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Upconversion Nanoparticles–Based Multiplex Protein Activation to Neuron Ablation for Locomotion Regulation

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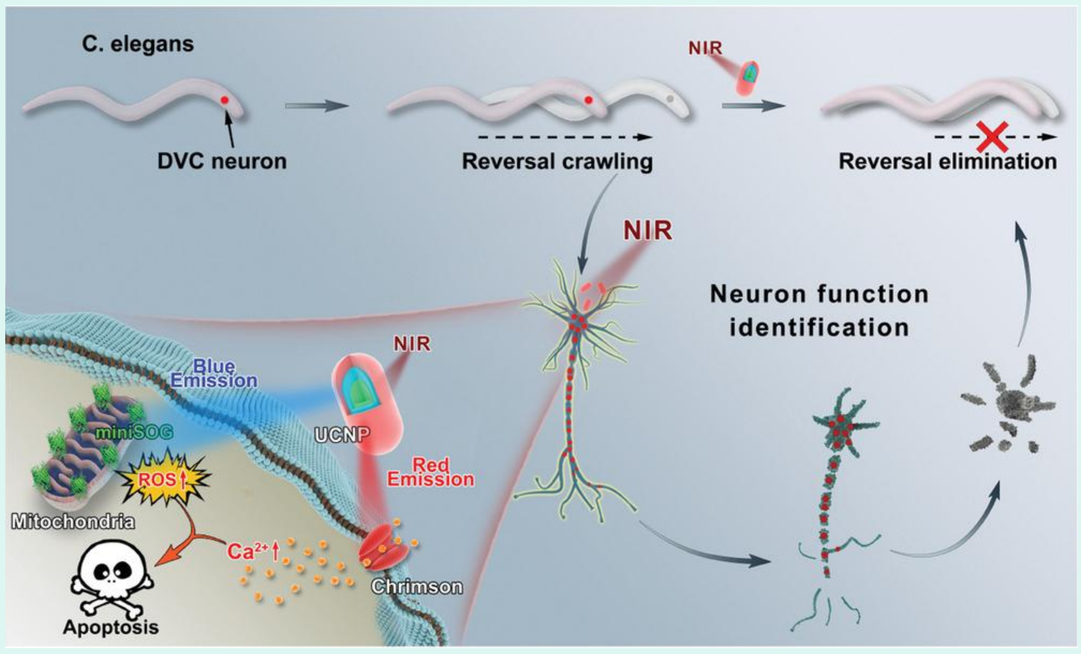

Scheme Schematic illustration of NIR light-induced neuron function identification strategy based on UCNPs-multiplex optogenetic protein activation system.

➢ Abstract

The optogenetic neuron ablation approach enables noninvasive remote decoding of specific neuron function within a complex living organism in high spatiotemporal resolution. However, it suffers from shallow tissue penetration of visible light with low ablation efficiency. This study reports a upconversion nanoparticle (UCNP)-based multiplex proteins activation tool to ablate deep-tissue neurons for locomotion modulation. By optimizing the dopant contents and nanoarchitecure, over 300-fold enhancement of blue and red emissions from UCNPs is achieved upon 808 nm irradiation. Such emissions simultaneously activate mini singlet oxygen generator and Chrimson, leading to boosted near infrared (NIR) light-induced neuronal ablation efficiency due to the synergism between singlet oxygen generation and intracellular Ca^{2+} elevation. The loss of neurons severely inhibits reverse locomotion, revealing the instructive role of neurons in controlling motor activity. The deep penetrance NIR light makes the current system feasible for in vivo deep-tissue neuron elimination. The results not only provide a rapidly adoptable platform to efficient photoablate single- and multiple-cells, but also define the neural circuits underlying behavior, with potential for development of remote therapy in diseases.

