Supplemental document

Video S1. Time-lapse intravital eSLAM imaging of mouse skin flap without image denoising.

Video S2. Time-lapse intravital eSLAM imaging of the mouse skin flap denoised by DeepCAD-RT.

Video S3. Time-lapse intravital eSLAM imaging of the mouse skin flap denoised by UDVD.

Video S4. Depth-resolved eSLAM imaging of *ex vivo* mouse kidney with SHG/green against THG/magenta contrasts (upper left), 2PAF/yellow aganist 3PAF/cyan contrasts (lower left), 2PAF lifetime contrast (upper right), and 3PAF lifetime contrast (lower right).

Table S1. Representative commercial Yb-based pp-FCPA lasers and optional OPA accessories

Model (vendor)	λ, f, and τ (low-bound)*	P	λ, f, and τ from optional OPA
Satsuma (Amplitude)	1030 nm, 0.5-40 MHz, 300 fs	5/10/20 W	Niji: 257-4000 nm, 0.5-2 MHz, 50 fs
Y-Fi (Thorlabs)	1035 nm, 1-10 MHz, 220 fs	3-20 W	Yi-F OPA: 1275-1800 nm, 1-3 MHz, 100 fs
Spirit 1030 (Newport)	1030 nm, 1-30 MHz, 400 fs	70/100/140 W (water cooled)	NOPA-VISIR: 650-900 & 1200-2500 nm, 1-4.3 MHz, 70 fs
Monaco (Coherent)	1035 nm, 1-50 MHz, 350 fs	40/60 W (water cooled)	Opera-F: 650-900 & 1200-2500 nm, 1-4 MHz, 70 fs
FemtoFibe vario 1030 HP (Toptica)	1030 nm, 1-10 MHz, 250 fs	8 W	N.A.
Impulse (Clark-MXR)	1030 nm, 2-25 MHz, 250 fs	20 W	N.A.
BlueCut (Menlosystem)	1030 nm, 1-10 MHz, 400 fs	10 W	N.A.
FCPA-DE (IMRA)	1045 nm, 1-5 MHz, 400 fs	20 W	N.A.

*Pulse width of sech2-profile that can be tuned (stretched) to several ps (up-bound) by a grating compressor.

Table S2. Representative supercontinuum generation in bulk media and photonic crystal fibers

Report	Input λ, f, and τ, respectively	Coupled P (or E)	Interactive medium (diameter, length)	Feature/comment
14	530 nm, Q-switch, 4-8 ps	(5mJ)	Bulk glass (1.2 mm, 2-1000 mm)	Discovery of supercontinuum generation under self-focusing
15	800 nm, 0.25 MHz, 170 fs	0.25 W (1 μJ)	Sapphire plate (~20 μm, <500 μm)	Bulk supercontinuum generation employed in commercial OPA
16	770 nm, ~80 MHz, 100 fs	(0.2 nJ)	Photonic crystal fiber (1.7 μm, 10 cm)	Widely accessible single-mode fiber supercontinuum generation
17	1070 nm, 40 MHz, 3.3 ps	1.5 W	Photonic crystal fiber (4 μm, 5-65 m)	Commercial all-fiber supercontinuum generation for the broadest spectra
22	1030 nm, 10 MHz, 300 fs	1.8 W	Photonic crystal fiber (15 μm, 25 cm)	High peak-power coherent fiber supercontinuum generation

Table S3. Three schemes of polarized coherent fiber supercontinuum (approach 3)

	Scheme 1	Scheme 2	Scheme 3
Master laser (vendor)	Satsuma 10W (Amplitude)	Satsuma 10W (Amplitude)	
Input (λ, f, and τ) *	1030 nm, 10 MHz, 280 fs	1031 nm, 40 MHz, 290 fs	1031 nm, 5 MHz, 290 fs
Photonic crystal fiber (vendor)	LMA-PM-15 (NKT Photonics)	NL-1050-NEG-PM (custom, NKT Photonics)	LMA-PM-40-FUD (NKT Photonics)
Core diameter (mode field diameter)	14.8 μm (12.6 μm @1064 nm)	2.4 μm (2.2 μm @1064 nm)	40 μm (32 μm @1064 nm)
Hole/pitch size; cladding diameter	4.9/9.8 μm; 230 μm	0.65/1.44 μm; 125 μm	7/26 μm; 450 μm
Fiber zero dispersion wavelength	1210 nm	Nonexistent	1260 nm
Focusing length, lens (vendor)	18.4 mm, C280TMD-B (Thorlabs)	3.1 mm, C330TME-B (Thorlabs)	50 mm, AC127-050-B (Thorlabs)
Coupled efficiency	75%	70%	79%
Coupling (output) P	1.2 W	0.22 W	3.44 W
Input peak intensity**	5 TW/cm^2	5 TW/cm^2	6 TW/cm^2
Collimating parabolic mirror	focal length 25 mm	focal length 10 mm	focal length 50 mm
Output PER	>50	>50	>30
Long-term fiber photodamage	present after 100±40 hrs accumulative operation	present after 10±2 hrs accumulative operation	absent after >2000 hrs accumulative operation
Number of fiber pieces	18	7	2
Fiber length	25 cm	25 cm	9.0 cm
Localization of photodamage	<10 cm beyond fiber entrance end	<1 cm beyond fiber entrance end	Not observed
Estimated Λ of LPFG	**1 mm**	**80 μm**	**~9 cm**

*Pulse width of sech2-shape from two similar lasers (Satsuma 10W, Amplitude) with a beam diameter of ~1.8 mm. **Assuming no pulse broadening from laser exit to coupling photonic crystal fiber.

Table S4. Comparison of FNWC with OPA as accessory for pp-FCPA lasers

Accessory	FNWC (SLM or prism compression) *	OPA
λ - tunable range (nm)	950-1110	Wide
f - variable range (MHz)	1-10	<5 (typically fixed)
τ - tunable range (fs)	40-400	~70 (typically not tuned)
P in mW (E in nJ)	20-200 (20)	up to 1000 (up to 250)
Independently tuned λ, f, and τ	demonstrated	not demonstrated
Fiber delivered output	demonstrated	not demonstrated
Portability/troubleshooting	possible/simple	limited/complex

* Performance is from Satsuma 10W (Amplitude) and can be further improved for f and P using Satsuma 20W.

