

## Supporting Information

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

*Limei Han<sup>a,+</sup>, Wenjia Duan<sup>a,+</sup>, Xinwei Li<sup>a,+</sup>, Cong Wang<sup>a</sup>, Ziyi Jin<sup>a</sup>, Yuting Zhai<sup>b,c</sup>,  
Chong Cao<sup>a</sup>, Luo Chen<sup>a</sup>, Wenjing Xu<sup>b,c</sup>, Ying Liu<sup>b,c</sup>, Yong-Yan Bai<sup>a</sup>, Jianfeng Feng<sup>b,c</sup>,  
Mao Ying<sup>d,e</sup>, Qi Yue<sup>\*d</sup>, Xiaoyong Zhang<sup>\*b,c</sup>, Cong Li<sup>\*a,f</sup>*

<sup>a</sup>Minhang Hospital and Key Laboratory of Smart Drug Delivery, Ministry of Education, School of Pharmacy, Fudan University, Shanghai, 201203, China

<sup>b</sup>Institute of Science and Technology for Brain-Inspired Intelligence, Fudan University, Shanghai 200433, China

<sup>c</sup>Key Laboratory of Computational Neuroscience and Brain-Inspired Intelligence, Ministry of Education, Fudan University, Shanghai 200433, China

<sup>d</sup>Department of Neurosurgery, Huashan Hospital, Fudan University, Shanghai 200040, China

<sup>e</sup>State Key Laboratory of Medical Neurobiology, School of Basic Medical Sciences and Institutes of Brain Science, Fudan University, Shanghai 200032, China

<sup>f</sup>Institute of Functional and Molecular Medical Imaging, Department of Radiology, Huashan Hospital, Fudan University, Shanghai 200040, China

\*Corresponding Author:

\*E-mail: congli@fudan.edu.cn

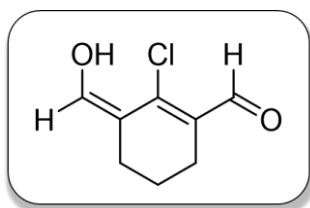
\*E-mail: xiaoyong\_zhang@fudan.edu.cn

\*E-mail: yueqi1989@126.com

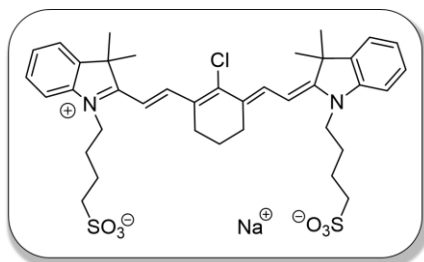
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## 1. Synthesis of molecular reporter IR7-SH

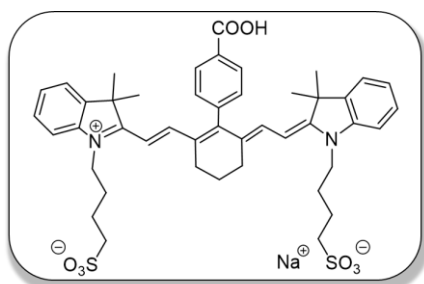


**1.1 Synthesis of compound 1.** Mixing 8.0 mL *N,N*-dimethylformamide (DMF) with 8.0 mL dichloromethane (DCM) and 7.2 mL POCl<sub>3</sub> in 7 mL DCM to obtain solution 1 and solution 2 respectively. Dropwise adding solution 2 into solution 1 in ice bath offered solution 3. Then cyclohexanone (2.0 g, 20.4 mM) in 10 mL DCM was dropwise added into solution 3. After continuously stirring at 65 °C 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%).



