SUPPORTING INFORMATION

An overlooked hepcidin-cadmium connection

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3

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# Supporting figures

**Scheme 1.** Comparison of sequences of hepcidin-25 and α-domain of human metallothionein 2 (Cys residues set in bold).

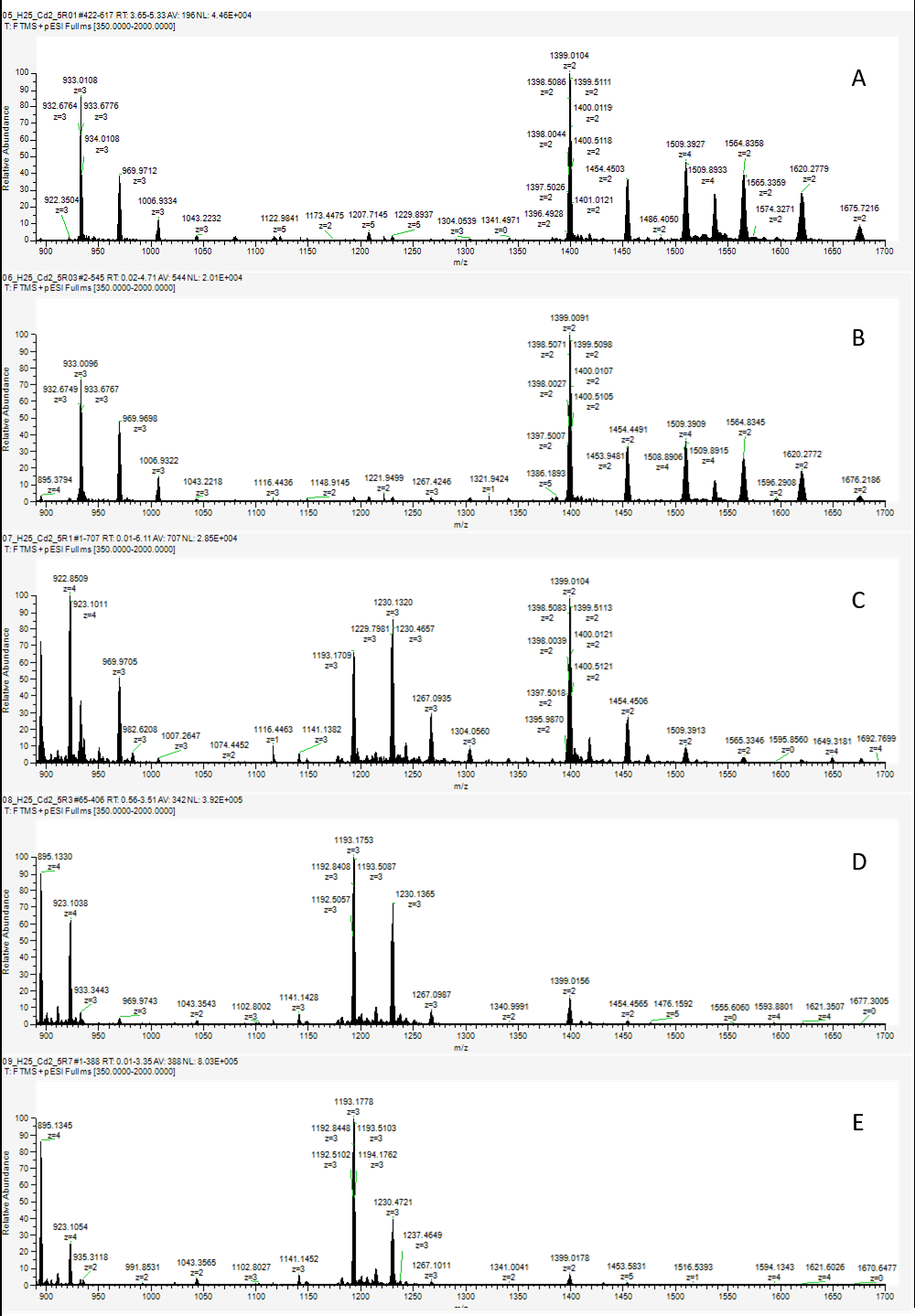
**MT2** KS**CC**S**CC**PVG**C**AK**C**AQG**C**I**C**KGASDK**C**S**CC**A

**hepcidin-25** DTHFPI**C**IF**CC**G**CC**HRSK**C**GM**CC**KT

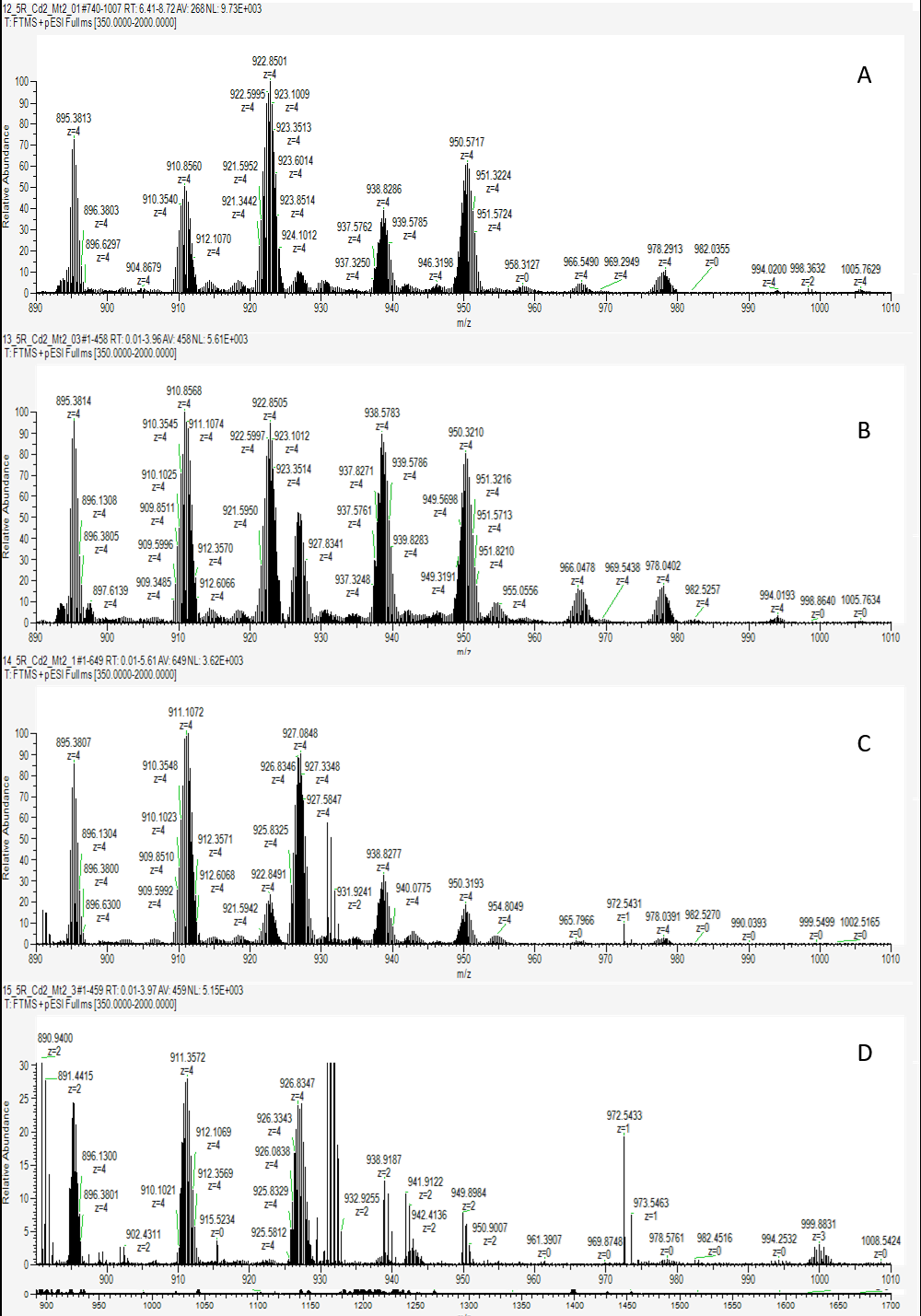




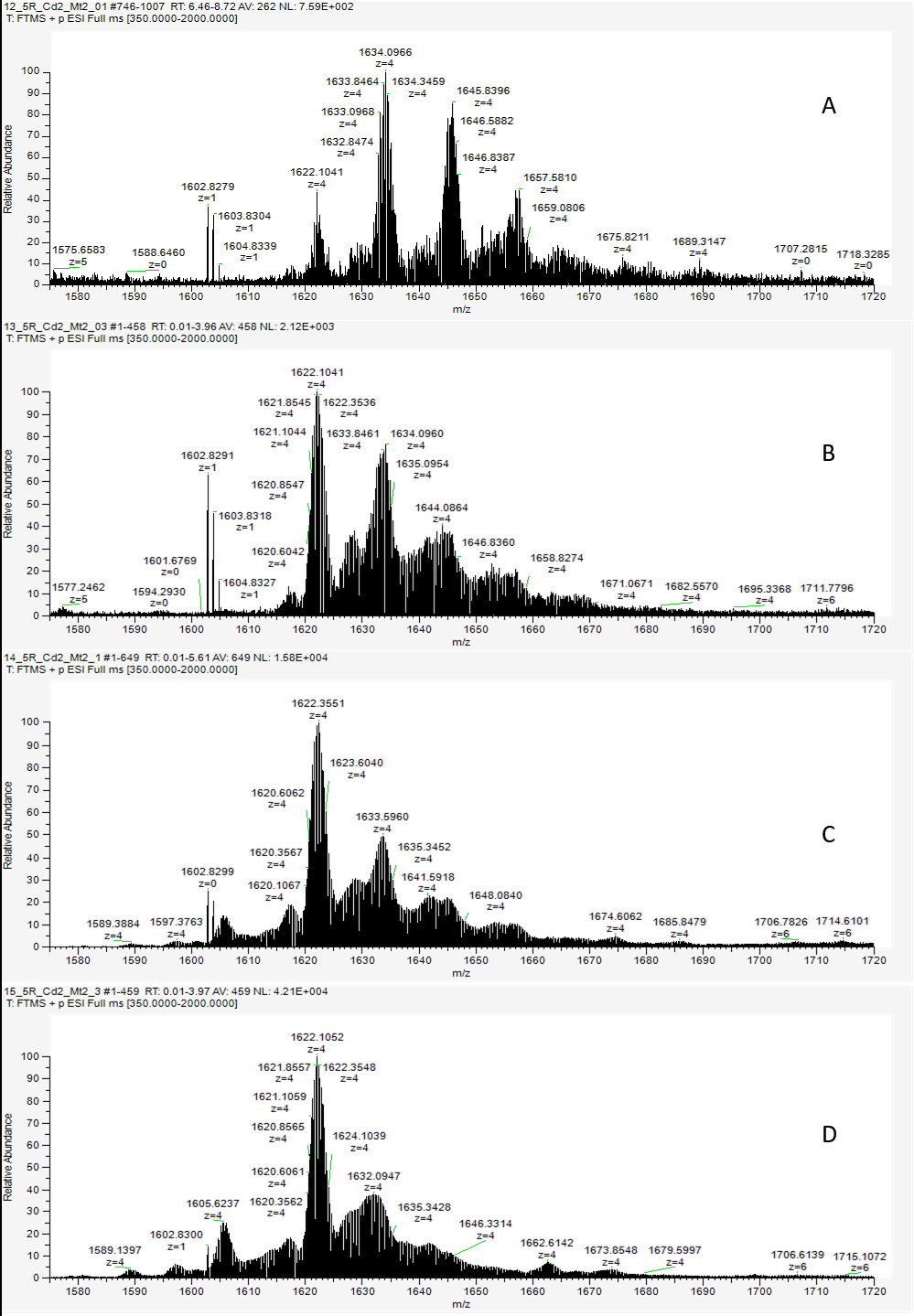