Table S5. Comparison of integrated pp-FCPA-FNWC laser with tunable solid-state femtosecond lasers.

	pp-FCPA-FNWC laser	Tunable solid-state femtosecond lasers
Tunable λ range (nm)	950-1110	690-1020 (Ti:sapphire) or 690-1300 (OPO)
Other tunable pulse parameters	τ (down to ~40 fs) and f (1-10 MHz in this study)	τ (typically, down to ~100 fs); f of ~80 MHz typically not tunable
E and P	high and moderate, respectively	moderate and high, respectively
Dependence of f on λ	no	yes (even though small)
Beam pointing stability	ensured by endless single-mode supercontinuum (intrinsic)	ensured by feedback beam-pointing correction (extrinsic)
Cooling	air cooling sufficient	water cooling required
Maintenance cost	low	high
Comments on multiphoton excitation of common fluorophores	missing 2-photon excitation across 690-950 nm can be recovered by 3-photon excitation across 690-950 nm	often sufficient by 2-photon excitation across 690-1020 nm, except for some with red-shifted emission across 1020-1300 nm

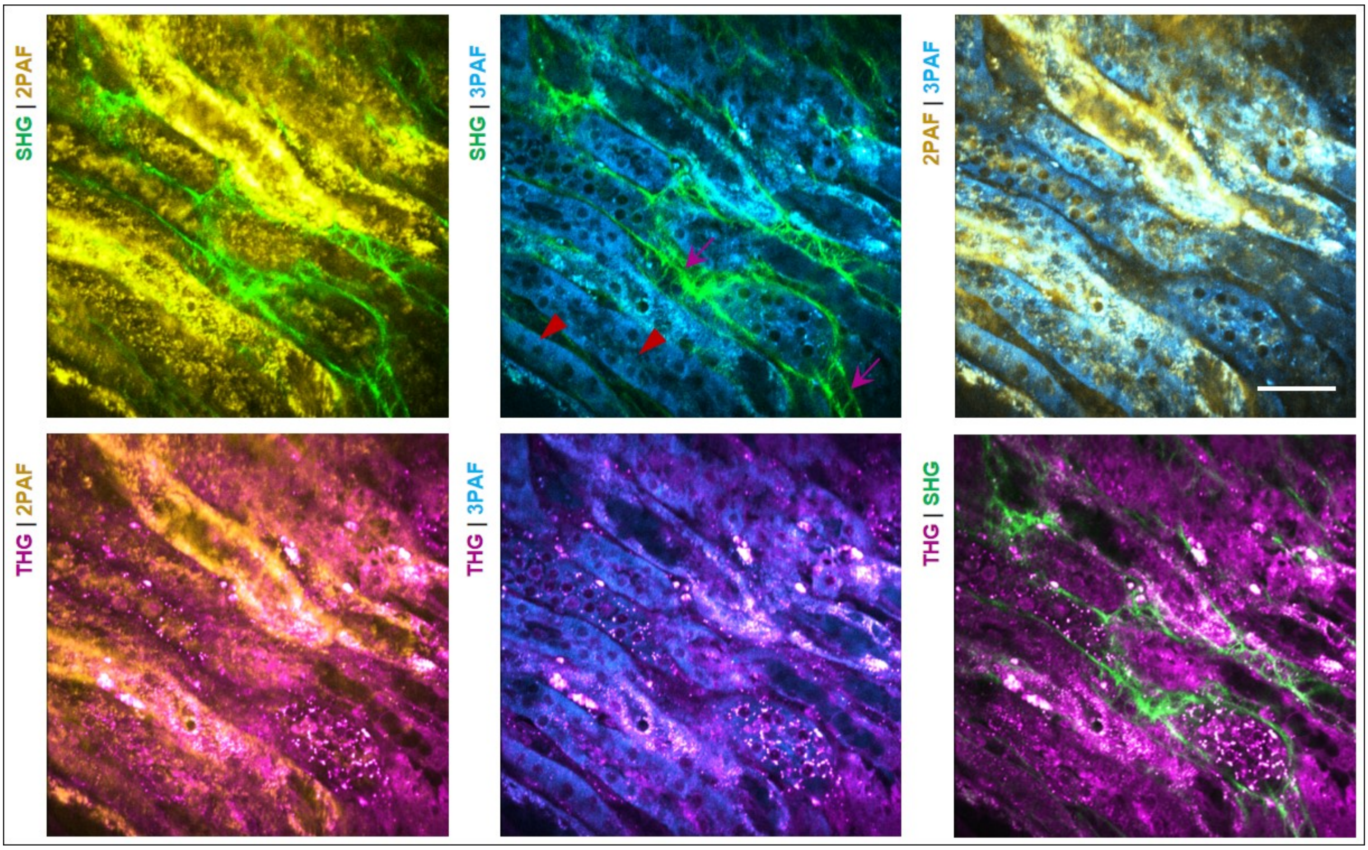

Fig. S1. Label-free regular SLAM images (17-s total acquisition time) of ex vivo rabbit kidney tissue excited by optical fiber-delivered FNWC output, with colored contrasts of second-harmonic generation (SHG), third-harmonic generation (THG), two-photon-excited auto-fluorescence (2PAF), and three-photon-excited auto-fluorescence (3PAF) showing live cells (arrowheads) and extracellular matrix (arrows). Scale bar: 50 μm.