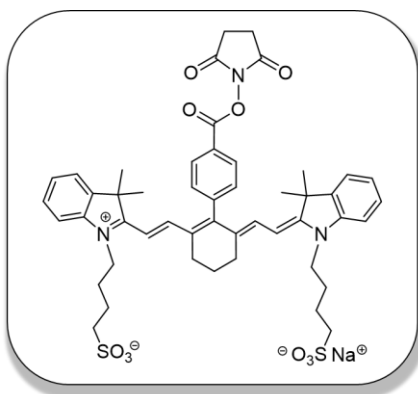
**1.3. Synthesis of IR783.** Sodium acetate (0.11 g, 1.4 mM), compound 1 (0.12 g, 0.7 mM) and 2 (0.41 g, 1.4 mM) were solved in acetic anhydride (13 mL). The mixture was stirred for 40 min at 70 °C. After cooling down to room temperature, superfluous ice-cold diethyl ether was added

and obtained a green color powder after filtration. The solid was further purified via silica gel chromatography (CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH=10:3) to give pure product (0.44 g, 0.59 mM, yield: 84%).



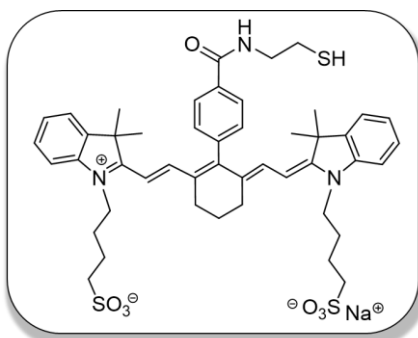
**1.4. Synthesis of compound 2.** IR783 (0.3 g, 0.4 mM), potassium carbonate (120 mg, 0.86 mM) and 4-hydroxyphenylboronic acid (120 mg, 0.72 mM) were dissolved in water (2 mL). The solution was heated to 95 °C before tetrakis(triphenylphosphine)palladium (27

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<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>OH=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%). <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) 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). <sup>13</sup>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

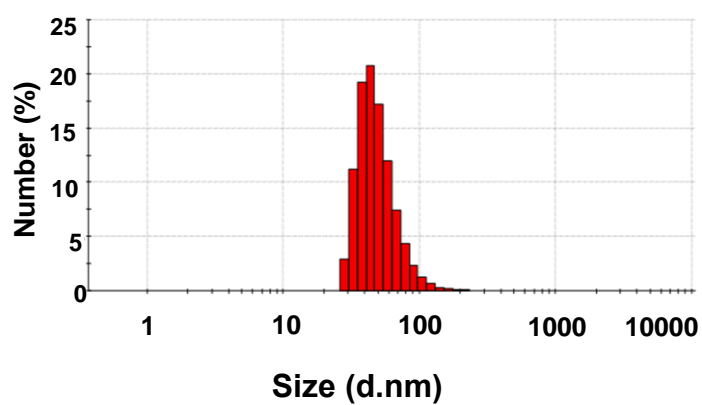


Figure S1. Hydrodynamic diameter of **AuS-IR7**.

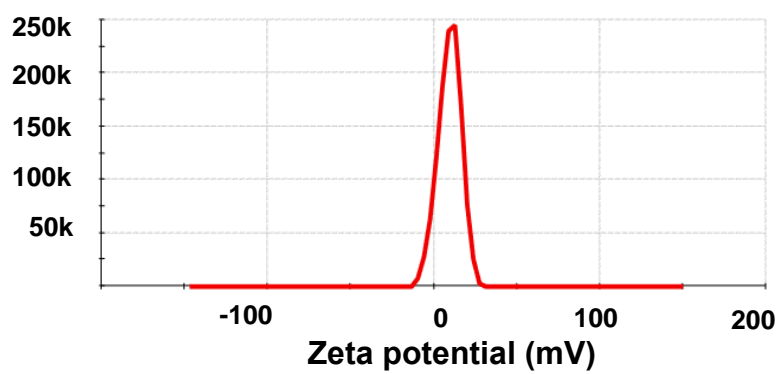


Figure S2. Zeta potential of **AuS-IR7**.

