

Table S1. The impact of various pathogens or derived virulence factors on the expression of β -defensins' genes and proteins, as well as the tests employed in different studies.

Study	Pathogen (or derived virulence factor)	Evaluated β -defensins ¹	Effect	Test	Sampling sites/ Evaluated cells	Study type
[19]	Subclinical mastitis	LAP DEFB1 BNBD3	detected	RT-PCR ²	Parenchymal and cistern tissue	<i>in vivo</i> -N ³
	Purulent mastitis caused by <i>Actinomyces pyogenes</i>	LAP DEFB401 BNBD9 BNBD12				
	Bloody mixed infection	DEFB1				
	Affected udder half, mixed infection	LAP BNBD9				
	Purulent mixed infection	LAP				
[28]	<i>S. uberis</i>	LAP	\uparrow^4	In situ hybridization/ RT-PCR	Epithelium from the cisternal, alveolar, and peripheral regions	<i>in vivo</i> -E ⁵
	<i>Staphylococcus</i> species <i>Corynebacterium</i> species <i>S. aureus</i>	LAP	\uparrow	In situ hybridization/ RT-PCR	Epithelium from the cisternal, alveolar, and peripheral regions	<i>in vivo</i> -N
[26]	<i>A. pyogenes</i> <i>E. coli</i> <i>S. aureus</i> <i>S. dysgalactiae</i> <i>S. canis</i> <i>S. uberis</i>	BNBD5	\uparrow	In situ hybridization/ RT-PCR	Deeper area of udder quarter/mammary epithelial cell	<i>in vivo</i> -N
[52]	LPS LTA	β -defensin (β -defensin sequences revealed the presence of LAP and TAP)	\uparrow (Response to LTA was lower)	qRT-PCR ⁶	BMECs ⁷	<i>ex vivo</i>
[100]	<i>S. aureus</i>	β -defensins	\uparrow	RT-PCR	BMECs	<i>ex vivo</i>
[56]	<i>E. coli</i>	β -defensins (universal defensin)	\uparrow	qRT-PCR	A deeper area of the udder quarter, 10 cm dorsal of the milk cistern/ regional udder lymph nodes and peripheral lymph nodes	<i>in vivo</i> -E
		BNBD5	\uparrow			
	<i>S. aureus</i>	β -defensins (universal defensin)	\leftrightarrow	qRT-PCR		

		BNBD5	↔			
	<i>E. coli</i>	LAP	Induced	IHC	BMECs	<i>in vivo</i> -E
[61]	<i>E. coli</i>	LAP DEFB1 BNBD4	↑	Affymetrix DNA- microarrays qRT-PCR	BMECs	<i>ex vivo</i>
[51]	LPS	LAP	↑	ELISA	Milk	<i>in vivo</i> -E
[11]	Live <i>S. aureus</i>	TAP	↓	RT-PCR	BMECs	<i>ex vivo</i>
	Killed <i>S. aureus</i>		↑			
[89]	<i>S. aureus</i>	TAP B-defensin	↔	RT-PCR	BMECs	<i>ex vivo</i>
[50]	<i>E. coli</i>	LAP TAP DEFB1	↑	Microarray analysis	Teat cistern lobulo-alveolar region	<i>in vivo</i> -E
[53]	LPS	LAP	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[68]	<i>S. aureus</i>	TAP	↓	RT-PCR	BMECs	<i>ex vivo</i>
[48]	<i>S. aureus</i>	DEFB1 DEFB4 DEFB5	↑	qRT-PCR	Alveolar, ductal, gland cistern and teat canal regions	<i>in vivo</i> -E
		LAP TAP	↔			
[90]	LPS	LAP	↑	RT-PCR	BMECs	<i>ex vivo</i>
[97]	<i>S. aureus</i>	TAP BNBD5	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[27]	<i>S. aureus</i>	LAP TAP DEFB1 BNBD5 BNBD10	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[98]	<i>S. aureus</i>	LAP TAP DEFB1 BNBD4 BNBD5 BNBD10	↑	qRT-PCR	BMECs	<i>ex vivo</i>
			↔			

