Supporting information for

The unique effect of Cu(II) in the metal-induced amyloid formation of β-2-microglobulin

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Table S1. Single scattering EXAFS fits for Ni-β2m. Fits carried out in r-space (Δk = 2 to 12.5 $Å^{-1}$; $\Delta R'$ = 1 to 2.5 Å) with a Kaiser-Bessel window with dk = 1, a *k*-weight = 3 and S_o = 0.9. Initial input metal-ligand distances were 2.0 Å for Ni-N(O), 2.3 Å for Ni-S and 2.4 Å for Ni-Br. #v number is the number of independent variables used in the fit.

Model	R factor	Reduced χ^2	χ^2	#v
XN	***where X is the number of nitrogen atoms (N)***			
'2N'	0.2791	60.64	1018.623	3
'3N'	0.1773	38.521	647.064	3
'4N'	0.1211	26.317	442.072	3
'5N'	0.0963	20.919	351.391	3
'6N'	0.094	20.426	343.105	3
'7N'	0.1082	23.511	394.933	3
AS	***where A is the number of sulfur atoms (S)***			
'2S'	0.2294	49.838	837.17	3
'3S'	0.1716	37.289	626.381	3
'4S'	0.1518	32.983	554.039	3
'5S'	0.1527	33.173	557.24	3
'6S'	0.1653	35.905	603.133	3
'7S'	0.1844	40.053	672.805	3
XNYN	***where X and Y are the number of nitrogen atoms (N) in separate shells***			
'2N1N'	0.1367	33.708	498.808	5
'2N2N'	0.0858	21.165	313.203	5
'3N1N'	0.0894	22.056	326.383	5
'4N1N'	0.0773	19.069	282.181	5
'5N1N'	0.081	19.973	295.555	5
'6N1N'	0.0946	23.331	345.244	5
'3N2N'	0.0764	18.841	278.808	5
'3N3N'	0.0834	20.575	304.466	5
'4N2N'	0.082	20.217	299.175	5
'5N2N'	0.0957	23.595	349.156	5
'4N3N'	0.0967	23.844	352.84	5

Model	R factor	Reduced χ^2	χ^2	#v
ASBS	***where A and B are the number of sulfur atoms (S) in separate shells***			
'2S1S'	0.1254	30.933	457.737	5
'2S2S'	0.1049	25.867	382.781	5
'3S1S'	0.1052	25.949	383.996	5
'4S1S'	0.103	25.391	375.731	5
'5S1S'	0.1114	27.481	406.659	5
'6S1S'	0.1653	40.758	603.133	5
'3S2S'	0.1013	24.985	369.725	5
'4S2S'	0.1079	26.609	393.752	5
'3S3S'	0.1059	26.125	386.599	5
'5S2S'	0.1202	29.643	438.655	5
'4S3S'	0.1162	28.665	424.176	5
XNAS	***where X is the number of nitrogen atoms (N) and A is the number of sulfur atoms (S) in separate shells***			
'2N1S'	0.1268	31.263	462.626	5
'1N2S'	0.1353	33.358	493.619	5
'2N2S'	0.1058	26.096	386.163	5
'3N1S'	0.0941	23.197	343.267	5
'1N3S'	0.1667	41.121	608.505	5
'1N4S'	0.1108	27.324	404.342	5
'4N1S'	0.0837	20.651	305.583	5
'2N3S'	0.0992	24.46	361.95	5
'3N2S'	0.0915	22.567	333.946	5
'5N1S'	0.0883	21.776	322.238	5
'1N5S'	0.1238	30.518	451.605	5
'4N2S'	0.0891	21.966	325.05	5
'2N4S'	0.0973	23.993	355.05	5
'3N3S'	0.0927	22.852	338.163	5
'6N1S'	0.0778	19.187	283.923	5
'1N6S'	0.1227	30.256	447.728	5
'5N2S'	0.091	22.452	332.241	5
'2N5S'	0.1131	27.891	412.72	5
'4N3S'	0.0918	22.637	334.976	5
'3N4S'	0.094	23.173	342.915	5

Table S2. Multiple-scattering EXAFS fits for Ni-β2m. Fits carried out in r-space (Δk = 2 to 12.5 $Å^{-1}$; $\Delta R'$ = 1 to 4.5 Å) with a Kaiser-Bessel window with dk = 1, a *k*-weight = 3 and S_o = 0.9. Imidazole scattering paths with an amplitude of 10% or higher were included. Initial input metal-ligand distances were 2.0 Å for Ni-N(O), 2.3 Å for Ni-S and 2.4 Å for Ni-Br. #v number is the number of independent variables used in the fit. Fits that did not converge or produced results outside the resolution of the instrument are not shown.

Model	R factor	Reduced χ^2	χ^2	#v
(XNWH)	***where X is the number of nitrogen atoms (N) and W is the number of imidazoles (H) in the same shell***			
'(1N1H)'	0.2913	67.3	1063.188	4
'(2N1H)'	0.1761	40.671	642.512	4
'(3N1H)'	0.1128	26.045	411.456	4
'(4N1H)'	0.0832	19.211	303.494	4
'(5N1H)'	0.0771	17.813	281.412	4
'(6N1H)'	0.0869	20.082	317.255	4
XNWH	***where X is the number of nitrogen atoms (N) and W is the number of imidazoles (H) in separate shells***			
'3N1H'	0.1124	27.714	410.109	5
'4N1H'	0.0824	20.317	300.65	5
'5N1H'	0.0755	18.63	275.691	5
'6N1H'	0.0837	20.652	305.612	5
'2N2H'	0.1293	31.889	471.887	5
'3N2H'	0.0898	22.138	327.598	5
'4N2H'	0.0774	19.092	282.525	5
'5N2H'	0.0843	20.778	307.469	5
(XNWH)YN	***where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and Y is the number of nitrogen atoms (N) in a separate shell***			
'(1N1H)1N'	0.145	38.358	529.254	6
'(2N1H)1N'	0.0858	22.705	313.285	6
'(3N1H)1N'	0.0645	17.048	235.227	6
'(4N1H)1N'	0.0632	16.705	230.496	6
'(5N1H)1N'	0.0734	19.418	267.925	6
(XNWH)AS	***where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and A is the number of sulfurs atoms (S) in a separate shell***			
'(1N1H)1S'	0.1473	38.948	537.403	6
'(2N1H)1S'	0.0949	25.087	346.151	6
'(3N1H)1S'	0.0754	19.936	275.073	6
'(4N1H)1S'	0.075	19.839	273.742	6
'(5N1H)1S'	0.0598	15.825	218.35	6