➢ Results

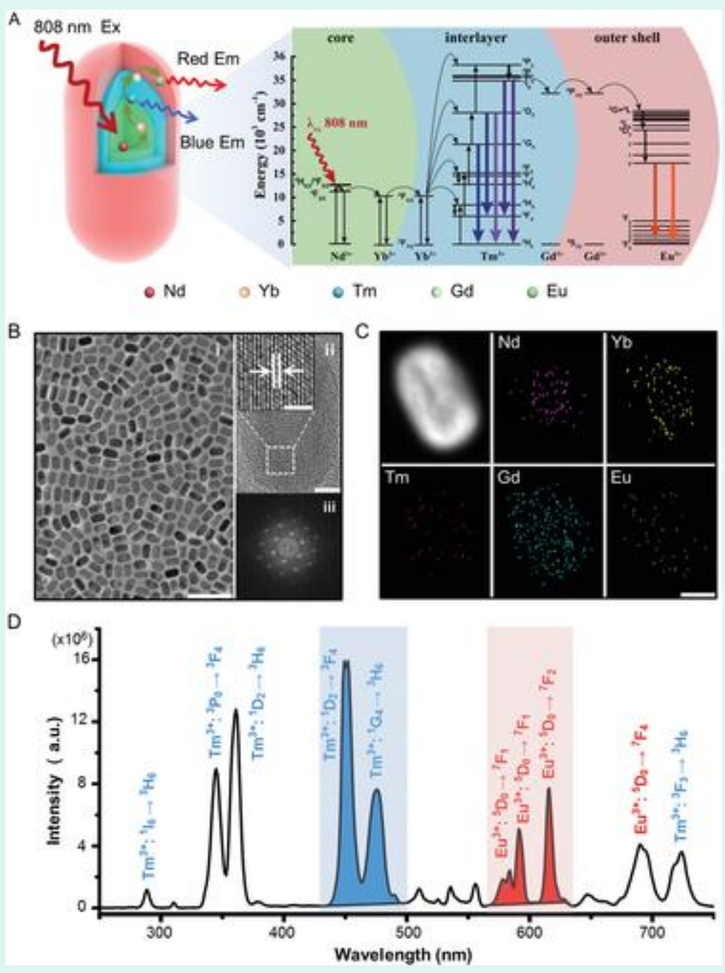

Figure 1 Synthesis and characterization of core/shell/shell UCNPs.

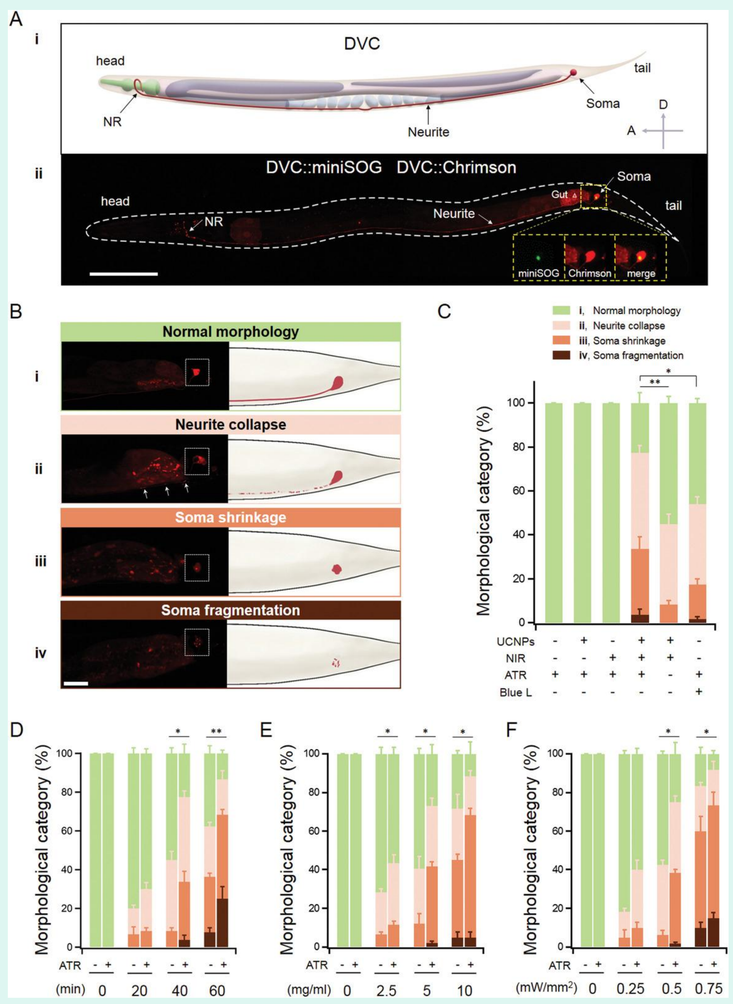

Figure 2 Multiplex optogenetic activation of miniSOG and Chrimson promotes the ablation of DVC interneuron with high-efficiency by UCNPs

