Supporting Informations

1. KTP Particles synthesis : Influence of the neutralization pH using K_2CO_3.

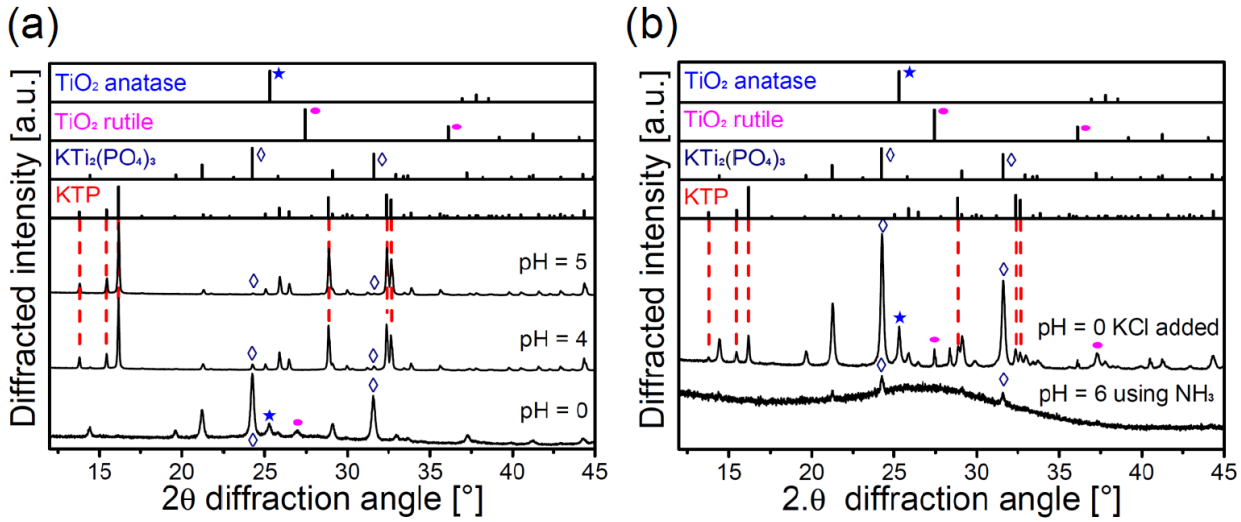

Figure S1. Influence of the synthesis parameters. (a) Powder X-Ray Diffraction diagrams for synthesis corresponding to different pH of neutralization. (b) Powder X-Ray Diffraction diagrams for synthesis without neutralization but still adding KCl (quantity corresponding to the one of K ion added with K_2CO_3 during standard synthesis) and for synthesis using NH3 instead of K_2CO_3. Diagrams corresponding to the different phases are shown on top according to the JCPDS files (n°01-078-1342 (KTP), n°01-076-3177 (TiO_2 anatase), n°01-076-0440 (TiO_2 rutile) and n°00-034-0131 ($KTi_2(PO_4)_3$)). The diagrams were obtained using Cu K_α radiation.

2. Setup for optical studies

The setup used for optical studies is shown in **Figure S2**.[1] It combines a customized two-photon scanning optical microscope with an AFM (Asylum Research, MFP-3D-BIO).

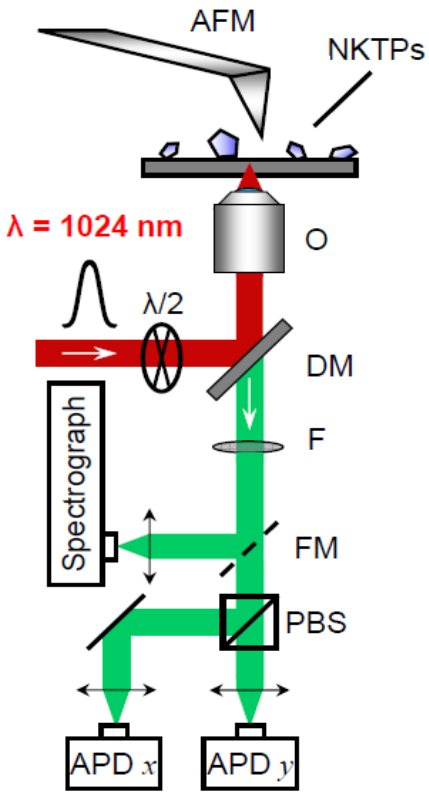

Figure S2. Setup used for the characterization of KTP nanoparticle at the individual level. AFM: tip of the atomic force microscope operated in contact mode. O: oil-immersion microscope objective (Olympus, x60, NA=1.35); DM: dichroic mirror; F: optical filter selecting the spectral detection window. FM: flipping mirror for either spectral analysis or polarization-sensitive characterization. Spectral analysis is realized using an imaging spectrograph equipped with a back-illuminated cooled charged-coupled-device array. Polarization-sensitive detection consists of a polarizing beamsplitter (PBS) and silicon avalanche photodiodes (APD) placed on the two output ports of the PBS. The polarization diagram is obtained by rotating the half-wave plate on the infrared excitation beam and recording the detected intensity on each APD. By choosing the filter F, we can observe the combined emission of SHG from KTP nanoparticles and TPL from dyes (720 nm shortpass filter) or we can select the SHG (510 nm bandpass filter).

