Tunable ON/OFF pH-Sensitive Nanoprobes

A series of pH-activatable micelles with tunable and ultra-sensitive pH response in the physiological range (5.0-7.4) are developed. These nanoparticles have fast temporal response (<5 ms), large increase of emission intensity between ON and OFF states (up to 55 times), and require a change of < 0.25 pH units for activation. Confocal imaging studies demonstrate that the nanoparticles are "silent" in the media at pH 7.4 but can be activated upon uptake in cells. Moreover, nanoparticles with transitions at pH 6.3 and 5.4 can be selectively activated in different endocytic compartments such as early endosomes (pH 5.9-6.2) and lysosomes (5.0-5.5). This nanoplatform offers many exciting opportunities in the development of nonlinear ON/OFF nanosystems for diagnostic imaging and drug delivery applications with minimal effect at physiological pH values (e.g. pH 7.4) but can be activated at acidic tumor pH values or in specific intracellular organelles (e.g. endosomes/lysosomes).

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