Electronic Supplementary Material (ESI) for Lab on a Chip.

Supplementary Information for

Versatile Tissue Lasers Based on High-Q Fabry-Pérot Microcavities

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1. Characteristics of the plano-plano and plano-concave FP cavities

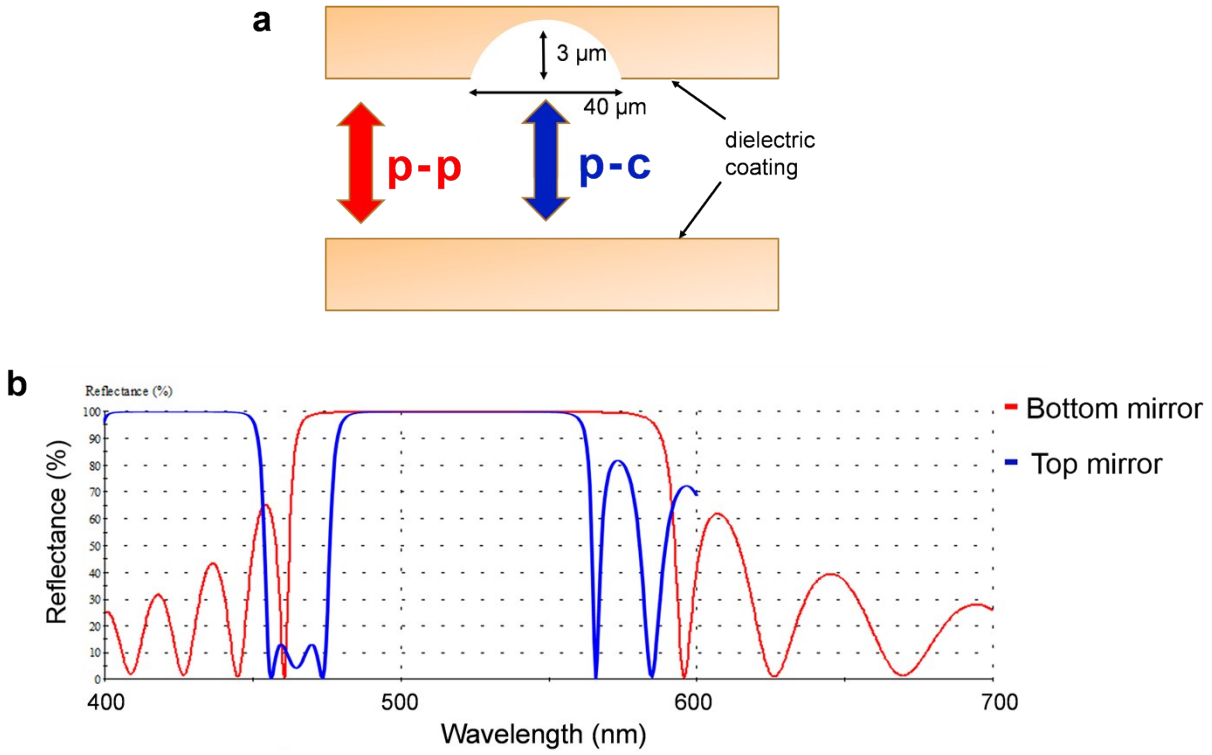

Figure S1. a, Schematic of the structure of the FP cavity, showing both the plano-plano (p-p) and the plano-concave (p-c) configuration. The concave well array on the top mirror was created using CO_2 laser ablation before dielectric coating. The two adjacent concave wells were 3 mm apart. The rest area on the mirror was flat. **b,** The reflectance spectra of the top mirror (blue curve) and the bottom mirror (red curve). Details of the fabrication of mirrors can be found in Methods and Ref. 1.