Model	R factor	Reduced χ^2	χ^2	#v
(XNWH)CBr where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and C is the number of bromine atoms (Br) in a separate shell				
'(1N1H)1Br'	0.2211	58.473	806.801	6
'(2N1H)1Br'	0.1255	33.198	458.059	6
'(3N1H)1Br'	0.0797	21.068	290.69	6
'(4N1H)1Br'	0.0642	16.981	234.301	6
'(5N1H)1Br'	0.0679	17.947	247.633	6
XNYNWH where X and Y are the number of nitrogen atoms (N) and W is the number of imidazoles (H) in separate shells				
'2N1N1H'	0.0767	21.873	279.921	7
'3N1N1H'	0.0605	17.252	220.784	7
'4N1N1H'	0.0617	17.583	225.024	7
'5N1N1H'	0.0731	20.833	266.622	7
'1N2N1H'	0.0727	20.724	265.218	7
'2N2N1H'	0.0596	17.003	217.597	7
'3N2N1H'	0.0624	17.794	227.72	7
'4N2N1H'	0.0742	21.153	270.719	7
'1N1N2H'	0.0936	26.7	341.7	7
'2N1N2H'	0.0673	19.179	245.448	7
'3N1N2H'	0.0616	17.556	224.68	7
'4N1N2H'	0.0695	19.822	253.684	7
XNASWH where X is the number of nitrogen atoms (N), A is the number of sulfur atoms (S) and W is the number of imidazoles (H) in separate shells				
'2N1S1H'	0.0948	27.039	346.046	7
'3N1S1H'	0.0753	21.486	274.973	7
'4N1S1H'	0.0749	21.356	273.306	7
'5N1S1H'	0.0568	16.208	207.425	7
'1N2S1H'	0.118	33.655	430.706	7
'2N2S1H'	0.0904	25.766	329.755	7
'3N2S1H'	0.0813	23.181	296.662	7
'4N2S1H'	0.0748	21.33	272.974	7
'2N1S2H'	0.0821	23.409	299.581	7
'3N1S2H'	0.0735	20.965	268.301	7
'4N1S2H'	0.0612	17.441	223.21	7
'1N2S2H'	0.1819	51.876	663.896	7
'2N2S2H'	0.0857	24.425	312.593	7
'3N2S2H'	0.0785	22.394	286.594	7
'1N1S3H'	0.1064	30.329	388.147	7
'2N1S3H'	0.08	22.807	291.883	7
'3N1S3H'	0.0802	22.858	292.53	7

Table S3. Table showing bond distances, σ^2 component of the Debye-Waller factors and energy shifts for relevant EXAFS fits from the multiple-scattering EXAFS fits for Ni-β2m (see above). Fits were carried out as described above. The fit in **bold** was determined to be the best model. Values in red are used to discount the model as they produce a physically unreasonable number.

Ni Model		Radius, R' (Å)	σ^2 (Å^2)	E_0 shift (eV)	R factor	Reduced χ^2
'(1N1H)1Br'	1 N/O	2.06(2)	-3(3)	1(4)	0.2210	58.47
	1 Im	2.06(2)	-1(5)			
	1 Br	2.43(2)	7(3)			
'(2N1H)1Br'	2 N/O	2.06(1)	-1(2)	1(3)	0.1255	33.20
	1 Im	2.06(1)	1(5)			
	1 Br	2.44(3)	8(3)			
'(3N1H)1Br'	3 N/O	2.061)	0(1)	0(2)	0.0797	21.07
	1 Im	2.06(1)	1(4)			
	1 Br	2.44(2)	8(2)			
'(4N1H)1Br'	**4 N/O**	**2.06(8)**	**2(1)**	**0(2)**	**0.0640**	**16.98**
	1 Im	**2.06(8)**	**1(4)**			
	1 Br	**2.44(3)**	**9(2)**			
'(5N1H)1Br'	5 N/O	2.06(8)	4(1)	0(1)	0.0679	17.95
	1 Im	2.06(8)	0(3)			
	1 Br	2.44(3)	11(4)			
'(5N1H)1S'[a]	5 N/O	2.07(7)	4(1)	1(1)	0.0598	15.82
	1 Im	2.07(7)	4(2)			
	1 S	2.66(2)	1(3)			
'5N1S1H'[a]	5 N/O	2.08(1)	4(1)	1(1)	0.0568	16.21
	1 Im	2.06(2)	4(2)			
	1 S	2.66(2)	0(2)			
'(4N1H)1N'	4 N/O	2.06(1)	0(1)	2(1)	0.0632	16.71
	1 Im	2.06(1)	2(4)			
	1 N	2.21(3)	-2(3)			
'2N2N1H'	2 N/O	2.02	-3(1)	2(2)	0.0596	17.00
	1 Im	2.09(3)	0(3)			
	2 N	2.15(2)	-2(2)			
'(3N1H)1N'	3 N/O	2.05(1)	-1(1)	2(2)	0.0644	17.05
	1 Im	2.05(1)	2(4)			
	1 N	2.19(2)	-4(2)			

[a]Models containing S-donor ligands were discounted since all the sulfur in β2m is associated with methionine residues or cysteine disulfides.

Table S4. Single scattering EXAFS fits for Cu-β2m. Fits carried out in r-space (Δk = 2 to 12.5 $Å^{-1}$; $\Delta R'$ = 1 to 2.5 Å) with a Kaiser-Bessel window with dk = 1, a *k*-weight = 3 and S_o = 0.9. Initial input metal-ligand distances were 2.0 Å for Cu-N(O), 2.3 Å for Cu-S and 2.4 Å for Cu-Br. #v number is the number of independent variables used in the fit.

