Supplementary material

Supplementary Table S1. Detailed apstatin interactions of APP-1 structures and PID-5 APP-RD (predicted, AlphaFold2 DB: Q9GUI6). Reference literature shown in parentheses: *Ce*APP-1 [24], *Pf*APP-1 [8,26] and *Ec*APP-1 [22,24].

Protein	Residues	Apstatin Interactions	
		APP-1	Apstatin
*Ce*APP-1	Arg78	NH1 NH1	O3 O4
	His392	NE2	O3
	Asp413	OD2 OD1 OD2	O1 N1 N1
	His487	NE2	O2
	His496	NE2	O2
	Glu522	OE1 OE1 OE2	O1 N2 O2
	Glu536	OE1 OE2	O1 O1
	Zn^{2+}_{A}	-	O1
	Zn^{2+}_{B}	-	N1 O1
*Pf*APP-1	Asp581	OD1	N1
	His653	NE2	O2
	Glu676	OE1	N2
	Mn^{2+}_{A}	-	O1 O2
	Mn^{2+}_{B}	-	O1
*Ec*APP-1	His243	NE2	O3
	Asp260	OD1	N1
	His361	NE2	O2
	Glu383	OE1	O1
	Mn^{2+}_{A}	-	O1
	Mn^{2+}_{B}	-	N1 O1
Predicted PID-5 APP-RD	Gln857	NE2	O1
	Glu929	OE1 OE1	N4 N5
	His932	NE2	N1
	Glu950	OE1	N5
	Arg979	NH1 NH2 NH2	O1 O1 O2
	Zn^{2+}_{A}	-	N1 O1

Supplementary Table S2. Complete interactions of *Ce*APP-1 with apstatin (PDB code: 4S2T). Equivalent residues in PID-5 APP-RD (AlphaFold2 DB: Q9GUI6) are shown on the same row and potential interactions of these residues with apstatin, in the binding pose from the highest scoring GOLD ligand docking, are shown.

***Ce*APP-1 residues**	**Apstatin interactions**	**PID-5 APP-RD residues**	**Potential apstatin interactions**
Tyr43	Hydrophobic	Leu492	Hydrophobic
Asp76	Hydrophobic	Asp525	Hydrophobic
Arg78	2 H-bonds side chain NH1 to apstatin O3 and O4	Gly527	Hydrophobic
Phe378	Hydrophobic	Gln825	Hydrophobic
Asp379	Hydrophobic	Pro826	Hydrophobic
Ile381	Hydrophobic	Ile828	Hydrophobic
His392	H-bond side chain NE2 to apstatin O3	Ala839	Hydrophobic
Asp413	3 H-bonds to apstatin and metal coordination OD1 to Zn^{2+}_B	Gln857	H-bond side chain NE2 to apstatin O1
Asp424	Metal coordination side chain OD1 to Zn^{2+}_B and OD2 to Zn^{2+}_A	Asn868	Lost metal coordination
His483	Hydrophobic	His928	Hydrophobic
Gly484	Hydrophobic	Glu929	2 H-bonds side chain OE1 to apstatin N4 and N5
Gly486	Hydrophobic	Gly931	Hydrophobic
His487	H-bond side chain NE2 to apstatin O2 and Zn^{2+}_A	His932	H-bond side chain NE2 to apstatin N1 and Zn^{2+}_A
His496	H-bond side chain NE2 to apstatin O2	Arg941	Hydrophobic
Arg505	Hydrophobic	Glu950	H-bond side chain OE1 to apstatin N5
Glu522	3 H-bonds to apstatin and metal coordination OE2 to Zn^{2+}_A	Glu967	Metal coordination side chain OE2 to Zn^{2+}_A
Arg534	Hydrophobic	Arg979	3 H-bonds side chain NH1 to apstatin O1, and NH2 to O1 and O2
Glu536	2 H-bonds to apstatin and metal coordination OE1 to Zn^{2+}_B and OE2 to Zn^{2+}_A	Gly981	Lost metal coordination
Zn^{2+}_A	Coordination to apstatin O1	Zn^{2+}_A	Coordination to apstatin N1 and O1
Zn^{2+}_B	Coordination to apstatin O1 and N1	-	-