2. Laser emission spectra of pure FITC in water and pure BODIPY in ethanol

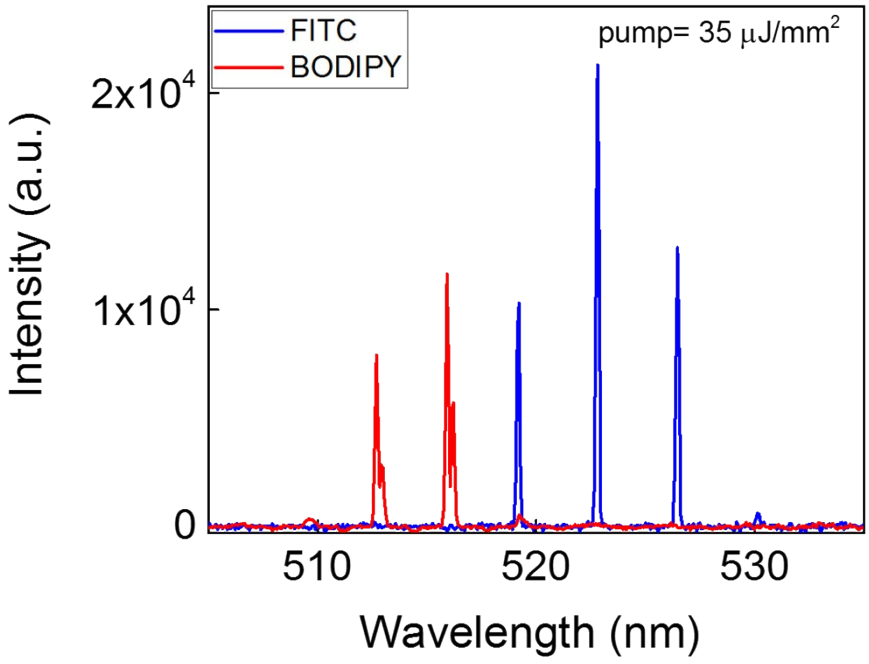

Figure S2. Laser emission spectra of FITC in water (blue curve), BODIPY in ethanol (red curve). Excitation wavelength=465 nm. Pump intensity=35 μJ/mm^2. [FITC]=2.0 mM. [BODIPY]=1.0 mM. Cavity length=30 μm. The lasing emission of FITC was within the range of 520 nm – 530 nm, whereas the lasing emission of BODIPY was within the range of 512 nm – 520 nm. The center of the lasing emission band for FITC is about 10 nm red-shifted with respect to that of BODIPY due to the slightly red-shift gain profile of FITC (see Fig. 1b). Note that the lasing emission band of both FITC and BODIY is much narrower than their respective fluorescence band. Consequently, the lasing emission can be distinguished between FITC and BODIPY, even though their fluorescence cannot be.

3. Simulation of lasing thresholds for FITC in muscle tissue

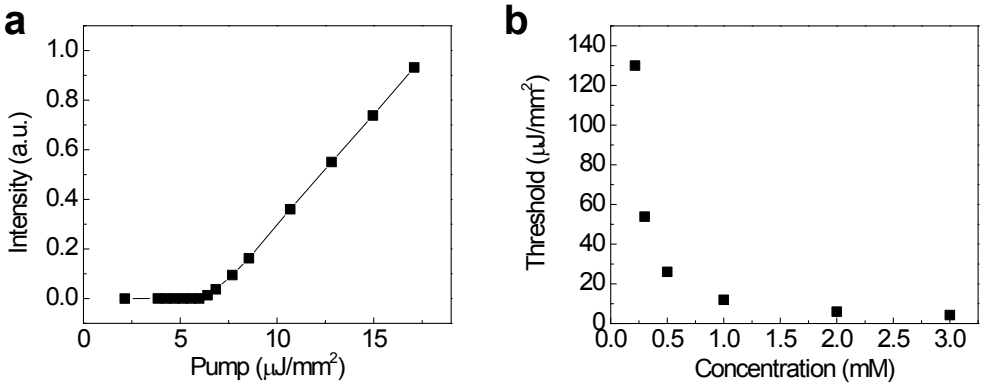

Figure S3. a, Lasing threshold simulation for the muscle tissue in the longitudinal direction shows a threshold of ~7 μJ/mm^2. FITC= 2 mM. Cavity length=30 μm. Tissue extinction coefficient=10 cm^{-1}. **b,** Lasing threshold vs. FITC concentration inside the muscle tissue. Other parameters are the same as in **a**.

