Femtosecond Laser Microscopy of Stem Cells

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Multiphoton femtosecond laser near-infrared microscopes, such as SHG/THG microscopes, two-photon/three-photon microscopes, and Raman/CARS microscopes, opened a new way to 3D live cell imaging. Furthermore, if multiphoton microscopes are operating at very high transient TW/cm^2 light intensities, highly localized destructive effects occur, that can be used for micro-/nanosurgery (1-2).
Stem cells are known to differ from normal cells by their self-renewing ability and capability of generating specialized cell types. There is the hope that stem cells/iPS cells may cure illnesses that remained incurable up to date as well as to engineer tissues/organs.
Femtosecond laser microscopes have been used to perform label-free optical metabolic imaging of stem cells by time-correlated single autofluorescence photon counting (3-7). Recently, they were also employed to perform optical reprogramming of adult skin cells to generate iPS cells by the generation of transient nanoholes and the diffusion of certain DNA cocktails into the cell's cytoplasm (8).
This presentation focuses on the application of femtosecond laser microscopy for multiphoton imaging and nanoprocessing of stem cells and induced pluripotent stem (iPS) cells.

1. Uchugonova. A., et al., "Targeted transfection of stem cells with sub-20 femtosecond laser pulses," *Opt. Exp.* **16**, 9357- 9364 (2008).
2. Uchugonova, A., et al., "Optical knock out of stem cells with extremely ultrashort femtosecond laser pulses," *J. Biophot.* **1**, 463-469 (2008)
3. König, K., Uchugonova, A., Gorjup, E., "Multiphoton fluoprescence Lifetime imaging of 3D stem cells spheroids during differentiation," *Microsc. Res. Tech.* **74**, 9-17 (2011)
4. Uchugonova, A. and König, K., "Two-photon autofluorescence and second harmonic imaging of adult stem cells," *J. Biomed. Opt.* **13**, 054068-8 (2008)
5. Uchugonova, A., et al., "Watching stem cells in the skin of living mice non-invasively," *Cell Cycle* **10(12)**, 1-4 (2011)
6. Uchugonova, A. "Multiphoton Autofluorescence Lifetime Imaging of Induced Pluripotent Stem Cells," *J. Biomed. Opt.* **22(6)**, 660018 (2017)
7. Uchugonova, A and Hoffman, MR. (2018) Non-invasive single-photon and multi- photon imaging of stem cells and cancer cells in mouse models. In König, K (Ed.) "Multiphoton Microscopy and Fluorescence Lifetime Imaging Applications in Biology and Medicine", Berlin, Boston De Gruyter, pp. 411-421
8. Uchugonova, A., et. al., "Optical reprogramming of human cells with an ultrashort femtosecond laser microfluidic transfection platform," *J. Biophotonics* **9(9)**, 942-7 (2016)