[74]	<i>E. coli</i> <i>S. aureus</i>	BNBD5	↑ (Response to <i>S. aureus</i> was lower)	qRT-PCR	BMECs	<i>ex vivo</i>
[18]	<i>S. aureus</i> <i>S. bovis</i> <i>S. dysgalactiae</i> <i>E. coli</i>	LAP	↑	ELISA	Milk	<i>in vivo</i> -N
[79]	<i>E. coli</i> <i>S. aureus</i>	LAP TAP	↑	Microfluidic high-throughput RT-qPCR	BMECs extracted from milk	<i>ex vivo</i>
[40]	<i>S. aureus</i> - coagulase- positive and coagulase-negative	LAP DEFB1 BNBD4 BNBD5 BNBD10 TAP	↑ No detected	qRT-PCR	Parenchyma	<i>in vivo</i> -N
[75]	<i>S. aureus</i>	LAP TAP BNBD5 BNBD10	↑ ↔	qRT-PCR	BMECs	<i>ex vivo</i>
[80]	LPS	LAP TAP EBD BNBD1 BNBD5 BNBD3 BNBD4 BNBD6 BNBD7 BNBD10 BNBD13	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[66]	<i>S. aureus</i>	LAP TAP DEFB1 BNBD4 BNBD5	↔	qRT-PCR	BMECs	<i>ex vivo</i>

BNBD10						
[62]	<i>E. coli</i>	LAP	↑	qRT-PCR	The teat cistern	<i>in vivo</i> -E
	<i>S. aureus</i>		↔			
[64]	LPS	LAP	↑	qRT-PCR	Sections of heifer udders	<i>ex vivo</i>
	LTA <i>S. aureus</i>		↔			
[84]	<i>S. aureus</i>	TAP BNBD5	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[86]	<i>S. aureus</i>	DEFB1 TAP LAP	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[81]	<i>E. coli</i>	BNBD5	↑	qRT-PCR	BMECs	<i>ex vivo</i>
[83]	LPS	BNBD5	↑	ELISA	BMECs	<i>ex vivo</i>
			↔	qRT-PCR	BMECs	<i>ex vivo</i>
	<i>E. coli</i>	TAP BNBD	↑ ↔	qRT-PCR		
[59]	Clinical mastitis	DEFB1 DEFB4A DEFB7 DEFB10	↑	RNA sequencing	Circulating leukocytes	<i>in vivo</i> -N
	Subclinical mastitis	DEFB1 DEFB4A DEFB7 DEFB10	↔			
[60]	<i>E. coli</i>	β-defensins	↑	RNA sequencing	Circulating Leukocytes	<i>in vivo</i> -N
[67]	<i>S. aureus</i>	LAP	↔	qRT-PCR	Precision-cut bovine udder slices/BMECs	<i>ex vivo</i>
[49]	Clinical mastitis	DEFB4	↑	ELISA	Serum	<i>in vivo</i> -N
	(<i>E. coli</i> <i>S. uberis</i>)		↔		Milk	
	Subclinical mastitis		↓		Serum	
	(<i>S. aureus</i> <i>S. uberis</i> <i>S. dysgalactiae</i>)		↓		Milk	

¹ LAP: Lingual antimicrobial peptide; TAP: Tracheal antimicrobial peptide; BNBD: Bovine neutrophil β -defensins [Alternative names of BNBD1-13 genes are DEFB1-13.
²real-time PCR. ³Incidence of infection naturally. ⁴ \uparrow : Upregulated; \leftrightarrow : No change; \downarrow : Downregulated. ⁵Incidence of infection experimentally. ⁶ quantitative real-time PCR.
⁷BMECs: Bovine mammary epithelial cells.