The FITC laser is described by:

$$\frac{dn(t)}{dt} = I_p(t)\sigma_{a,p}[N_0 - n(t)] - \frac{\sigma_{e,l}c}{\varepsilon}n(t)q(t) + \frac{\sigma_{a,l}c}{\varepsilon}[N_0 - n(t)]q(t) - \frac{n(t)}{\tau_0} \quad (1)$$

$$\frac{dq(t)}{dt} = \frac{Fc}{\varepsilon V}\sigma_{e,l}n(t) + \frac{Fc}{\varepsilon}\sigma_{e,l}n(t)q(t) - \frac{Fc}{\varepsilon}\sigma_{a,l}[N_0 - n(t)]q(t) - \frac{q(t)}{\tau_q} \quad (2)$$

In these equations, n is the concentration of the excited FITC molecules and q is the photon density of a lasing mode at FITC emission band. I_p is the photon fluence at the excitation wavelength (465 nm). $\sigma_{a,p}$ is the absorption cross section of FITC at the excitation wavelength. N_0 is the total concentration of FITC. $\sigma_{a,l}/\sigma_{e,l}$ is the absorption/emission cross section of FITC at the lasing wavelength. c is the speed of light in vacuum. ε is the refractive index of the tissue. τ_f is the fluorescence lifetimes of FITC. τ_q denotes the lifetime of the photon in the lasing mode and is determined by $\tau_q = (\frac{1}{\tau_0} + \frac{1}{\tau_s})^{-1}$, where $\tau_0 = \frac{\lambda Q_0}{2\pi c}$ results from the loss of mirrors (Q_0, empty cavity quality factor; λ, lasing wavelength) and $\tau_s = \frac{\varepsilon}{c\alpha}$ results from the attenuation of light by the presence of tissue (α, tissue extinction coefficient). With the round trip loss limited by the transmission of the bottom mirror (0.5%), Q_0 of an FP cavity with a cavity length of 30 μm is 1.9e5. The extinction coefficient of tissue, $\alpha = \alpha_s + \alpha_a$, where α_s is scattering loss and α_a is the absorption of myoglobin. Here we consider only the forward scattering, since the thickness of the muscle tissue is far less than 1 mm. Therefore, we can simply use the reduced scattering coefficient for muscle in simulation, which is approximately 9 cm^{-1} according to Refs. 2,3). The myoglobin absorption coefficient is 1 cm^{-1}. V is the mode volume and F is the fraction of the mode volume

occupied by the tissue.

To simulate the pulse excitation condition, we assume the excitation photon fluence I_p to be Gaussian with a full width at half maximum (FWHM) of 5 ns. Pump intensity is determined by temporal integral of I_p from time zero to infinity.

The coupled rate equations are numerically solved in Matlab for different conditions. Output intensity is determined by temporal integral of q(t) assuming a constant out-coupled rate. Parameters used in the simulation are summarized in Table S1 below.

Table S1. Simulation parameters

Symbols	Description	Numeric values
$\sigma_{a,p}$	Absorption cross section at excitation wavelength	1.25e-16 cm^2
$\sigma_{a,l}$	Absorption cross section at lasing wavelength	<1e-19 cm^2
$\sigma_{e,l}$	Emission cross section at lasing wavelength	1.19e-16 cm^2
c	Speed of light in vacuum	30 cm/ns
ε	Refractive index of tissue	1.40
τ_f	Fluorescence lifetime of FITC	4.1 ns
V	Volume of the electromagnetic mode	2.7e-8 cm^3
F	Fraction of mode volume occupied by the dye molecules	1
Q_0	Empty cavity quality factor (cavity length=30 μm)	1.9e5
λ	Lasing wavelength	550 nm
α	Tissue extinction coefficient	$\alpha_s + \alpha_a$
α_s	Tissue scattering loss	9 cm^{-1}
α_a	Myoglobin absorption loss	1 cm^{-1}

