Fig. S1 XRD diffraction pattern of the core, core-shell and the core-shell-shell nanoparticles and the standard reference pattern β-NaYF4 (JCPDS-16-0334, bottom).

Fig. S2 TEM images of NaYF₄: Yb/Ho (8/1%) core (24.4 nm), NaYF₄: Yb/Ho (8/1%)@NaYF₄:Nd(20%) core-shell (34.5 nm) and NaYF₄: Yb/Ho (8/1%)@NaYF₄:Nd(20%)@ NaYF₄ core-shell-shell (45.2 nm) nanoparticles.

Fig. S3 Log-log plots of the $^5$S$_2 \rightarrow ^5$I$_8$ (540 nm) and $^5$F$_5 \rightarrow ^5$I$_8$ (650 nm) luminescence intensities for NaYF₄: Yb/Ho(8/1%)@NaYF₄: Nd (20%)@NaYF₄ nanoparticles excited by 808 nm laser.
Fig. S4 Room-temperature NIR emission spectra of NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$: Nd (20%) nanoparticles coated with 1.5 nm inert NaYF$_4$ shell (pink line), 5 nm inert NaYF$_4$ shell (dark red line), and NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$: Nd(20%) (blue line) nanoparticles respectively. All active layers were kept about 5 nm. The spectra were recorded under excitation by 808 nm continuous-wave (CW) laser.

Fig. S5 Room-temperature NIR emission spectra of NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$:Nd(20%) and NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$:Nd(20%)@NaYF$_4$ with different thickness of active layer ((a) for 0.4 nm, (b) for 1.5 nm and (c) for 4.2 nm). The spectra were recorded under excitation by a 808 nm continuous-wave (CW) laser.
Fig. S6  Room-temperature NIR emission spectra of NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$:Nd(x%) and NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$:Nd(x%)@NaYF$_4$ (a) x=10 %, (b) x= 20 %, (c) x= 30 %, (d) x= 50 %. The spectra were recorded under excitation by a 808 nm continuous-wave (CW) laser.

Fig. S7 (a) Energy diagram displaying the quenching mechanism of Ho$^{3+}$ by Nd$^{3+}$. (b) Room-temperature upconversion emission spectra of NaYF$_4$: Yb/Ho(8/1%) nanoparticles and NaYF$_4$: Yb/Ho(8/1%)@NaYF$_4$: Nd (x%)@NaYF$_4$ (x=10, 20,
30) nanoparticles with 980 nm laser excitation.

Fig. S8 TEM images of NaYF₄:Yb/Ho (8/1%) core, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd(20%) core-shell, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd (20%)@NaYF₄ core-shell-shell with 0.4 nm NaYF₄:Nd (20%) active-shell.

Fig. S9 TEM images of NaYF₄:Yb/Ho (8/1%) core, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd(20%) core-shell, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd (20%)@NaYF₄ core-shell-shell with 1.5 nm NaYF₄:Nd (20%) active-shell.

Fig. S10 TEM images of NaYF₄:Yb/Ho (8/1%) core, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd(20%) core-shell, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd (20%)@NaYF₄ core-shell-shell with 2.6 nm NaYF₄:Nd (20%) active-shell.

Fig. S11 TEM images of NaYF₄:Yb/Ho (8/1%) core, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd(20%) core-shell, NaYF₄:Yb/Ho (8/1%)@NaYF₄:Nd (20%)@NaYF₄ core-shell-shell with 4.2 nm NaYF₄:Nd (20%) active-shell.
Fig. S12 Room-temperature upconversion emission spectra of \( \text{NaYF}_4: \text{Yb/Ho} \) (8/1%) @ \( \text{NaYF}_4: \text{Nd} \) (20%) @ \( \text{NaYF}_4 \) core-shell-shell samples A-D (A for 0.4 nm, B for 1.5 nm, C for 2.6 nm and D for 4.2 nm active layer in thickness, respectively).

Fig. S13 Room-temperature upconversion emission spectra of \( \text{NaYF}_4: \text{Yb/Ho}(8/1\%) \) @ \( \text{NaYF}_4: \text{Nd}(20\%) \) @ \( \text{NaYF}_4 \) with different \( \text{NaYF}_4: \text{Nd}(20\%) \) thickness active-shell (A,B,C,D) before and after conjugated RB.
Fig. S14 UV-Vis absorption spectra of UCNPs-RB nanoconjugates incubated with RB of different concentrations. The numbers of RB per nanoparticle are also given.