## **Electronic Supplementary Information**

## The Roles of Surface Chemistry, Dissolution Rate, and Delivered Dose in the

## **Cytotoxicity of Copper Nanoparticles**

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Figure S1. ATR-IR spectra of TA: (a) pure sample and (b) on the surface of copper nanoparticles.



**Figure S2.** Dissolution kinetic curves for Cu-MHA at the concentration of (a) 10, (b) 25, (c) 50 and (d) 100  $\mu$ g/mL, respectively.



**Figure S3.** *In vitro* dosimetry of copper samples at (a) 1, (b) 50, and (c) 100  $\mu$ g/mL, respectively (S: copper in supernatant, not associated with cells; P: copper in pellet, associated with cells).



**Figure S4.** Luciferase response plots of intensity at a function of log (concentration) at exposure time of 24 h.



Figure S5. TEM micrograph of Cu-MOA (25  $\mu$ g/mL) incubated with A549luc cells for 4 h exposure.



**Figure S6.** TEM micrographs of (a, b) Cu-MOA, (c, d) Cu-MDA, (e, f) Cu-MHA and (g. h) Cu-TA after the oxidation for (a, c, e, g) 20 and (b, d, f, h) 48 h, respectively, in PBS at room temperature. Insets are corresponding photographs of the samples after oxidation.

Amount (µg-Cu/mL)	10	25	50	100	Mean±SD
Cu-MOA*	(2.62)	(2.46)	(2.70)	(2.08)	(2.47±0.27)
Cu-MDA	1.41	1.65	1.36	0.91	1.33±0.31
Cu-MHA	1.68	1.79	1.68	1.13	1.57±0.30
Cu-TA*	(5.89)	(5.53)	(4.31)	(4.36)	(5.02±0.81)

Table S1. Values of reaction order of copper in its dissolution at different concentrations

\*  $R^2$  values for these two samples are < 0.9, thus the reactions were complex and could not be analyzed as simple dissolutions, so the values are shown in parentheses.

Table S2. S<sub>max</sub> of luciferase response of copper samples at exposure time of 24 h without defining  $I_t$ .

		$\mathcal{O}$ $l^{2}$					
Type of Cu NPs	Cu-MOA	Cu-MDA	Cu-MHA	Cu-TA			
$S_{max}$ (ug-Cu/mL)*	$3194 \pm 2405$	$236 \pm 122$	$398 \pm 349$	$367 \pm 113$			
$\max(\mathbf{P} \mathbf{B} + \mathbf{m})$							
* Average with standard deviation.							

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