4. Lasing profile of muscle tissue + FITC with various tissue thicknesses

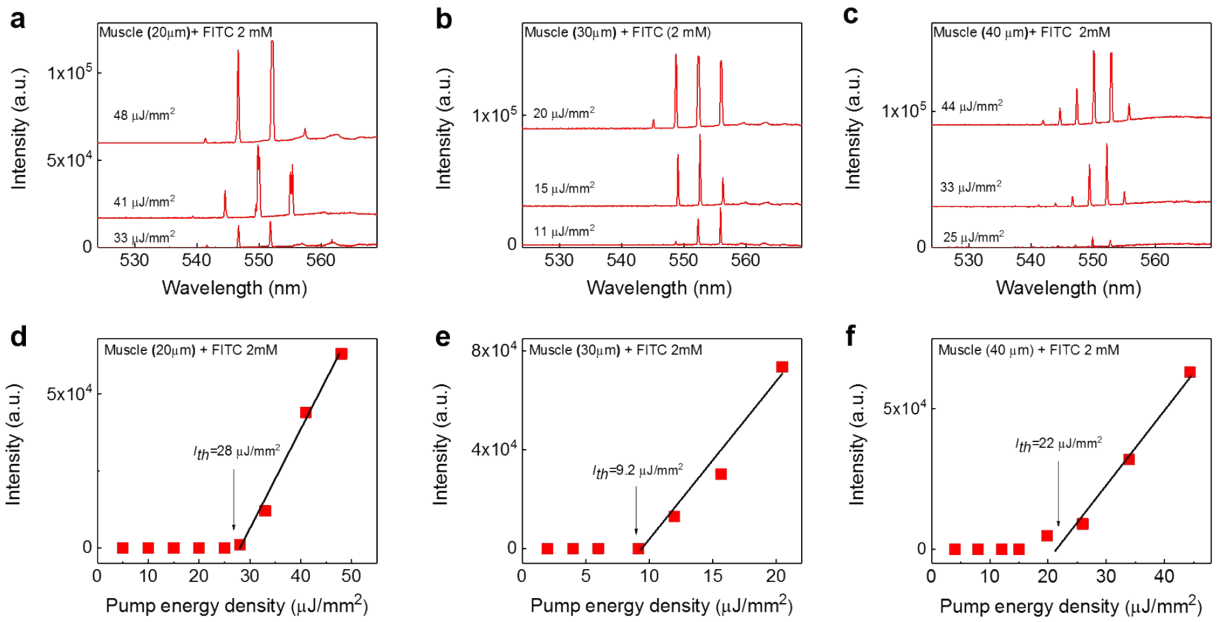

Figure S4. a-c, Lasing spectra of muscle tissue doped with FITC (2 mM) under various pump energy densities by with the cavity length of (**a**) 20 μm, (**b**) 30 μm, and (**c**) 40 μm. All curves are vertically shifted for clarity. **d-f**, Spectrally integrated (540 nm – 560 nm) laser output as a function of pump energy density extracted from (**a**), (**b**), and (**c**), respectively. Solid lines show the linear fit above the threshold. Excitation wavelength=465 nm.