Model	R factor	Reduced χ^2	χ^2	#v
XN	***where X is the number of nitrogen atoms (N)***			
'2N'	0.2336	5.964	97.353	3
'3N'	0.2527	6.453	105.347	3
'4N'	0.3061	7.817	127.599	3
'5N'	0.3703	9.454	154.336	3
'6N'	0.4322	11.036	180.151	3
'7N'	0.4858	12.405	202.495	3
AS	***where A is the number of sulfur atoms (S)***			
'2S'	0.3423	8.74	142.675	3
'3S'	0.3717	9.491	154.941	3
'4S'	0.4002	10.218	166.806	3
'5S'	0.4246	10.842	176.982	3
'6S'	0.4457	11.381	185.792	3
'7S'	0.4645	11.86	193.603	3
XNYN	***where X and Y are the number of nitrogen atoms (N) in separate shells***			
'2N1N'	0.1527	4.442	63.634	5
'2N2N'	0.1836	5.342	76.524	5
'3N1N'	0.1813	5.275	75.563	5
'4N1N'	0.2329	6.776	97.058	5
'3N2N'	0.2353	6.846	98.067	5
'5N1N'	0.2962	8.618	123.453	5
'4N2N'	0.299	8.701	124.634	5
'3N3N'	0.229	6.664	95.453	5
'6N1N'	0.3625	10.548	151.098	5
'5N2N'	0.3664	10.661	152.711	5
'4N3N'	0.2973	8.651	123.913	5

Model	R factor	Reduced χ^2	χ^2	#v
ASBS	***where A and B are the number of sulfur atoms (S) in separate shells***			
'2S1S'	0.1682	4.895	70.117	5
'2S2S'	0.1977	5.753	82.401	5
'3S1S'	0.2092	6.087	87.189	5
'4S1S'	0.3519	10.241	146.698	5
'3S2S'	0.2276	6.622	94.854	5
'5S1S'	0.4038	11.751	168.325	5
'4S2S'	0.2587	7.528	107.826	5
'3S3S'	0.277	8.061	115.473	5
'6S1S'	0.4457	12.97	185.792	5
'5S2S'	0.2452	7.135	102.207	5
'4S3S'	0.3091	8.995	128.842	5
XNAS	***where X is the number of nitrogen atoms (N) and A is the number of sulfur atoms (S) in separate shells***			
'2N1S'	0.1798	5.233	74.952	5
'1N2S'	0.1648	4.794	68.677	5
'2N2S'	0.2002	5.825	83.434	5
'3N1S'	0.2452	7.134	102.185	5
'1N3S'	0.165	4.8	68.759	5
'1N4S'	0.1653	4.81	68.903	5
'4N1S'	0.2075	6.037	86.477	5
'2N3S'	0.2028	5.901	84.524	5
'3N2S'	0.2465	7.172	102.732	5
'5N1S'	0.1983	5.771	82.671	5
'1N5S'	0.1943	5.653	80.976	5
'4N2S'	0.2533	7.372	105.598	5
'2N4S'	0.2017	5.869	84.062	5
'3N3S'	0.2435	7.085	101.492	5
'6N1S'	0.2011	5.851	83.809	5
'1N6S'	0.2185	6.358	91.068	5
'5N2S'	0.2325	6.766	96.917	5
'2N5S'	0.1885	5.486	78.584	5
'4N3S'	0.2767	8.052	115.339	5
'3N4S'	0.2406	7.001	100.281	5

Table S5. Multiple-scattering EXAFS fits for Cu-β2m. Fits carried out in r-space (Δk = 2 to 12.5 $Å^{-1}$; $\Delta R'$ = 1 to 4.5 Å) with a Kaiser-Bessel window with dk = 1, a *k*-weight = 3 and S_o = 0.9. Imidazole scattering paths with an amplitude of 10% or higher were included. Initial input metal-ligand distances were 2.0 Å for Cu-N(O), 2.3 Å for Cu-S and 2.4 Å for Cu-Br. #v number is the number of independent variables used in the fit. Fits that did not converge or produced results outside the resolution of the instrument are not shown.

Model	R factor	Reduced χ^2	χ^2	#v
(XNWH)	***where X is the number of nitrogen atoms (N) and W is the number of imidazoles (H) in the same shell***			
'(1N1H)'	0.1267	3.446	52.806	4
'(2N1H)'	0.1045	2.843	43.572	4
'(3N1H)'	0.0996	2.709	41.514	4
'(4N1H)'	0.1015	2.761	42.304	4
'(5N1H)'	0.1062	2.888	44.255	4
XNWH	***where X is the number of nitrogen atoms (N) and W is the number of imidazoles (H) in separate shells***			
'1N1H'	0.1223	3.56	50.995	5
'2N1H'	0.0883	2.57	36.817	5
'3N1H'	0.0802	2.335	33.441	5
'4N1H'	0.0827	2.407	34.475	5
'5N1H'	0.0888	2.583	36.993	5
'1N2H'	0.1235	3.593	51.462	5
'2N2H'	0.1165	3.389	48.546	5
'3N2H'	0.1175	3.42	48.991	5
'4N2H'	0.1196	3.481	49.86	5
(XNWH)YN	***where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and Y is the number of nitrogen atoms (N) in a separate shell***			
'(1N1H)1N'	0.0489	1.531	20.398	6
'(2N1H)1N'	0.0499	1.562	20.806	6
'(3N1H)1N'	0.0697	2.181	29.065	6
'(4N1H)1N'	0.0884	2.766	36.857	6
'(1N1H)2N'	0.0833	2.606	34.728	6
'(1N1H)3N'	0.0804	2.516	33.519	6
(XNWH)CBr	***where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and C is the number of bromine atoms (Br) in a separate shell***			
'(1N1H)1Br'	0.0926	2.897	38.594	6
'(2N1H)1Br'	0.0799	2.498	33.284	6
'(3N1H)1Br'	0.0784	2.453	32.687	6
'(4N1H)1Br'	0.0806	2.522	33.607	6
'(5N1H)1Br'	0.0842	2.634	35.1	6

Model	R factor	Reduced χ^2	χ^2	#v
XNWHCBr where X is the number of nitrogen atoms (N), W is the number of imidazoles (H), and C is the number of bromine atoms (Br) shell in separate shells				
'1N1H1Br'	0.0923	3.122	38.473	7
'2N1H1Br'	0.0747	2.527	31.146	7
'3N1H1Br'	0.0675	2.282	28.127	7
'4N1H1Br'	0.0666	2.253	27.768	7

Table S6. Table showing bond distances, σ^2 component of the Debye-Waller factors and energy shifts for relevant EXAFS fits from the multiple scattering EXAFS fits for Cu-β2m (see above). Fits were carried out as described above. The fit in **bold** was determined to be the best model. Values in red are used to discount the model as they produce a physically unreasonable number.