**Figure S1.** 100 μM 5R-hepcidin in 100mM HEPES pH 7.4, titrated with Cd(NO3)2 (top) and Zn(NO3)2 (bottom). Cd(II) and Zn(II) to peptide ratios are color coded on the plots.



**Figure S2.** Native mass spectra of 10 μM Hepcidin-25 with 20 μM Cd(II) acetate with varying concentration of 5R-hepcidin: A) 1 μM, B) 3 μM, C) 10 μM, D) 30 μM, E) 70 μM in ammonium acetate pH 7.4.



**Figure S3.** Native mass spectra of 10 μM 5R-hepcidin with 20 μM Cd(II) acetate with varying concentration of metallothionein MT2A: A) 1 μM, B) 3 μM, C) 10 μM, D) 30 μM in ammonium acetate pH 7.4 Due to high noise and differing intensities, for better clarity only fragment for 5R-hepcidin is shown, the fragment with peaks associated with MT2A is shown in Fig. S4.



**Figure S4.** Native mass spectra of 10 μM 5R-hepcidin with 20 μM Cd(II) acetate with varying concentration of metallothionein MT2A: A) 1 μM, B) 3 μM, C) 10 μM, D) 30 μM in ammonium acetate pH 7.4 Due to high noise and differing intensities, for better clarity only peaks associated with MT2A is shown, the spectrum fragment with peaks associated with 5R-hepcidin is shown in Fig. S3.