### 3. Development of mouse dorsal skin window chamber

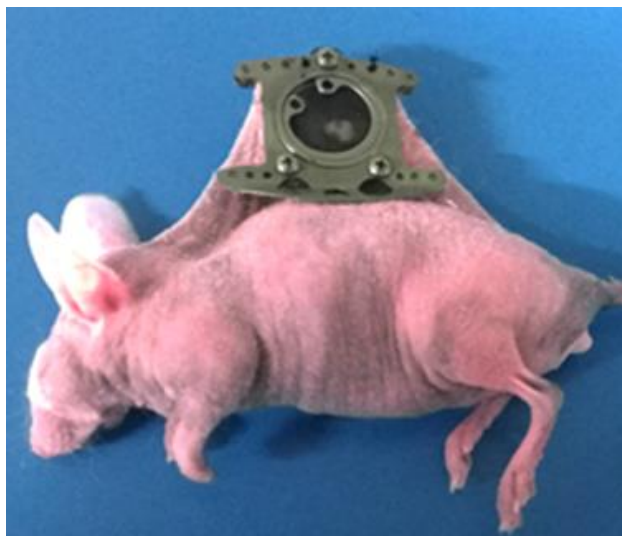


Figure S3. Picture of mouse dorsal skin window chamber model bearing a C6 glioma xenograft.

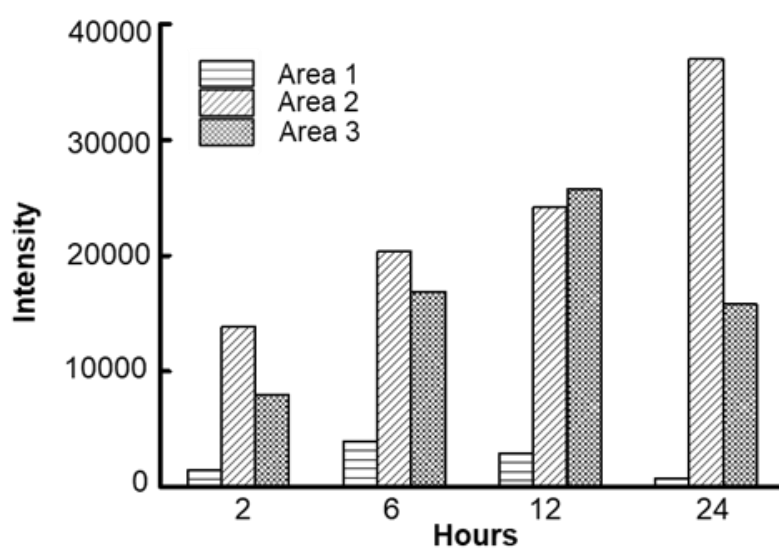


Figure S4. Raman signal intensities at the selected locations in mouse dorsal skin window chamber at 2, 6, 12 and 24 h post **AuS-IR7** injection.