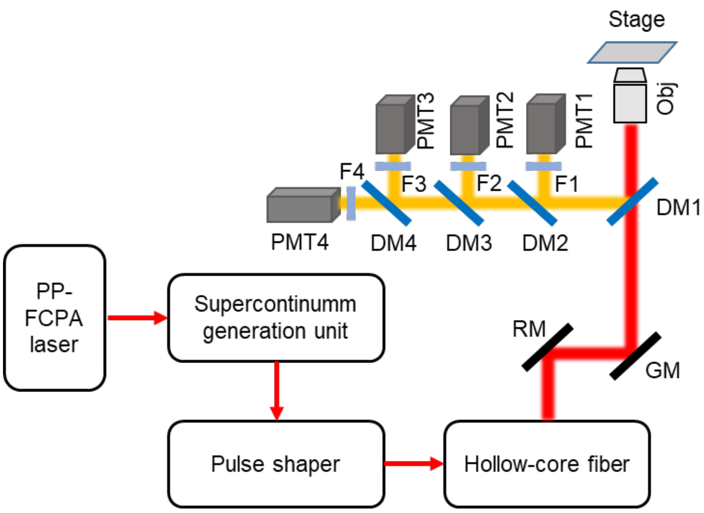

Fig. S2. Schematic of the eSLAM platform. Femtosecond pulses emitted by the PP-FCPA laser are coupled into a large-core PCF to generate a supercontinuum. A pulse shaper is used to select the excitation window and compensate for the dispersion so that the output pulse reaches the near-transform-limited at the sample, and then coupled into the hollow-core fiber for imaging. RM - resonant mirror, GM - galvo mirror, DM - dichroic mirror, Obj - objective, F - filter. DM1-DM4 edge: 925nm, 376nm, 484nm, 580nm. F1-F4 spectral band: 365-375 nm, 417-477 nm, 543-566 nm, 593-643 nm. Other details can be found in Table 1.

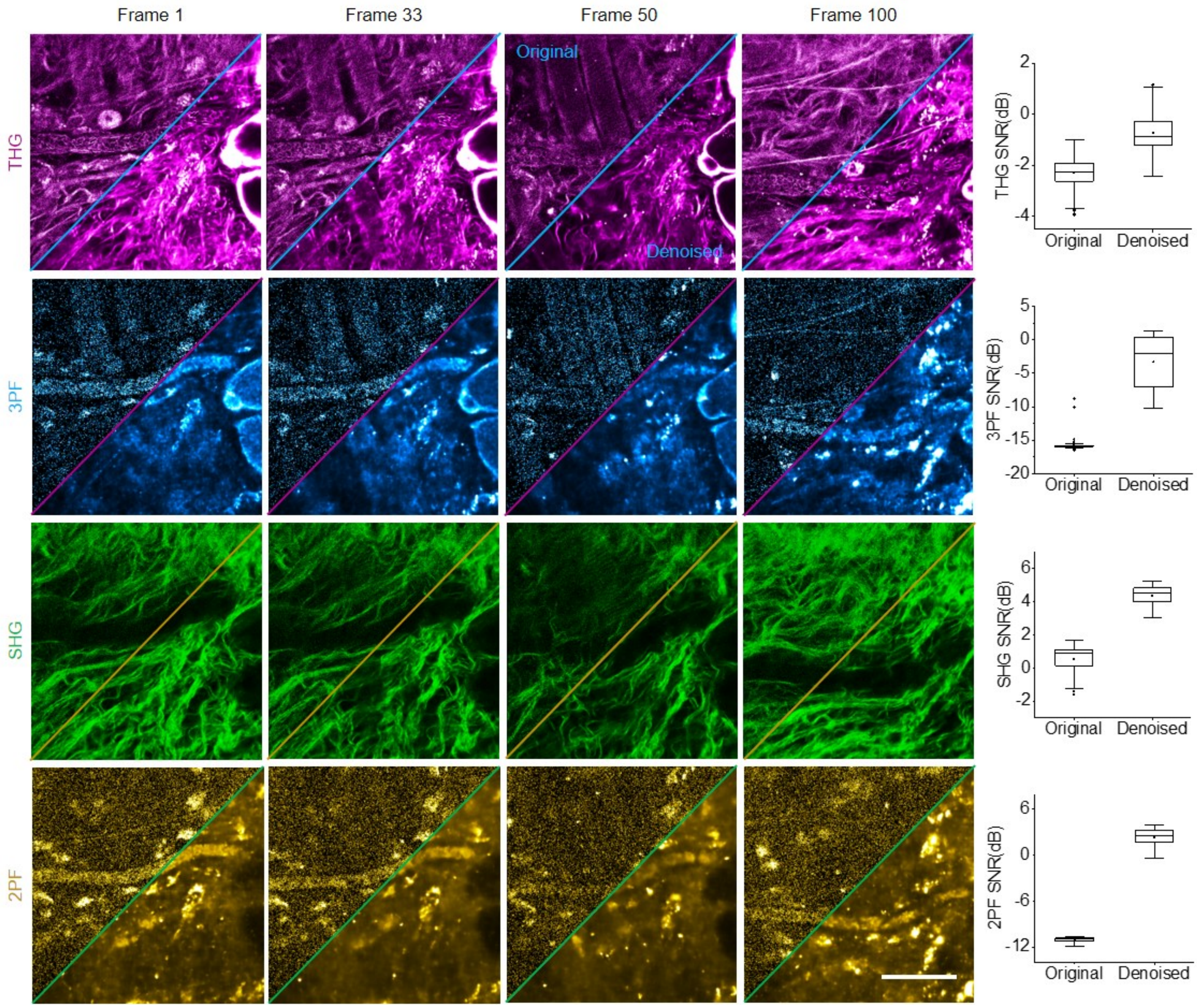

Fig. S3. Time-lapse intravital eSLAM imaging of mouse skin flap across the modalities of THG, 3PAF, SHG, and 2PAF without (upper left) and with UDVD denoising (lower right). The box and whisker plots show the corresponding SNR improvement (right panel). Scale bar: 50 μm.