5. Lasing profile of muscle tissue with various FITC concentrations

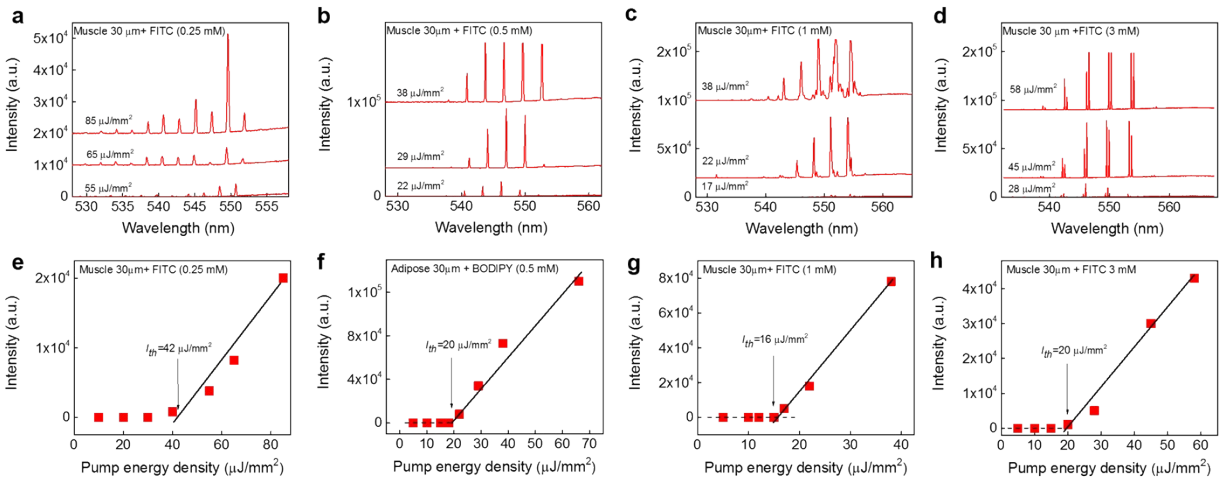

Figure S5. a-d, Lasing spectra of muscle tissue doped with FITC (cavity length fixed at 30 μm) under various pump energy densities with FITC concentration of (**a**) 0.25 mM, (**b**) 0.5 mM, (**c**) 1.0 mM, and (**d**) 3.0 mM. All curves are vertically shifted for clarity. **e-h**, Spectrally integrated (540 nm – 560 nm) laser output as a function of pump energy density extracted from (**a**), (**b**), (**c**), and (**d**), respectively. Solid lines show the linear fit above the threshold. Excitation wavelength=465 nm.

6. Light-guiding effect along myofibrils

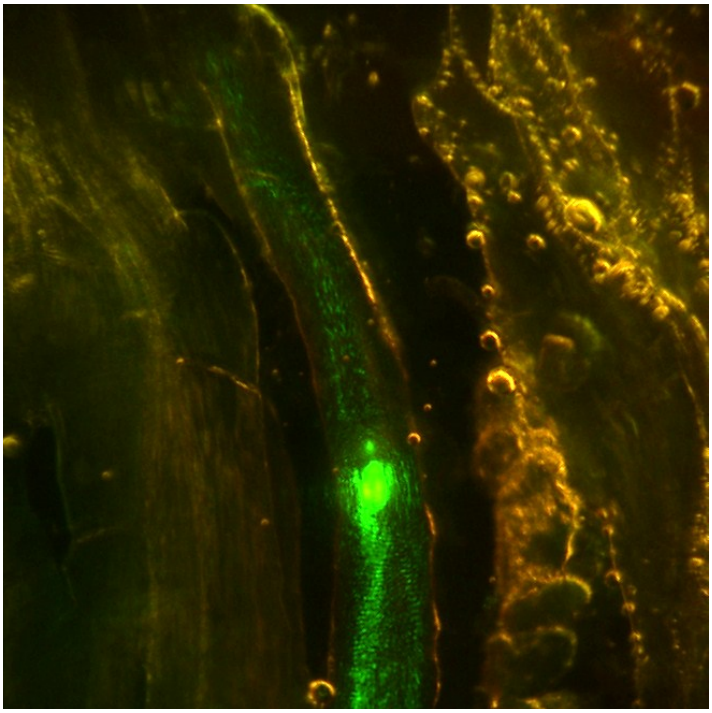

Figure S6. Strong light-guiding effect along the myofibrils can be clearly observed under a high pump intensity (72 μJ/mm^2), which shows that propagation loss is smaller along myofibrils than across myofibrils. Tissue thickness=30 μm. [FITC]=2.0 mM. Excitation wavelength=465 nm.