Cu Model		Radius, R' (Å)	σ^2 (Å^2)	E_0 shift (eV)	R factor	Reduced χ^2
'(1N1H)1Br'	1 N/O	1.95(1)	3(4)	-1(2)	0.0926	2.897
	1 Im	1.95(1)	-2(1)			
	1 Br	2.40(2)	11(2)			
'(2N1H)1Br'	2 N/O	1.95(1)	12(4)	-1(2)	0.0799	2.498
	1 Im	1.95(1)	-1(1)			
	1 Br	2.40(2)	11(2)			
'(3N1H)1Br'	**3 N/O**	**1.95(1)**	**18(5)**	**-2(1)**	**0.0784**	**2.453**
	1 Im	**1.95(1)**	**2(1)**			
	1 Br	**2.40(2)**	**12(2)**			
'(4N1H)1Br'	4 N/O	1.95(1)	24(5)	-2(1)	0.0806	2.522
	1 Im	1.95(1)	-1(1)			
	1 Br	2.39(2)	12(2)			
'(5N1H)1Br'	5 N/O	1.95(1)	30(5)	-3(1)	0.0842	2.634
	1 Im	1.95(1)	-9(3)			
	1 Br	2.39(3)	12(3)			
'(2N1H)1N'	2 N/O	1.97(1)	4(2)	3(1)	0.0499	1.562
	1 Im	1.97(1)	-2(1)			
	1 N	2.16(1)	-2(1)			
'(3N1H)1N'	3 N/O	1.97(1)	11(3)	1(1)	0.0697	2.181
	1 Im	1.97(1)	-3(1)			
	1 N	2.17(2)	0(2)			
'4N1H1Br'	4 N/O	2.02(4)	3(1)	0(2)	0.0666	2.253
	1 Im	1.95(1)	0(1)			
	1 Br	2.40(3)	12(3)			
'3N1H1Br'	3 N/O	2.01(4)	20(5)	0(2)	0.0674	2.282
	1 Im	1.95(1)	-3(1)			
	1 Br	2.40(2)	13(3)			
'3N1H'	3 N/O	2.01(3)	16(4)	0(2)	0.0802	2.334
	1 Im	1.95(1)	-3(1)			

Table S7. Single scattering EXAFS fits for Zn-β2m. Fits carried out in r-space (Δk = 2 to 12.5 $Å^{-1}$; $\Delta R'$ = 1 to 2.5 Å) with a Kaiser-Bessel window with dk = 1, a *k*-weight = 3 and S_o = 0.9. Initial input metal-ligand distances were 2.0 Å for Zn-N(O), 2.3 Å for Zn-S and 2.4 Å for Zn-Br. #v number is the number of independent variables used in the fit.

Model	R factor	Reduced χ^2	χ^2	#v
XN	***where X is the number of nitrogen atoms (N)***			
'2N'	0.4183	246.808	4145.85	3
'3N'	0.328	193.551	3251.243	3
'4N'	0.2825	166.67	2799.694	3
'5N'	0.2667	157.384	2643.709	3
'6N'	0.2709	159.839	2684.959	3
'7N'	0.2879	169.889	2853.772	3
AS	***where A is the number of sulfur atoms (S)***			
'2S'	0.3475	205.04	3444.237	3
'3S'	0.27	159.348	2676.709	3
'4S'	0.2352	138.763	2330.925	3
'5S'	0.2248	132.657	2228.359	3
'6S'	0.2287	134.965	2267.124	3
'7S'	0.2408	142.098	2386.939	3
XNYN	***where X and Y are the number of nitrogen atoms (N) in separate shells***			
'2N1N'	0.1865	124.896	1848.186	5
'2N2N'	0.1794	120.139	1777.797	5
'3N1N'	0.173	115.906	1715.159	5
'4N1N'	0.1886	126.336	1869.508	5
'3N2N'	0.1986	133.047	1968.807	5
'5N1N'	0.221	148.043	2190.718	5
'4N2N'	0.2341	156.828	2320.716	5
'3N3N'	0.2439	163.371	2417.541	5
'6N1N'	0.2625	175.813	2601.653	5
'5N2N'	0.2775	185.844	2750.088	5
'4N3N'	0.2877	192.681	2851.261	5

Model	R factor	Reduced χ^2	χ^2	#v
ASBS	***where A and B are the number of sulfur atoms (S) in separate shells***			
'2S1S'	0.1231	82.444	1219.999	5
'2S2S'	0.1301	87.126	1289.271	5
'3S1S'	0.1296	86.807	1284.561	5
'4S1S'	0.2334	156.328	2313.313	5
'3S2S'	0.1574	105.42	1559.996	5
'5S1S'	0.2248	150.587	2228.359	5
'4S2S'	0.223	149.372	2210.386	5
'3S3S'	0.195	130.606	1932.685	5
'6S1S'	0.2272	152.184	2251.996	5
'5S2S'	0.2208	147.903	2188.645	5
'4S3S'	0.232	155.399	2299.573	5
XNAS	***where X is the number of nitrogen atoms (N) and A is the number of sulfur atoms (S) in separate shells***			
'2N1S'	0.1176	78.793	1165.965	5
'1N2S'	0.123	82.357	1218.713	5
'2N2S'	0.1389	93.062	1377.111	5
'3N1S'	0.1333	89.29	1321.294	5
'1N3S'	0.1357	90.919	1345.408	5
'1N4S'	0.1579	105.766	1565.107	5
'4N1S'	0.17	113.864	1684.943	5
'2N3S'	0.1709	114.491	1694.227	5
'3N2S'	0.1766	118.294	1750.496	5
'5N1S'	0.2132	142.811	2113.297	5
'1N5S'	0.1307	87.542	1295.437	5
'4N2S'	0.2093	140.215	2074.883	5
'2N4S'	0.1935	129.642	1918.421	5
'3N3S'	0.2018	135.142	1999.81	5
'6N1S'	0.2411	161.491	2389.723	5
'1N6S'	0.1532	102.589	1518.101	5
'5N2S'	0.2224	148.952	2204.171	5
'2N5S'	0.1224	82.001	1213.436	5
'4N3S'	0.2145	143.675	2126.084	5
'3N4S'	0.2106	141.098	2087.941	5