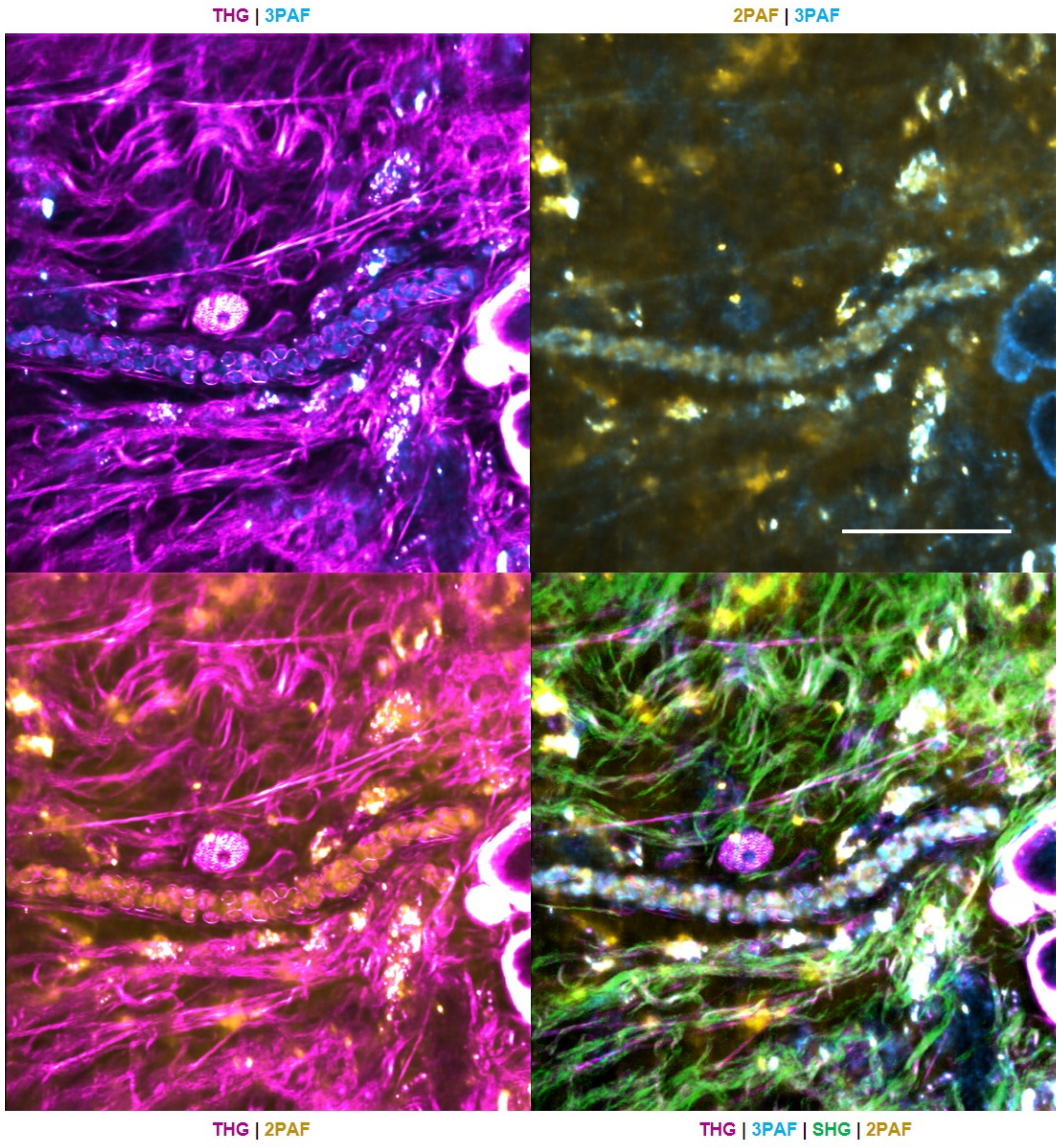

Fig. S4. intravital eSLAM imaging of mouse skin flap at one instance showing the presence of intracellular 2PAF/yellow, 3PAF/cyan, and THG/magenta signals in different parts of single biconcave disk-shaped blood cells. Scale bar: 50 µm.

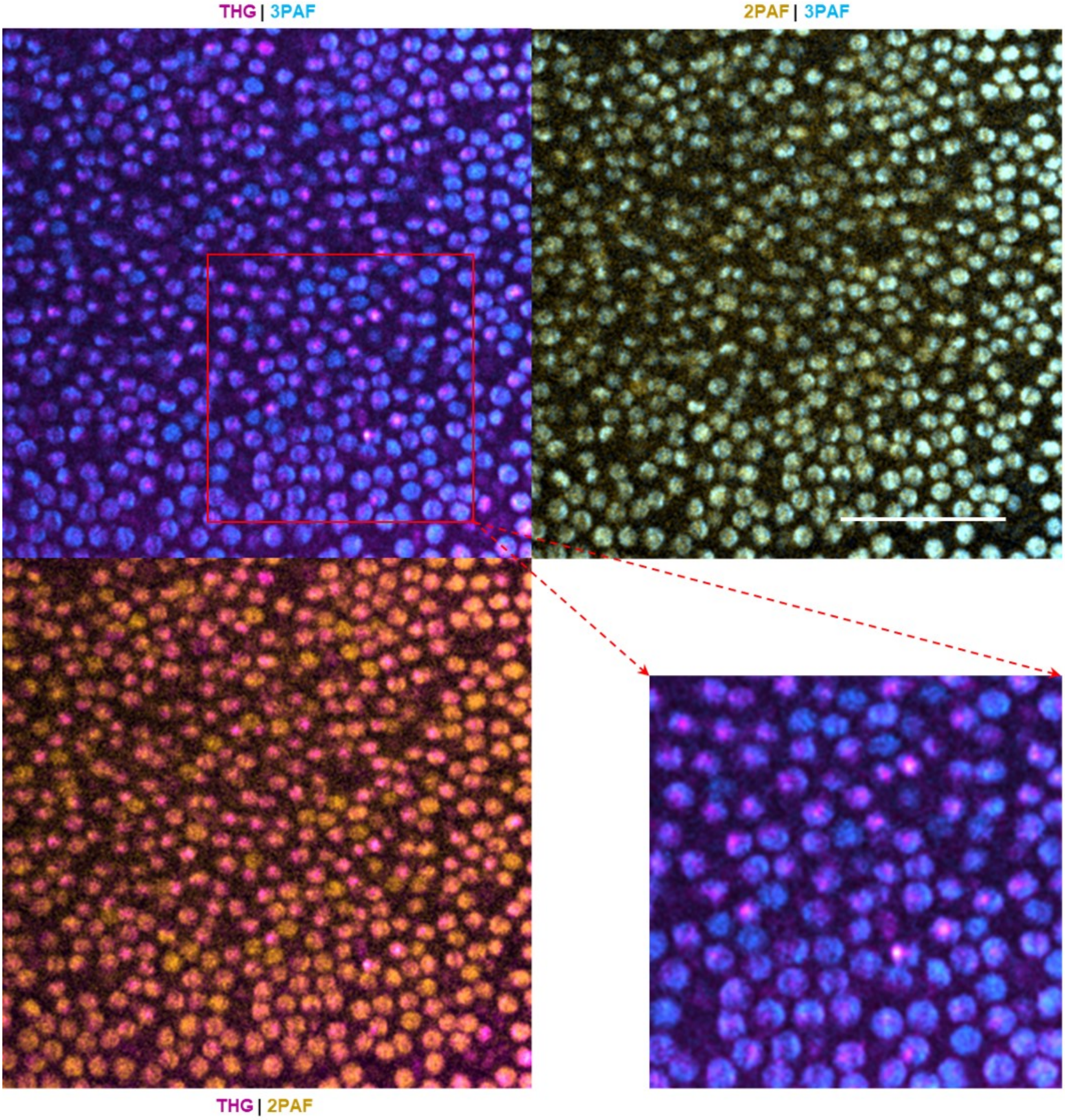

Fig. S5. Mouse blood smear from eSLAM imaging confirms the presence of intracellular 2PAF/yellow, 3PAF/cyan, and THG/magenta signals in different parts of single blood cells. Scale bar: 50 µm.

