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Super-Resolution Imaging and Enhanced Spontaneous Neuritogenesis with Nanodiamond Probe

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Extended Abstract

Regeneration of defective neurons in central nervous system is a highlighted issue for neurodegenerative disease treatment [1]. Various tissue engineering approaches have focused on neuritogenesis to achieve the regeneration of damaged neuronal cells because damaged neurons often fail to achieve spontaneous restoration of neonatal neurites [2]. Meanwhile, as a result of the demand for a better diagnosis, studies of super-resolution imaging techniques in fluorescence microscopy have triggered the technological development to surpass the classical resolution dictated by the optical diffraction limit for precise observations of neuronal behaviors [3].

In this study, the multi-functions of nanodiamonds (NDs) as neuritogenesis promoters and super-resolution imaging probes were studied. In vitro and ex vivo images were visualized through two-photon microscopy using NDs as imaging probes and the direct stochastic optical reconstruction microscopy (dSTORM) process was performed for the super-resolution reconstruction owing to the photoblinking properties of NDs, thereby addressing the problem of image distortion due to nano-sized particles, including size expansion and the challenge in distinguishing the nearby located particles. Furthermore, NDs were endocytosed by HT-22 hippocampal neuronal cells and promoted spontaneous neuritogenesis without any differentiation factors, where NDs exhibited no significant toxicity in vitro or in vivo with their outstanding biocompatibility. Additionally, ex vivo imaging of the mouse brain was performed 24 h after the intravenous injection of NDs and confirmed that NDs could penetrate the blood-brain barrier (BBB) and retain their photoblinking property for dSTORM application.

In conclusion, it is demonstrated that the NDs are capable of dSTORM super-resolution imaging, neuritogenic facilitation, and BBB penetration, suggesting their remarkable potential in biological applications.

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