Supporting Information

Surface-enhanced resonance Raman scattering guided brain tumor surgery showing prognostic benefit in rat models

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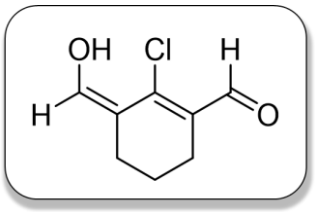
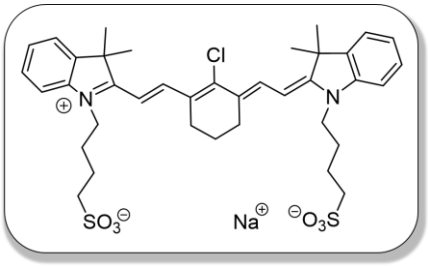
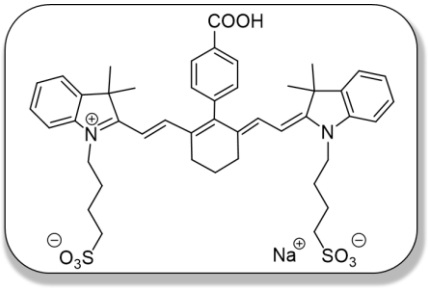
1. Synthesis of molecular reporter IR7-SH



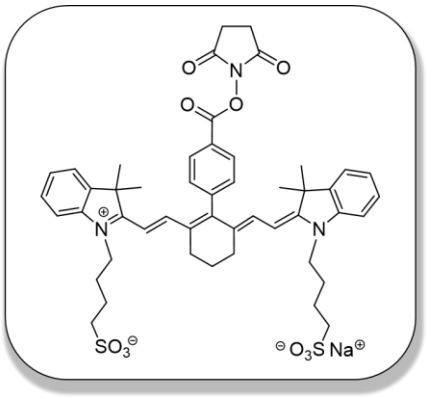
1.1 Synthesis of compound 1. Mixing 8.0 mL *N*,*N*-dimethylformamide (DMF) with 8.0 mL dichloromethane (DCM) and 7.2 mL $POCl_3$ in 7 mL DCM to obtain solution 1 and solution 2 respectively. Dropwise adding solution 2 into solution 1 in ice bath offered solution 3. Then cyclohexanone (2.0 g, 20.4 mM) in 10 mL DCM was dropwise added into solution 3. After continuously stirring at 65 ℃ for 3 h, the reactive mixture was poured into 50 g ice. The water-layer was collected and filtered to obtain aiming product as a yellow solid (2.75g, 15.9 mM, yield: 78%).



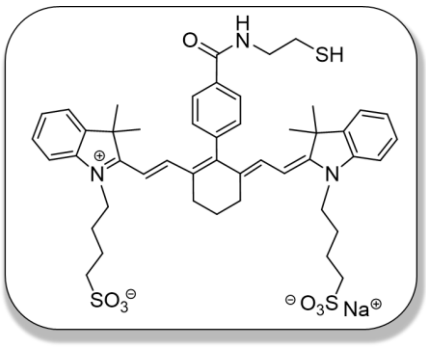
1.3. Synthesis of IR783. Sodium acetate (0.11 g, 1.4 mM), compound 1 (0.12 g, 0.7 mM) and 2 (0.41 g, 1.4 mM) were solved in acetic anhydride (13 mL). The mixture was stirred for 40 min at 70 ℃. After cooling down to room temperature, superfluous ice-cold diethyl ether was added and obtained a green color powder after filtration. The solid was further purified via silica gel chromatography (CH_2Cl_2:CH_3OH=10:3) to give pure product (0.44 g, 0.59 mM, yield: 84%).



1.4. Synthesis of compound 2. IR783 (0.3 g, 0.4 mM), potassium carbonate (120 mg, 0.86 mM) and 4-hydroxyphenylboronic acid (120 mg, 0.72 mM) were dissolved in water (2 mL). The solution was heated to 95 ℃ before tetrakis(triphenylphosphine)palladium (27 mg, 0.023 mM) was added. The mixture was stirred for 2 h and TLC showed new compound has been produced. The product was purified via silica gel chromatography (CH_2Cl_2:CH_3OH=10:3) to give the purple solid (0.29 g, 0.35 mM, yield: 88%).



