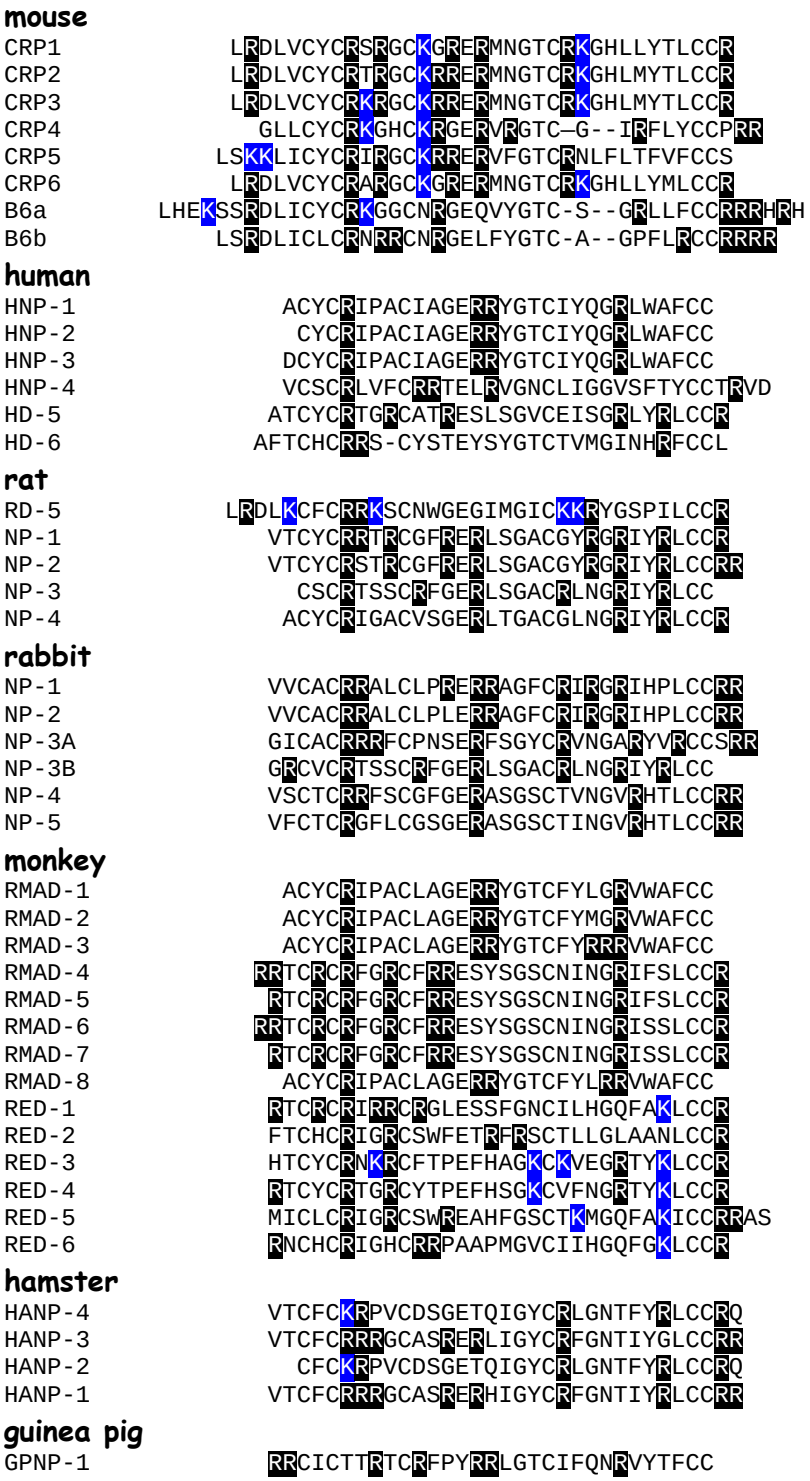
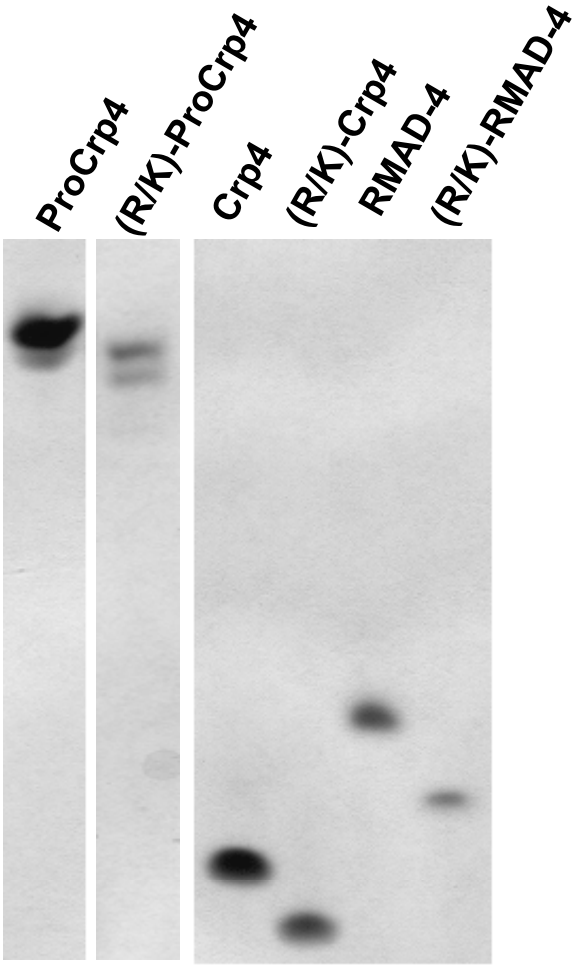
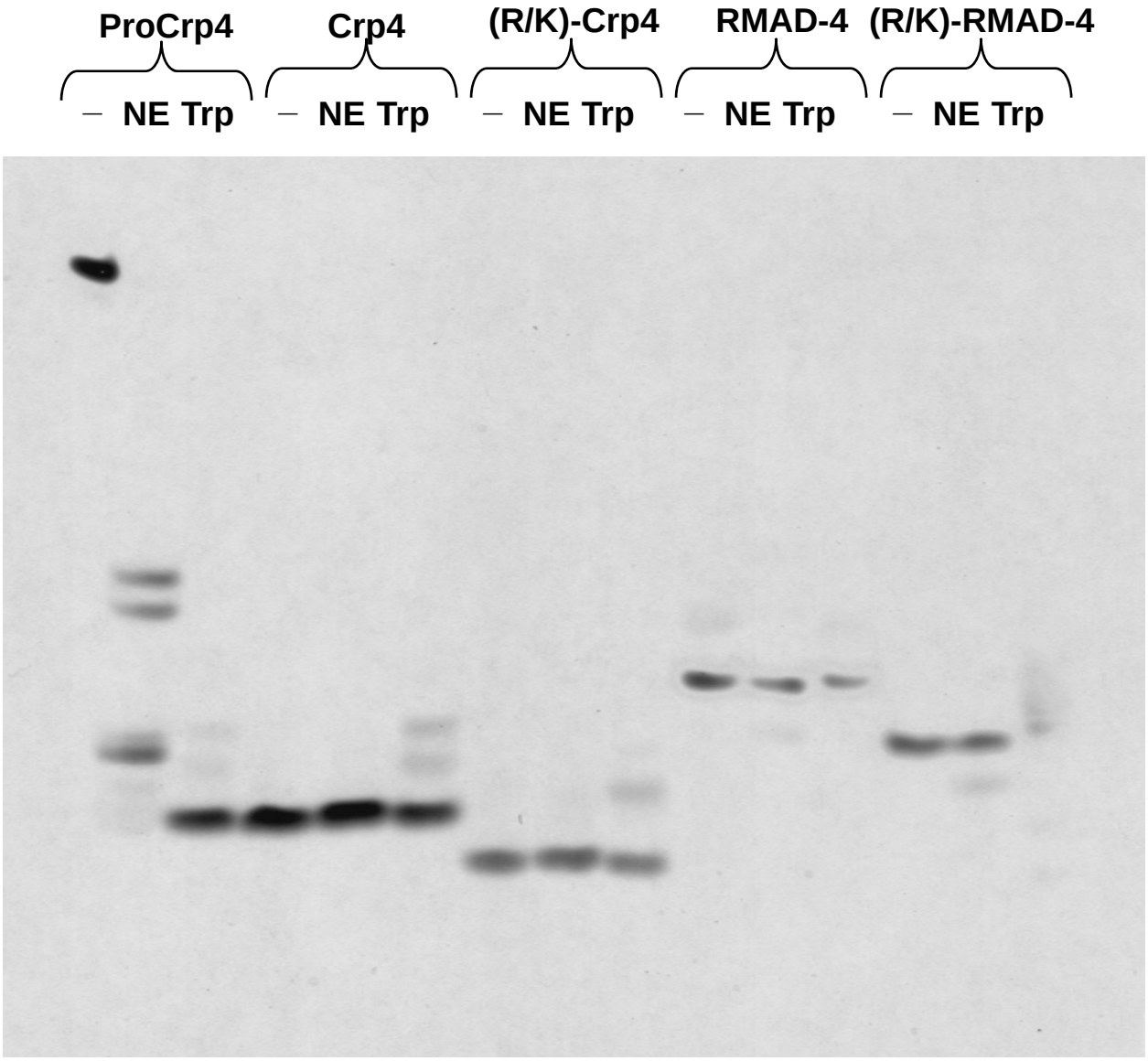


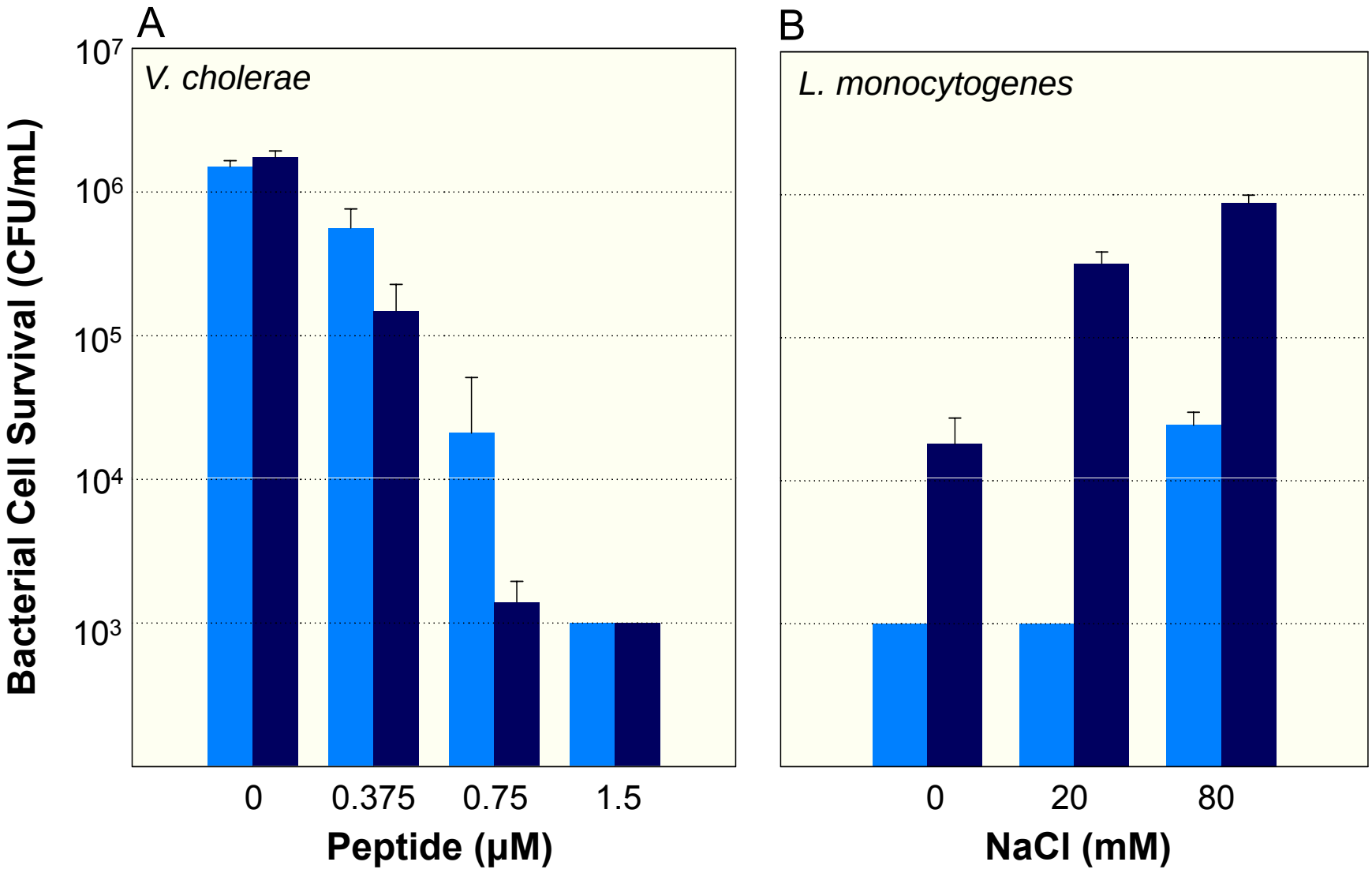
Supplementary Figure S1. An alignment of representative known mammalian α-defensins illustrates an Arg:Lys ratio of 9:1. Arg residue positions are highlighted in black and Lys positions in blue.



Supplementary Figure S2. Twelve micrograms proCrp4 and (R/K)-proCrp4 and 6 µg samples of Crp4, (R/K)-Crp4, RMAD-4, and (R/K)-RMAD-4 were resolved by acid-urea-PAGE and stained with Coomassie Blue.



