Supporting Information

Quantitative imaging of 2 nm monolayer-protected gold nanoparticle distributions in tissues using laser ablation inductively-coupled plasma mass spectrometry (LA-ICP-MS)

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TEM images of AuNPs

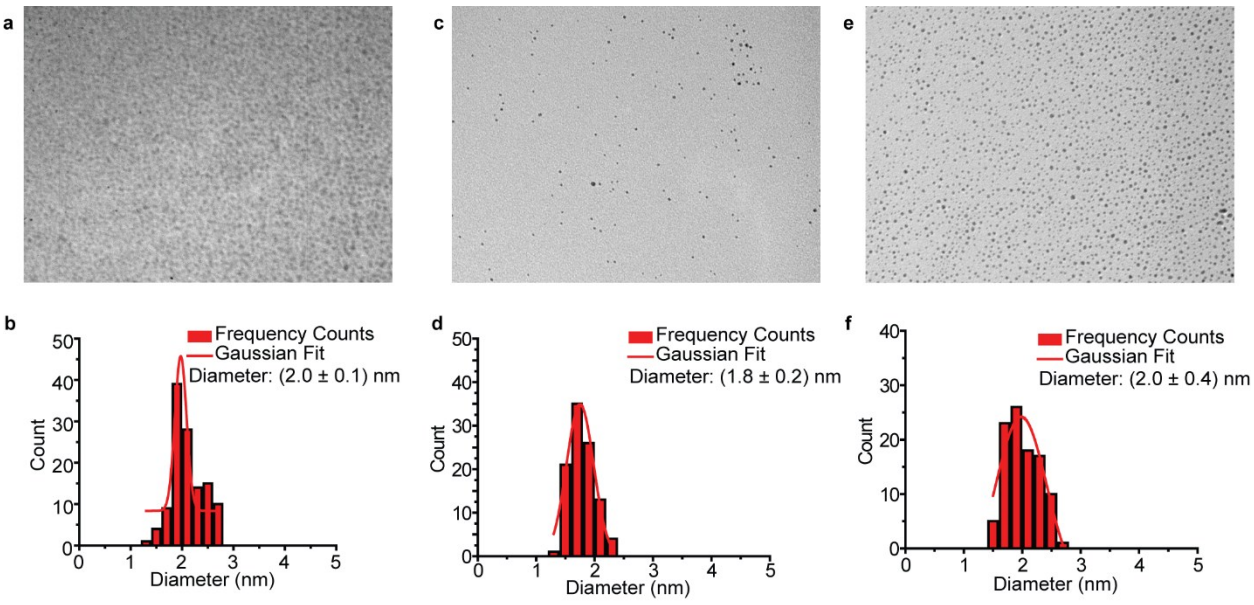


Figure S1. a) TEM image and b) core size distribution of AuNP 1, c) TEM image and d) core size distribution of AuNP 2, e) TEM image and f) core size distribution of AuNP 3

Sample holder preparation

To prepare the sample holder for matrix matched standards, a 50 mL centrifuge tube was cut at the 35 mL line and the top part of the tube with the cap was used. The tube was then filled with optical cutting temperature (OCT) solution. Five Edvotek 0.5-10 µL ultra pipet tips were attached to a piece of tape and slowly placed into the OCT solution. The resulting set up was placed in a freezer until the OCT solution was completely frozen. The embedded tips were then removed with tweezers, and the gold nanoparticle-tissue homogenate mixture was deposited into the five spaces that remained in the frozen OCT.

