$BiFeO_3$ harmonic nanoparticle (BFO-HNPs) use for the stem cell tracking: Labeling investigation by non linear microscopy and X-ray fluorescence

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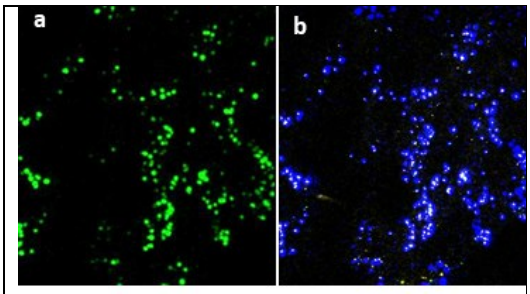
Duchenne Muscular Dystrophy is the most common form of degenerative muscle disease; currently, there is no effective treatment. In 2011, our group showed that an adult stem cell population (MuStem) isolated from healthy dog skeletal muscle induces long-term muscle repair and striking clinical efficacy after its systemic delivery in clinically relevant dystrophic dog. During last years, our group isolated the human counterparts (hMuStem) [1]. To achieve the full therapeutic potential of the hMuStem cells, their homing process, survival and engraftment post-transplantation must be clearly understood. $BiFeO_3$ harmonic nanoparticles (BFO-HNPs) were used as probes for the hMuStem cell tracking [2]. We demonstrate the possibility of identifying <100 nm BFO-HNPs in depth of muscle tissue at more than 1 mm from the surface by multiphoton microscopy. Based on this successful assessment, we monitor over 14 days any modification on proliferation and morphology features of the hMuStem cells upon exposure to BFO-HNPs revealing their high biocompatibility. To complete these studies, the stability of BFO-HNPs was followed in the labeled hMuStem cells by investigation of Bi and Fe X-ray fluorescence mapping on both Nanoscopium (Soleil, Gif-sur-Yvette, France) and ID16B (ESRF, Grenoble, France) beamlines. In this work, correlation between non-linear microscopy and X-Ray fluorescence was done. Bi and Fe X-Ray fluorescence allowed us to localize with high resolution the BFO-HNPs in the labeled hMuStem cells and the variation of Bi/Fe ratio was analyzed to detect possible dissociation of the nanoparticles in the labeled cells.



a: Second Harmonic Generation from BFO-HNPs observed by biphotonic microscopy. b: Bismuth X-ray fluorescence from BFO-HNPs detected on Nanoscopium beamline (Synchrotron Soleil)

References:

[1] J. Lorant, C. Saury and C.C Collaborator "Skeletal muscle regenerative potential of human MuStem cells following transplantation into injured skeletal muscle". Mol Ther, 26(2):618-633 (2018).

[2] L. Dubreil, I. Leroux and C.C. Collaborator "Multi-harmonic Imaging in the Second Near-Infrared Window of Nanoparticle-Labeled Stem Cells as a Monitoring Tool in Tissue Depth" *ACS Nano.*, 25,11(7):6672-6681 (2017).