Supplementary Figure S3. Sensitivity of Lys-substituted α-defensins to neutrophil elastase (NE) and trypsin (Trp) proteolysis. Twelve micrograms of proCrp4 and 6 µg of Crp4, (R/K)-Crp4, RMAD-4 and (R/K)-RMAD-4 were incubated in 50 mM ammonium bicarbonate alone (-), with NE in 50 mM Tris, 150 mM NaCl (pH 7.5) at 37 ºC for 2 h at a substrate:enzyme ratio of 40:1 NE , or with Trp in 50 mM ammonium bicarbonate at a 50:1 substrate:enzyme ratio for 2 h (see “Materials and Methods”).



Supplementary Figure S4. In panel A, five replicate bactericidal peptide assays were performed using RMAD-4 (light blue) and (R/K)-RMAD-4 (dark blue) at 1.5 μM, 0.75 μM, 0.375 μM and 0 μM against *V. cholerae*. Log-phase bacteria were exposed to peptide for 1 h in PIPES-TSB buffer (see "Materials and Methods"). Following peptide exposure, the bacteria were plated on TSB-agar plates and surviving bacteria were counted as CFU/ml after growth overnight at 37 °C. (B) Five replicate bactericidal peptide assays of RMAD-4 (light blue) and (R/K)-RMAD4 (dark blue) activity at 1.5 μM concentration against *L. monocytogenes.* Log-phase bacteria were exposed to peptides for 1 h in PIPES-TSB buffer, or in PIPES-TSB supplemented with 20 mM or 80 mM NaCl for 1 h. Following peptide exposure, the bacterial cell survival was determined as in panel A (see "Material and Methods"). Error bars denote standard deviation from the mean.