7. Lasing profile of adipose tissue + BODIPY with various thickness

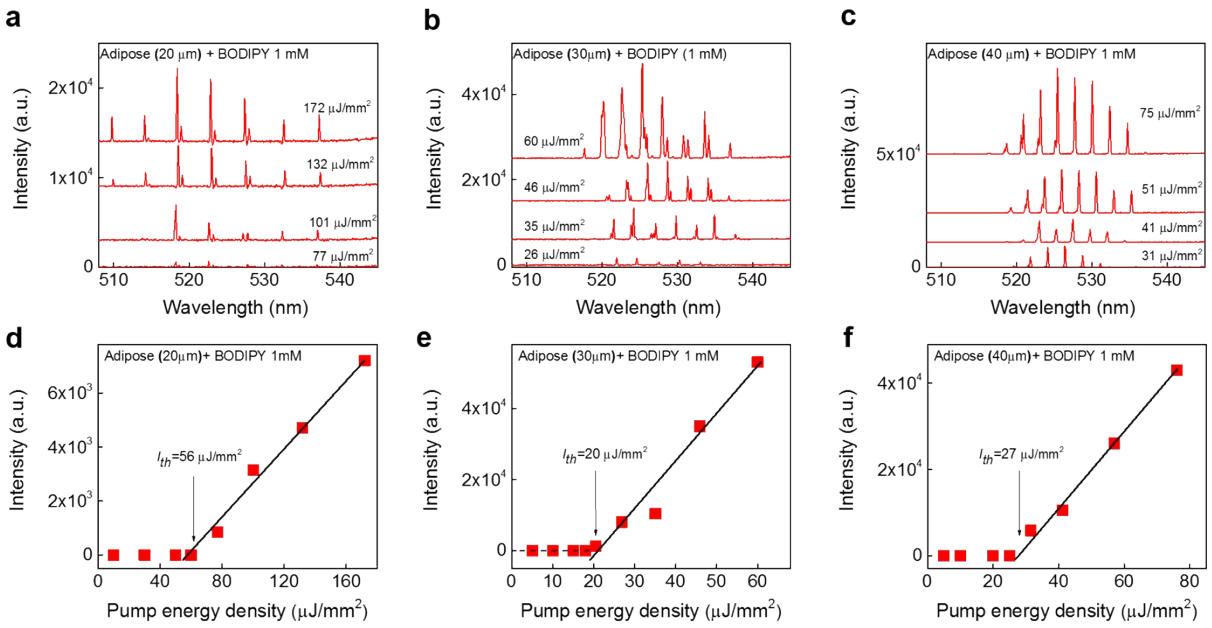

Figure S7. a-c, Lasing spectra of adipose tissue doped with BODIPY (1.0 mM) under various pump energy densities with the cavity length of (**a**) 20 μm, (**b**) 30 μm, and (**c**) 40 μm. All curves are vertically shifted for clarity. **d-f**, Spectrally integrated (515 nm – 535 nm) laser output as a function of pump energy density extracted from (**a**), (**b**), and (**c**), respectively. Solid lines show the linear fit above the threshold. Excitation wavelength=465 nm.

8. Lasing profile of adipose tissue with various BODIPY concentrations

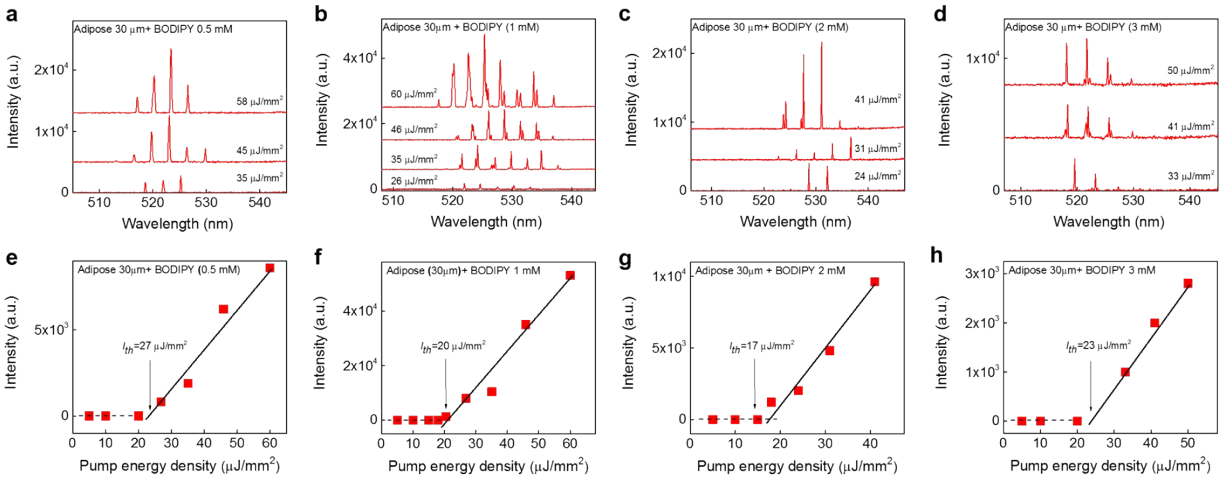

Figure S8. a-d, Lasing spectra of adipose tissue doped with BODIPY (cavity fixed at 30 μm) under various pump energy densities with BODIPY concentration of (**a**) 0.5 mM, (**b**) 1.0 mM, (**c**) 2.0 mM, and (**d**) 3.0 mM. All curves are vertically shifted for clarity. **e-h**, Spectrally integrated (515 nm – 535 nm) laser output as a function of pump energy density extracted from (**a**), (**b**), (**c**), and (**d**), respectively. Solid lines show the linear fit above the threshold. Excitation wavelength=465 nm.

