

McCann et al  
**Supplementary Figures and Tables**

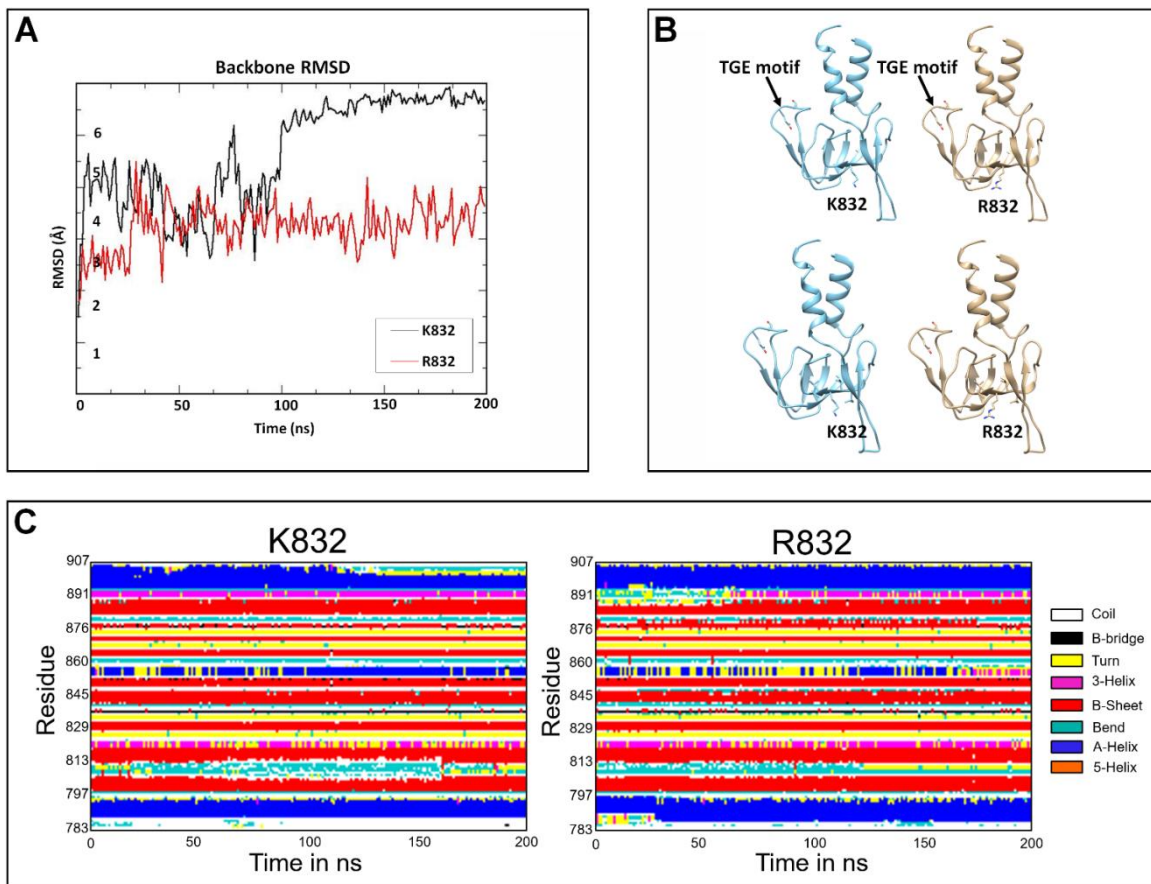
**Table 1. Demographic and biological variables of healthy individuals that are either carriers or non-carriers of R832 and K952.** Values reported are means and SD. Normal, healthy levels range from 16-24uM for serum Cu and 20-40mg/dL for serum Cp [3].

	<b>Mean</b>	<b>Standard Deviation</b>
<b>Age (years)</b>	65.19	12.857
<b>MMSE score</b>	28	1.91
<b>Copper (uM)</b>	13.5524	2.877
<b>Ceruloplasmin (mg/dL)</b>	25.6731	5.50615
<b>non-Ceruloplasmin copper (uM)</b>	1.4347	2.27155
<b>Copper: Ceruloplasmin</b>	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, <i>et. al.</i> , 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, <i>et. al.</i> , 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, <i>et. al.</i> , 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, <i>et. al.</i> , 2014
p.T1220M	p.K832R, p.R952K	N/A	N/A	hepatic	N/A	N/A	N/A	Haas, <i>et. al.</i> , 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, <i>et. al.</i> , 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  $\beta$ -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.