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Light controlled nanoparticles for deep tissue optogenetics?

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In the last decade, optogenetics has emerged as a powerful tool to investigate the workings of the nervous system and has been branded as the breakthrough of the decade. It provides invaluable insight into the mechanisms underlying diseases such as epilepsy, Parkinson's, etc. and has enormous therapeutic potential. However, this technique has yet to be realized in clinical practice since the visible light (usually blue light) required for excitation of light-sensitive proteins necessitates invasive implantation of optical fibers for light delivery. Near Infrared (NIR) light has excellent tissue penetrating capabilities in comparison to visible light but cannot be used directly for optogenetics. So we propose to use lanthanide doped Upconversion Nanoparticles (UCNs) as nanotransducers to convert NIR light to visible light for optogenetic application. This allows optogenetic manipulations to be performed in deep tissues and prevents the use of invasive optical fibers to be implanted. Here we report a quasi-CW NIR excitation regime that significantly enhances high energy-photon (UV and blue) emissions from UCNs. We then use UCNs for optogenetic manipulations *in vitro* and in *C. elegans* (expressing channel rhodopsin). Our findings indicate that using the quasi-CW NIR excitation regime, enables the activation of channel rhodopsin with a lower average NIR excitation power and lower concentration of UCNs without causing any phototoxicity and heating up effects. The findings reported herewith have overcome the current bottleneck in using UCNs for photoactivation and is foreseen to accelerate the use of UCNs in *in vivo* and clinical photoactivation.

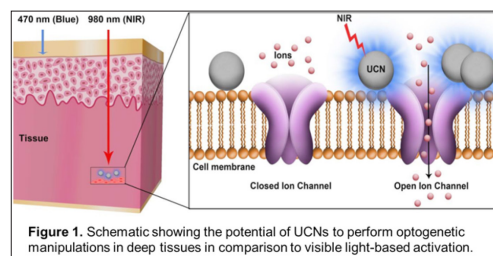


Figure 1. Schematic showing the potential of UCNs to perform optogenetic manipulations in deep tissues in comparison to visible light-based activation.

Biography

Muthu Kumara Gnanasammandhan Jayakumar is a Biomedical Engineer with 9 years research experience in the fields of nanomedicine, gene therapy, drug delivery, bioimaging and optogenetics. He is currently a Research Fellow in the Department of Biomedical Engineering, National University of Singapore, Singapore. He has authored/co-authored several peer reviewed publications in esteemed journals including Nature Medicine, Chemical Society Reviews, Nature Protocols and PNAS. He also has successfully coauthored several multi-institutional grants and has a patent on fluorescent upconversion nanoparticles. He has worked extensively with clinicians, academicians, industrialists and venture capitalists.

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