Supplementary information for

A mixed-valence biotinylated Cu(I/II) complex for tumor-targeted chemodynamic therapy accompanied with GSH depletion

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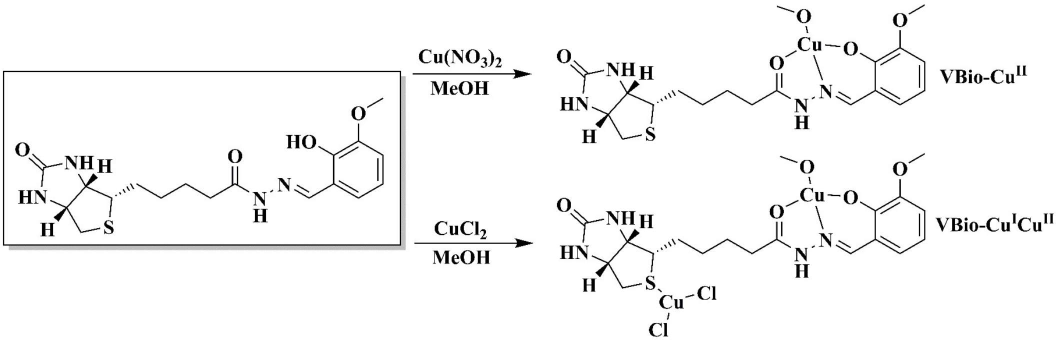


Scheme S1. Preparation of **VBio-Cu^{II}** and **VBio-Cu^{I}Cu^{II}**.

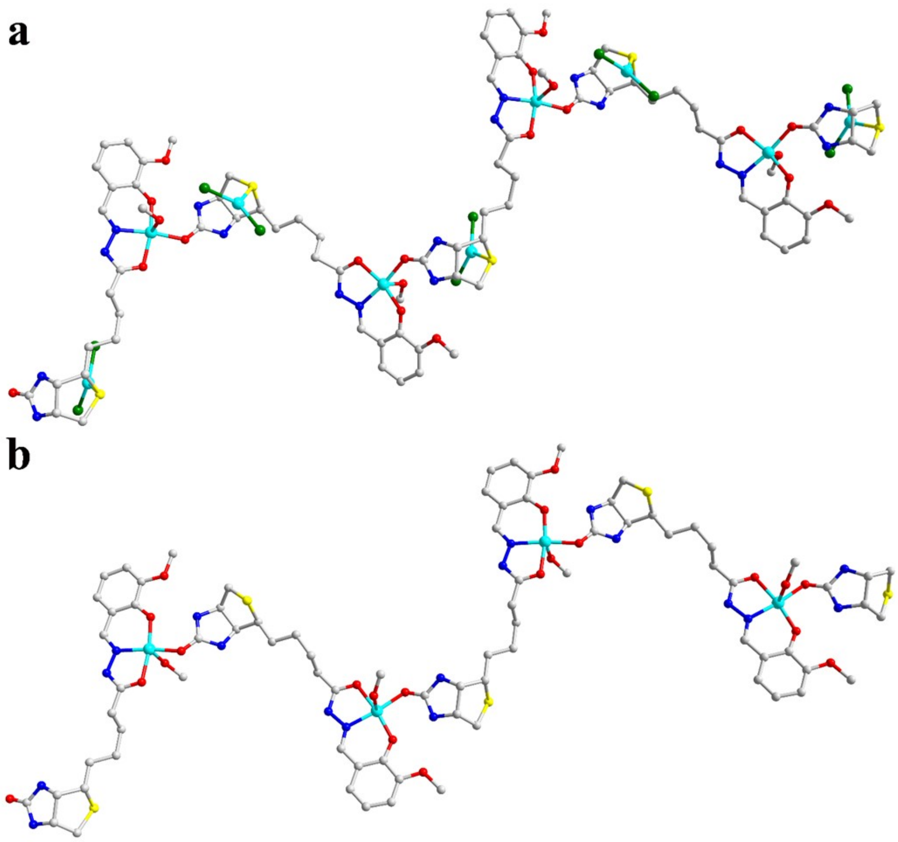


Fig. S1. 1D crystalline structure of **VBio-Cu^{I}Cu^{II}** (a) and **VBio-Cu^{II}** (b) (hydrogen atoms are omitted for clarity).