9. Comparison of Signal-to-Background Ratio (SBR)

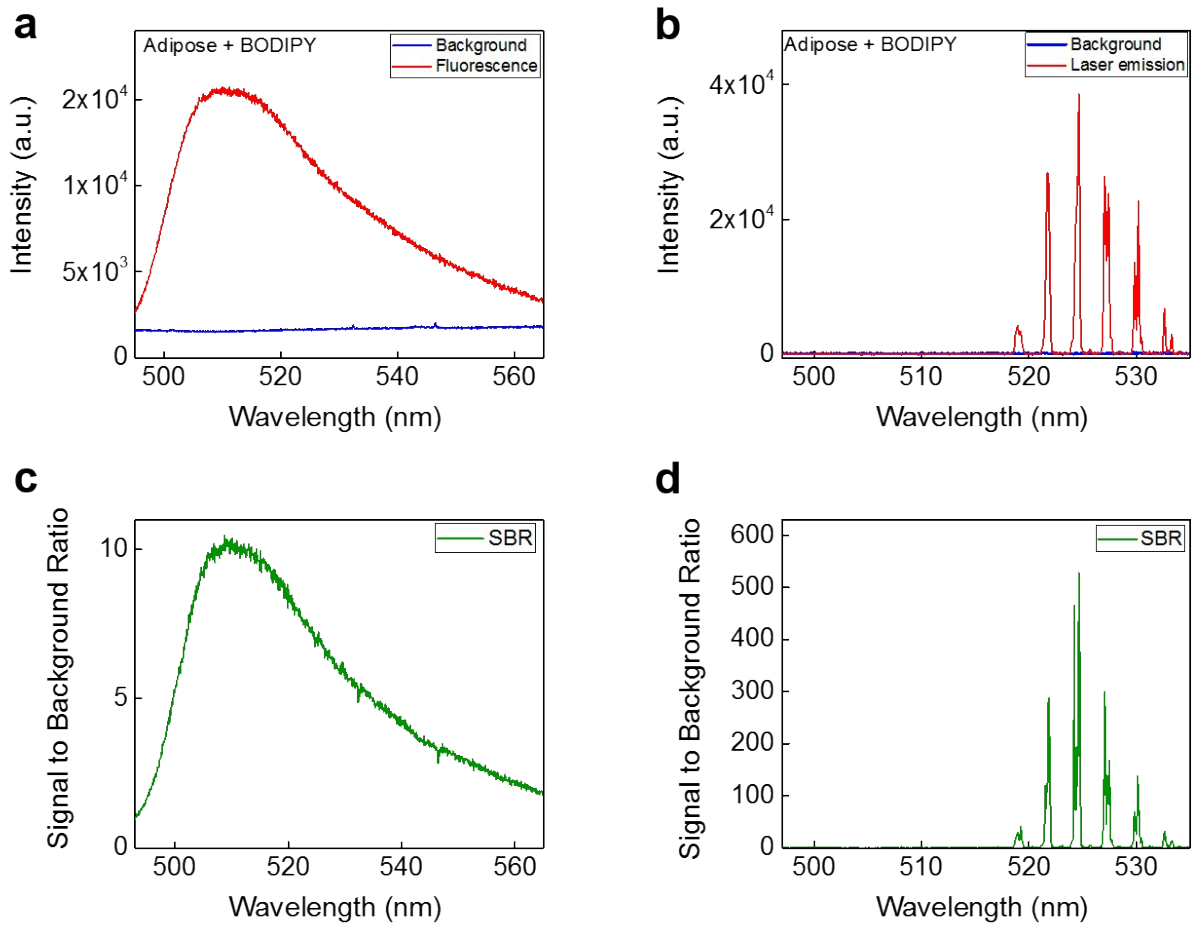

Figure S9. Comparison of the signal to background ratio (SBR) between fluorescence and lasing emission. **a**, Fluorescence spectrum of adipose tissue stained with BODIPY (red) and its background (blue). **b**, Lasing spectrum of adipose tissue stained with BODIPY and its background (blue). **c**, SBR extracted from **a** showing the maximal value of about 10. **d**, SBR extracted from **b** showing the maximal value of about 500. All the background signals were measured using the tissue sites without staining under the same configuration. [BODIPY]=1.0 mM. Pump energy density=60 μJ/mm^2. Excitation wavelength=465 nm. Fluorescence was measured by removing the top mirror.