**Chemical Structure of 10:** CC1(C)C(=C2C(=CC=C2N1CCCC[S-](=O)(=O)[O-])C=C3C(=C(C(=C3)C(=C4C(=CC=C4)C(=C5C(=CC=C5)C(=O)NCCS)C=C6C(=CC=C6)C(=C7C(=CC=C7)N(C)C)C=C8C(=CC=C8)C(=C9C(=CC=C9)C(=C10C(=CC=C10)C(=C11C(=CC=C11)C(=C12C(=CC=C12)C(=C13C(=CC=C13)C(=C14C(=CC=C14)C(=C15C(=CC=C15)C(=C16C(=CC=C16)C(=C17C(=CC=C17)C(=C18C(=CC=C18)C(=C19C(=CC=C19)C(=C20C(=CC=C20)C(=C21C(=CC=C21)C(=C22C(=CC=C22)C(=C23C(=CC=C23)C(=C24C(=CC=C24)C(=C25C(=CC=C25)C(=C26C(=CC=C26)C(=C27C(=CC=C27)C(=C28C(=CC=C28)C(=C29C(=CC=C29)C(=C30C(=CC=C30)C(=C31C(=CC=C31)C(=C32C(=CC=C32)C(=C33C(=CC=C33)C(=C34C(=CC=C34)C(=C35C(=CC=C35)C(=C36C(=CC=C36)C(=C37C(=CC=C37)C(=C38C(=CC=C38)C(=C39C(=CC=C39)C(=C40C(=CC=C40)C(=C41C(=CC=C41)C(=C42C(=CC=C42)C(=C43C(=CC=C43)C(=C44C(=CC=C44)C(=C45C(=CC=C45)C(=C46C(=CC=C46)C(=C47C(=CC=C47)C(=C48C(=CC=C48)C(=C49C(=CC=C49)C(=C50C(=CC=C50)C(=C51C(=CC=C51)C(=C52C(=CC=C52)C(=C53C(=CC=C53)C(=C54C(=CC=C54)C(=C55C(=CC=C55)C(=C56C(=CC=C56)C(=C57C(=CC=C57)C(=C58C(=CC=C58)C(=C59C(=CC=C59)C(=C60C(=CC=C60)C(=C61C(=CC=C61)C(=C62C(=CC=C62)C(=C63C(=CC=C63)C(=C64C(=CC=C64)C(=C65C(=CC=C65)C(=C66C(=CC=C66)C(=C67C(=CC=C67)C(=C68C(=CC=C68)C(=C69C(=CC=C69)C(=C70C(=CC=C70)C(=C71C(=CC=C71)C(=C72C(=CC=C72)C(=C73C(=CC=C73)C(=C74C(=CC=C74)C(=C75C(=CC=C75)C(=C76C(=CC=C76)C(=C77C(=CC=C77)C(=C78C(=CC=C78)C(=C79C(=CC=C79)C(=C80C(=CC=C80)C(=C81C(=CC=C81)C(=C82C(=CC=C82)C(=C83C(=CC=C83)C(=C84C(=CC=C84)C(=C85C(=CC=C85)C(=C86C(=CC=C86)C(=C87C(=CC=C87)C(=C88C(=CC=C88)C(=C89C(=CC=C89)C(=C90C(=CC=C90)C(=C91C(=CC=C91)C(=C92C(=CC=C92)C(=C93C(=CC=C93)C(=C94C(=CC=C94)C(=C95C(=CC=C95)C(=C96C(=CC=C96)C(=C97C(=CC=C97)C(=C98C(=CC=C98)C(=C99C(=CC=C99)C(=C100C(=CC=C100)C(=C101C(=CC=C101)C(=C102C(=CC=C102)C(=C103C(=CC=C103)C(=C104C(=CC=C104)C(=C105C(=CC=C105)C(=C106C(=CC=C106)C(=C107C(=CC=C107)C(=C108C(=CC=C108)C(=C109C(=CC=C109)C(=C110C(=CC=C110)C(=C111C(=CC=C111)C(=C112C(=CC=C112)C(=C113C(=CC=C113)C(=C114C(=CC=C114)C(=C115C(=CC=C115)C(=C116C(=CC=C116)C(=C117C(=CC=C117)C(=C118C(=CC=C118)C(=C119C(=CC=C119)C(=C120C(=CC=C120)C(=C121C(=CC=C121)C(=C122C(=CC=C122)C(=C123C(=CC=C123)C(=C124C(=CC=C124)C(=C125C(=CC=C125)C(=C126C(=CC=C126)C(=C127C(=CC=C127)C(=C128C(=CC=C128)C(=C129C(=CC=C129)C(=C130C(=CC=C130)C(=C131C(=CC=C131)C(=C132C(=CC=C132)C(=C133C(=CC=C133)C(=C134C(=CC=C134