Lifetime-engineered nanoparticles unlock multiplexed *in vivo* imaging

With the support by the National Natural Science Foundation of China, a study by the research group led by Prof. Zhang Fan (张凡) from the Department of Chemistry, State Key Laboratory of Molecular Engineering of Polymers, Shanghai Key Laboratory of Molecular Catalysis and Innovative Materials and iChem, Fudan University demonstrated that fluorescence lifetime is capable and reliable for quantitatively multiplexing biomarkers for cancer diagnosis *in vivo*, which was published in *Nature Nanotechnology* (2018, 13: 941—946).

Cancer has been one of the major threats to human beings for centuries. Diagnostic and prognostic classifications of tumors extensively rely on immunohistochemistry (IHC) performed *ex vivo*, requiring tissue samples collected via biopsy. However, IHC is semi-quantitative and subjective, which may result in variation of the results due to the biopsy, sample processing and scoring procedures. Besides, it is time- and labor-consuming, and cannot quantify multiple biomarkers simultaneously. It also has the risk of tumour cell reseeding following biopsy. Therefore, it is challenge to develop a new strategy for precise diagnosis of cancer without the surgery.

Prof. Zhang and his coworkers have recently reported a conceptual advance by creating lifetime-engineered lanthanide nanoparticles emitting in the second near-infrared (NIR-II) window and illustrated the feasibility for multiplexed *in vivo* imaging. In their work, they devised a core/multi-shell structure based on lanthanide nanoparticles. Through a systematic approach of controlled energy relay as well conventional doping method, an unprecedented dynamic ranges spanning 3 orders of magnitude for lifetime tuning upon a single emission band. The manipulated lifetimes of NIR-II nanoparticles are independent of absolute intensity and therefore more tolerant to the ambient background. They showed that even the signal-to-noise ratio of conventional intensity measurement dropped below 1.5; the lifetimes remained consistent and could be robustly detected from deep tissues. The universality of the energy relay for tuning lifetime was demonstrated by creating other lanthanide ions emitting in the NIR-II window. They also demonstrated the multiplexed quantification of tumor biomarker expressions *in situ*, which yielded results correlated well with conventional western blot and IHC tests but was non-invasive and simpler.

In short, this work reports the first-ever NIR-II probes with much more robust and reliable lifetime tunability for *in vivo* multiplexed imaging of practical opportunities, which is expected to shift the paradigm for the related material sciences and technologies.

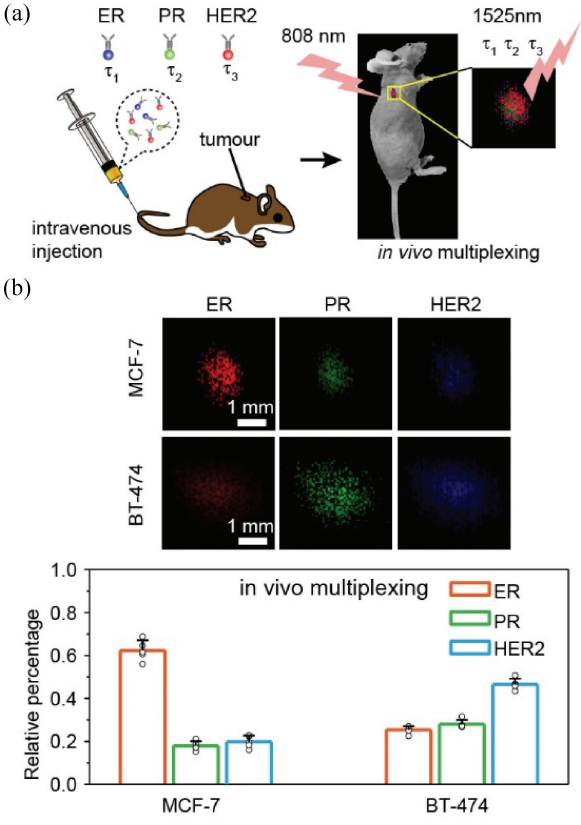

Figure Procedures and results for in vivo multiplexing of cancer biomarkers using lifetime channle.