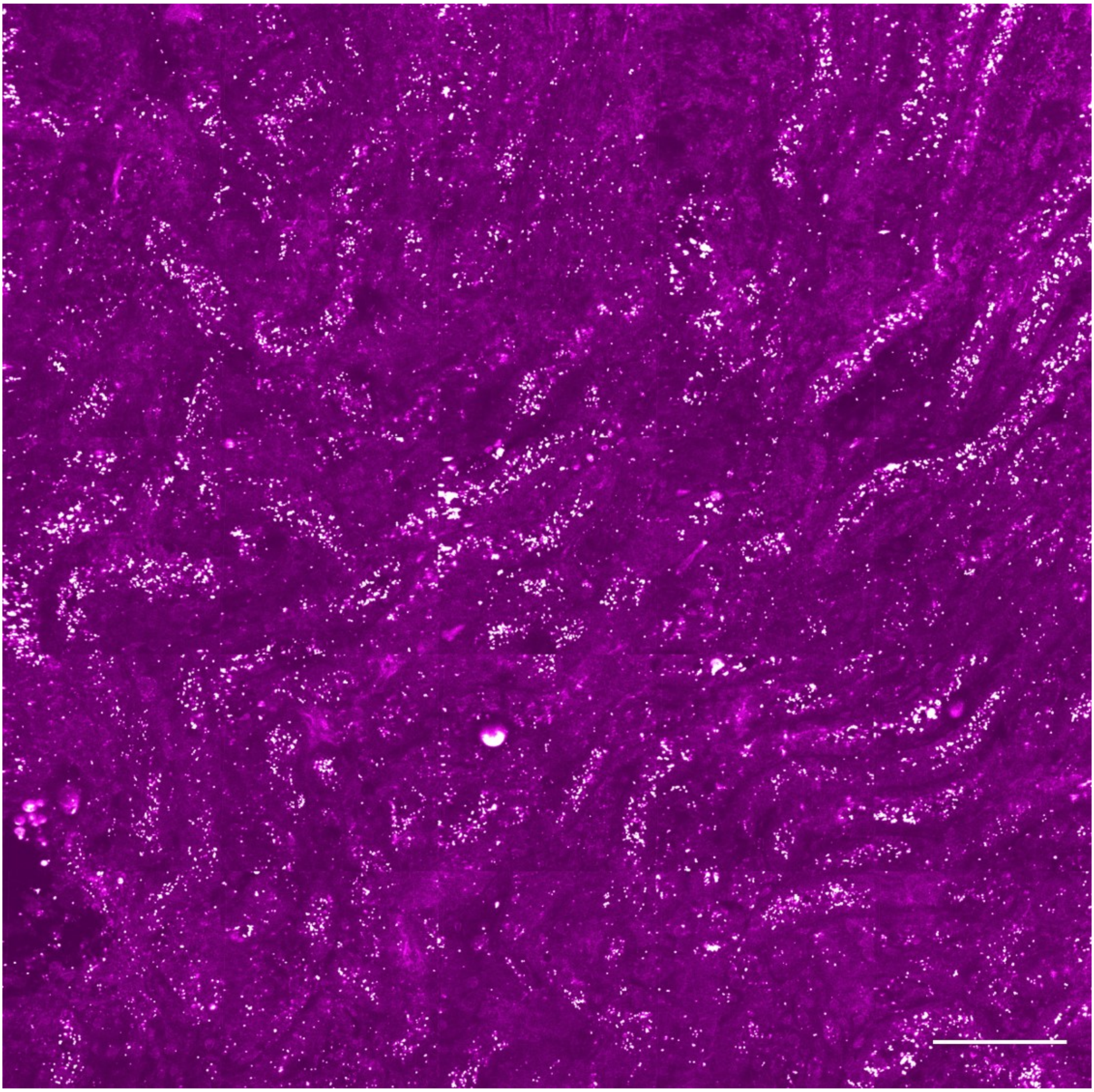

Fig. S6a. THG image of ex vivo mouse kidney from mosaic eSLAM imaging. Scale bar: 100 µm.