)C(=C135C(=CC=C135)C(=C136C(=CC=C136)C(=C137C(=CC=C137)C(=C138C(=CC=C138)C(=C139C(=CC=C139)C(=C140C(=CC=C140)C(=C141C(=CC=C141)C(=C142C(=CC=C142)C(=C143C(=CC=C143)C(=C144C(=CC=C144)C(=C145C(=CC=C145)C(=C146C(=CC=C146)C(=C147C(=CC=C147)C(=C148C(=CC=C148)C(=C149C(=CC=C149)C(=C150C(=CC=C150)C(=C151C(=CC=C151)C(=C152C(=CC=C152)C(=C153C(=CC=C153)C(=C154C(=CC=C154)C(=C155C(=CC=C155)C(=C156C(=CC=C156)C(=C157C(=CC=C157)C(=C158C(=CC=C158)C(=C159C(=CC=C159)C(=C160C(=CC=C160)C(=C161C(=CC=C161)C(=C162C(=CC=C162)C(=C163C(=CC=C163)C(=C164C(=CC=C164)C(=C165C(=CC=C165)C(=C166C(=CC=C166)C(=C167C(=CC=C167)C(=C168C(=CC=C168)C(=C169C(=CC=C169)C(=C170C(=CC=C170)C(=C171C(=CC=C171)C(=C172C(=CC=C172)C(=C173C(=CC=C173)C(=C174C(=CC=C174)C(=C175C(=CC=C175)C(=C176C(=CC=C176)C(=C177C(=CC=C177)C(=C178C(=CC=C178)C(=C179C(=CC=C179)C(=C180C(=CC=C180)C(=C181C(=CC=C181)C(=C182C(=CC=C182)C(=C183C(=CC=C183)C(=C184C(=CC=C184)C(=C185C(=CC=C185)C(=C186C(=CC=C186)C(=C187C(=CC=C187)C(=C188C(=CC=C188)C(=C189C(=CC=C189)C(=C190C(=CC=C190)C(=C191C(=CC=C191)C(=C192C(=CC=C192)C(=C193C(=CC=C193)C(=C194C(=CC=C194)C(=C195C(=CC=C195)C(=C196C(=CC=C196)C(=C197C(=CC=C197)C(=C198C(=CC=C198)C(=C199C(=CC=C199)C(=C200C(=CC=C200)C(=C201C(=CC=C201)C(=C202C(=CC=C202)C(=C203C(=CC=C203)C(=C204C(=CC=C204)C(=C205C(=CC=C205)C(=C206C(=CC=C206)C(=C207C(=CC=C207)C(=C208C(=CC=C208)C(=C209C(=CC=C209)C(=C210C(=CC=C210)C(=C211C(=CC=C211)C(=C212C(=CC=C212)C(=C213C(=CC=C213)C(=C214C(=CC=C214)C(=C215C(=CC=C215)C(=C216C(=CC=C216)C(=C217C(=CC=C217)C(=C218C(=CC=C218)C(=C219C(=CC=C219)C(=C220C(=CC=C220)C(=C221C(=CC=C221)C(=C222C(=CC=C222)C(=C223C(=CC=C223)C(=C224C(=CC=C224)C(=C225C(=CC=C225)C(=C226C(=CC=C226)C(=C227C(=CC=C227)C(=C228C(=CC=C228)C(=C229C(=CC=C229)C(=C230C(=CC=C230)C(=C231C(=CC=C231)C(=C232C(=CC=C232)C(=C233C(=CC=C233)C(=C234C(=CC=C234)C(=C235C(=CC=C235)C(=C236C(=CC=C236)C(=C237C(=CC=C237)C(=C238C(=CC=C238)C(=C239C(=CC=C239)C(=C240C(=CC=C240)C(=C241C(=CC=C241)C(=C242C(=CC=C242)C(=C243C(=CC=C243)C(=C244C(=CC=C244)C(=C245C(=CC=C245)C(=C246C(=CC=C246)C(=C247C(=CC=C247)C(=C248C(=CC=C248)C(=C249C(=CC=C249)C(=C250C(=CC=C250)C(=C251C(=CC=C251)C(=C252C(=CC=C252)C(=C253C(=CC=C253)C(=C254C(=CC=C254)C(=C255C(=CC=C255)C(=C256C(=CC=C256)C(=C257C(=CC=C257)C(=C258C(=CC=C258)C(=C259C(=CC=C259)C(

