Non-covalent assemblies of upconverting nanoparticles with porphyrin-dendrimers for multiphoton imaging and sensing

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Lanthanide-based upconverting nanoparticles (UCNPs) form a class of imaging agents with unique nonlinear optical properties. However, utilization of UCNPs in biomedical arena has been hampered by the lack of robust methods of their solubilization and surface functionalization. Here we show that non-covalent modification of UCNPs with polyanionic porphyrin-dendrimers converts them into stable, water-soluble, non-toxic imaging probes. UCNP-to-porphyrin excitation energy transfer enables analyte-sensitive detection by upconverted luminescence. As an example we demonstrate that UCNP/porphyrin-dendrimers make up ratiometric pH nanosensors for physiological pH range. Exceptionally high apparent multiphoton absorption cross-sections of dendritic UCNPs combined with their excellent bio-compatibility make them directly suitable for physiological imaging. Using a low power continuous wave (CW) laser for excitation we performed mapping of mouse cortical vasculature with micron-scale resolution down to 400 μm under the brain surface, setting the first precedent of true in vivo two-photon microscopy with CW sources.