Table S8. Multiple-scattering EXAFS fits for Zn-β2m. Fits carried out in r-space (Δk = 2 to 12.5 $Å^{-1}$; $\Delta R'$ = 1 to 4.5 Å) with a Kaiser-Bessel window with dk = 1, a *k*-weight = 3 and S_o = 0.9. Imidazole scattering paths with an amplitude of 10% or higher were included. Initial input metal-ligand distances were 2.0 Å for Zn-N(O), 2.3 Å for Zn-S and 2.4 Å for Zn-Br. #v number is the number of independent variables used in the fit. Fits that did not converge or produced results outside the resolution of the instrument are not shown.

Model	R factor	Reduced χ^2	χ^2	#v
(XNWH)	***where X is the number of nitrogen atoms (N) and W is the number of imidazoles (H) in the same shell***			
'(1N1H)'	0.383	240.314	3796.446	4
'(2N1H)'	0.2841	178.275	2816.368	4
'(3N1H)'	0.2344	147.044	2322.98	4
'(4N1H)'	0.216	135.507	2140.713	4
'(5N1H)'	0.2176	136.554	2157.261	4
XNWH	***where X is the number of nitrogen atoms (N) and W is the number of imidazoles (H) in separate shells***			
'1N1H'	0.3463	231.981	3432.815	5
'2N1H'	0.2832	189.681	2806.867	5
'3N1H'	0.2343	156.959	2322.662	5
'4N1H'	0.2158	144.571	2139.336	5
'5N1H'	0.217	145.33	2150.576	5
(XNWH)AS	***where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and A is the number of sulfurs atoms (S) in a separate shell***			
'(1N1H)1S'	0.0916	65.768	907.462	6
'(2N1H)1S'	0.0923	66.331	915.231	6
'(3N1H)1S'	0.1231	88.403	1219.772	6
'(4N1H)1S'	0.1522	109.349	1508.786	6
'(1N2H)1S'	0.0739	53.062	732.143	6
'(2N2H)1S'	0.0924	66.38	915.896	6
'(3N2H)1S'	0.1388	99.717	1375.876	6
'(1N3H)1S'	0.0718	51.614	712.168	6
'(2N3H)1S'	0.0961	69.017	952.293	6
'(3N3H)1S'	0.1428	102.58	1415.384	6
'(1N1H)2S'	0.1023	73.48	1013.864	6
'(2N1H)2S'	0.1359	97.595	1346.597	6
'(3N1H)2S'	0.16	114.966	1586.281	6

Model	R factor	Reduced χ^2	χ^2	#v
(XNWH)CBr	***where X is the number of nitrogen atoms (N), W is the number of imidazoles (H) in the same shell and C is the number of bromine atoms (Br) in a separate shell***			
'(1N1H)1Br'	0.1521	109.248	1507.391	6
'(2N1H)1Br'	0.0895	64.311	887.354	6
'(3N1H)1Br'	0.0714	51.274	707.472	6
'(4N1H)1Br'	0.0757	54.382	750.356	6
'(5N1H)1Br'	0.0894	64.215	886.029	6
'(1N1H)2Br'	0.1514	108.733	1500.278	6
'(2N1H)2Br'	0.1033	74.191	1023.673	6
'(3N1H)2Br'	0.0908	65.2	899.614	6
'(4N1H)2Br'	0.0949	68.138	940.159	6
'(1N2H)1Br'	0.0924	66.395	916.108	6
'(2N2H)1Br'	0.0615	44.184	609.638	6
'(3N2H)1Br'	0.0623	44.786	617.956	6
'(4N2H)1Br'	0.0754	54.186	747.644	6
'(1N3H)1Br'	0.0706	50.708	699.659	6
'(2N3H)1Br'	0.0596	42.846	591.186	6
'(3N3H)1Br'	0.073	52.458	723.806	6

Table S9. Table showing bond distances, σ^2 component of the Debye-Waller factors and energy shifts for relevant EXAFS fits from the multiple-scattering EXAFS fits for Zn-β2m (see above). Fits were carried out as described above. The fit in **bold** was determined to be the best model. Values in red are used to discount the model as they produce a physically unreasonable number.

Zn Model		Radius, R' (Å)	σ^2 (Å^2)	E_0 shift (eV)	R factor	Reduced χ^2
'(1N2H)1Br'	1 N/O	1.98(1)	0(3)	-8(2)	0.0924	66.39
	2 Im	1.98(1)	4(2)			
	1 Br	2.37(1)	6(1)			
'(2N2H)1Br'	**2 N/O**	**1.99(1)**	**4(2)**	**-8(2)**	**0.0615**	**44.18**
	2 Im	**1.99(1)**	**5(2)**			
	1 Br	**2.38(1)**	**6(1)**			
'(3N2H)1Br'	3 N/O	1.99(1)	7(2)	-8(2)	0.0623	44.78
	2 Im	1.99(1)	5(2)			
	1 Br	2.38(1)	7(1)			
'(4N2H)1Br'	4 N/O	1.99(1)	11(3)	-8(2)	0.0754	54.19
	2 Im	1.99(1)	4(2)			
	1 Br	2.37(1)	7(1)			
'(2N3H)1Br	2 N/O	1.99(1)	4(2)	-8(2)	0.0596	42.85
	3 Im	1.99(1)	8(2)			
	1 Br	2.38(1)	6(1)			
'(1N3H)1Br'	1 N/O	1.99(1)	1(3)	-8(2)	0.0706	50.71
	3 Im	1.99(1)	6(2)			
	1 Br	2.37(1)	6(1)			
'(3N1H)1Br'	3 N/O	1.98(1)	5(2)	-9(2)	0.0714	51.27
	1 Im	1.98(1)	3(3)			
	1 Br	2.37(1)	6(1)			
'(1N3H)1S'	1 N/O	1.95(1)	-3(1)	-10(2)	0.0718	51.61
	3 Im	1.95(1)	11(3)			
	1 S	2.23(1)	1(1)			
'(3N3H)1Br'	3 N/O	1.99(1)	8(3)	-8(2)	0.0730	52.46
	3 Im	1.99(1)	7(3)			
	1 Br	2.38(1)	7(1)			
'(1N2H)1S'	1 N/O	1.96(1)	-3(1)	-10(2)	0.0739	53.06
	2 Im	1.96(1)	8(3)			
	1 S	2.23(1)	1(1)			