3. Biocompatibility test of the KTP nanoparticles.

As biocompatibility is a key parameter of any biological use of a nanoprobe, we quantified the potential impact of KTP nanoparticles on the dendritic growth of cortical neurons. Dendrites of cultured cortical were identified on the basis of the expression of the microtubule-associated protein 2 (MAP2). MAP2 is a protein which belongs to the microtubule-associated protein family, involved in microtubule assembly and specifically enriched in dendrites, implicating a role in determining and stabilizing dendritic shape during neuron development dendrites.[2,3] We took advantage of this staining to quantify dendrite morphology as a toxicological marker **(Figure S3a)**. Since the cortical neuron dendritic follows a strict time-dependent development, this sequence can be used as a bona fide test for neurotoxicology.[4] Total dendritic length was measured at DIC2 as 27.9 $\pm$ 1.9 μm and 36.5 $\pm$ 3.7μm for control and KTP nanoparticles conditions, respectively. At DIC4, the total dendritic length was respectively 61.6 $\pm$ 7.4 μm and 61.5 $\pm$ 8.3μm **(Figure S3b and S3c)**. Altogether, these results indicate that the KTP nanoparticles did not modify the dendritic morphology during this four-day critical period of neuronal development, corresponding to the absence of KTP nanoparticles induced intracellular toxicity.

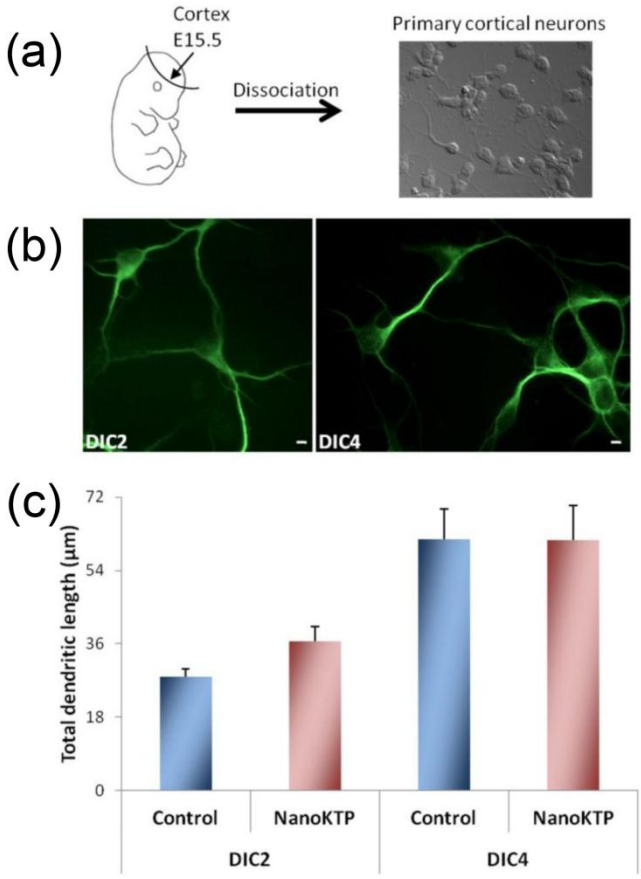

Figure S3. Test of biocompatibility based on the quantitative analysis of dendritic growth. (a) Schematic representation of mouse cortex microdissected at embryonic day 15.5 (E15.5). Neurons were isolated and plated as indicated in Methods. Dissociated neurons are incubated with the solution of KTP nanoparticles (concentration 100 µg/µL) during 30 minutes and plated. (b) Example of a cultured cortical neuron which uptook KTP nanoparticles at day in culture 0 (DIC0), fixed at DIC2 and DIC4 and stained for MAP2 (in green). (c) Quantification of total dendritic length at DIC2 and DIC4 for control neurons (Control) and neurons that uptook the KTP nanoparticles (NanoKTP). No statistically significant differences were measured during this time length. Scale bar: 10 µm.

REFERENCES

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