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## 5. Pictures of facilities used for in vivo visualization

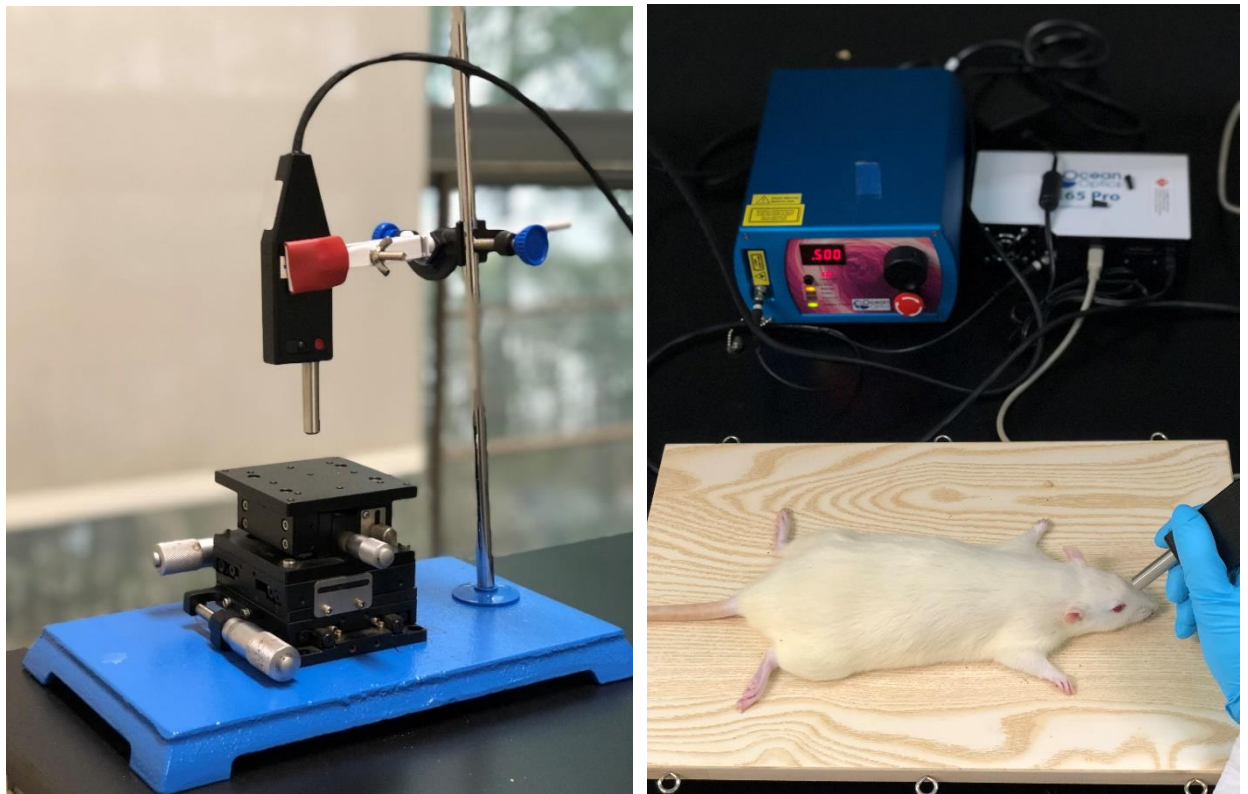


Figure S5. The pictures of facilities used for in vivo visualization of glioma in mouse skin window chamber (left) and SERRS-guided glioma surgery (right).