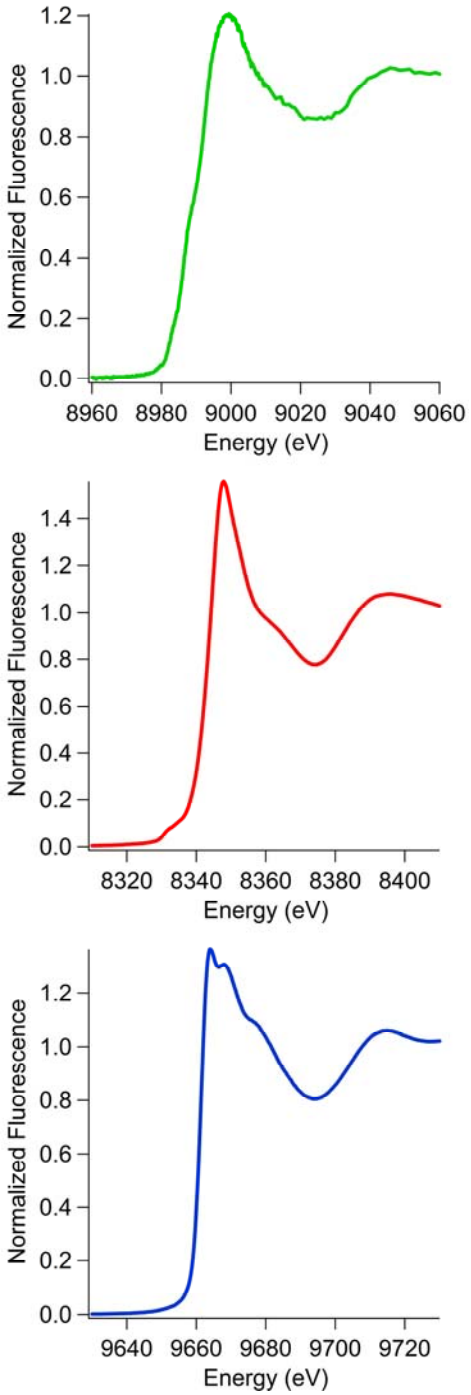

Figure S1. Metal K-edges XANES spectra from Table 1 for metal complexes of β2m in 150 mM KBr, 25 mM MOPS (pH = 7.4) and 10% glycerol in the presence of Cu(II) (green), Ni(II) (red), and Zn (blue).

Table S10: XANES analysis of metal complexes of β2m in 150 mM KBr, 25 mM MOPS (pH = 7.4) and 10% glycerol in the presence of Cu(II), Ni(II), and Zn(II).

	1s→3d peak area ($\times 10^{-2}$ eV)	1s→4pz observed	Coordination number	Edge energy (eV)
Cu(II)	NA	shoulder	NA	8987.2
Ni(II)	5.2(7)	No	6	8344.5
Zn(II)	NA	NA	5	9661.4

