Supplementary Table 1. MIC of *M. haemolytica* A2.

A)

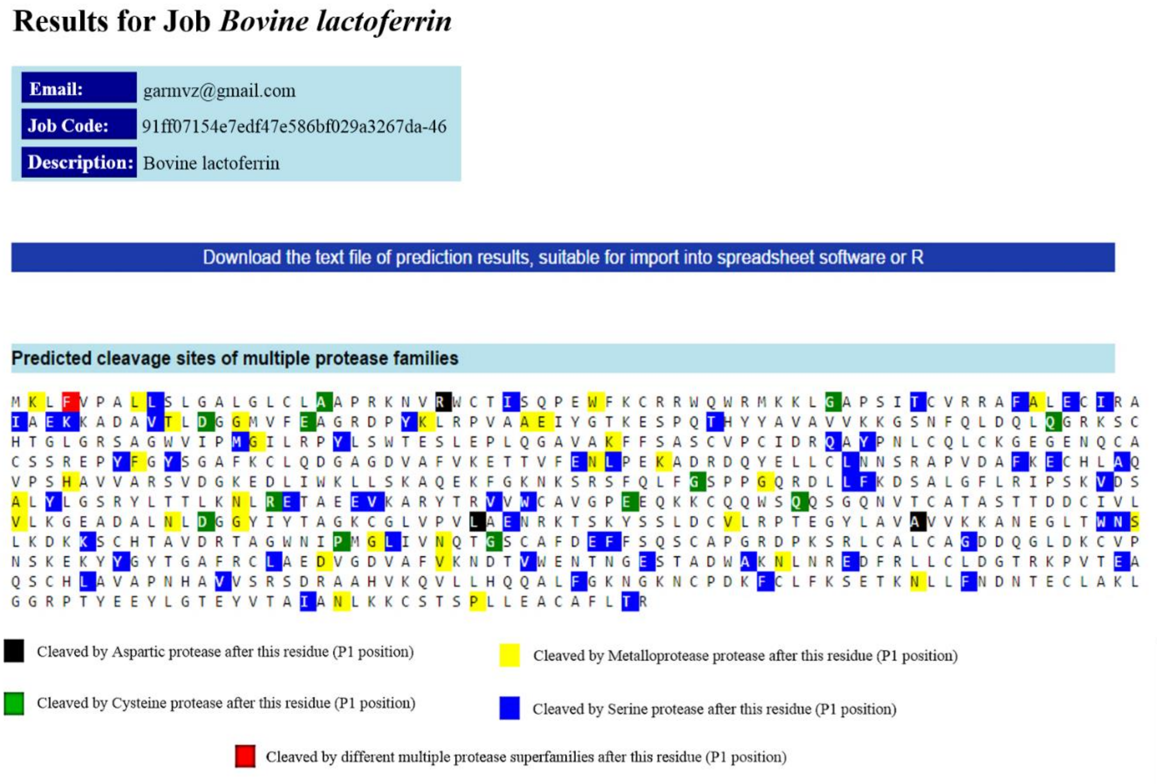
	10^6 CFU	Ct	7.5 µM	11.5 µM	15. 5 µM	19.5 µM	23.5 µM
O.D.	0.024+/-0.005	0.461+/-0.016	0.433+/-0.033	0.076+/-0.014	0.029+/-0.007	0.021+/-0.012	0.007+/-0.010

B)

	10^6 CFU	Ct	7.5 µM	11.5 µM	15. 5 µM	19.5 µM	23.5 µM
O.D.	0.023+/-0.005	0.158+/-0.015	0.170+/-0.013	0.112+/-0.008	0.033+/-0.014	0.027+/-0.010	0.012+/-0.013

OD_{595} values for MIC was obtained by the microdilution technique in broth. Cultures were carried out in agitation (200 RPM) **(A)** or static conditions **(B)** at 37 °C/24 h. The initial inoculum corresponded to 10^6 CFU (O.D. of 0.02) of *M. haemolytica* A2. Ct, control sample without apo-BLf treatment. The values are reported in $O.D._{595}$ nm. and are the average of six independent experiments.