1.5 Synthesis of compound 3. Compound 3 (190 mg, 0.24 mM) was dissolved in anhydrous DMF (4 mL) and N-hydroxysuccinimide (33 mg, 0.29 mM) and 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide was then added for reaction. The mixture was kept in dark for 12 h to get a green solution. A dark green precipitate was obtained after the solution was added dropwise to iced diethyl ether (50 mL) and filtered. The precipitated was washed 2-3 times by anhydrous acetonitrile and then dissolved by iced water less than 5 mL (pH = 4-6). The product was dried under vacuum to give a loose green solid (183 mg ,0.2 mM, yield: 82%).



1.6 Synthesis of IR783-SH. Compound 3 (64 mg, 0.07mM) was mixed with cysteamine hydrochloride (4.79 mg, 0.042 mM) and trimethylamine (4.98 mg, 0.049mM) in anhydrous DMF and reacted in dark for 8 h to get a green mixture. The solution was added dropwise to iced diethyl ether (50 mL) and a green precipitate was obtained after filtration. The solid was washed 2-3 times by anhydrous acetonitrile and then dissolved by iced water less than 5 mL (pH = 4-6). The product was dried under vacuum to give a loose green solid (48.8 mg, 0.054 mM, yield: 78%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.09 (d, J = 7.1 Hz, 2H), 7.58 – 7.44 (m, 1H), 7.33 – 7.25 (m, 6H), 7.21 (d, J = 6.7 Hz, 2H), 7.12 (t, J = 11.0 Hz, 4H), 6.18 (d, J = 13.9 Hz, 2H), 4.06 (s, 4H), 3.74 (t, J = 7.8 Hz, 2H), 2.84 – 2.79 (m, 6H), 2.71 – 2.67 (m, 4H), 1.85 (m, 10H), 1.54 (t, 1H), 1.10 (m, J = 10.4 Hz, 12H). ^{13}C NMR (151 MHz, MeOD) δ 178.55, 173.34, 149.21, 144.31, 143.62, 142.15, 135.29, 132.73, 131.13, 129.76, 128.81, 126.00, 123.31, 119.68, 111.93, 101.21, 51.83, 49.85, 44.78, 38.39, 28.06, 27.22, 26.90, 25.66, 23.57, 22.51.

2. Hydrodynamic diameter and Zeta potential of AuS-IR7

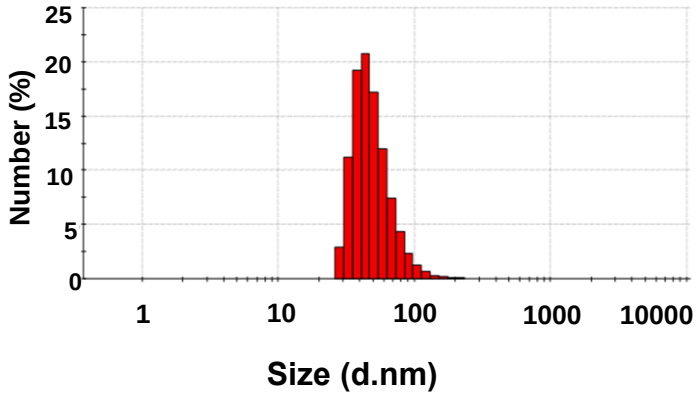


Figure S1. Hydrodynamic diameter of **AuS-IR7**.

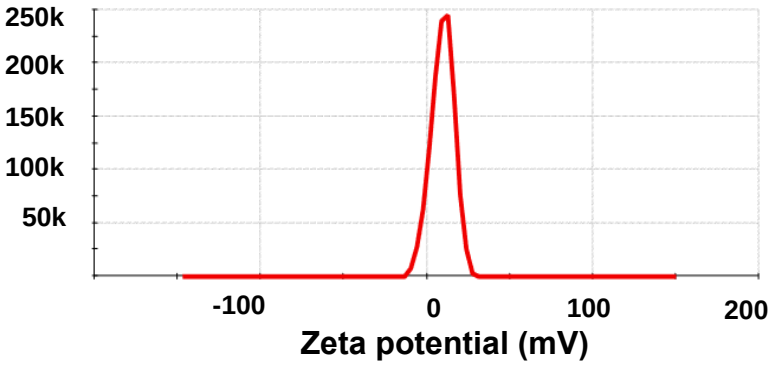


Figure S2. Zeta potential of **AuS-IR7**.