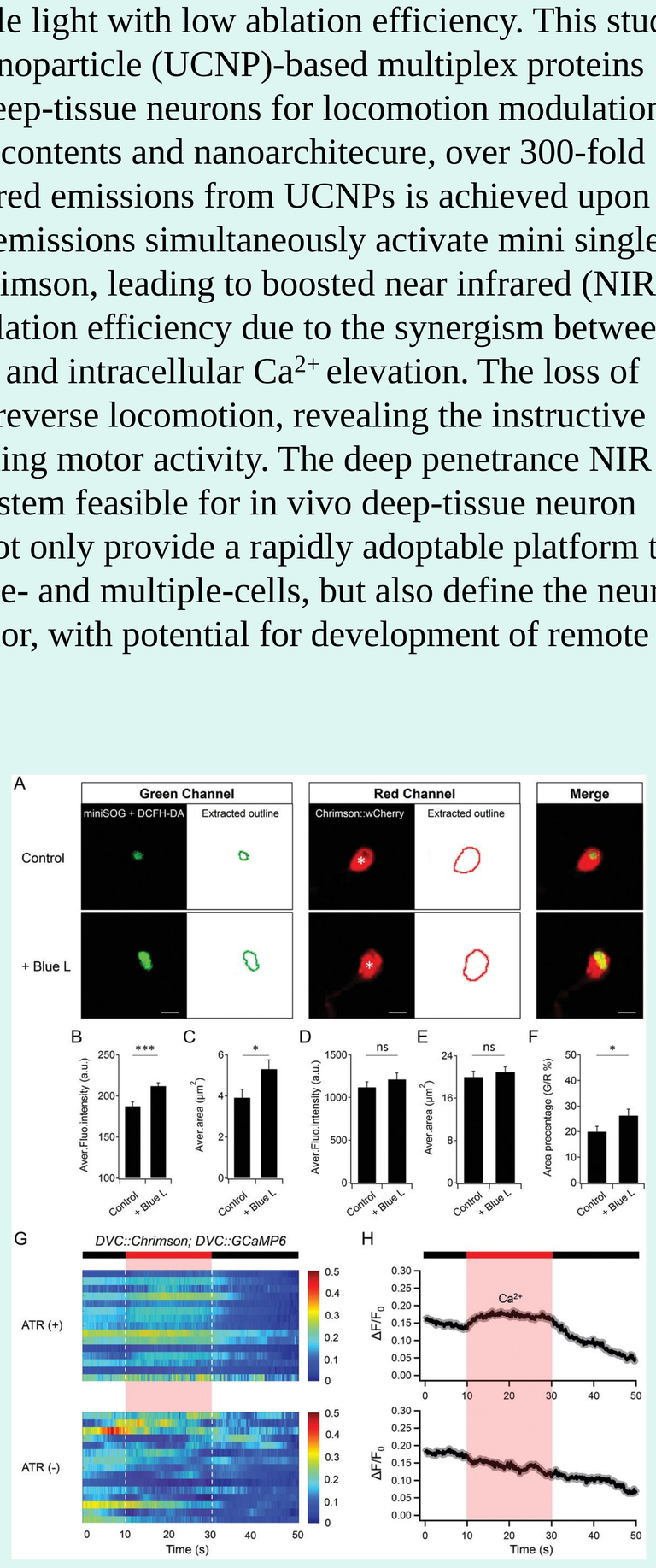

Figure 3 ROS generation and Ca^{2+} elevation in DVC neuron by the irradiation of blue and red lights, respectively.

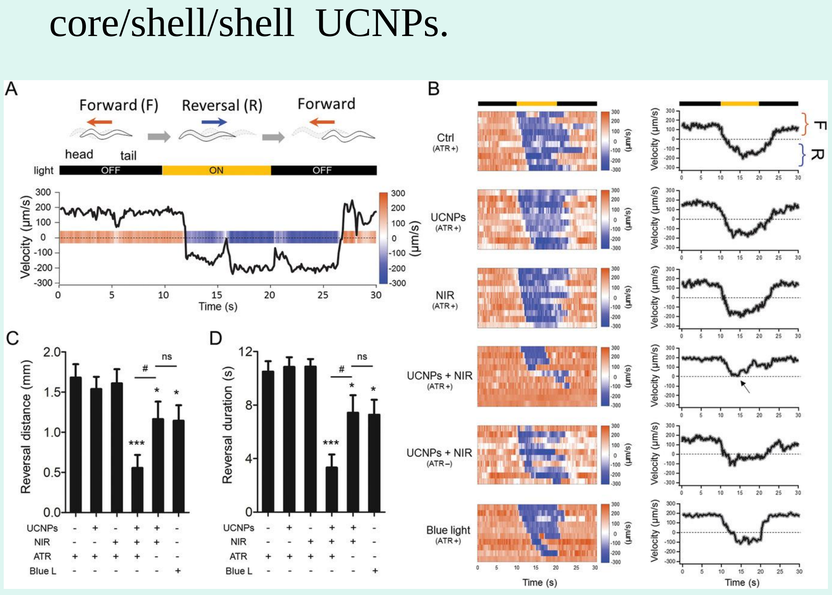

Figure 4 Simultaneous optogenetic activation of miniSOG and Chrimson by UCNPs promotes locomotion behavior inhibition rate in C. elegans.

➢ Conclusion

The newly developed optogenetic method also enables deep-tissue neuron elimination. This strategy not only holds great potential to ablate single- and multiple-cells in high spatiotemporally precise manner, it also opens new possibility to decipher cell function and activities, and potentially, benefit for the development of new technologies and therapeutic treatment toward diseases.

➢ Reference

ZHANG Y, ZHANG W, ZENG K, et al. Upconversion Nanoparticles-Based Multiplex. Protein Activation to Neuron Ablation for Locomotion Regulation [J]. Small, 2020, 16(8): e1906797

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