

defensins and cancer

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Authors

- **Jonathan Gonzalez**

 [XXXX-XXXX-XXXX-XXXX](#) ·  [jonzalez](#)

Department of Something, University of Whatever · Funded by Grant XXXXXXXX

- **None**

 [XXXX-XXXX-XXXX-XXXX](#)

Department of Something, University of Whatever; Department of Whatever, University of Something

Abstract

In humans, endogenous Antimicrobial peptides (AMP) are part of the immune system and act against pathogens. Defensins compose a class of AMPs that have activity against gram-positive and -negative bacteria and viruses. Their role in innate immunity as microbicidal and immunoregulatory agents that orchestrate cross-talk with the adaptive immune system, and, most recently, their association with cancer. Defensins produced by cells in the course of innate host defence serve as signals which initiate, mobilise, and amplify adaptive immune host defences. Linkage of defensins to weak tumour antigens potentiates their immunoadjuvant effects. Defensins use multiple cellular receptors, which endows them with the capacity to marshal adaptive host defences against microbial invaders. Recently, findings related to specific activation pathways of some of defensins have led investigators to associate them with pro-tumoral activity, contributing to a tumorigenic microenvironment. This review summarizes current knowledge of defensins to discuss their role in tumour growth, tumour monitoring and cancer treatment, is substantial interest in the identification of circulating human tumor-derived proteins in serum for the purposes of early cancer diagnosis.

Introduction

The AMP are polypeptides of fewer than 100 amino acids contain a positive net charge (from +2 to +9), high lysine and arginine content, and a significant number of hydrophobic residues ($\geq 30\%$) [1](#).

These properties permit the peptides to fold into amphipathic conformations upon contact with cell membranes, and the positively charged polar face help the molecules bind to the membrane through electrostatic interaction with the negatively charged head groups of phospholipids [2](#).

AMP have been isolated and characterized from a wide range of animal, plant and bacterial species and are known to play important roles in the host defence system and innate immunity [3](#)

The history of AMPs dates back to 1922 with the discovery of lysozyme by Alexander Flemming. The first reported animal originated AMP is defensin, which was isolated from rabbit leukocytes in 1956 [4](#). at the same time, it was also proven that human leukocytes contain AMPs in their lysosomes.

for mammals, there are two main genetic categories for AMP, have been implicated in antimicrobial activity of phagocytes, inflammatory and epithelial secretions. Defensins are widely distributed in epithelial cells and phagocytes, [5](#). Cathelicidins are structurally and evolutionarily distinct antimicrobial peptides that are similar to defensins in abundance and distribution [6](#)

The great diversity of AMP differs from one animal species to another. In this review I will focus on defensins because, defensins are particularly prominent in humans, as evidenced by the large number of expressed human genes [6](#), the various forms that are present in human tissues, and the ubiquitous occurrence of defensins in inflamed or infected human tissues [1](#).

Subclasses and antimicrobial activity defensins

Mammalian defensins are cationic AMP, with relatively arginine-rich nonglycosylated peptides with a molecular mass of 3.5–4.5 kDa. Their structure typically contains three intramolecular disulphide bridges between six cysteine residues [7](#). As mentioned for AMP in general, the classification of defensins is based on their structure, which divides them into three groups: α -defensins, β -defensins, and θ -defensins. In α -defensins, intramolecular bonding occurs between cysteines 1-6, 2-4, and [8](#), whereas in β -defensins it is between 1-5, 2-4, and 3-6 [9](#). Human defensins are produced in leukocytes and are also secreted by different epithelial cells and mucosal tissues. These human peptides have antimicrobial activity against a large number of gram-positive and -negative bacteria, fungi, and viruses [10](#). (table 1)

Although these disulfide bonds in cytheins appear to have a close relationship with microbial activity, it has been reported that the three disulfides or the order of connectivity is not an essential characteristic for activity in defensins, since even if cytokines defend them they still have antimicrobial activity [11](#).