3. Development of mouse dorsal skin window chamber

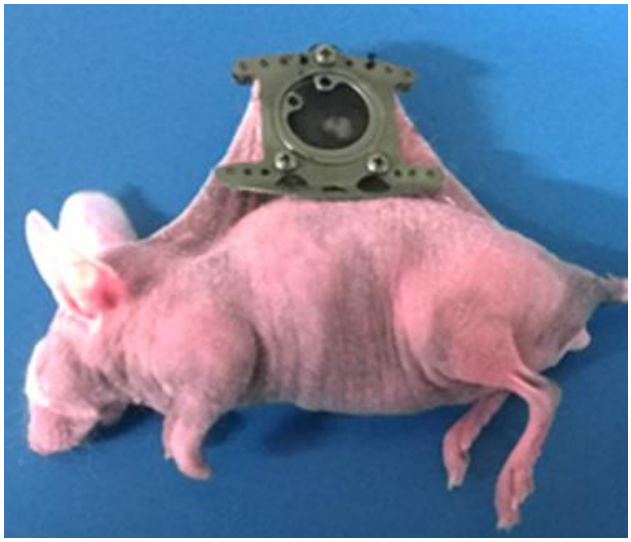


Figure S3. Picture of mouse dorsal skin window chamber model bearing a C6 glioma xenograft.

