University of Basel

Swiss Nanoscience Institute

PAUL SCHERRER INSTITUT PSI

Swiss Nanoscience Institute
Center of Excellence supported by the University of Basel and the Canton of Aargau

Targeted scintillator nanoparticles for X-ray-mediated optogenetics in behaving mice

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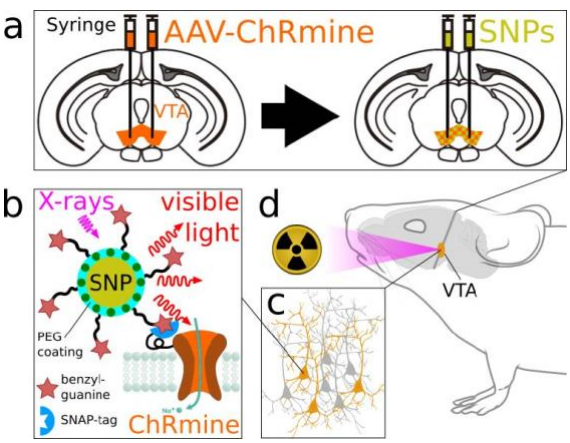
Join our interdisciplinary team of chemists, neurobiologists and X-ray physicists to work on the next generation of wireless, minimally invasive X-ray mediated optogenetic tools. What we offer:

- Access to cutting-edge research infrastructure at the Paul Scherrer Institute (PSI) and the University of Basel
- Mentorship for personal and professional development
- Generous research support

The successful candidate will be working both at the Paul Scherrer Institute as well as at the Department of Chemistry at University of Basel. The student will become a member of the Swiss Nanoscience Institute (SNI) PhD school and will benefit from personal support, career and soft skills training and both social and scientific SNI events. The earliest starting date for the position is January 1st 2023.

Project Description. Manipulating the activity of well-defined groups of neurons is an important tool for probing the function and connectivity of neuronal circuits [1,2]. In optogenetics, light-switchable transmembrane proteins are expressed in specific groups of neurons which can be depolarized (excited) or hyperpolarized (inhibited) by visible light with high temporal precision [3]. But the penetration depth of visible light is limited to a few hundreds of micrometres from the brain surface [4]. Conventional optogenetics requires an invasive surgery to implant tethered optical fibres that are relatively thick and increase the risk of brain tissue damage and neuroinflammation. Therefore, X-ray mediated optogenetic manipulation has been proposed as a minimal invasive alternative [5]. We aim to develop functionalized and biocompatible scintillator nanoparticles (SNPs) that can adhere to cell membrane-localised light-switchable proteins in neurons. If exposed to X-ray radiation, these SNPs will emit visible light which activates the light-switchable proteins. This project is part of a larger interdisciplinary effort at the PSI with the goal of developing a pipeline for low-dose focal X-ray-mediated optogenetics and in vivo two-photon calcium imaging in behaving mice. Biocompatible, functionalized scintillator nanoparticles could become a very interesting non-invasive alternative for optogenetic therapies of neurological diseases in humans.

Interested? Then apply on phd.nanoscience.ch.
For further information please contact: adrian.wanner@psi.ch



X-ray mediated optogenetics. a) The schematic shows a coronal section of a mouse brain. Modified adeno-associated viruses (AAV) are injected with a syringe into deep brain regions such as the ventral tegmental area (VTA). The AAVs release artificial DNA into infected cells that codes for light-switchable proteins such as the red-shifted channelrhodopsin ChRmine. About 4 weeks after the AAV injection the light-switchable proteins have been integrated into the cell membranes of the neurons of interest. Subsequently, scintillator nanoparticles (SNPs) are injected into the same area. b) The surface of the SNPs will be functionalized such that the particles can associate with the light-switchable proteins. d) Up on radiation with focused X-rays, the SNPs emit visible light which activates the light-switchable proteins in the neurons of interest (see c)) in order to excite or inhibit them.

1] Ditterich et al. Nat Neurosci. 2003;6: 891–898. [2] Salzman et al. Nature. 1990;346: 174–177. [3] Boyden et al. Nat Neurosci. 2005;8: 1263–1268. [4] Aravanis et al. J Neural Eng. 2007;4: S143–56. [5] Bartley et al. Front Synaptic Neurosci. 2019;11: 24.