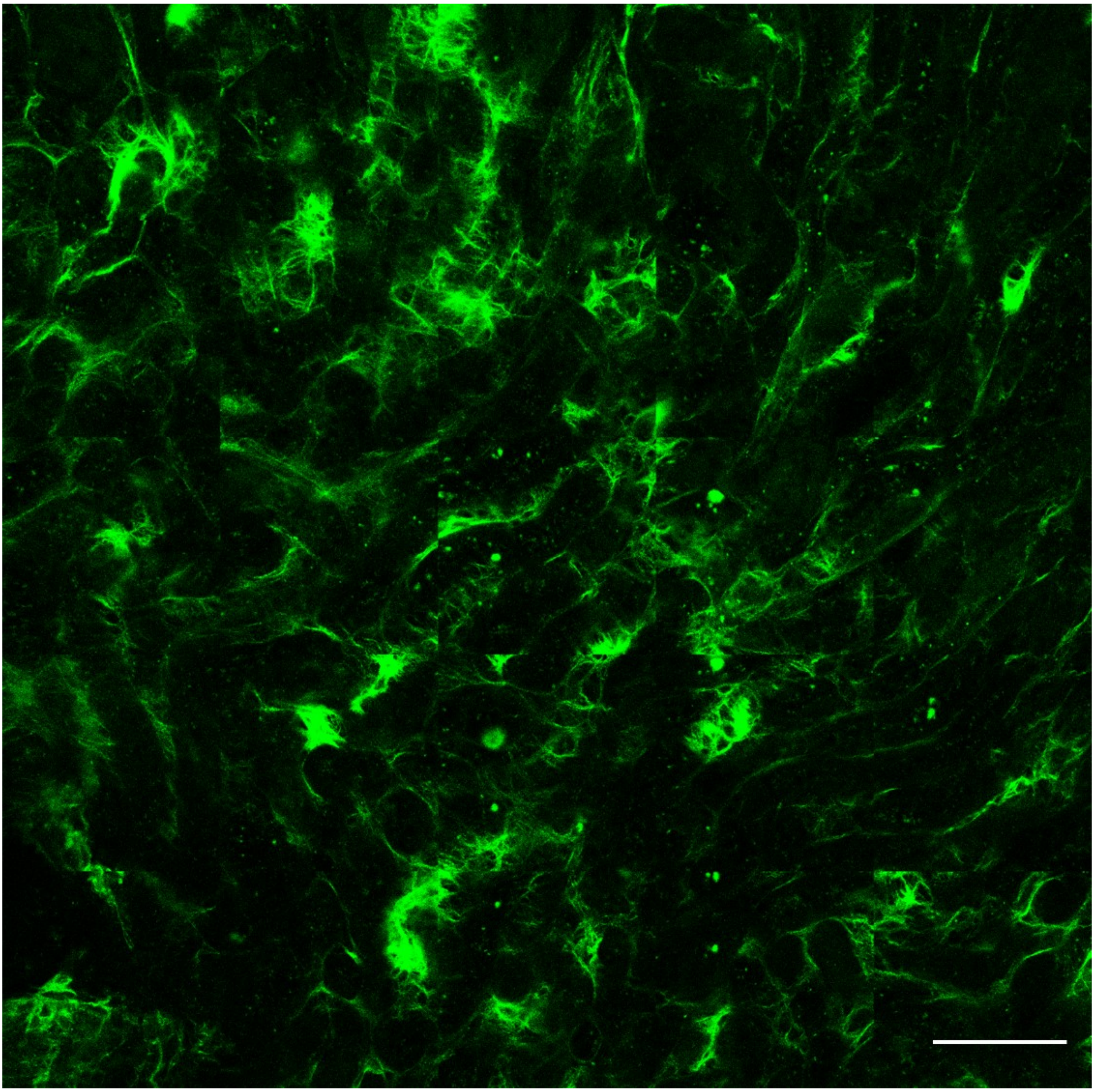

Fig. S6b. SHG image of ex vivo mouse kidney from mosaic eSLAM imaging. Scale bar: 100 µm.

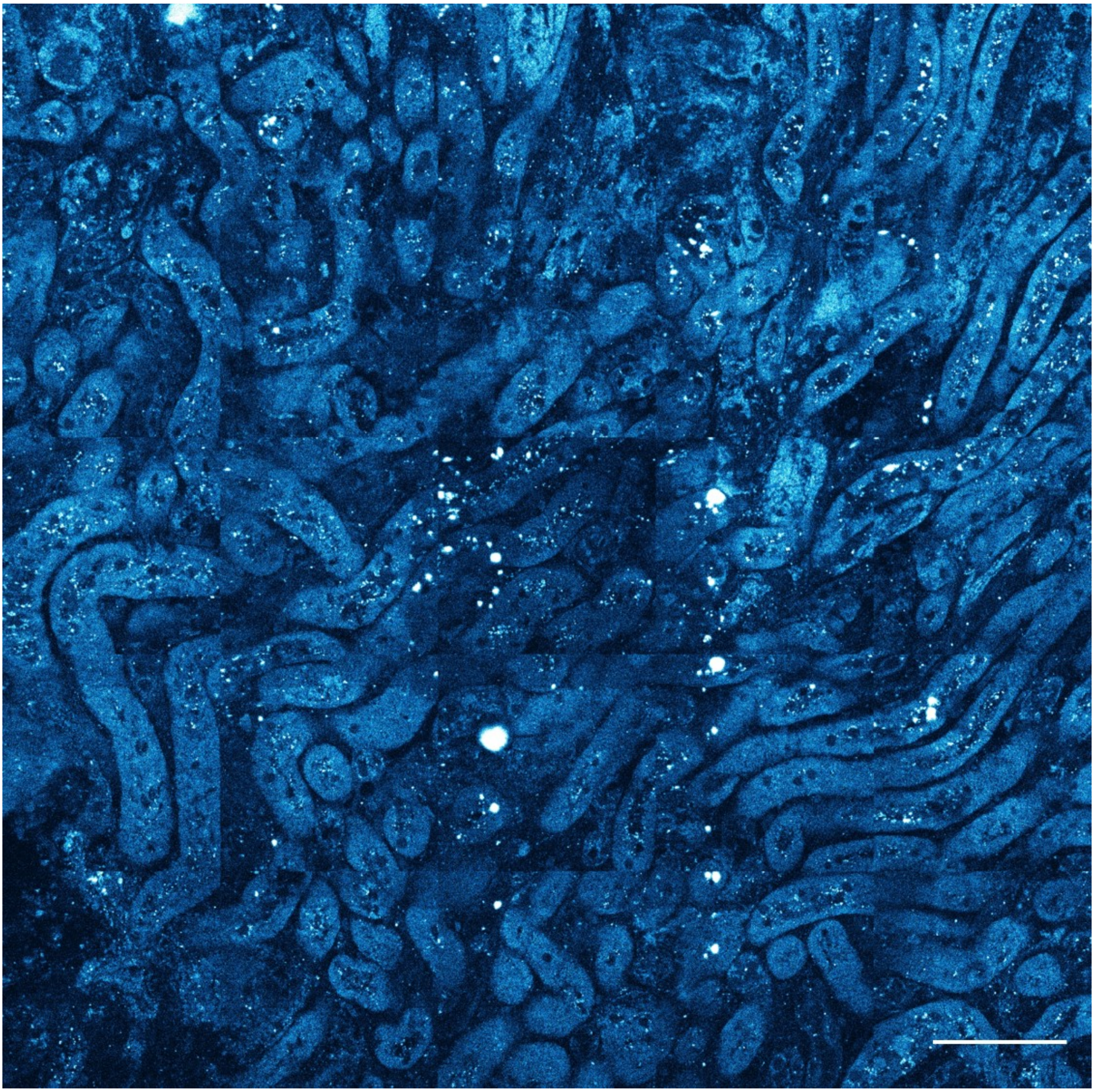

Fig. S6c. 3PAF intensity image of ex vivo mouse kidney from mosaic eSLAM imaging. Scale bar: 100 µm.

