

Electronic Supporting information for the manuscript entitled:

Functionalized Gold Nanoparticles: Detailed *In Vivo* Multimodal Microscopic Brain Distribution Study

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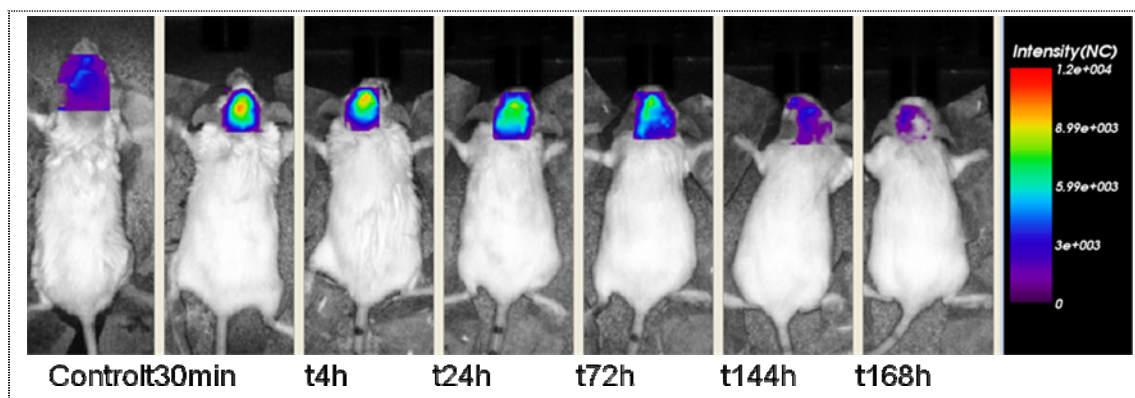


Fig. S1 *In vivo* images and fluorescence intensity map of the head of a mouse injected intravenously with PNP nanoparticles in which the albumin is labeled with Cy 5.5 in comparison to an untreated control. The series of images shows the intensity profile between 30 min and 7 days. The assessment of the nanoparticle fluorescence was done after background subtraction of the intrinsic autofluorescence measured in the control mouse.



Fig. S2 Tomographic reconstructions of the brain of an untreated mouse. The upper panel shows the transverse plane and the lower panel depicts the sagittal plane.