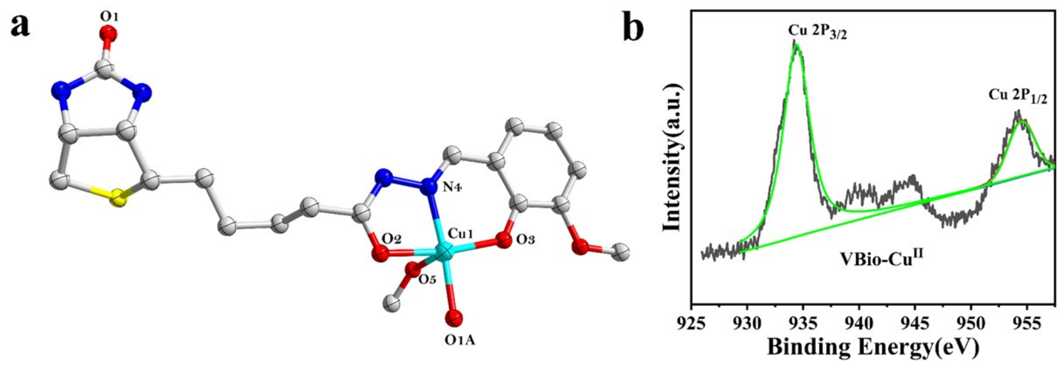


Fig. S2. (a) Crystal structure of **VBio-Cu^{II}**, anions, hydrogen atoms and solvent molecules are omitted for clarity. (b) XPS spectrum of **VBio-Cu^{II}**. The XPS data confirmed the only presence of Cu(II) in complex **VBio-Cu^{II}**, which exhibited Cu $2p_{3/2}$ and Cu $2p_{1/2}$ peaks at 933.7 and 953.8 eV.[1-2]

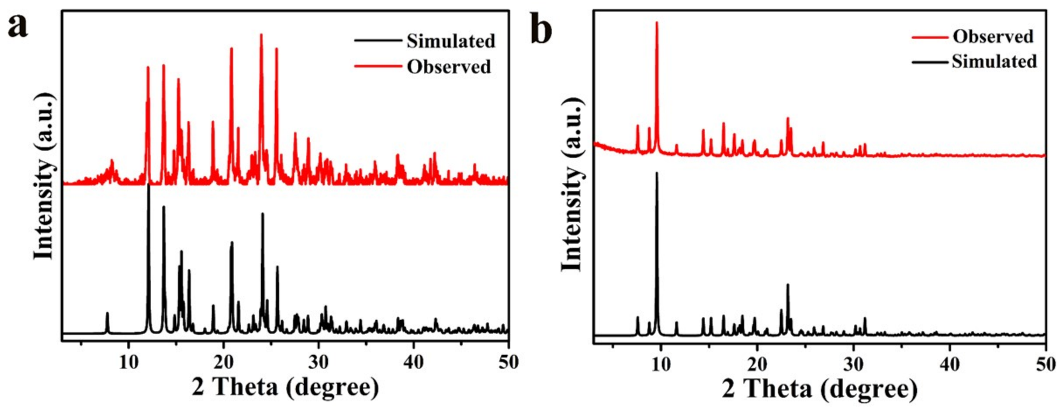
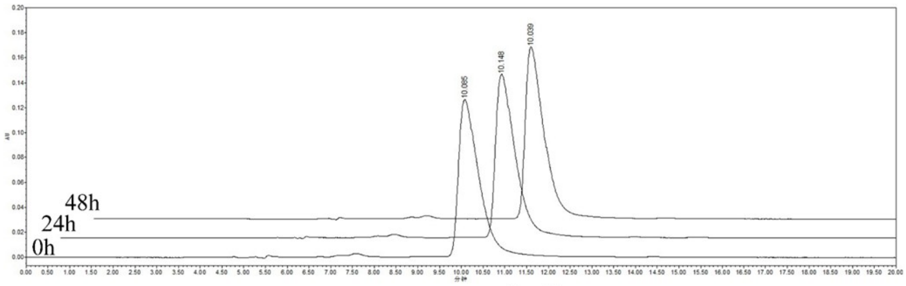
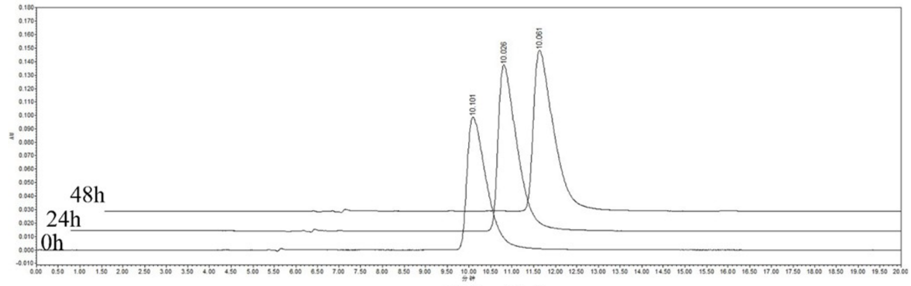


