Docket #: S19-017

Ultra-bright ~ 1600 nm Emitting Nanoparticles for NIR-IIb Molecular Imaging with Clinical Potential

Stanford researchers in the Dai Lab have developed the first ultra-bright cubic-phase erbium-based rare-earth nanoparticles (α-ErNPs) with down-shifting luminescence at ~ 1600 nm for *in vivo* NIR-IIb (1500-1700 nm) imaging with deep penetration and high clarity. The 11-fold increase in brightness enables excitation by low power, low cost LED for exceptionally crisp, dynamic imaging *in vivo* at a high frame rate. The highly biocompatible, hydrophilic crosslinked polymer coated nanoparticles provided about 90% biliary excretion from mice in 2 weeks, which can enable clinical translation with minimal toxicity concerns. This invention also shows potential for multiplexed, time resolved imaging, when used in combination with other nanoparticle compositions. Applications include cancer immunotherapy prediction as well as cancer diagnosis, monitoring and image-guided cancer surgery.

Figure

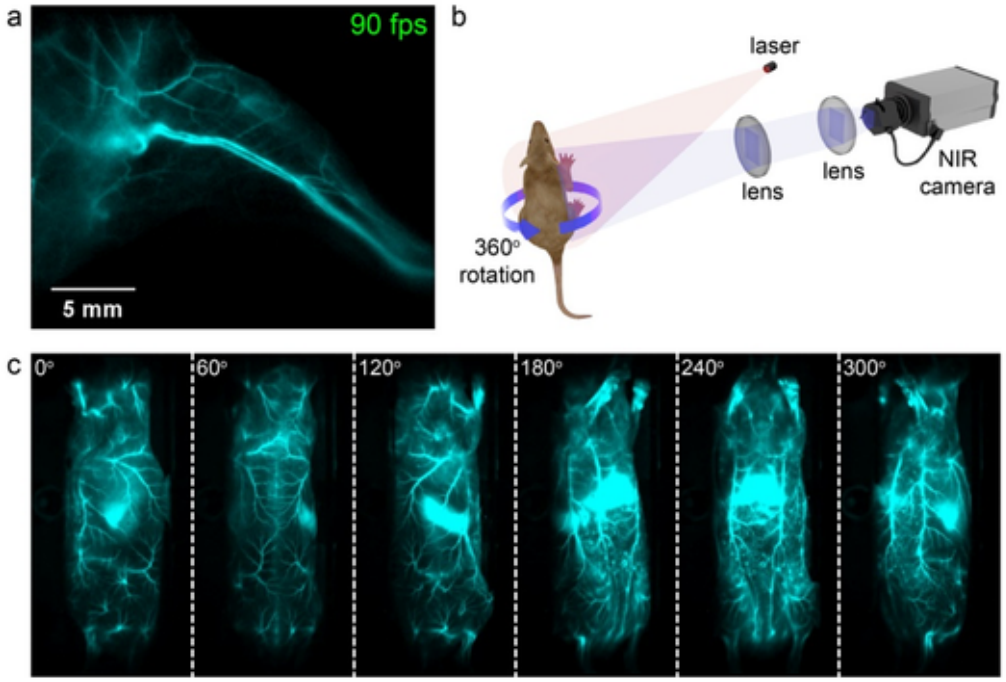

Figure description - Ultrafast and rotation imaging of mouse vascular structure. (a) Ultrafast *in vivo* imaging of mouse hindlimb. The exposure time for each image acquisition was 1.11 ms, while the overhead time of the camera is 10 ms. Therefore, the frame rate we used for ultrafast imaging is 1 / (1.11 ms + 10 ms) = 90 Hz (or 90 frames per second). **(b)** Schematic of the experimental setup for 360 ^{o} rotation imaging of mouse whole-body. **(c)** *In vivo* NIR-IIb imaging of the mouse whole-body from different degree (0^{o}, 60^{o}, 120^{o}, 180^{o}, 240^{o}, and 300^{o}).

Stage of Research

- ***In vivo* mice experiments**

Applications

- **High resolution deep tissue *in vivo*** imaging useful for immunotherapy prediction as well as for diagnosis, monitoring and image-guided cancer surgery
- **Can complement current molecular imaging modalities** including positron-emission tomography (PET), single-photon emission computed tomography (SPECT), and fluorescence-based imaging in the NIR-I 1000 nm range and NIR-IIa 1000-1300 nm range

Advantages

- **Ultra-bright** - 11 times brighter than hexagonal-phase nanoparticles
- **Fast with low cost** - Low power, low cost light emitting diodes (LED) can be used to excite the particles *in vivo*, achieving a record setting dynamic imaging in NIR-IIb at a speed of 90 frames per second (fps)
- **High resolution and sensitivity** - imaging with sub-centimeter tissue penetration and micrometer image resolution and unprecedented T/NT ratio > 40, ~ 4-10 times higher than any previous in vivo fluorescence imaging due to zero background in NIR-IIb. The imaging sensitivity matches radio-tracers
- **For the first time, two-plex molecular imaging can be done at the same** ~ 1600 nm wavelength by performing lifetime-resolved imaging
- **Long luminescence lifetime** of ErNPs (~ 4.6 ms in aqueous solution)
- **Potential for human clinical translation** due to high biocompatibility, low toxicity and rapid excretion in 2 weeks.

Publications

- Yeteng Zhong, Zhuoran Ma, Feifei Wang, Xi Wang, Yijun Yang, Yulai Liu, Xiang Zhao, Jiachen Li, Haotian Du, Mingxi Zhang, Qiuhong Cui, Shoujun Zhu, Qinchao Sun, Hao Wan, Ye Tian, Qiang Liu, Weizhi Wang, K. Christopher Garcia and Hongjie Dai. "In vivo molecular imaging for immunotherapy using ultra-bright near-infrared-IIb rare-earth nanoparticles." *Nature Biotechnology*. September 2019.

Patents

- Published Application: WO2020251639
- Published Application: 20220145175

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