Supplementary Figure Legends

Fig. 1. *In vivo* flow cytometry (FC) integrating photoacoustic (PA), photothermal (PT), fluorescent and transmission digital microscope (TDM) technique.

Fig. 2. High-resolution (300 nm) optical TDM imaging of single melanoma cell *in vitro* (**left single image**) at different cross-sections (**right colored images**) (distances indicate the different positions of objective focus).

Fig. 3. Histology of melanoma metastasis (brown color, arrows) **(a)** in the sentinel (mandibular) lymph nodes of the mouse with ear tumor, 28th day after inoculation; H&E 100x, **(b)** adjacent to the adrenal gland, the mouse with skin tumor, 21th day after inoculation, H&E, 200x; **(c)** in the lung of the mouse with ear tumor, 28th day after inoculation, H&E, 100x (green line contours micrometastasis).

Fig. 4. Gene expression as a function of time after tumor inoculation (lower signal is equivalent to higher expression).

Fig. 5. A. Schematic of the detection of PA signals with an unfocused ultrasound transducer from ~200 μm peripheral blood vessel in intact animal skin with depth location of 0.3-0.5 mm through ~3.6-mm two skin layers. **B.** PA signals from vessels in intact skin (**top**), with additional one (**middle**) and two skin layers (**bottom**). Laser parameters**:** 532 nm; 50 mJ/cm^2. **C.** The detection of PA signals from ~0.9 mm mouse aorta with the depth location of 2.5 mm (from mouse back) with transducer through almost whole mouse body (irradiation from bottom, distance from aorta to

transducer is 11 mm). Laser parameters**:** 850 nm; 100 mJ/cm^2. **D.** PA signals from aorta (**top**), surrounding tissue (**middle**) and PA signals from simultaneously irradiated vessels at approximate depths of 0.3 mm and 2.4 mm (**bottom, 1 µs/div**) showing time-resolved discrimination of deep vessel in the presence of background from superficial vessels and strongly pigmented skin. Laser parameters**:** 850 nm; 100 mJ/cm^2.

Fig. 6. Pigmentation of MALME-3M human melanoma cells after 48-hr incubation with well-established agents (40): IBMX (1 µM), PD98059 (10 µM), and in combination (50:50, 10 µM), 4 x 10^6 cells in each well.

Fig. 7. The portable PAFC prototype with green pilot laser (**A**) for clinical studies on humans (**B**) consisted of a miniature focused ultrasound transducer and an optical fiber with cylindrical lens tip. **C.** Ultrasound image (General Electric Logiq 700) of ~1.5-mm hand vein at 1.5 mm depth and deep arteries. **D**. Near-infrared (NIR) image at wavelength 880 nm of arm (48).