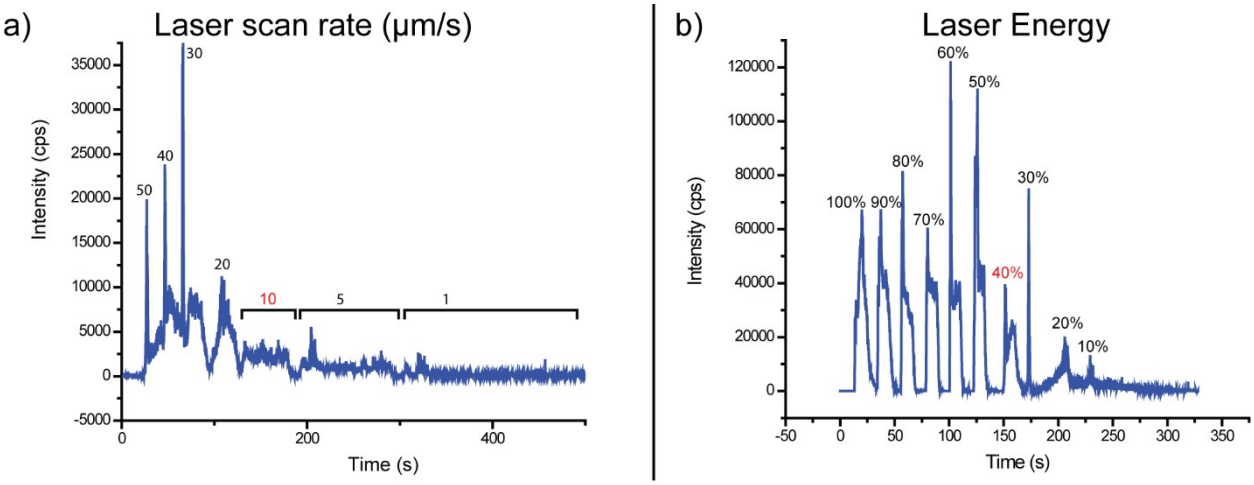


Figure S2. Identification of laser ablation condition for optimal resolution. a) Optimization of the laser scan rate showing the homogeneous ablation at 10 µm/s. b) Optimization of the laser energy showing homogeneous signal at a laser energy percentage of 40%, which corresponds to 3.34 J. Optimal values were identified by finding conditions that lead to relatively constant signals over a 500 µm space of inkjet-printed AuNPs. Relatively constant signals over a wide spatial range, rather than the most abundant signals, are important for obtaining images that more accurately reflect the spatial distributions of the element of interest (i.e. gold). The large signal spikes associated with some laser ablation conditions tend to result in lower image quality and fidelity. For example, large signal spikes at the interfaces of tissue regions (e.g. red pulp/white pulp interface in the spleen) can compromise the distribution information at these interfaces.

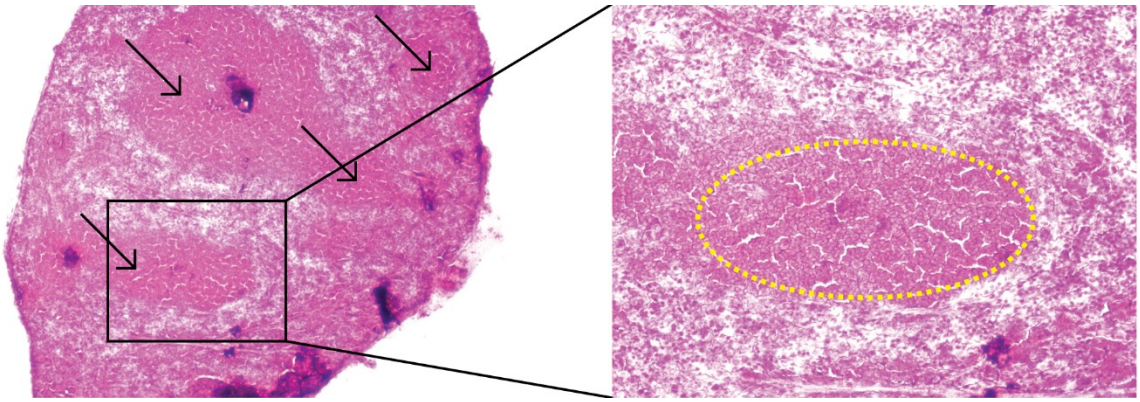


Figure S3. An example H&E stain images of the spleen, illustrating a means by which the red and white pulp can be distinguished. In addition to visual inspection as a means of distinguishing the red and white pulp regions, the white pulp appears as a denser purple color upon using an H&E stain, whereas the red pulp appears less dense. In the image on the left, black arrows indicate white pulp regions. A zoomed-in region on the right provides a closer image of the white pulp region as seen upon staining. The margins of the white pulp are highlighted by a yellow dashed line).

