Supplementary Information for

Copper (Cu^{2+}) Ion Induced Misfolding of Tau Protein R3 Peptide Revealed by Enhanced Molecular Dynamics Simulation

Jing Jing[1,2], Gao Tu[2], Hongyan Yu[1,2], Rong Huang[3,4], Xianquan Ming[5], Haiqing Zhan[5], Feng Zhan[1*], Weiwei Xue[2,3*]

[1] *The Key Laboratory of Nonferrous Metal Materials and New Processing Technology of Ministry of Education, Guangxi University, Nanning 530004, China*

[2] *School of Pharmaceutical Sciences and Innovative Drug Research Centre, Chongqing Key Laboratory of Natural Product Synthesis and Drug Research, Chongqing University, Chongqing 401331, China*

[3] *Central Nervous System Drug Key Laboratory of Sichuan Province, Luzhou 646106, China*

[4] *Sichuan Credit Pharmaceutical Co., Ltd., Luzhou 646106, China*

[5] *CITIC Dameng Mining Industries Ltd, Nanning 530028, China*

***Corresponding Author**

Dr. Weiwei Xue

Email: xueww@cqu.edu.cn

Dr. Feng Zhan

Email: fzhan_gxu@126.com

Table S1. The residues interaction networks (RINs) of Cu^{2+}-R3 and R3 peptide systems. Atom names are reported according to the PDB standard. The hydrogen bond (HBOND) has been split into main chain (MC) and side chain (SC) interactions. For Van der Waals (VDW) interaction, the distance is calculated considering atom surface instead of atom center

Systems	NodeId1	NodeId2	Interaction	Distance (Å)	Angle (°)	Atom1	Atom2
Cu^{2+}-R3	2: THR	5: CYS	HBOND:MC_MC	3.243	26.684	O	N
	4: LYS	9: GLY	VDW:MC_MC	3.562	-999.9 [a]	C	C
	4: LYS	13: HIS	HBOND:SC_SC	2.992	37.74	NZ	ND1
	6: GLY	9: GLY	HBOND:MC_MC	3.253	23.235	O	N
	6: GLY	10: ASN	HBOND:MC_MC	3.106	14.599	O	N
	7: SER	10: ASN	HBOND:MC_MC	3.279	47.195	O	N
	7: SER	11: ILE	HBOND:MC_MC	2.87	9.961	O	N
	8: LEU	12: HIS	HBOND:MC_MC	3.145	35.822	O	N
	9: GLY	12: HIS	HBOND:MC_MC	3.341	41.872	O	N
	9: GLY	13: HIS	HBOND:MC_MC	3.014	26.591	O	N
	10: ASN	13: HIS	HBOND:MC_MC	3.381	45.736	O	N
	10: ASN	14: LYS	HBOND:MC_MC	3.027	17.129	O	N
	10: ASN	14: LYS	VDW:SC_SC	3.779	-999.9	ND2	CE
	11: ILE	14: LYS	HBOND:MC_MC	3.239	53.4	O	N
R3	4: LYS	7: SER	HBOND:MC_MC	3.207	18.396	O	N
	4: LYS	7: SER	VDW:MC_SC	3.994	-999.9	C	CB
	6: GLY	9: GLY	HBOND:MC_MC	3.219	52.209	O	N
	14: LYS	17: GLY	HBOND:SC_MC	3.218	59.035	NZ	O
	14: LYS	17: GLY	VDW:SC_MC	3.427	-999.9	CB	C
	15: PRO	18: GLY	HBOND:MC_MC	2.907	38.986	O	N

[a] For VDW interactions and IAC it is not possible to infer any angle and the -999.9 (NULL) value is assigned.

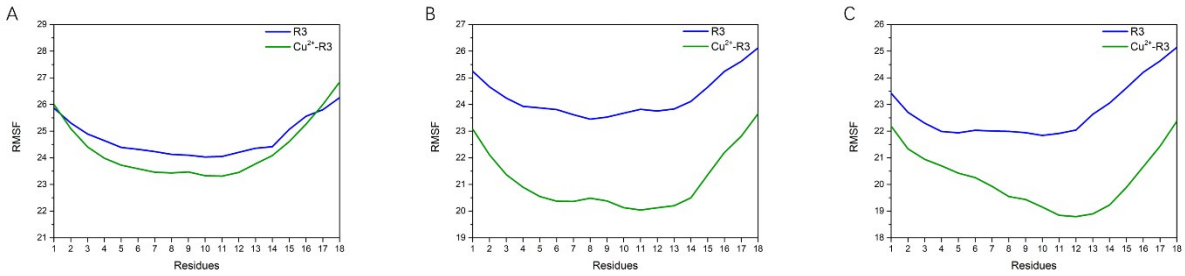

Figure S1. (A-C) Root mean square fluctuation (RMSF) values of 1/2 R3 peptide and Cu^{2+}-R3 peptide system during the three independents 1000 ns GaMD simulations. The blue and green lines represent 1/2 R3 peptide and Cu^{2+}-R3 peptide system.