10. Lasing in muscle tissue with FITC-phalloidin

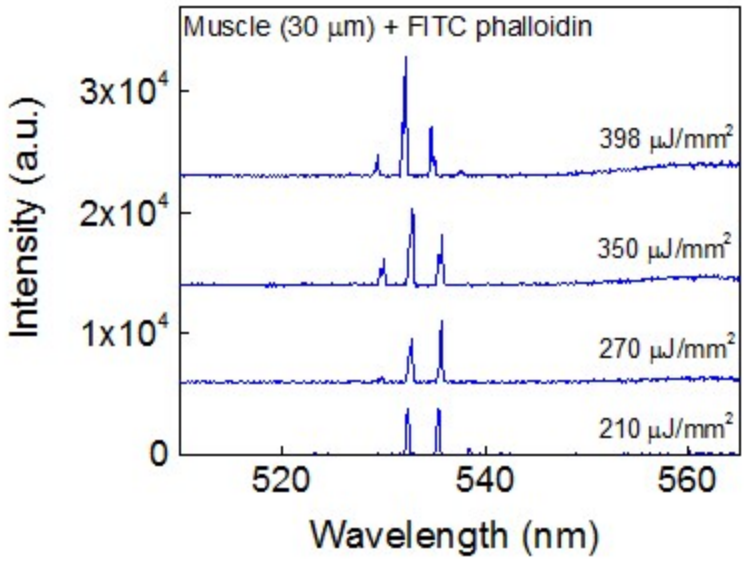

Figure S10. Examples of lasing spectra of the muscle tissue stained with FITC-phalloidin under various pump energy densities. The lasing is centered around 535 nm. This blue shift with respect to the lasing emission around 550 nm for 1 mM FITC is typical for a laser when the gain medium concentration decreases[4,5]. Tissue thickness=30 μm. [FITC-phalloidin]=10 μM. Excitation wavelength=465 nm. The muscle tissue was arranged longitudinally. Curves are vertically shifted for clarity.

11. Lasing profile of muscle tissue + FITC using a concave top mirror

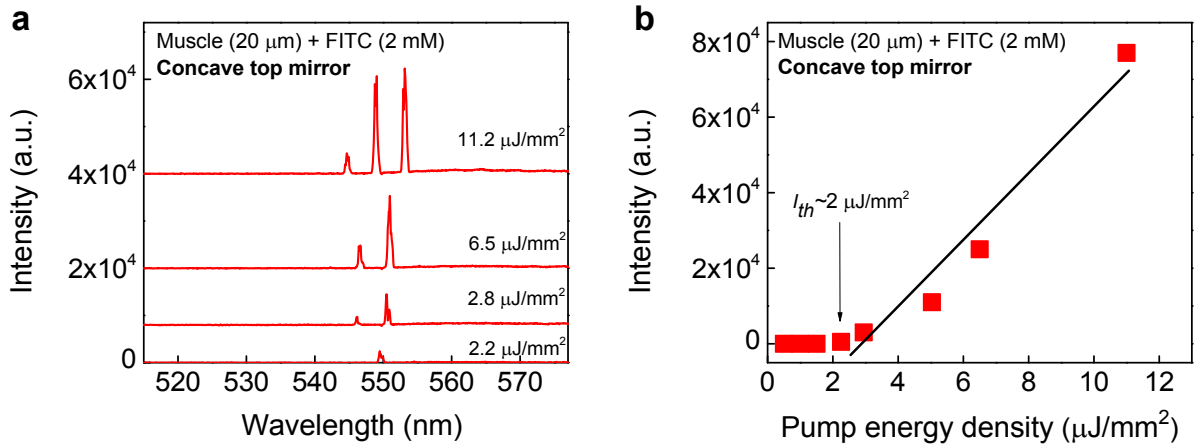

Figure S11. a, Examples of lasing spectra of muscle tissue stained with FITC using a concave top mirror under various pump energy densities. **b**, Spectrally integrated (540 nm – 560 nm) laser output as a function of pump energy density extracted from (**a**). Solid line is the linear fit above the threshold, showing a lasing threshold of approximately 2 μJ/mm^2. Tissue thickness=20 μm. [FITC]=2.0 mM. Excitation wavelength=465 nm.

References

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