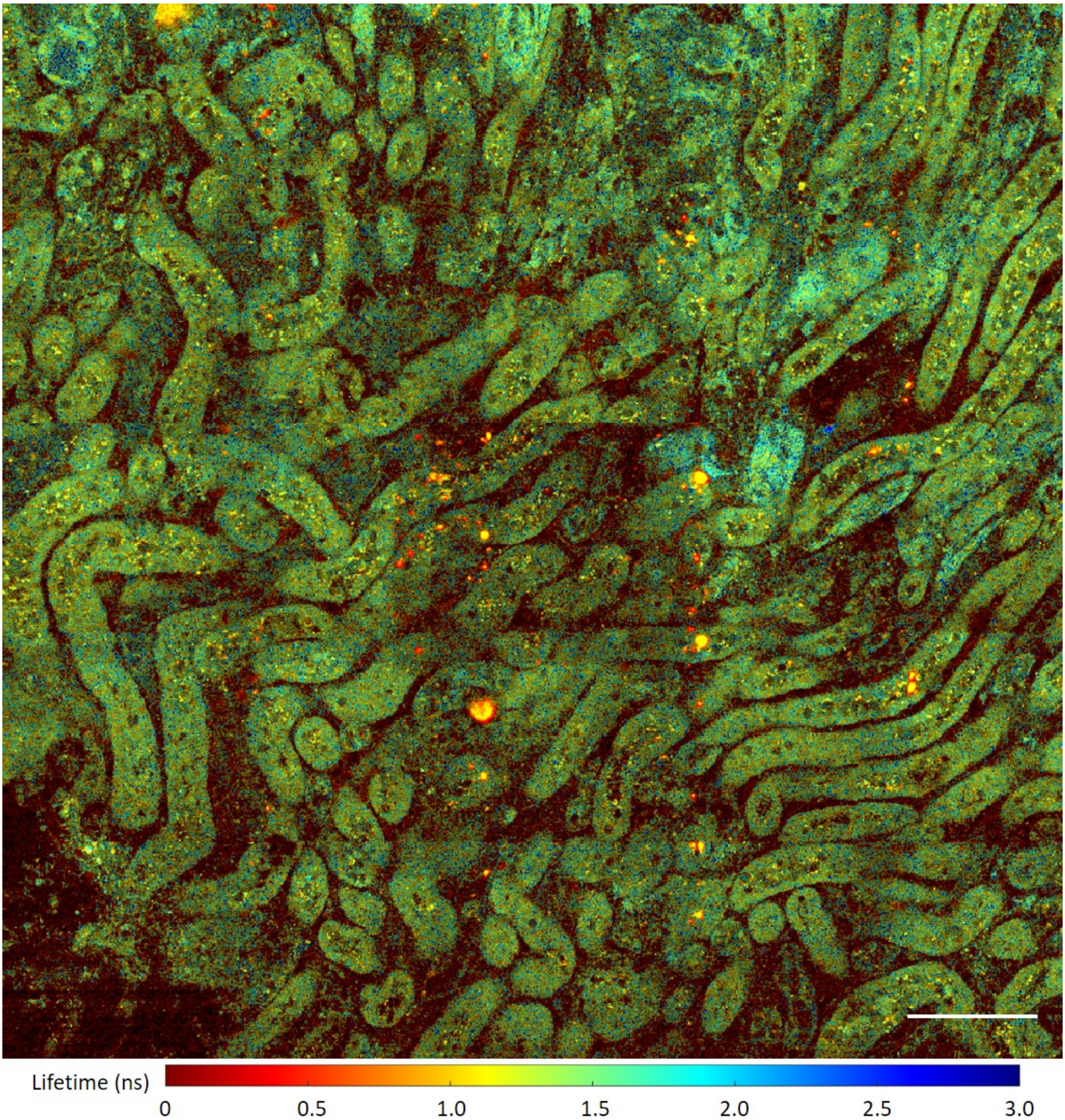

Fig. S6d. 3PAF lifetime image of ex vivo mouse kidney from mosaic eSLAM imaging. Scale bar: 100 µm.