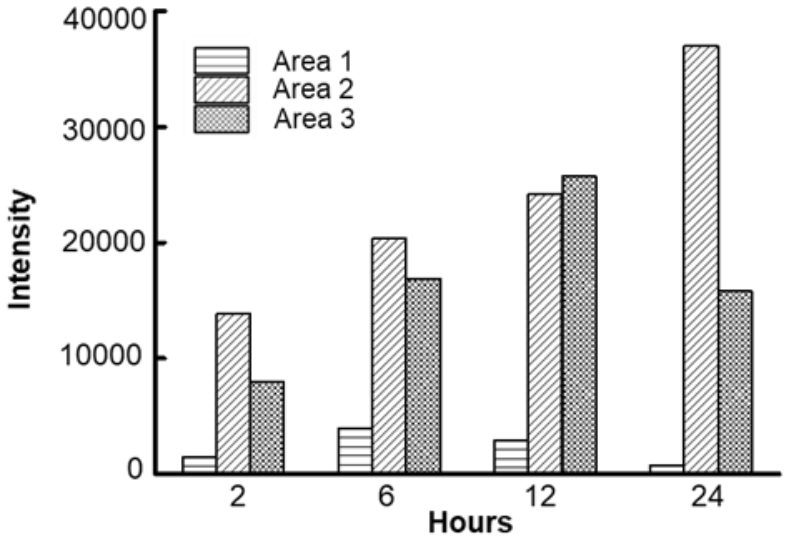
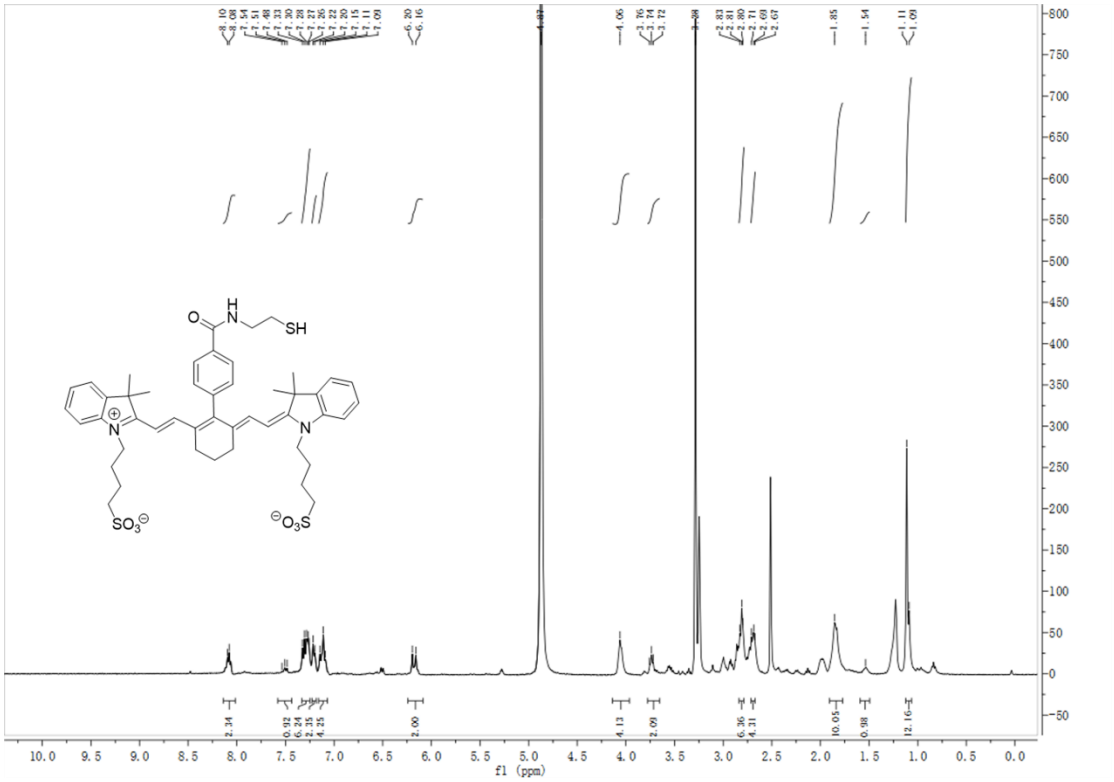
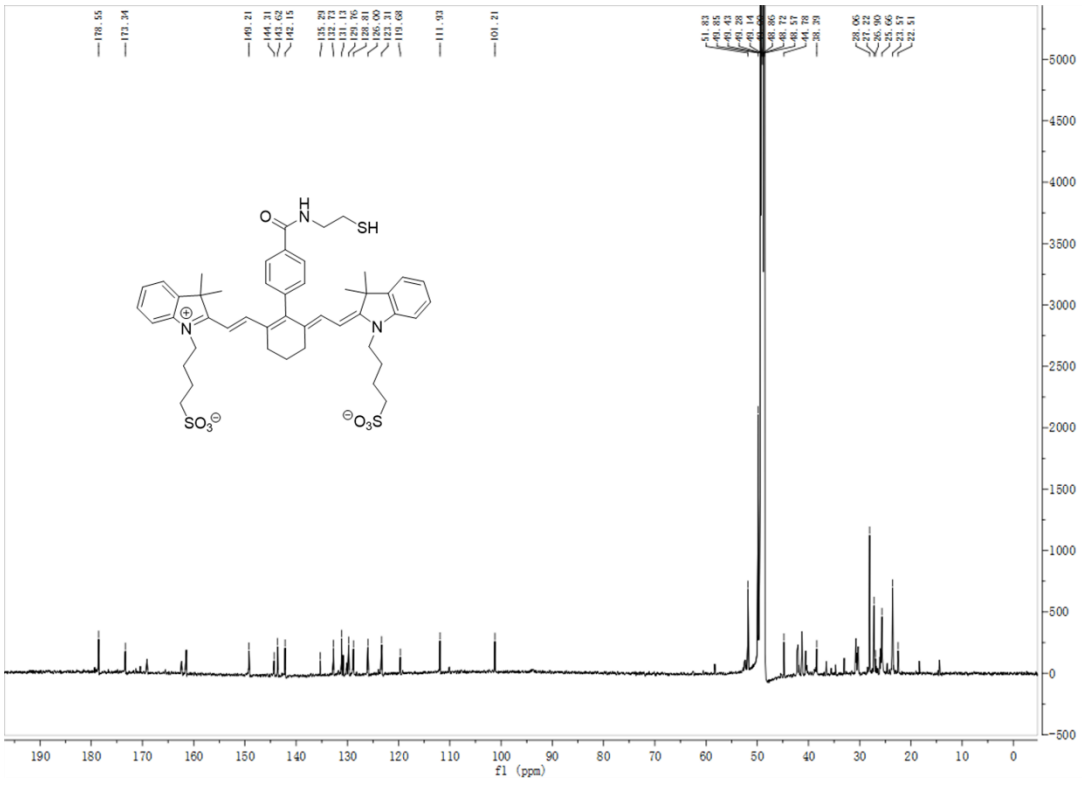


Figure S4. Raman signal intensities at the selected locations in mouse dorsal skin window chamber at 2, 6, 12 and 24 h post **AuS-IR7** injection.

