NIR-II Fluorescent Probes for in vivo Multiplexed Biodetection

Fan Zhang

No.2005, Songhu Road, Yangpu District, Shanghai, China
Department of Chemistry & Laboratory of Advanced Materials & Collaborative Innovation Center of Chemistry for Energy Materials & State Key Laboratory of Molecular Engineering of Polymers, Fudan University
Shanghai, China
zhang_fan@fudan.edu.cn

Fluorescent imaging and sensing with high spatio-temporal resolution and sensitivity allow the direct visualization of dynamic biological interests at different levels of components from the molecules, cells in vitro to the tissues, organs in vivo. Disastrous light attenuation and background autofluorescence in tissue at conventional imaging window of 400-900 nm have limited this technique for in vivo analysis, but they both decrease at progressively longer wavelength. Over the past decade, advances in the development of functional fluorophores operating in the second near-infrared window (NIR-II; 1000-1700 nm) have allowed the investigations of deep anatomical features in vivo with high resolution and sensitivity. However, inhomogeneous signal attenuation due to biological matter hampers the application of multiple-wavelengths NIR-II probes to multiplexed imaging. Here we present lanthanide-doped NIR-II nanoparticles with engineered luminescence lifetimes for in vivo quantitative imaging using time-domain multiplexing. To achieve this, we devise a systematic approach based on controlled energy relay that creates a tunable lifetime range spanning 3 orders-of-magnitude upon a single emission band. We consistently resolve selected lifetimes from the NIR-II nanoparticle probes at depths up to 8 mm in biological tissues, where signal-to-noise ratio derived from intensity measurements drops below 1.5. We demonstrate that robust lifetime coding is independent of tissue penetration depth, and we apply in vivo multiplexing to identify tumour subtypes in living mice. Our results correlate well with standard ex vivo immunohistochemistry assays, suggesting that luminescence lifetime imaging could be used as a minimally invasive approach for disease diagnosis.

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