α -Defensins	sequence
HNP-1	ACYCRIPACIAGERRYGTCIYQGRLWAFCC
HNP-2	CYCRIPACIAGERRYGTCIYQGRLWAFCC
HNP-3	DCYCRIPACIAGERRYGTCIYQGRLWAFCC
HNP-4	VCSCRLVFCRRETLRVGNCLIGGVSTFYCCTRVD
HNP-5	ATCYCRTGRCATRESLSGVCEISGRLYRLCCR

α -Defensins	sequence
HNP-6	TCHCR-RSCYSTEYSYGTCTVMGINHRFCCL

β -defensins	sequence
hBD-1	GNFLTGLGHRSDHYN CVSSGGQCLYSACPIFTKIQT CYRGKAKCCK
hBD-2	GIGDPVTC LKSGAICHPVFCPRRYKQIGT CGLPGTKCCKKP
hBD-3	GIINTLQKYYCVRGGRC AVLSCLPKEEQIGK CSTRGRKCRRKK
hBD-4	EFELDRI CGYGTCARK-KCRSQEYRIGRC PN-TYACCLRKWDESLNRTKP

α -defensins

The α -defensins were described, which have been isolated from the granules of polymorphonuclear neutrophil leukocytes. Because of their distribution in the granules of the leucocytes, they were named human neutrophil peptides 1-4 (HNP1-4) [12](#) They are constitutively produced by myeloid precursor cells. However, recent reports suggest that their production can be induced by activated CD8 T cells as well [p@mid:12183052](#), in contrast, HD-5 and HD-6 are enteric defensins stored in the granules of Paneth cells, processing of 'pro-HD-5' is mediated by one or more isoforms of Paneth cell trypsin [24](#) . Although the main sites of human α -defensins production are leukocytes and Paneth cells, the human female reproductive tract expresses HD-5, When induced to degranulate, neutrophils and Paneth cells release these α defensins locally [13](#).

These six peptides are human α -defensins, whose typical structure consists of 29-35 amino acids [14]. (Table1) demonstrates the difference in structure between α - and β -defensins.

α -defensins are synthesized as inactive prepro- α -defensins whose maturation requires the cleavage of a signal peptide to produce pro- α -defensins. Then, the NH₂-terminal neutralizing pro fragment is cleaved by cellular proteases [[\[???\]](#); [1339298](#); [8601627](#)]. Mature HNP-1, HNP-2 and HNP-3 appear to have similar bioactivities.

Mature HNP-1 3 are 3 kDa peptides comprising 6 characteristic, highly conserved cysteine residues and 3 intra-molecular disulfide bonds. HNP-2 is the smallest human defensin (29 amino-acids) and differs from HNP1 and HNP3 by the absence of only one, N-terminal amino-acid residue in HNP-1 is alanine and aspartate in HNP3 [14](#)

β -defensins

References

1. Defensins: antimicrobial peptides of innate immunity

Tomas Ganz

Nature Reviews Immunology (2003-09) <https://doi.org/cx6gzg>

DOI: [10.1038/nri1180](https://doi.org/10.1038/nri1180) · PMID: [12949495](https://pubmed.ncbi.nlm.nih.gov/12949495/)

2. Animal antimicrobial peptides: an overview.

D Andreu, L Rivas

Biopolymers (1998) <https://www.ncbi.nlm.nih.gov/pubmed/10333735>

DOI: [10.1002/\(sici\)1097-0282\(1998\)47:6<415::aid-bip2>3.0.co;2-d](https://doi.org/10.1002/(sici)1097-0282(1998)47:6<415::aid-bip2>3.0.co;2-d) · PMID: [10333735](https://pubmed.ncbi.nlm.nih.gov/10333735/)

3. Design of an α -helical antimicrobial peptide with improved cell-selective and potent anti-biofilm activity

Shi-Kun Zhang, Jin-wen Song, Feng Gong, Su-Bo Li, Hong-Yu Chang, Hui-Min Xie, Hong-Wei Gao, Ying-Xia Tan, Shou-Ping Ji

Scientific Reports (2016-06-08) <https://doi.org/ggt4kh>

DOI: [10.1038/srep27394](https://doi.org/10.1038/srep27394) · PMID: [27271216](https://pubmed.ncbi.nlm.nih.gov/27271216/) · PMCID: [PMC4897634](https://pubmed.ncbi.nlm.nih.gov/pmc/PMC4897634/)

4. PHAGOCYTIN: A BACTERICIDAL SUBSTANCE FROM POLYMORPHONUCLEAR LEUCOCYTES

James G. Hirsch

The Journal of Experimental Medicine (1956-05-01) <https://doi.org/dzvswf>

DOI: [10.1084/jem.103.5.589](https://doi.org/10.1084/jem.103.5.589) · PMID: [13319580](https://pubmed.ncbi.nlm.nih.gov/13319580/) · PMCID: [PMC2136631](https://pubmed.ncbi.nlm.nih.gov/pmc/PMC2136631/)