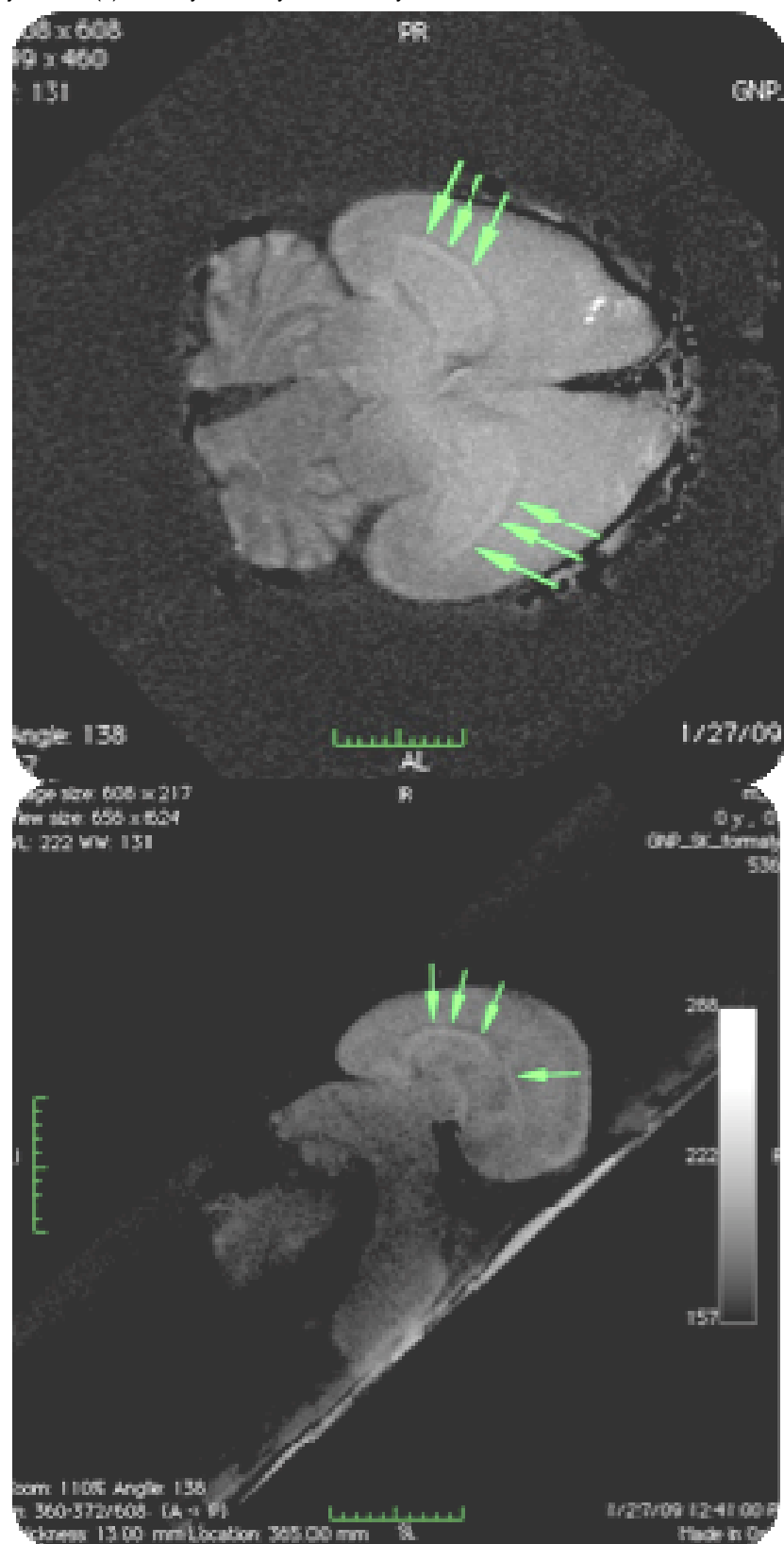


Fig. S3 Tomographic reconstructions of the brain 1 week after injection of the PNP nanoparticles. The upper panel shows the transverse plane and the lower panel depicts the sagittal plane. Green arrows highlight the boundary of lamellae separating the different thalamic subparts, areas in which a higher contrast was found.

