.H.; Yue, B.; Zhou, S.; Zhang, M. TO17: A teleost antimicrobial peptide that induces degradation of bacterial nucleic acids and inhibits bacterial infection in red drum, *Sciaenops ocellatus*. *Fish Shellfish Immunol.* **2018**, 72, 639–645. [CrossRef]
97. Rahnamaeian, M.; Cytryńska, M.; Zdybicka-Barabas, A.; Dobszlaff, K.; Wiesner, J.; Twyman, R.M.; Zuchner, T.; Sadd, B.M.; Regoes, R.R.; Schmid-Hempel, P.; et al. Insect antimicrobial peptides show potentiating functional interactions against Gram-negative bacteria. *Proc. Biol. Sci.* **2015**, 282, 20150293. [CrossRef] [PubMed]

98. Chileveru, H.R.; Lim, S.A.; Chairatana, P.; Wommack, A.J.; Chiang, I.L.; Nolan, E.M. Visualizing attack of *Escherichia coli* by the antimicrobial peptide human defensin 5. *Biochemistry* **2015**, *54*, 1767–1777. [CrossRef]
99. Maria-Neto, S.; Cândido Ede, S.; Rodrigues, D.R.; de Sousa, D.A.; da Silva, E.M.; de Moraes, L.M.; Otero-Gonzalez Ade, J.; Magalhães, B.S.; Dias, S.C.; Franco, O.L. Deciphering the magainin resistance process of *Escherichia coli* strains in light of the cytosolic proteome. *Antimicrob. Agents Chemother.* **2012**, *56*, 1714–1724. [CrossRef] [PubMed]
100. Kobayashi, S.; Takeshima, K.; Park, C.B.; Kim, S.C.; Matsuzaki, K. Interactions of the novel antimicrobial peptide buforin 2 with lipid bilayers: Proline as a translocation promoting factor. *Biochemistry* **2000**, *39*, 8648–8654. [CrossRef]
101. Subbalakshmi, C.; Sitaram, N. Mechanism of antimicrobial action of indolicidin. *FEMS Microbiol. Lett.* **1998**, *160*, 91–96. [CrossRef]
102. Sousa, D.A.; Porto, W.F.; Silva, M.Z.; da Silva, T.R.; Franco, O.L. Influence of Cysteine and Tryptophan Substitution on DNABinding Activity on Maize γ -Hairpinin Antimicrobial Peptide. *Molecules* **2016**, *21*, 1062. [CrossRef] [PubMed]
103. Lee, J.K.; Park, S.C.; Hahm, K.S.; Park, Y. Antimicrobial HPA3NT3 peptide analogs: Placement of aromatic rings and positive charges are key determinants for cell selectivity and mechanism of action. *Biochim. Biophys. Acta* **2013**, *1828*, 443–454. [CrossRef]
125. Okuda, K.; Zendo, T.; Sugimoto, S.; Iwase, T.; Tajima, A.; Yamada, S.; Sonomoto, K.; Mizunoe, Y. Effects of bacteriocins on methicillin-resistant *Staphylococcus aureus* biofilm. *Antimicrob. Agents Chemother.* **2013**, *57*, 5572–5579. [CrossRef]
126. Overhage, J.; Campisano, A.; Bains, M.; Torfs, E.C.; Rehm, B.H.; Hancock, R.E. Human host defense peptide LL-37 prevents bacterial biofilm formation. *Infect. Immun.* **2008**, *76*, 4176–4182. [CrossRef]
130. de la Fuente-Núñez, C.; Reffuveille, F.; Haney, E.F.; Straus, S.K.; Hancock, R.E. Broad-spectrum anti-biofilm peptide that targets a cellular stress response. *PLoS Pathog.* **2014**, *10*, e1004152. [CrossRef]
131. De la Fuente-Núñez, C.; Reffuveille, F.; Mansour, S.C.; Reckseidler-Zenteno, S.L.; Hernández, D.; Brackman, G.; Coenye, T.; Hancock, R.E. D-enantiomeric peptides that eradicate wild-type and multidrug-resistant biofilms and protect against lethal *Pseudomonas aeruginosa* infections. *Chem. Biol.* **2015**, *22*, 196–205. [CrossRef]

132. Pletzer, D.; Wolfmeier, H.; Bains, M.; Hancock, R.E.W. Synthetic Peptides to Target Stringent Response-Controlled Virulence in a *Pseudomonas aeruginosa* Murine Cutaneous Infection Model. *Front. Microbiol.* **2017**, *8*, 1867. [CrossRef]
133. Sutton, J.M.; Pritts, T.A. Human beta-defensin 3: A novel inhibitor of *Staphylococcus*-produced biofilm production. Commentary on “Human β -defensin 3 inhibits antibiotic-resistant *Staphylococcus* biofilm formation”. *J. Surg. Res.* **2014**, *186*, 99–100. [CrossRef]
134. Zhu, C.; Tan, H.; Cheng, T.; Shen, H.; Shao, J.; Guo, Y.; Shi, S.; Zhang, X. Human β -defensin 3 inhibits antibiotic-resistant *Staphylococcus* biofilm formation. *J. Surg. Res.* **2013**, *183*, 204–213. [CrossRef]
135. De la Fuente-Núñez, C.; Korolik, V.; Bains, M.; Nguyen, U.; Breidenstein, E.B.; Horsman, S.; Lewenza, S.; Burrows, L.; Hancock, R.E. Inhibition of bacterial biofilm formation and swarming motility by a small synthetic cationic peptide. *Antimicrob. Agents Chemother.* **2012**, *56*, 2696–2704. [CrossRef]
137. Luca, V.; Stringaro, A.; Colone, M.; Pini, A.; Mangoni, M.L. Esculentin(1-21), an amphibian skin membrane-active peptide with potent activity on both planktonic and biofilm cells of the bacterial pathogen *Pseudomonas aeruginosa*. *Cell Mol. Life Sci.* **2013**, *70*, 2773–2786. [CrossRef]
138. Ansari, J.M.; Abraham, N.M.; Massaro, J.; Murphy, K.; Smith-Carpenter, J.; Fikrig, E. Anti-Biofilm Activity of a Self-Aggregating Peptide against *Streptococcus mutans*. *Front. Microbiol.* **2017**, *8*, 488. [CrossRef]
141. Zhang, J.; Chen, C.; Chen, J.; Zhou, S.; Zhao, Y.; Xu, M.; Xu, H. Dual Mode of Anti-Biofilm Action of G3 against *Streptococcus mutans*. *ACS Appl. Mater. Interfaces* **2020**, *12*, 27866–27875. [CrossRef]