4. Supplemented spectra of IR7-SH



^{1}H NMR spectrum of IR7-SH in CD_3OD-d_4.



^{13}C NMR spectrum of IR7-SH in MeOD.

5. Pictures of facilities used for in vivo visualization

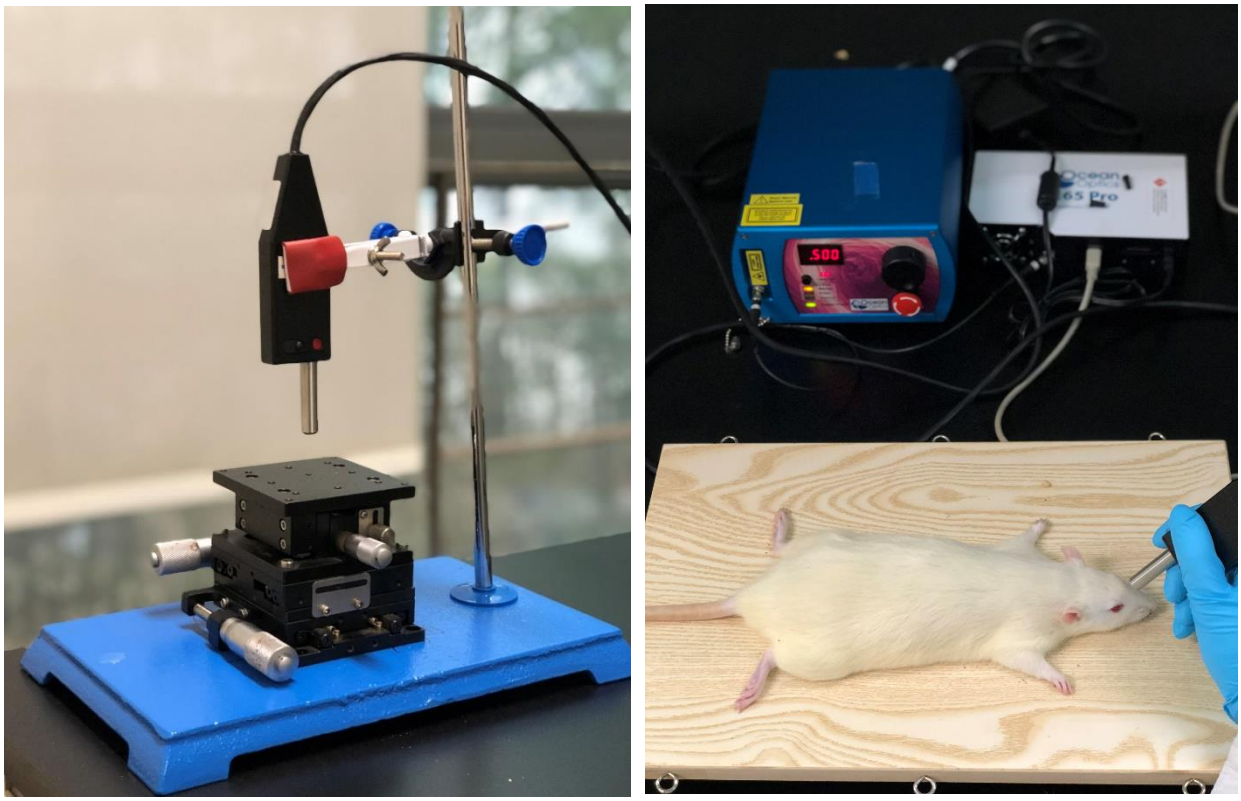


Figure S5. The pictures of facilities used for in vivo visualization of glioma in mouse skin window chamber (left) and SERRS-guided glioma surgery (right).