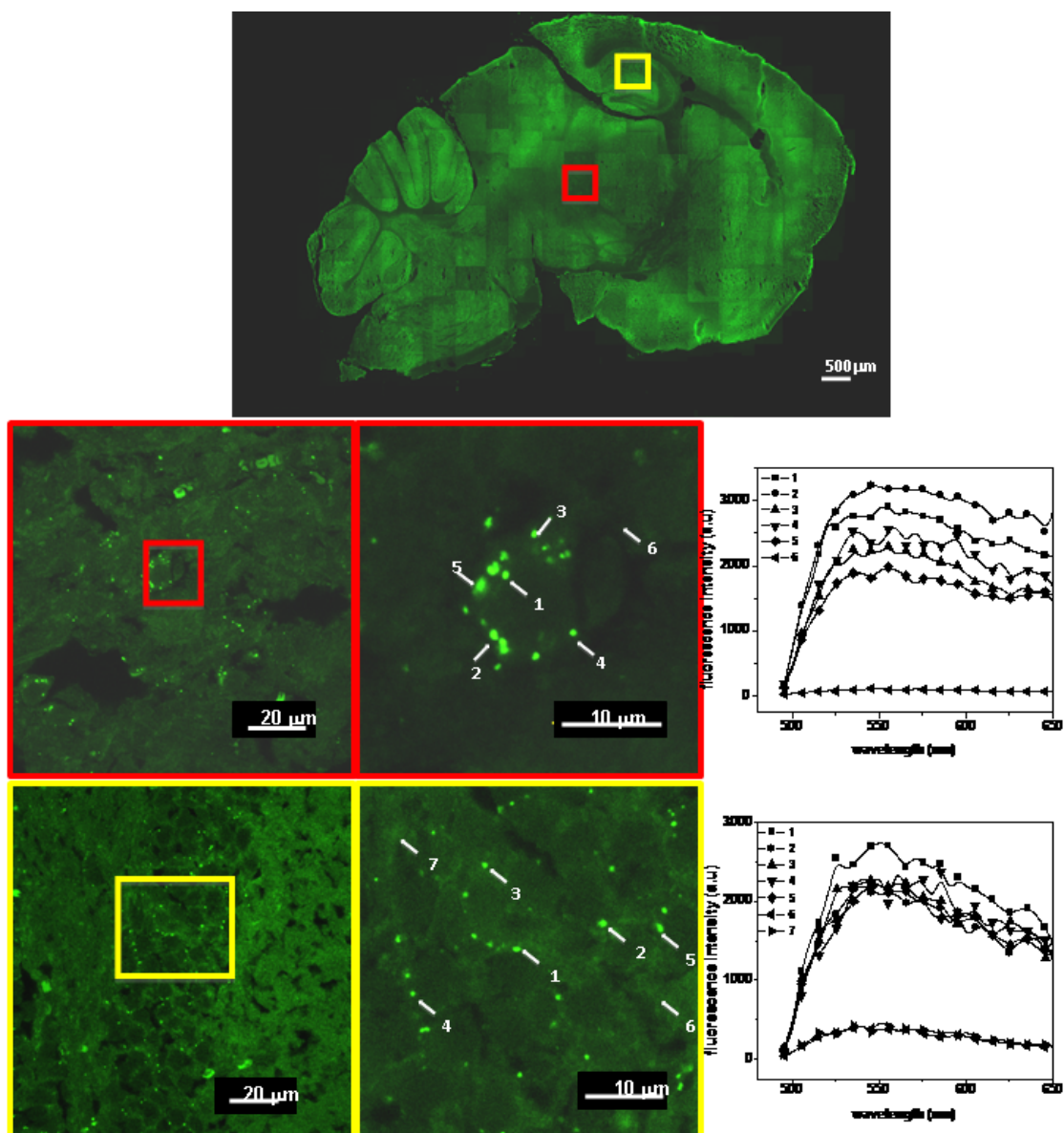