A)



Results for Job *Bovine lactoferrin*

Email:	garmvz@gmail.com
Job Code:	91ff07154e7edf47e586bf029a3267da-46
Description:	Bovine lactoferrin

Download the text file of prediction results, suitable for import into spreadsheet software or R

Predicted cleavage sites of multiple protease families

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M K L F V P A L L S L G A L G L C L A A P R K N V R W C T I S Q P E W F K C R R W Q W R M K K L G A P S I T C V R R A F A L E C I R A
I A E K K A D A V T L D G G M V F E A G R D P Y K L R P V A A E I Y G T K E S P Q T H Y Y A V A V V K K G S N F Q L D Q L Q G R K S C
H T G L G R S A G W V I P M G I L R P Y L S W T E S L E P L Q G A V A K F F S A S C V P C I D R Q A Y P N L C Q L C K G E G E N Q C A
C S S R E P Y F G Y S G A F K C L Q D G A G D V A F V K E T T V F E N L P E K A D R D Q Y E L L C L N N S R A P V D A F K E C H L A Q
V P S H A V V A R S V D G K E D L I W K L L S K A Q E K F G K N K S R S F Q L F G S P P G Q R D L L F K D S A L G F L R I P S K V D S
A L Y L G S R Y L T T L K N L R E T A E E V K A R Y T R V V W C A V G P E E Q K K C Q Q W S Q Q S G Q N V T C A T A S T T D D C I V L
V L K G E A D A L N L D G G Y I Y T A G K C G L V P V L A E N R K T S K Y S S L D C V L R P T E G Y L A V A V V K K A N E G L T W N S
L K D K K S C H T A V D R T A G W N I P M G L I V N Q T G S C A F D E F F S Q S C A P G R D P K S R L C A L C A G D D Q G L D K C V P
N S K E K Y Y G Y T G A F R C L A E D V G D V A F V K N D T V W E N T N G E S T A D W A K N L N R E D F R L L C L D G T R K P V T E A
Q S C H L A V A P N H A V V S R S D R A A H V K Q V L L H Q Q A L F G K N G K N C P D K F C L F K S E T K N L L F N D N T E C L A K L
G G R P T Y E E Y L G T E Y V T A I A N L K K C S T S P L L E A C A F L T R
```

■ Cleaved by Aspartic protease after this residue (P1 position)

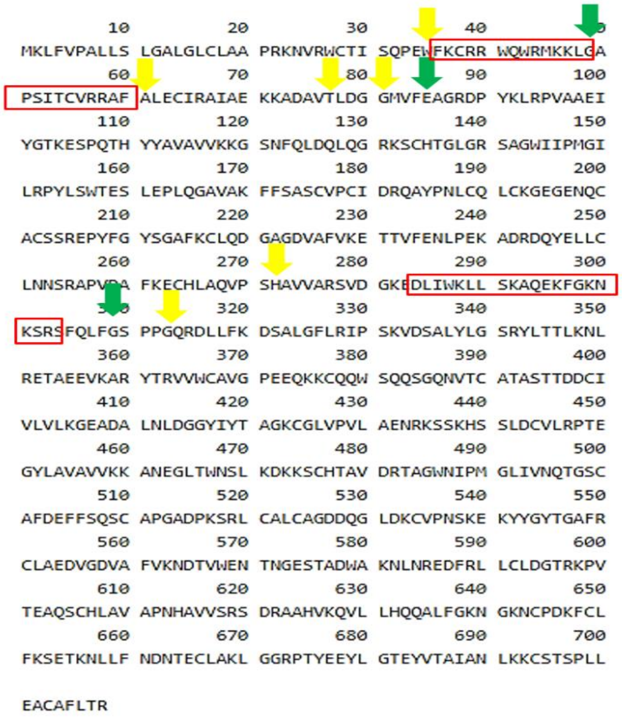
🟨 Cleaved by Metalloprotease protease after this residue (P1 position)

🟩 Cleaved by Cysteine protease after this residue (P1 position)

🟦 Cleaved by Serine protease after this residue (P1 position)

🟥 Cleaved by different multiple protease superfamilies after this residue (P1 position)

B)



