



Scheme 1. Schematic Illustration of the construction of FMUP nanoagent and the underlying anticancer mechanism. (A) FMUP nanoagent containing UCNP as the core and photoacid (pHP) encapsulated in the FA-doped nanoagent shell by one-pot self-assembly. The FMUP nanoagent was synthesized by coordination of carboxyl groups on BTC and FA with Fe^{3+} . The UCNP as the core was located in the shell and simultaneously the pHP was loaded in the pore of the nanoagent. (B) Corresponding anticancer mechanism of FMUP nanoagent. ① Active internalization of FMUP in tumor cells helped by FA functionalization. ② Lysosome escape of FMUP induced by the increase of osmotic pressure after NIR light irradiation. ③ Fe^{2+} and H^+ release from FMUP upon NIR light irradiation. ④ Photoacidification of intracellular microenvironment induced calcium influx and therefore calcium overload in the mitochondria and simultaneously generated a key acidic environment for efficient Fenton reactions. The release of Fe^{2+} and photoacidification synergistically reinforced Fenton reactions and therefore produced a large number of $\cdot\text{OH}$ within the close proximity of mitochondria. ⑤ As a result, the calcium overloaded and plentiful $\cdot\text{OH}$ enabled dual damage to mitochondria and further induced cell death.