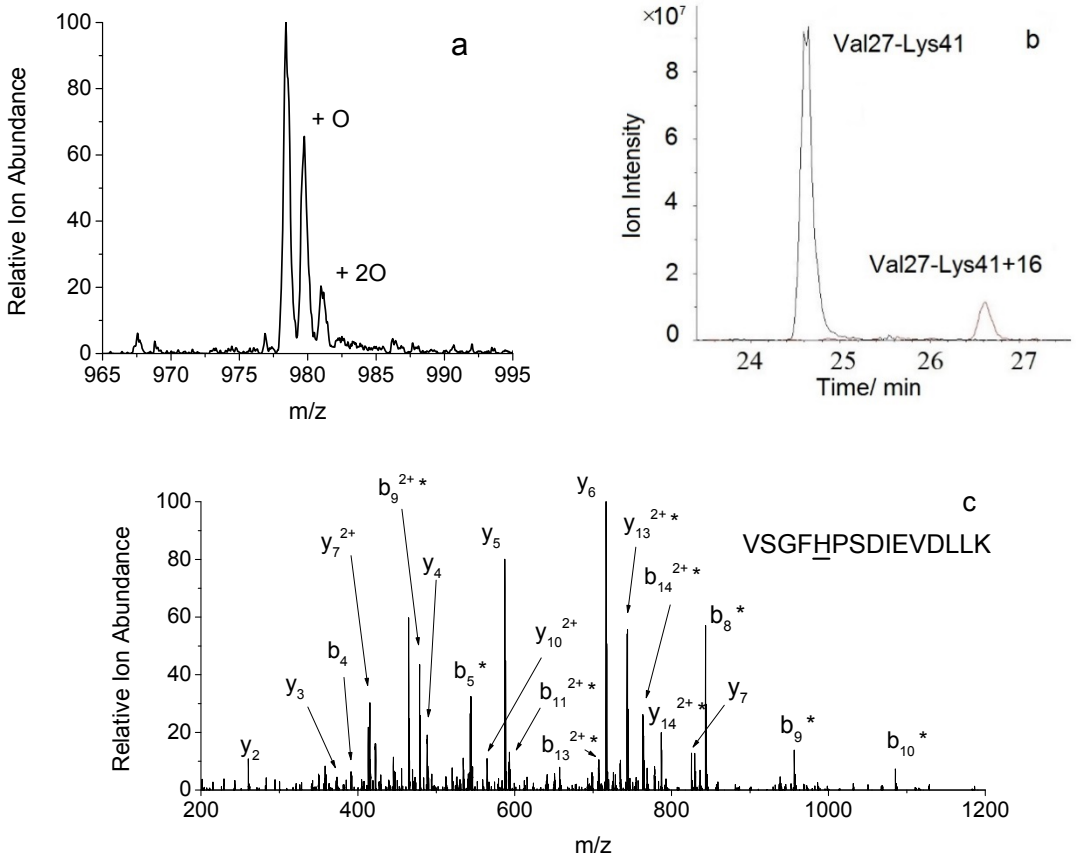

Figure S2. (a) ESI mass spectrum around + 12 charge states of β2m after the MCO reaction with Ni(II). Legend: +1O, addition of 16 Da; +2O, addition of 32 Da. (b) Extracted ion chromatogram of the unmodified (m/z 828.4) and modified (m/z 836.4) forms of the peptide Val27-Lys41 after the MCO reaction of β2m-Ni(II). The oxidation percentage was determined by comparing the LC-MS intensities of modified and unmodified peptide containing the amino acid of interest. (c) CID mass spectrum of $[Val27\text{-}Lys41+16]^{3+}$, showing oxidation occurs at His31. The peaks labeled with asterisks correspond to oxidized product ions.

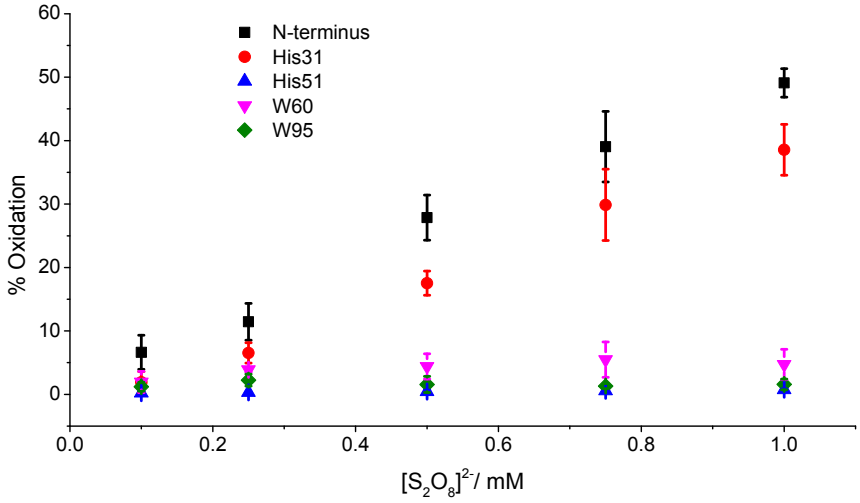

Figure S3. Oxidation percentages for modified residues after 200 μM β2m was reacted with 250 μM $NiSO_4$, 5 mM ascorbate, and 0.1-1 mM $S_2O_8^{2-}$ in 150 mM potassium acetate and 25 mM MOPS at pH 7.4 and 25 ºC.

Calculations to estimate the percent decrease in Cu(II)-β2m loading in the presence and absence of 3 mM Ni(II) with 100 μM β2m and 150 μM Cu(II) present. Dissociation constants previously reported (K_d^{Cu} = 2.5 μM, K_d^{Ni} = 400 μM) were used for these calculations.

Sample	β2m-Cu(II)-Ni(II)			β2m-Cu(II)	
	β2m	Cu(II)	Ni(II)	β2m	Cu(II)
Conc/ μM	100	150	3000	100	150
[β2m-Ni]/ μM		19		0	
[β2m-Cu]/ μM		77		96	
	Percent decrease of β2m-Cu : 19.7%				

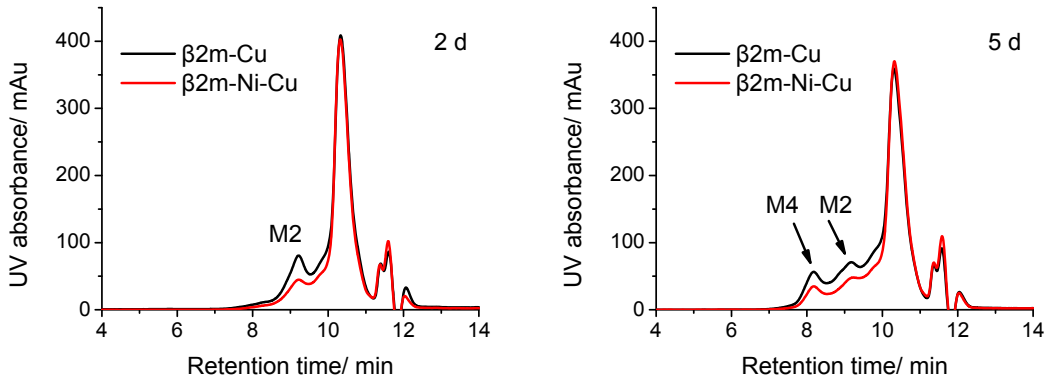

Figure S4. SEC analyses of 100 μM β2m and 150 μM $CuSO_4$ incubated without (black) and with 3 mM $NiSO_4$ (red) in 500 mM urea, 150 mM potassium acetate and 25 mM MOPS at pH 7.4 and 37 ºC