Fig. S3. XRD analysis of **VBio-Cu^{I}Cu^{II}** (a) **and VBio-Cu^{II}** (b).



VBio-Cu^{I}Cu^{II}



VBio-Cu^{II}

Fig. S4. Stability test of **VBio-Cu^{I}Cu^{II}** and **VBio-Cu^{II}** after incubation in PBS (pH=7.4) for different times.

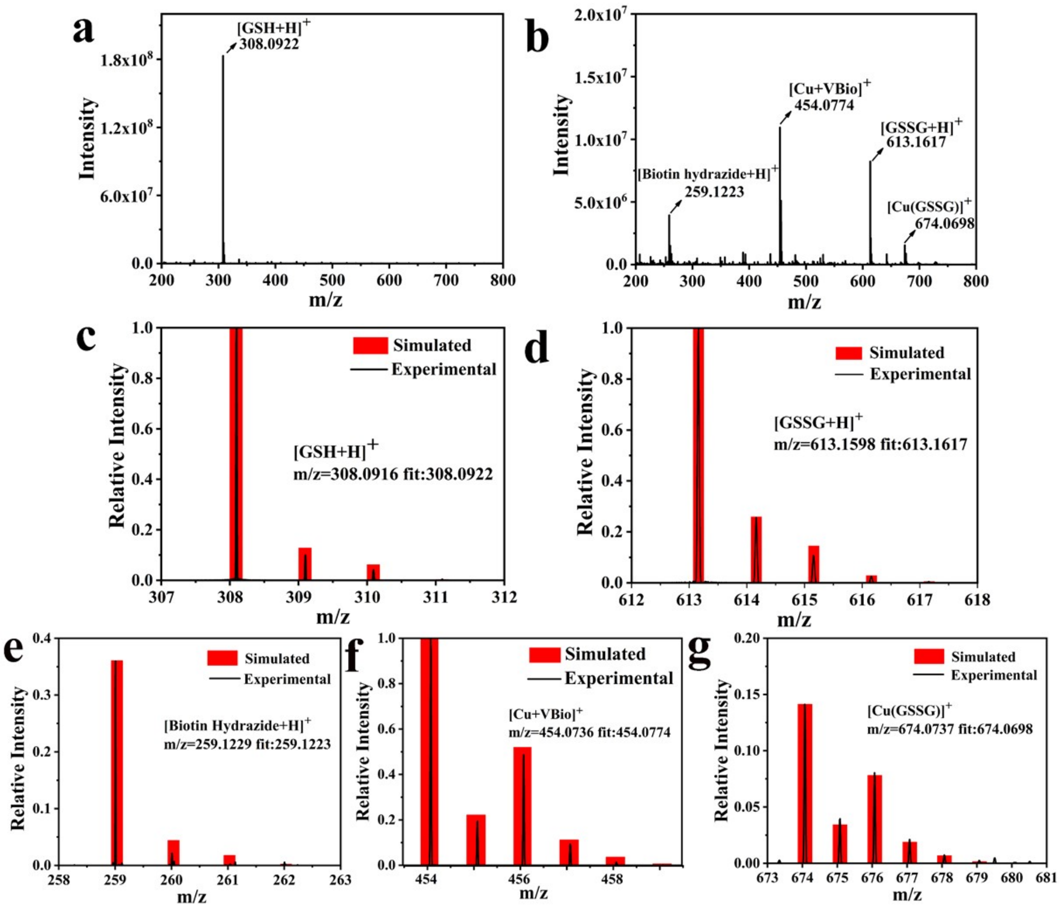


Fig. S5. High resolution mass spectrometry before (a) and after (b) the addition of **VBio-Cu^{I}Cu^{II}** into GSH solution under nitrogen atmosphere in PBS (pH=7.4, 5 % DMF). (c) Corresponding superposed simulated and experimental spectra from (a). (d-g) Corresponding superposed simulated and experimental spectra from (b).

