Supporting Information

Structure-Activity Relationships for Biodistribution, Pharmacokinetics and Excretion of Atomically Precise Nanoclusters in a Murine Model

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Table of Contents

Fig. S1: Polyacrylamide gel of Au\(_{102}(p\text{MBA})_{44}\) S2

Fig. S2: Graph of relative amounts of compounds 1-3 in urine and feces S2

Fig. S3: Graph of relative amounts of compounds 4,5, and the Au\(_{102}\) 1:1 exchange compound in urine and feces S3

Fig. S4-S7: Atomistic models of Au\(_{25}\)-based compounds S3-S5

Fig. S8-S10: Atomistic models of Au\(_{102}\)-based compounds S5-S6

The chemical and biological properties of the compounds discussed in the main text are calculated and predicted from the atomistic models in Fig. S4-S10

Fig. S11-S13: Percent dosed in tissues of the Au\(_{25}\)-based compounds S7-S8

Fig. S14-S15: Percent dosed in tissues of the Au\(_{102}\)-based compounds S8-S9

Fig. S16: \(^1\)H NMR of compound 5 S9

Table S1: Information on Au\(_{102}\)-based 1:1 ligand exchange compound S10

Fig. S17: Blood drug concentration vs. time curves of Au\(_{102}\)-based compounds S10
Fig. S1 Polyacrylamide gel electrophoresis of \( \text{Au}_{102}(p\text{MBA})_{44} \) that shows the purity of the compound.

Fig. S2 Relative amounts of compounds 1-3 in urine and feces at 6, 12, and 24 hours post injection time.
**Fig. S3** Relative amounts of compounds 4, 5, and the 1:1 exchange Au\(_{102}\)-based compound (Au\(_{102}\)PMBA\(_{44}\) exchanged with HS-(CH\(_2\))\(_{11}\)EG\(_4\)-OH) in urine and feces at 6, 12, and 24 hours post injection time.

**Fig. S4** Au\(_{25}\)(GSH)\(_{18}\), Compound 1
**Fig. S5** $\text{Au}_{25}(\text{GSH})_9(\text{OEG})_9$, (OEG = HS-(CH$_2$)$_6$-EG-OH), Compound 2

**Fig. S6** $\text{Au}_{25}(\text{GSH})_6(\text{OEG})_{12}$, (OEG = HS-(CH$_2$)$_6$-EG-OH), Compound 3
**Fig. S7** \( \text{Au}_{25}(\text{OEG})_{18}, \) (OEG = HS-(CH\(_2\))\(_6\)-EG-OH)

**Fig. S8** \( \text{Au}_{102}(\rho\text{MBA})_{44}, \) Compound 4
**Fig. S9** \( \text{Au}_{102}(\rho\text{MBA})_{25}(\text{OEG})_{19}, \text{(OEG} = \text{HS-(CH}_2\text{)}_{11}\text{-EG-OH}) \), Compound 5

**Fig. S10** \( \text{Au}_{102}(\text{OEG})_{44}, \text{(OEG} = \text{HS-(CH}_2\text{)}_{11}\text{-EG-OH}) \)
**Fig. S11** Percent dosed in tissue for compound 1 at noted post-injection time points.

**Fig. S12** Percent dosed in tissue for compound 2 at noted post-injection time points.
Fig. S13 Percent dosed in tissue for compound 3 at noted post-injection time points.

Fig. S14 Percent dosed in tissue for compound 4 at noted post-injection time points. Data points of liver are not included.
**Fig. S15** Percent dosed in tissue for compound 5 at noted post-injection time points. Data points of liver are not included.

**Fig. S16** $^1$H NMR of compound 5
Table S1 Information on Au$_{102}$-based 1:1 exchanged compound

<table>
<thead>
<tr>
<th>Calculated Stokes Diameter (nm)$^a$</th>
<th>Net Surface Charge (e$^-$)</th>
<th>Surface Charge Density (Charge/Å$^2$)</th>
<th>Hydrophobic Surface Area (%)</th>
<th>Expected Clearance Mechanism % Renal / % RES</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.92</td>
<td>22$^-$</td>
<td>1.8×10$^{-4}$ (-)</td>
<td>74%</td>
<td>40 / 60</td>
</tr>
</tbody>
</table>

Ligand exchange reaction of Au$_{102}$(pMBA)$_{44}$ with 23-mercapto-3,6,9,12-tetraoxatricosan-1-ol [HS-(CH$_2$)$_{11}$-EG$_4$-OH]

A 500 µM solution of Au$_{102}$pMBA$_{44}$ (6.6 µmol, 178 mg in 13.37 mL H$_2$O) and a 0.1 M solution of HS-(CH$_2$)$_{11}$-EG$_4$-OH (0.79 mmol, 304 mg in 7.90 mL THF) were prepared. For the 1:1 incoming ligand:outgoing ligand reaction: 3 mL of Au$_{102}$pMBA$_{44}$ solution and 0.66 mL of HS-(CH$_2$)$_{11}$-EG$_4$-OH solution were mixed and diluted with H$_2$O to a final volume of 15 mL. Then the reaction was shaken at rt for 1 h, then the crude product was purified by ultrafiltration spin columns (5000 Da cutoff) and was washed with 3 x 10 mL 1:1 H$_2$O:MeOH. The remaining orange liquid was placed into a 15 mL conical and lyophilized until dry.

The Au$_{102}$-based 1:1 exchanged compound was dissolved in 5% DMSO, 5% Tween-80 in 90% D5W solution. The particle solutions were filtered through a 0.45 micron filter, and the dosage concentrations were determined after the filtration step. Approximate dosage concentration for this compound was 3.14 x 10$^{-5}$ M.

Fig. S17 Blood drug concentration vs. time curves of Au$_{102}$-based compounds