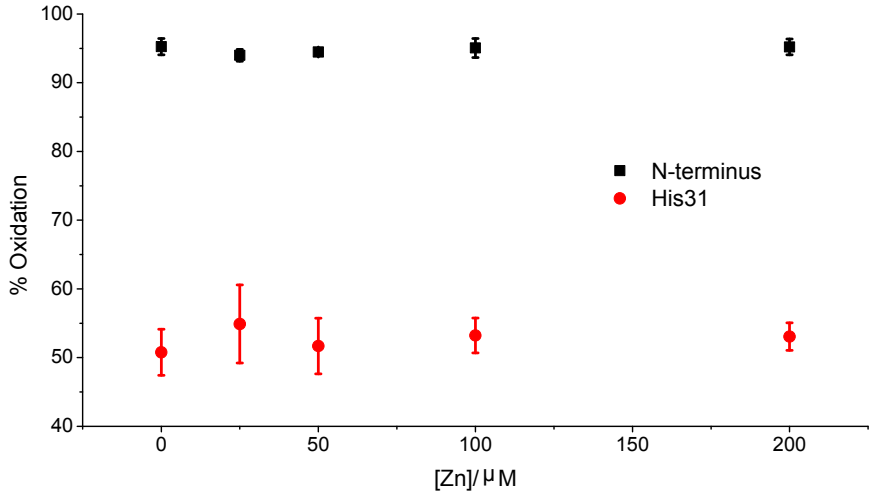

Figure S5. Oxidation percentages of the N-terminus and His31 after 5 μM β2m is reacted with 5 μM $CuSO_4$, 0-200 μM $ZnSO_4$, 0.5 mM ascorbate, and 25 μM $S_2O_8^{2-}$ in 150 mM potassium acetate and 25 mM MOPS at pH 7.4 and 25 ºC for 1 min.

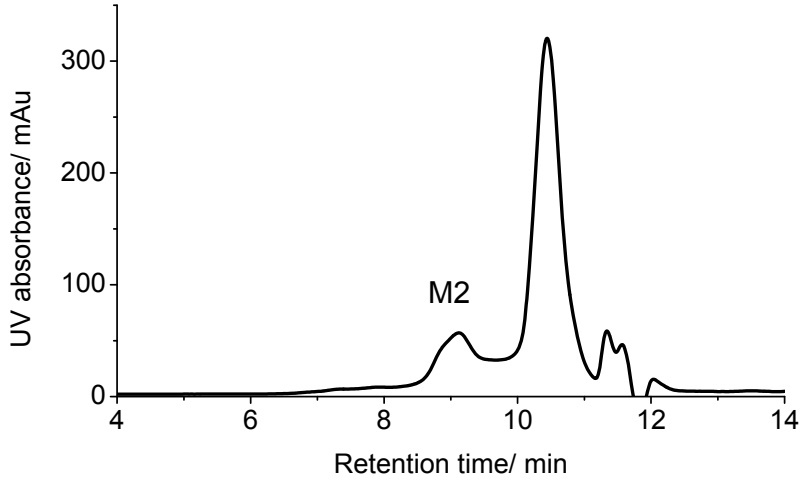

Figure S6. SEC analysis of 100 μM β2m and 100 μM $ZnSO_4$ incubated in a solution containing 150 mM potassium acetate and 25 mM MOPS at pH 7.4 and 37 ºC for 1 day.

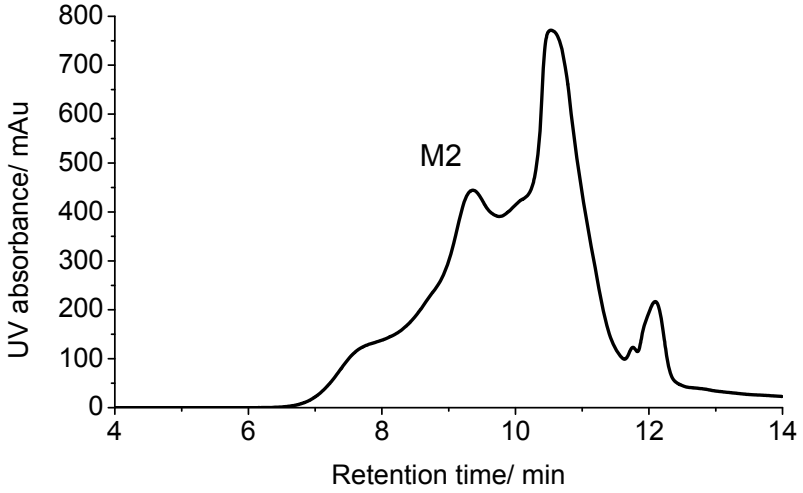

Figure S7. SEC analysis of 2 mM β2m and 1.2 mM $ZnSO_4$ equilibrated in 150 mM KBr and 25 mM MOPS at pH 7.4 and 25 ºC.

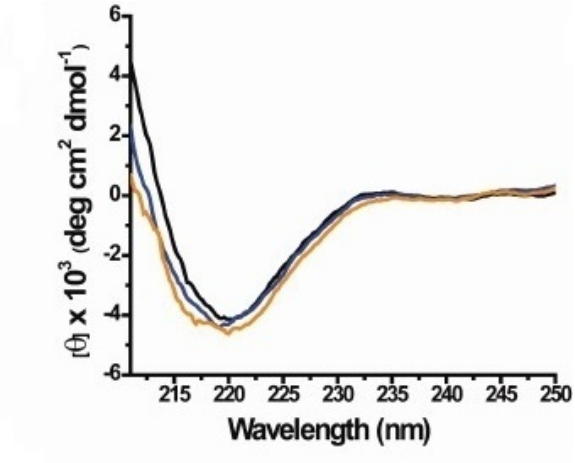

Figure S8. Far-UV CD spectra of β2m in the absence (black) and presence of divalent metal ions: Cu(II) (blue), Ni(II) (green), and Zn(II) (orange).

Table S11. Global hydrogen deuterium exchange rates of the amide hydrogens for β2m incubated in the absence and presence of Cu(II)/ Ni(II)/ Zn(II)

		HDX results (Fast)		HDX results (Slow)		
		# D	Rate / min	# D	Rate/ min	Total # D
β2m		40.67 ± 0.85	8.37 ± 0.42	15.83 ± 3.24	0.14 ± 0.05	56.5 ± 2.4
	Cu(II)	46.5 ± 3.5	8.54 ± 0.41	20.6 ± 4.3	0.039 ± 0.019	67.0 ± 7.8
β2m	Ni(II)	50.5 ± 5.4	9.6 ± 3.0	16.19 ± 2.84	0.05 ± 0.04	66.7 ± 4.0
	Zn(II)	49.1 ± 2.3	8.1 ± 0.23	18.36 ± 2.66	0.041 ± 0.017	67.4 ± 0.3