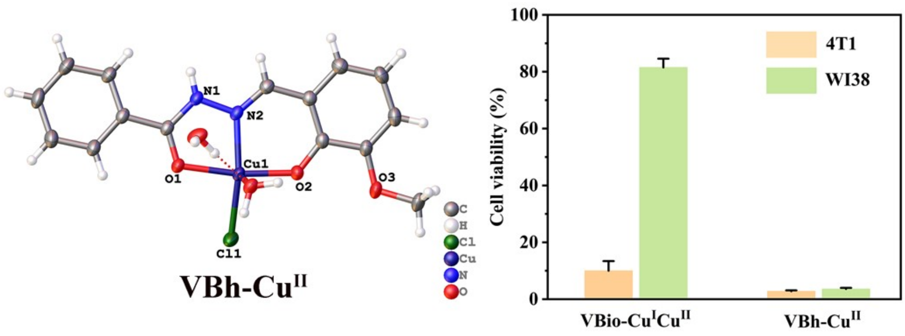


Fig. S6. Crystal structure of **VBh-Cu^{II}** (left). Cell viability of 4T1/WI38 cells after treatment with 25 μM **VBio-Cu^{I}Cu^{II}** (presence of 100 μM H_2O_2) or **VBh-Cu^{II}** for 48 h (right).

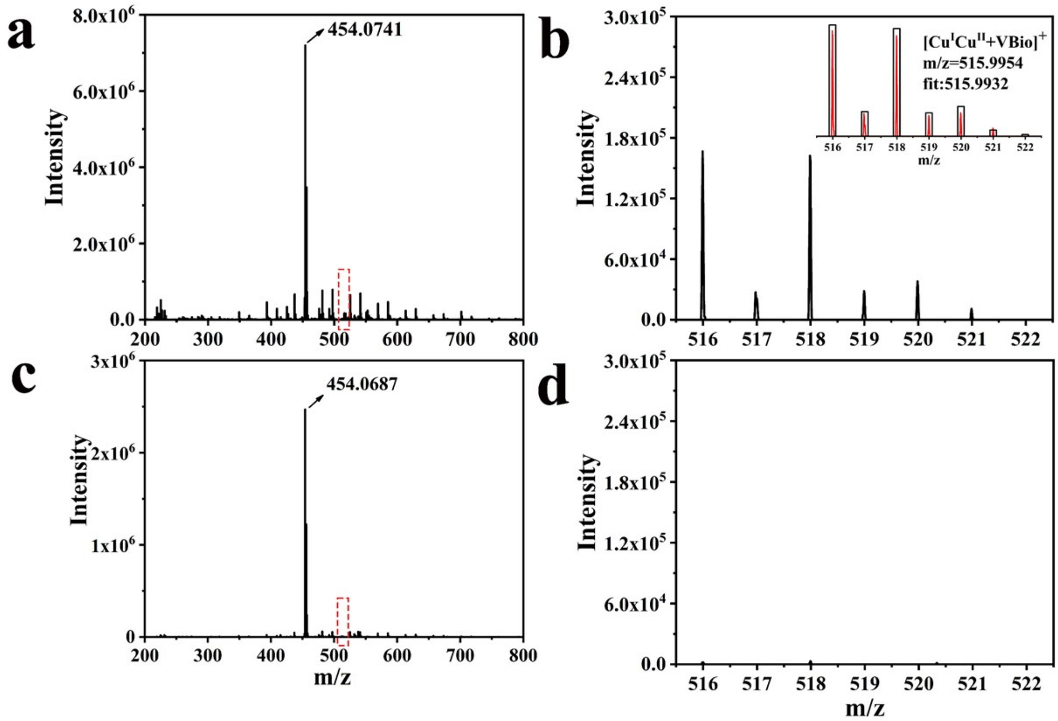


Fig. S7. (a-b) High resolution mass spectrometry and corresponding amplification area of **VBio-Cu^{I}Cu^{II}**, insert in (b): corresponding superposed simulated and experimental spectra. (c-d) High resolution mass spectrometry and corresponding amplification area of **VBio-Cu^{II}**.