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        60         70         80         90        100
PSITCVRRAF ALECIRAIAE KKADAVTLDG GMVFEAGRDP YKLRPVAAEI
       110        120        130        140        150
YGTKESPQTH YYAVAVVKKG SNFQLDQLQG RKSCHTGLGR SAGWIIPMGI
       160        170        180        190        200
LRPYLSWTES LEPLQGAVAK FFSASCVPCI DRQAYPNLCQ LCKGEGENQC
       210        220        230        240        250
ACSSREPYFG YSGAFKCLQD GAGDVAFVKE TTVFENLPEK ADRDQYELLC
       260        270        280        290        300
LNNSRAPVDA FKECHLAQVP SHAVVARSVD GKEDLIWKLL SKAQEKFGKN
       3 0        320        330        340        350
KSRSFQLFGS PPGQRDLLFK DSALGFLRIP SKVDSALYLG SRYLTTLKNL
       360        370        380        390        400
RETAEEVKAR YTRVVWCAVG PEEQKKCQQW SQQSGQNVTC ATASTTDDCI
       410        420        430        440        450
VLVLKGEADA LNLDGGYIYT AGKCGLVPVL AENRKSSKHS SLDCVLRPTE
       460        470        480        490        500
GYLAVAVVKK ANEGLTWNSL KDKKSCHTAV DRTAGWNIPM GLIVNQTGSC
       510        520        530        540        550
AFDEFFSQSC APGADPKSRL CALCAGDDQG LDKCVPNSKE KYYGYTGAFR
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CLAEDVGDVA FVKNDTVWEN TNGESTADWA KNLNREDFRL LCLDGTRKPV
       610        620        630        640        650
TEAQSCHLAV APNHAVVSRS DRAAHVKQVL LHQQALFGKN GKNCPDKFCL
       660        670        680        690        700
FKSETKNLLF NDNTECLAKL GGRPTYEEYL GTEYVTAIAN LKKCSTSPLL

EACAFLTR
```
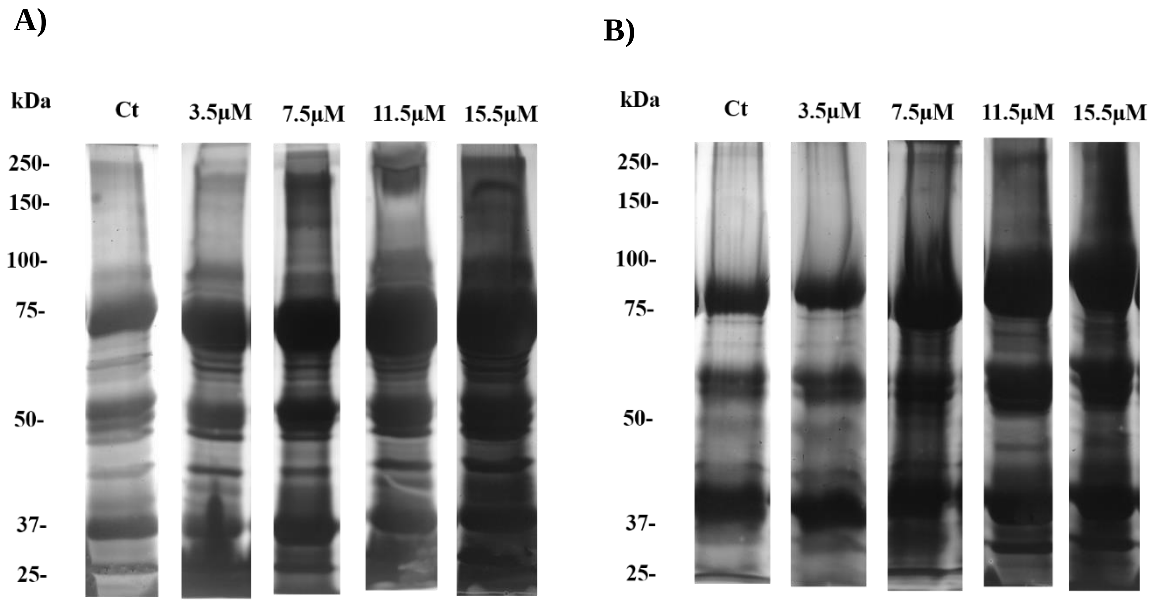

Supplementary Figure 1. Susceptible cleavage sites of BLf by proteases. A. Predicted sites of cleavage by proteases**. B.** Antimicrobial peptides, Lcins and lactoferrampin obtained by cleavage of metallo- and cysteine- proteases**.** Results obtained with the protease cleavage prediction software PROSPER (https://prosper.erc.monash.edu.au/).



Supplementary Figure 2. SDS-PAGE of outer membrane vesicles (OMVs) (A) and culture supernatants (CS) (B) proteins from *M. haemolytica* A2 cultured in the presence of apo-BLf. Ct, control sample without apo-BLf. Electrophoresis was performed at 10%. A result representative of three independent experiments is shown.