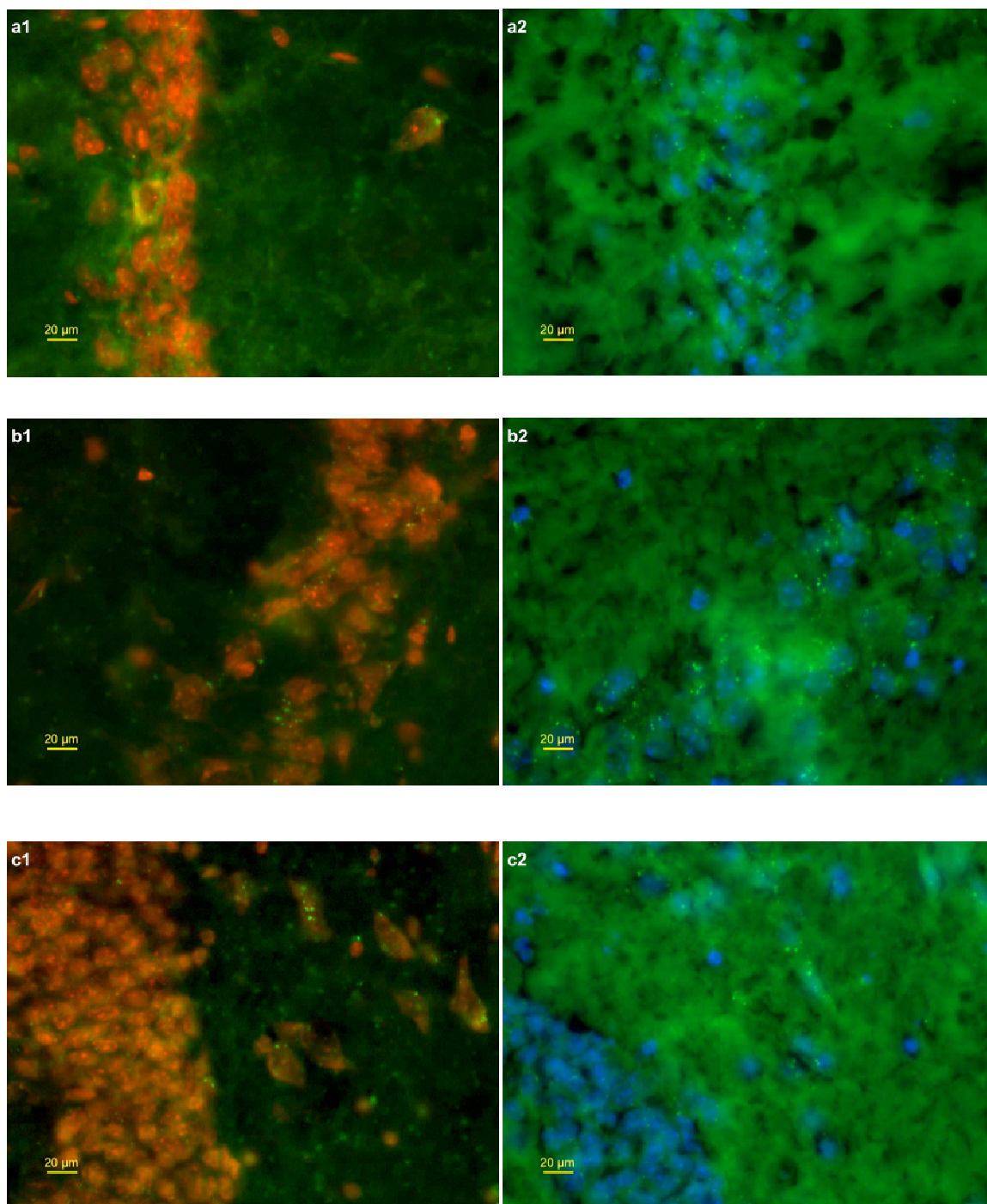