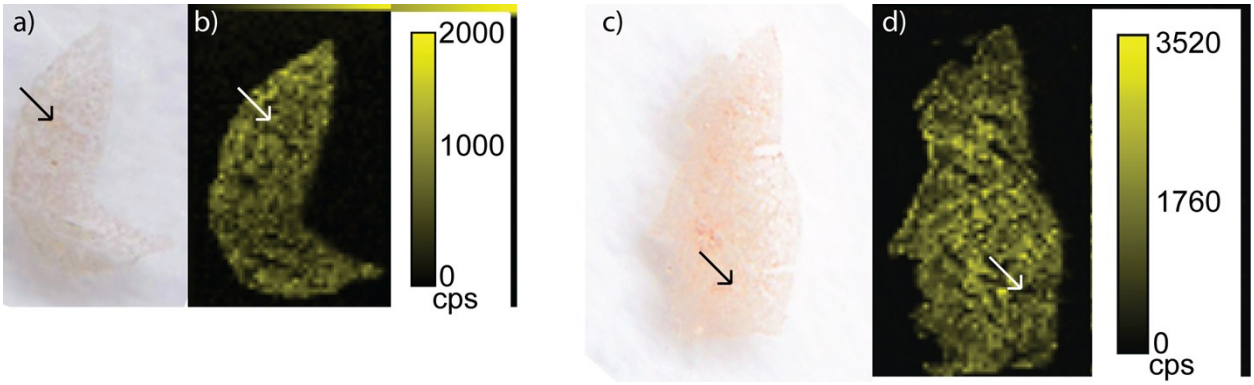
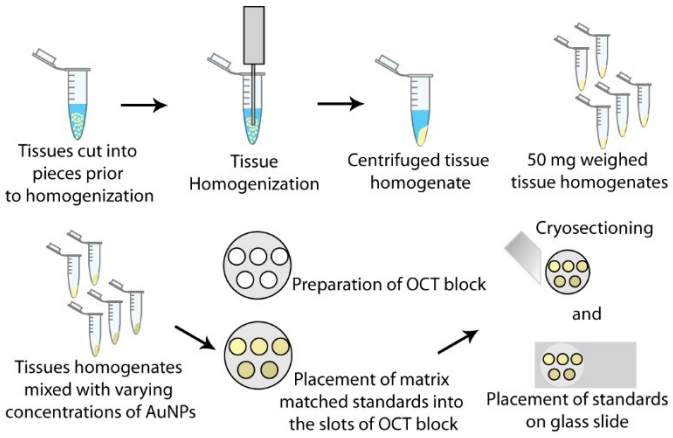


Figure S4. a) Optical image of a liver tissue taken from a mouse injected with AuNP 2. b) LA-ICP-MS image of the same liver tissue showing the distribution of gold. c) Optical image of a liver tissue taken from a mouse injected with AuNP 3. d) LA-ICP-MS image of the same liver tissue showing the distribution of gold. (cps = counts per second)

Matrix matched standardization method

Chicken breast and beef liver were purchased from a local market and used as the matrix-matched standards for spleen and liver, respectively. After homogenization, 50 mg of the

homogenates were weighed and mixed with 50 µL of varied concentration of AuNPs. The preparation of the matrix matched samples is illustrated in Scheme S1. The mixtures were then transferred into a homemade sample holder to be sliced into the desired thickness using the cryostat microtome and used without further treatment for the quantification purpose.



Scheme S1. Illustration of matrix-matched standard preparation.