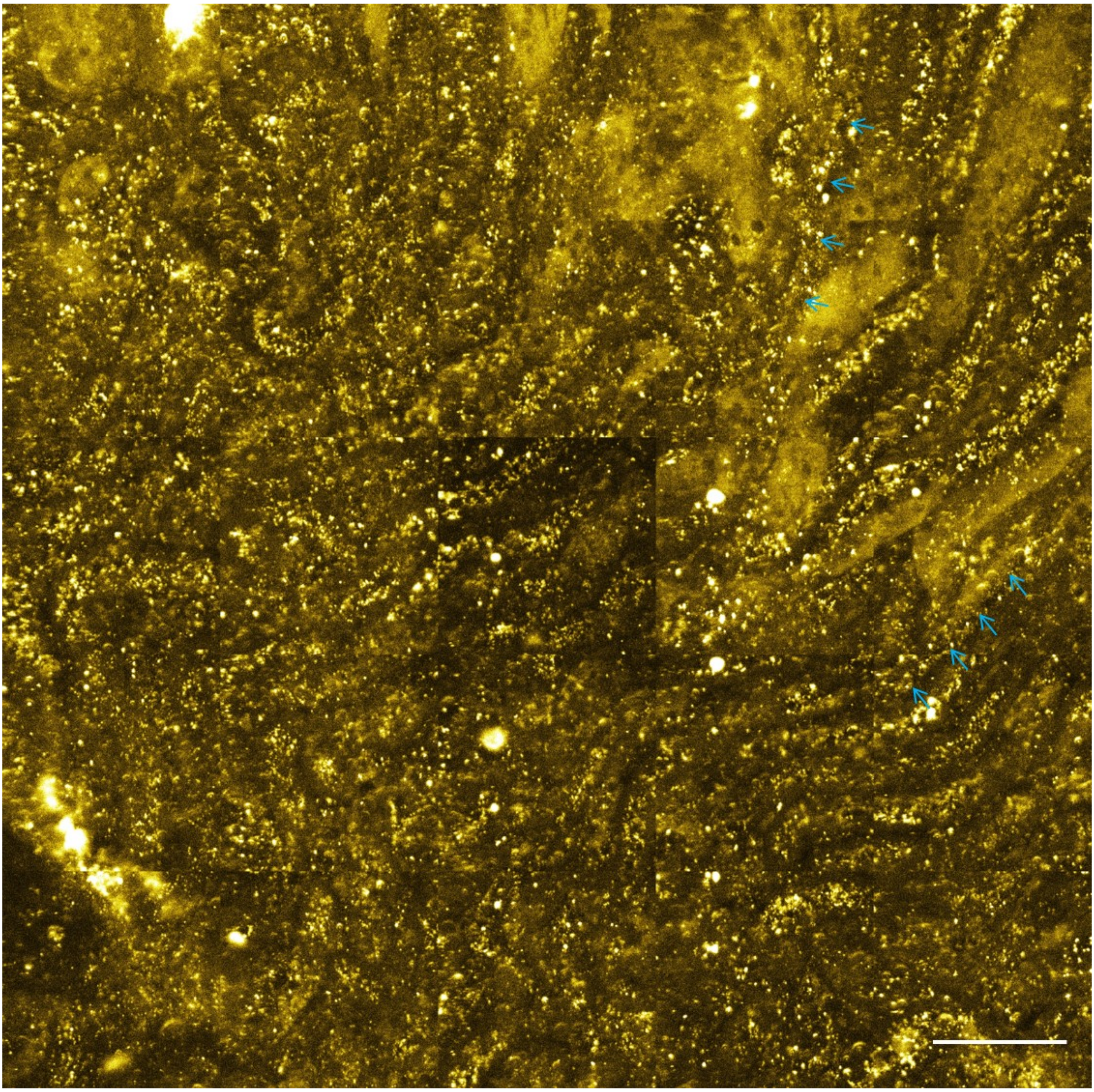

Fig. S6e. 2PAF intensity image of ex vivo mouse kidney from mosaic eSLAM imaging. Scale bar: 100 µm.

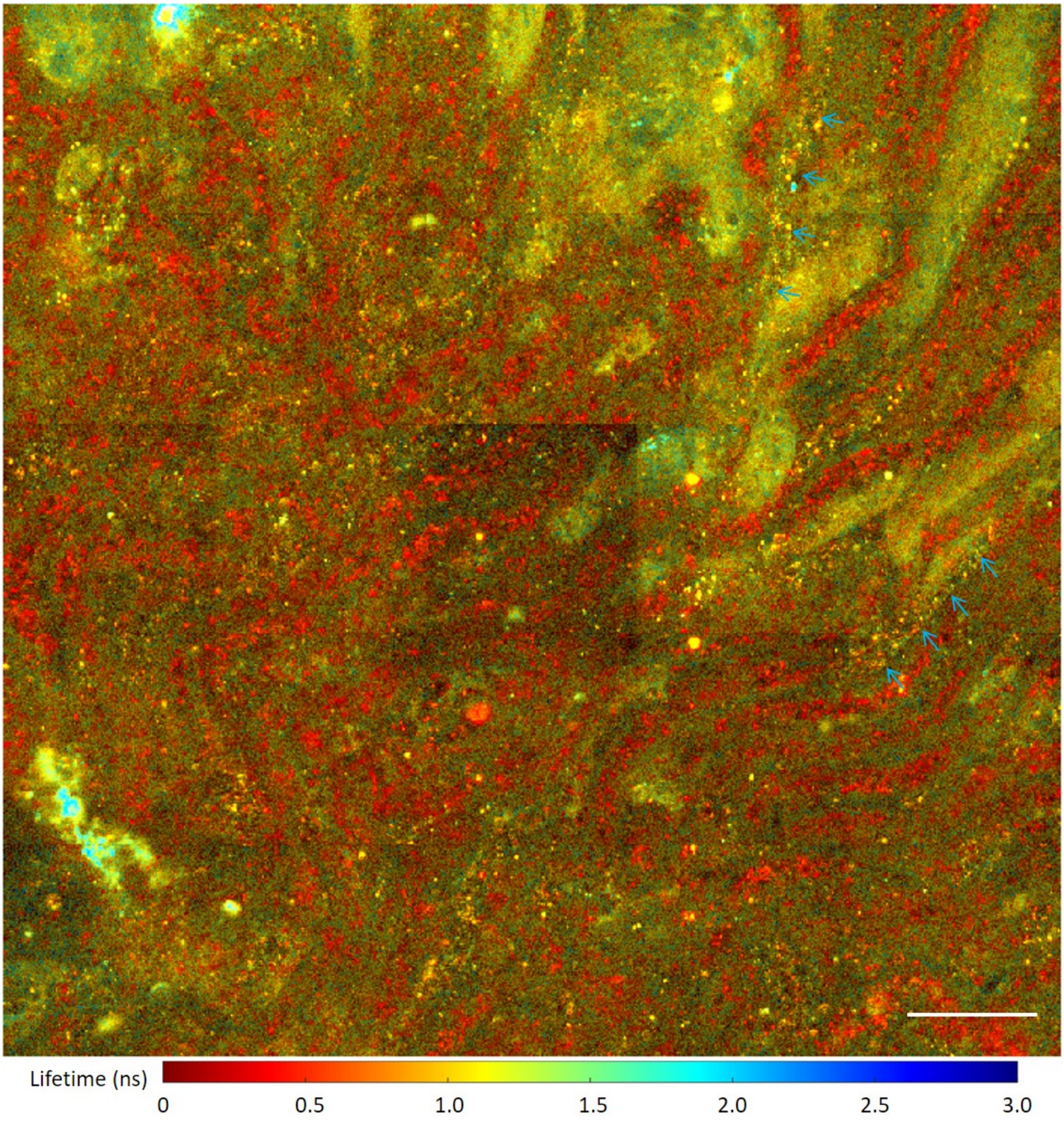

Fig. S6f. 2PAF lifetime image of ex vivo mouse kidney from mosaic eSLAM imaging. Scale bar: 100 μm.