Intraneuronal transport measurement by tracking the optical non-linear response of nanoparticles

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Brain diseases involve a large network of genes displaying subtle changes in their expression. Abnormalities of intraneuronal transport have been linked to genetic risk factors found in patients but current techniques cannot detect minor changes. Our team has developed a sensitive method relying on spontaneous internalization and subsequent single particle tracking of fluorescent nanodiamonds in endosomes of mouse hippocampal neurons in 2D cultures. This method is able to detect slight alterations of intraneuronal transport in neurons from transgenic mouse models displaying a genetic risk factor of a neuropsychiatric disease [1].

The extent of this technique to more realistic and complex 3D neuronal network can benefit from the use of non-linear crystals that can be excited in the near-infrared spectral window in which tissue are transparent, allowing to study intraneuronal transport in deep tissues. We will present our first results regarding the tracking of translation and rotational motion of endosomes in 2D-cultures using non-linear nanocrystals displaying second harmonic response detected by fast scanning 2-photon excited microscopy (Fig.1).

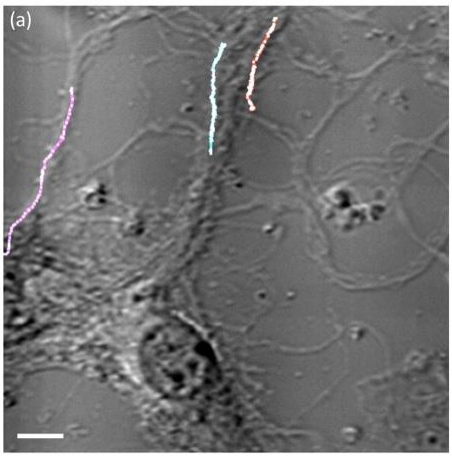

Figure 1: Tracking of second harmonic generation (SHG) of non-linear crystals of $KTiPO_4$ (KTP, size ≈ 140 nm) internalized inside 2D-cultures of mouse cortical neurons. Dott contrast image of a neuron overlapped with 3 representative trajectories of nanoKTP. 2-photon microscope of *France Life Imaging* PIMPA platform (Orsay), λ_{exc}=890 nm, laser power ≈1 mW, SHG detection filter: 448±20 nm. Scale bar: 10 µm.

[1] S. Haziza, *et al.,* « Fluorescent nanodiamond tracking reveals intraneuronal transport abnormalities induced by brain-disease-related genetic risk factors," Nat. Nanotech. **12**, 322 (2017).