Fig. S4 CLSM images of an entire brain slice in low (a) (20X magnification) resolution. Selected areas (as highlighted in (a) with colored squares) with high particle concentration were imaged with higher magnification. (b) Red square (100X) – thalamus; (c) yellow (100X) - hippocampus CA1 cells. The adjacent spectra of the emission signal depict validation of the presence of nanoparticles labeled with FITC.



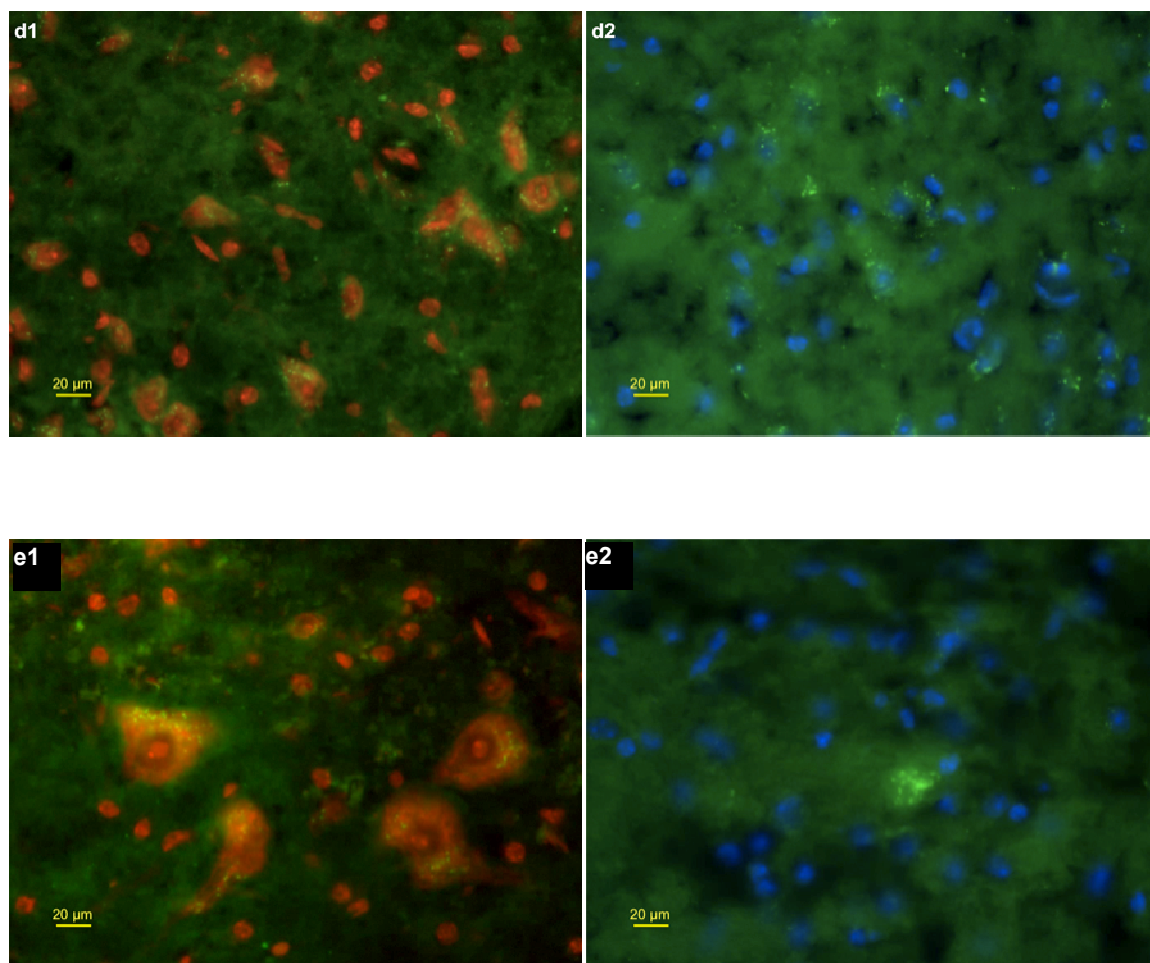


Fig. S5 Cellular distribution of the nanoparticles in specific neuronal regions of the brain was visualized using a combination of different labels. The green bright dots are clusters of PSS/PAH+HSA coated gold nanoparticles labeled with FITC (arrows); cell bodies (Nissl) are labeled red and the nucleus (DAPI) blue. The general green color of the tissue is the autofluorescence of the cells. The left column of images (x1) depicts the double stain Nissl/FITC while the right column of images (x2) shows (DAPI/FITC). The images a to c are from the hippocampal region: (a) CA1 pyramidal cells, (b) pyramidal cells of the CA3 region, and (c) cells from the dentate gyrus. The images depicted in (d) are from the thalamus; and (e) cells in the medulla towards the spinal cord.

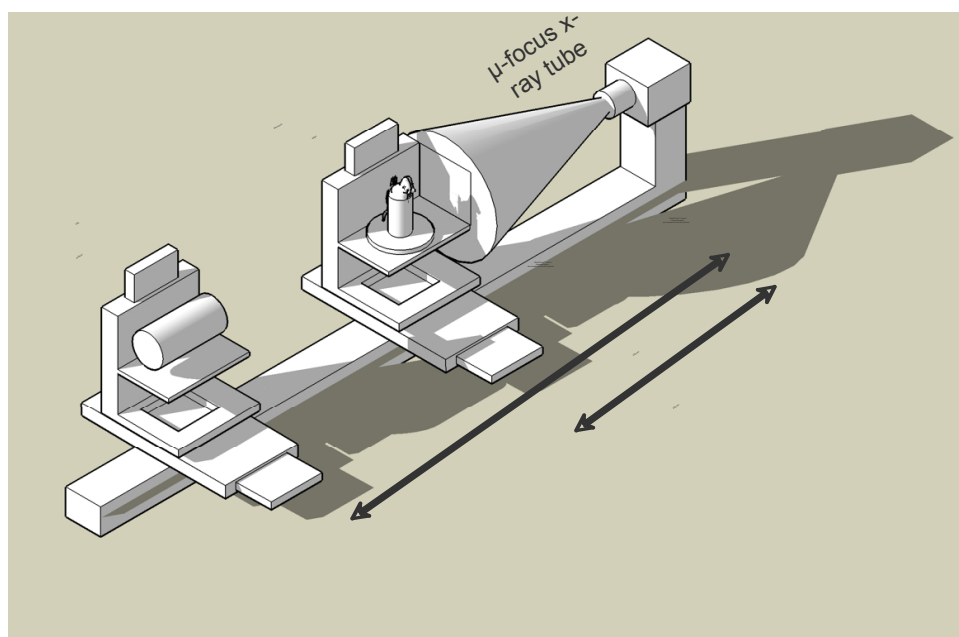


Fig. S6 Sketch of the imaging set-up at the TOMOLAB