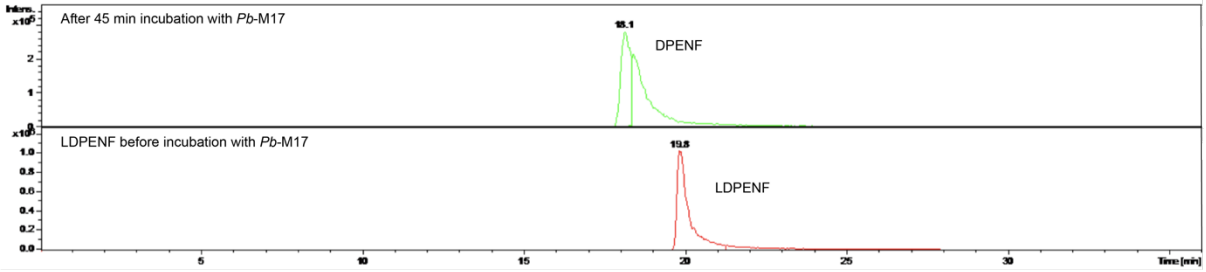
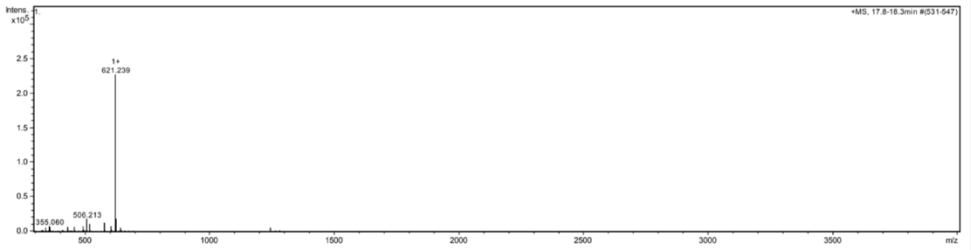
SUPPLEMENTARY MATERIAL

Supplementary Figure S1. Sequence alignment of *Pf*A-M1, *Pv*-M1 and *Pb*-M1, colored by domain.
Amino acid sequence alignment of *Pf*A-M1, *Pv*-M1 and *Pb*-M1. Domain I highlighted in blue, domain II in yellow, domain III in green and domain IV in pink. N-terminal truncation sites and C-terminal histidine site are labeled, conserved metal-binding residues are marked with 'x' and conserved active site residues boxed.

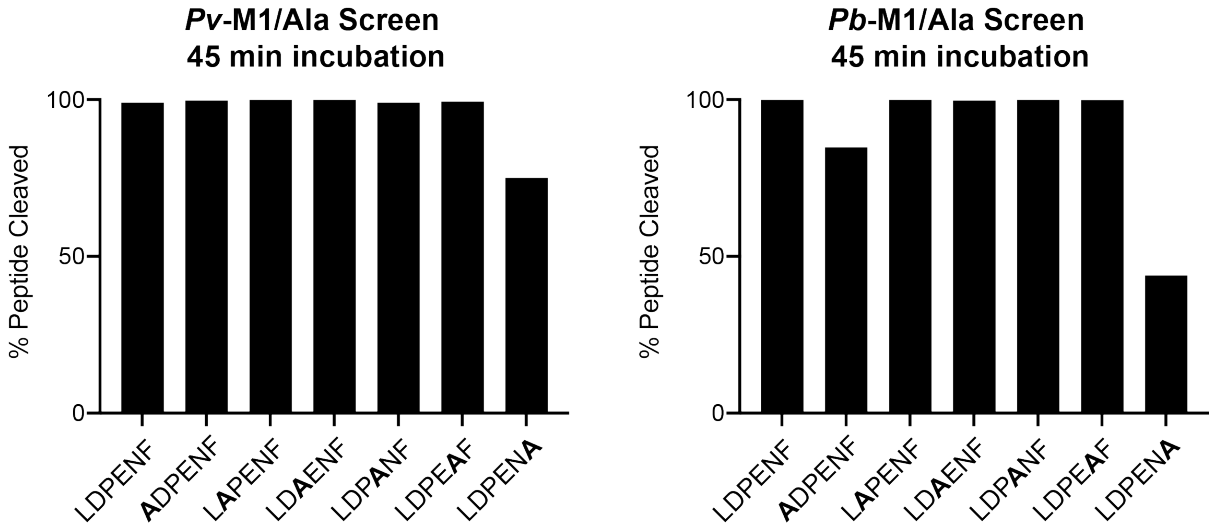
Supplementary Figure S2. Sequence alignment of *Pf*A-M17, *Pv*-M17 and *Pb*-M17, colored by domain.
Amino acid sequence alignment of *Pf*A-M17, *Pv*-M17 and *Pb*-M17. Domain I highlighted in blue, domain II in yellow, and domain III in green. N-terminal truncation sites and C-terminal histidine site are labeled, conserved metal-binding residues are marked with ‘x’ and conserved active site residues boxed.