Table S1. Crystal data and structure refinement for two complexes.

Complex	**VBio-Cu^I^Cu^II^**	**VBio-Cu^II^**
Empirical formula	$C_{19}H_{27}Cl_2Cu_2N_4O_5S$	$C_{19}H_{28}CuN_5O_9S$
Formula weight	621.48	566.06
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1$
a (Å)	6.8033 (6)	5.3882 (9)
b (Å)	22.7687 (12)	23.305 (2)
c (Å)	8.1373 (7)	10.0694 (13)
α (°)	90.00	90.00
β (°)	108.401 (9)	94.765 (15)
γ (°)	90.00	90.00
Volume (Å^3)	1196.04 (17)	1263.4 (3)
Z	2	2
D_{calc} (g cm^{-3})	1.726	1.729
F(000)	634	588
Reflections collected	7641	7309
Independent reflections	4494	4435
R_{int}	0.046	0.064
Goodness-of-fit on F^2	1.05	1.03
R_1, wR_2 [$I \geq 2\sigma (I)$]	0.0568, 0.0938	0.066, 0.01233
R_1, wR_2[all data]	0.0933, 0.1121	0.01275, 0.01651

Table S2. Selected bond lengths (Å) and angles (°) for two copper complexes.

VBio-Cu^{I}Cu^{II}			
Cu1—O3	1.891 (7)	Cu1—O5	2.314 (9)
Cu1—N4	1.928 (8)	Cu2—Cl1	2.221 (4)
Cu1—O1A	1.947 (7)	Cu2—S1	2.235 (3)
Cu1—O2	2.005 (7)	Cu2—Cl2	2.260 (3)
O3—Cu1—N4	89.7 (3)	O3—Cu1—O5	95.2 (3)
O3—Cu1—O1A	96.7 (3)	N4—Cu1—O5	92.8 (4)
N4—Cu1—O1A	172.4 (4)	O1A—Cu1—O5	90.6 (3)
O3—Cu1—O2	165.0 (3)	O2—Cu1—O5	96.5 (3)
N4—Cu1—O2	80.4 (3)	Cl1—Cu2—S1	119.94 (13)
O1A—Cu1—O2	92.5 (3)	Cl1—Cu2—Cl2	115.50 (14)
S1—Cu2—Cl2	122.95 (13)		
VBio-Cu^{II}			
Cu1—O3	1.882 (6)	Cu1—O2	1.995 (6)
Cu1—N4	1.943 (8)	Cu1—O1A	1.927 (6)
Cu1—O5	2.365 (8)		
O3—Cu1—N4	90.9 (3)	O3—Cu1—O5	97.9 (3)
O3—Cu1—O2	168.9 (3)	O3—Cu1—O1A	95.9 (2)
N4—Cu1—O5	94.7 (3)	N4—Cu1—O2	81.1 (3)
O2—Cu1—O5	90.4 (3)	O1A—Cu1—N4	172.2 (3)
O1A—Cu1—O5	88.2 (3)	O1A—Cu1—O2	91.7 (3)

Reference

1. J. Wang, J. Ren, Q. Tang, X. Wang, Y. Wang, Y. Wang, Z. Du, W. Wang, L. Huang, L.A. Belfiore and J. Tang, An Efficient Cyan Emission from Copper (II) Complexes with Mixed Organic Conjugate Ligands, *Materials*, 2022, **15**, 1719.

2. B. Ma, S. Wang, F. Liu, S. Zhang, J. Duan, Z. Li, Y. Kong, Y. Sang, H. Liu, W. Bu and L. Li, Self-Assembled Copper-Amino Acid Nanoparticles for in Situ Glutathione ″AND″ H_2O_2 Sequentially Triggered Chemodynamic Therapy, *J. Am. Chem. Soc.*,

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