Electronic Supplementary Material (ESI) for Metallomics.

McCann et all

Supplementary Figures and Tables

Table 1. Demographic and biological variables of healthy individuals that are either carriers or non-carries of R832 and K952. Values reported are means and SD. Normal, healthy levels range from 16-24uM for serum Cu and 20-40mg/dL for serum Cp [3].

	Mean	Standard Deviation
Age (years)	65.19	12.857
MMSE score	28	1.91
Copper (uM)	13.5524	2.877
Ceruloplasmin (mg/dL)	25.6731	5.50615
non-Ceruloplasmin copper (uM)	1.4347	2.27155
Copper:Ceruloplasmin	7.0625	1.11833

Table 2. Presence of R832 and K952 in patients with Wilson disease and corresponding clinical symptoms.

WD Mutation	ATP7B SNPs	Age of diagnosis	Sex	Phenotype	KF Ring	Serum Cu (µg/dL)	Cp (mg/dL)	Source
p.A990P	p.K832R	14	F	hepatic	Y	22	5	Brage, *et. al*, 2007
p.P768L	p.R952K	28	M	hepatic	N	70	14	
p.G691R	p.K832R, p.R952K	3	F	liver cirrhosis, subclinical hepatitis	Y	N/A	N/A	Scvortova, *et. al.*, 2013
p.G691R	p.K832R, p.R952K	12	M	liver cirrhosis, subclinical hepatitis	Y	N/A	N/A	
N/A	p.K832R, p.R952K	9	F	trigonocephaly, biparietal widening, hypertelorism, hepatomegaly	N	26	5	Cogulu, *et. al.*, 2005
N/A	p.K832R, p.R952K	13	M	trigonocephaly, biparietal widening, hypertelorism, hepatomegaly	N	13.3	5	
p.	p.K832R, p.R952K	24	F	ataxia, dystonia, tremor	Y	0.111	N/A	Lu, *et. al.*, 2014
p.T1220M	p.K832R, p.R952K	N/A	N/A	hepatic	N/A	N/A	N/A	Haas, *et. al.*, 1999
c. 2008-2013 del	p.K832R	N/A	N/A	hepatic	N/A	N/A	N/A	
p.R969Q, p.H1069Q	p.K832R	N/A	N/A	hepatic	N/A	N/A	N/A	
p.C985T, p.I1148T	p.R952K	N/A	N/A	hepatic	N/A	N/A	N/A	
pH1069Q	p.K832R	17	M	neurological, cirrhosis	Y	N/A	3.5	Cocoş, *et. al.*, 2014
pH1069Q	p.K832R	18	M	neurological	Y	N/A	0.9	
pH1069Q	p.K832R	19	F	neurological	Y	N/A	2.6	
pH1069Q	p.K832R	6	M	high ALT and AST	N	N/A	0.4	
pH1069Q	p.K832R	7	F	high ALT and AST	N	N/A	0.1	
pH1069Q	p.K832R	19	M	neurological	Y	N/A	1.2	
pH1069Q	p.K832R	20	M	neurological, cirrhosis	Y	N/A	2.3	

Supplementary Figure 1

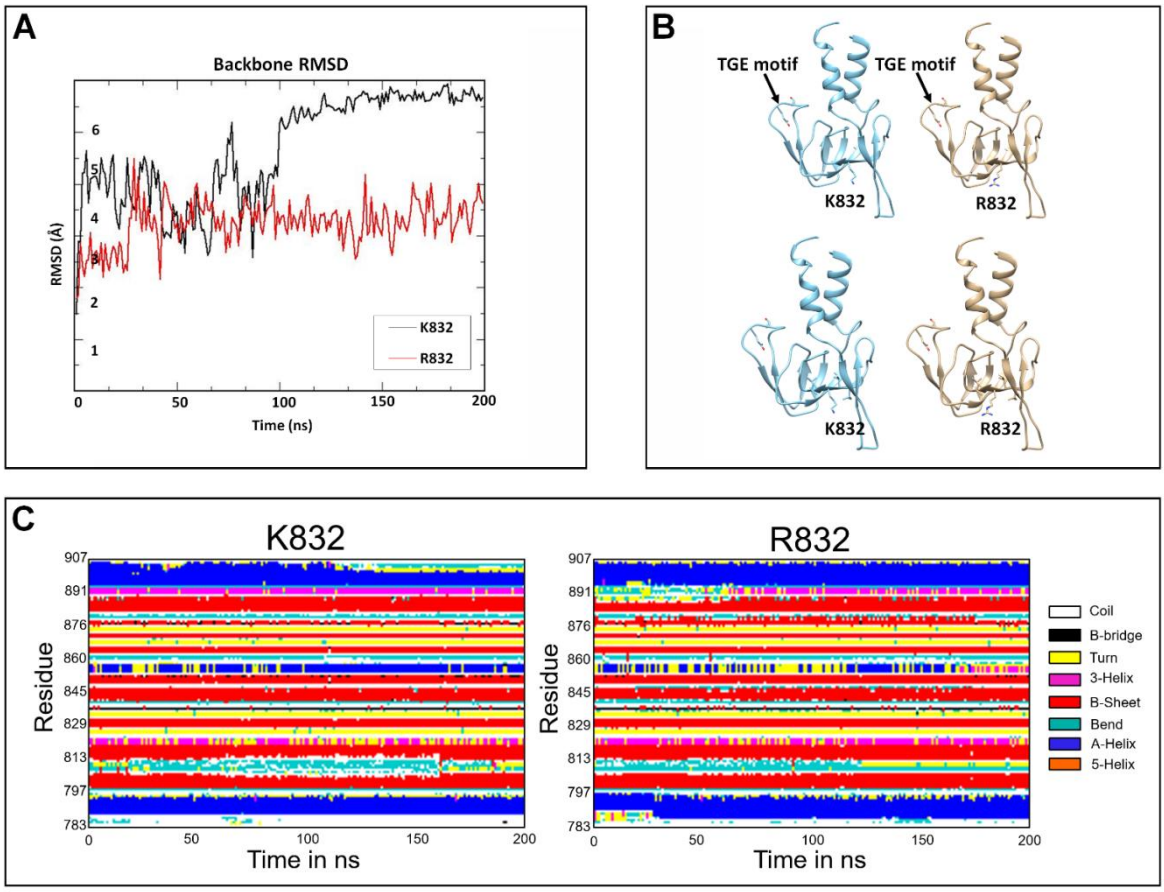

Fig S1. MD simulations of the isolated A-domain.
(A) Root mean square deviation (RMSD) differs between the domain containing K832 or R832. The backbone RMSD of the 200 nanosecond all-atom MD simulation for K832 (black) and R832 (red). **(B)** Ribbon models of the isolated K832 and R832 A-domain with the K832R residues shown as sticks. *Top panel,* residues in the TGE motif—T858, G859, E860—are shown as sticks. *Bottom panel,* residues neighboring K832R in the β-sheet 3—I830, V831, V833, and V834—highlighted as sticks. **(C)** Effects of the 832 SNPs on the secondary structure of the A-domain. The secondary structural changes on the A-domain due to K832 (left) and R832 (right), shown as a DSSP secondary structure time series diagram.