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Near-Infrared Optogenetic Manipulation of a Channelrhodopsin via Upconverting Nanoparticles

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Abstract : Optogenetics is an innovative technology now widely adopted by researchers in different fields of the biological sciences. However, due to the weak tissue penetration capability of the short wavelengths used to activate light-sensitive proteins, an invasive light guide has been used in animal studies for photoexcitation of target tissues. Upconverting nanoparticles (UCNPs), which transform near-infrared (NIR) light to short-wavelength emissions, can help address this issue. To improve optogenetic performance, we enhance the target selectivity for optogenetic controls by specifically conjugating the UCNPs with light-sensitive proteins at a molecular level, which shortens the distance as well as enhances the efficiency of energy transfer. We tagged V5 and Lumio epitopes to the extracellular N-terminal of channelrhodopsin-2 with an mCherry conjugated at the intracellular C-terminal (VL-ChR2m) and then bound NeutrAvidin-functionalized UCNPs (NAv-UCNPs) to the VL-ChR2m via a biotinylated antibody against V5 (bV5-Ab). We observed an apparent energy transfer from the excited UCNP (donor) to the bound VL-ChR2m (receptor) by measuring emission-intensity changes at the donor-receptor complex. The successful patch-clamp electrophysiological test and an intracellular Ca2+ elevation observed in the designed UCNP-ChR2 system under optogenetic manipulation confirmed the practical employment of UCNP-assisted NIR-optogenetic functionality. This work represents a significant step toward improving therapeutic optogenetics.

Keywords : Channelrhodopsin-2, near infrared, optogenetics, upconverting nanoparticles
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