Spectrum for peak observed in green trace, after incubation with *Pb*-M17



Supplementary Figure S3. Representative mass spectrometry trace of LDPENF digestion by *Pb*-M17. After 45 min of incubation, only one product at a molecular weight of 621 Da is observed. This correlated to the removal of the single amino acid residue Leu from the N-terminus of hexapeptide LDPENF, producing pentapeptide DPENF. Trace is representative of cleavage results obtained for each aminopeptidase – in each experiment only peptides of molecular weights 734 Da (LDPENF) and 621 Da (DPENF) were observed.



Supplementary Figure S4. Digestion of Ala screen peptides by *Pv*-M1 and *Pb*-M1 in 45-min incubation period. Template hexapeptide (LDPENF) and Ala screen peptides were digested to almost 100% in the 45-min incubation period at 37˚C. *Pv*-M1 and *Pb*-M1 showed decreased activity levels against peptides ADPENF and LDPENA.

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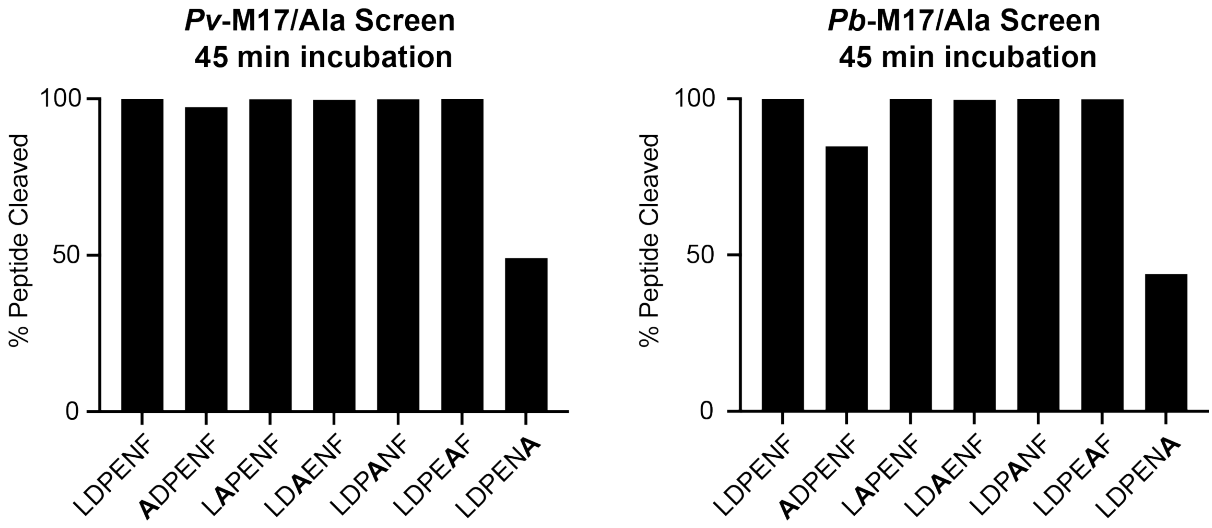
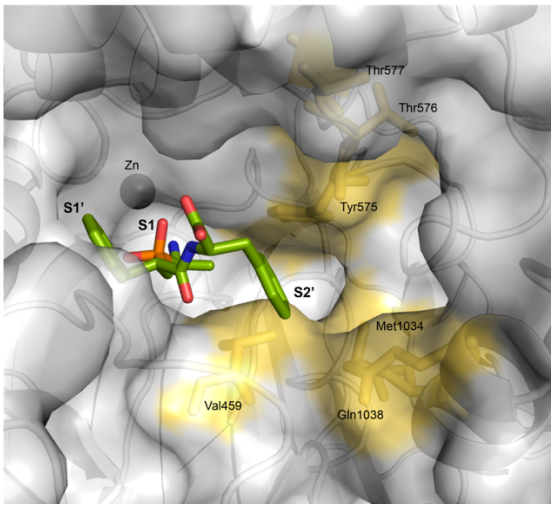


Supplementary Figure S5. Digestion of Ala screen peptides by *Pv*-M17 and *Pb*-M17 in 45-min incubation period. Template hexapeptide (LDPENF) and Ala screen peptides were digested to almost 100% in the 45-min incubation period at 37˚C. *Pv*-M17 and *Pb*-M17 showed decreased activity levels against peptides ADPENF and LDPENA compared to LDPENF.



Supplementary Figure S6. APN inhibitor PL250 docked into *Pf*A-M1 X-ray crystal structure with P2' subsite highlighted.
E. coli APN X-ray crystal structure in complex with PL250 (PDB ID: 2ZXG) used to dock PL250 (green sticks) into *Pf*A-M1 X-ray crystal structure (PDB ID: 3EBG). S1, S1' and S2' pockets labelled. Residues postulated