Time-Gated LRET Using NIR Long-lived Luminescent Upconversion Nanoparticles for Nucleic Acid Detection

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Accurate quantification of nucleic acids is critical for early disease diagnosis and molecular monitoring. However, conventional detection strategies rely on complex, multi-step enzymatic amplification, and exhibit limited sensitivity. Here, we report a time-gated luminescence resonance energy transfer (TG-LRET) biosensing strategy for rapid and ultrasensitive detection of microRNAs (miRNAs) within 10 minutes. This strategy employs lanthanide-doped upconversion nanoparticles (UCNPs) with extended near-infrared (NIR) lifetimes as LRET donors, hereafter referred to as NIR long-lived donors (L-donors). The donors are designed with a core/shell/shell nanostructure ($NaYbF_4$@$NaYF_4$:10%Yb,1%Tm@$NaYF_4$), in which spatial separation between Yb^{3+} sensitizers and Tm^{3+} activators leads to prolonged lifetime while maintaining high emission intensity at 800 nm. This configuration establishes an extended energy migration and transfer pathway, effectively suppressing the immediate reactivation of Tm^{3+} ions deactivated by LRET. The TG-LRET using the L-donor (L-TG-LRET) enables attomolar-level detection of three cancer-associated miRNAs (miR-21, miR-155, and miR-375), demonstrating higher sensitivity than conventional polymerase chain reaction (PCR). Furthermore, the L-TG-LRET successfully quantified miRNAs in cell lysates, plasma, and plasma-derived exosomes. These results suggest that luminescence lifetime tuning of UCNPs represents an effective approach for enhancing LRET sensitivity, offering a highly sensitive strategy for biomolecular detection in clinical diagnostics.

References

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Figures

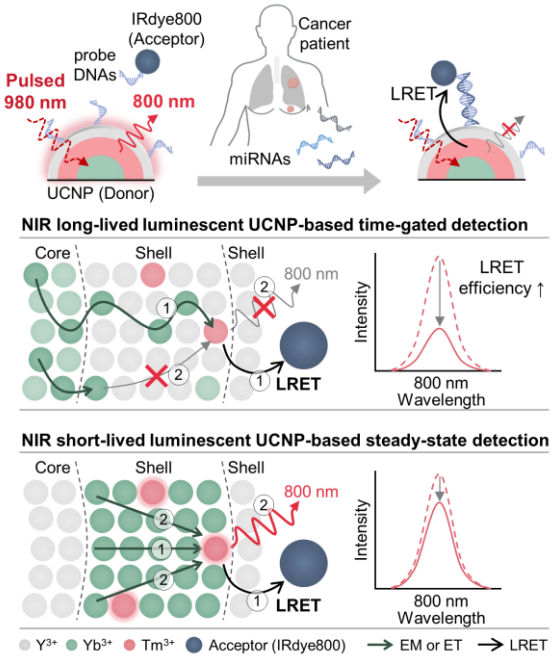

Figure 1: Schematic illustration of miRNA detection based on LRET. The probe DNAs are complementary to the respective target miRNAs. IRDye800 is an acceptor. TG-LRET using NIR long-lived UCNP as a donor exhibits higher sensitivity than SS-LRET using NIR short-lived UCNP as a donor.