5. Defensins. Natural peptide antibiotics of human neutrophils.

T Ganz, ME Selsted, D Szklarek, SS Harwig, K Daher, DF Bainton, RI Lehrer

Journal of Clinical Investigation (1985-10-01) <https://doi.org/bb8wz4>

DOI: [10.1172/jci112120](https://doi.org/10.1172/jci112120) · PMID: [2997278](https://pubmed.ncbi.nlm.nih.gov/2997278/) · PMCID: [PMC424093](https://pubmed.ncbi.nlm.nih.gov/pmc/PMC424093/)

6. Cathelicidins: a novel protein family with a common proregion and a variable C-terminal antimicrobial domain.

M Zanetti, R Gennaro, D Romeo

FEBS letters (1995-10-23) <https://www.ncbi.nlm.nih.gov/pubmed/7589491>

DOI: [10.1016/0014-5793\(95\)01050-o](https://doi.org/10.1016/0014-5793(95)01050-o) · PMID: [7589491](https://pubmed.ncbi.nlm.nih.gov/7589491/)

7. Mammalian defensins in the antimicrobial immune response

Michael E Selsted, Andre J Ouellette

Nature Immunology (2005-05-19) <https://doi.org/bcth9d>

DOI: [10.1038/ni1206](https://doi.org/10.1038/ni1206) · PMID: [15908936](https://pubmed.ncbi.nlm.nih.gov/15908936/)

8. Antimicrobial activity, mechanism of action, and methods for stabilisation of defensins as new therapeutic agents

Meri Amerikova, Ivanka Pencheva El-Tibi, Vania Maslarska, Stanislav Bozhanov, Konstantin Tachkov

Biotechnology & Biotechnological Equipment (2019-05-11) <https://doi.org/ggt6q5>

DOI: [10.1080/13102818.2019.1611385](https://doi.org/10.1080/13102818.2019.1611385)

9. Defensins and host defense.

T Ganz

Science (New York, N.Y.) (1999-10-15) <https://www.ncbi.nlm.nih.gov/pubmed/10577203>

DOI: [10.1126/science.286.5439.420](https://doi.org/10.1126/science.286.5439.420) · PMID: [10577203](https://pubmed.ncbi.nlm.nih.gov/10577203/)

10. Defensins: endogenous antibiotic peptides of animal cells.

RI Lehrer, T Ganz, ME Selsted

Cell (1991-01-25) <https://www.ncbi.nlm.nih.gov/pubmed/1988144>

DOI: [10.1016/0092-8674\(91\)90632-9](https://doi.org/10.1016/0092-8674(91)90632-9) · PMID: [1988144](https://pubmed.ncbi.nlm.nih.gov/1988144/)

11. Antibacterial activity of human neutrophil defensin HNP-1 analogs without cysteines.

Jobin Varkey, Ramakrishnan Nagaraj

Antimicrobial agents and chemotherapy (2005-11)

<https://www.ncbi.nlm.nih.gov/pubmed/16251296>

DOI: [10.1128/aac.49.11.4561-4566.2005](https://doi.org/10.1128/aac.49.11.4561-4566.2005) · PMID: [16251296](https://pubmed.ncbi.nlm.nih.gov/16251296/) · PMCID: [PMC1280114](https://pubmed.ncbi.nlm.nih.gov/PMC1280114/)

12. Current status of defensins and their role in innate and adaptive immunity.

Periathamby Antony Raj, Andrew R Dentino

FEMS microbiology letters (2002-01-02) <https://www.ncbi.nlm.nih.gov/pubmed/11786250>

DOI: [10.1111/j.1574-6968.2002.tb10979.x](https://doi.org/10.1111/j.1574-6968.2002.tb10979.x) · PMID: [11786250](https://pubmed.ncbi.nlm.nih.gov/11786250/)

13. [Structure and function of enteric alpha defensins in norm and pathology].

IG Nikitina, Iu A Bukurova, GS Krasnov, EN Grineva, VL Karpov, NA Lisitsyn, SF Beresten'

Molekuliarnaia biologiya <https://www.ncbi.nlm.nih.gov/pubmed/22642099>

PMID: [22642099](https://pubmed.ncbi.nlm.nih.gov/22642099/)

14. Human defensins as cancer biomarkers and antitumour molecules.

Nathalie Droin, Jean-Baptiste Hendra, Patrick Ducoroy, Eric Solary

Journal of proteomics (2009-01-11) <https://www.ncbi.nlm.nih.gov/pubmed/19186224>

DOI: [10.1016/j.jprot.2009.01.002](https://doi.org/10.1016/j.jprot.2009.01.002) · PMID: [19186224](https://pubmed.ncbi.nlm.nih.gov/19186224/)