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Selective Intracellular Activation by Designing pH-Sensitive and Tunable Fluorescent Nanoparticle KEJIN ZHOU, YIGUANG WANG, XIAONAN HUANG, MILAN POUDEL, GANG HUANG, KATE LUBY-PHELPS, JINMING GAO — Integration of nanotechnology with molecular biology and medical imaging has propelled the development of various nanoscopic imaging probes and targeted therapeutics. Despite great advances, it remains a formidable challenge to create highly biointeractive nanosystems that can respond to subtle changes in physiological stimuli (e.g. pH, enzymes) to achieve desired biological specificity. Here we report a set of robust, pH-activatable micelle nanoprobes with tunable pH transitions in the physiological range. These nanoprobes have a fast fluorescence response (<5 ms), up to 55-fold increase of emission intensity between OFF and ON states, and only require <0.25 pH unit for activation (vs. 2 pH unit for small molecular dyes). Nanoprobes with different transition pH can be selectively activated in specific endocytic compartments such as early endosomes or lysosomes. This capability allows for the development of pH-activatable imaging probes or nanocarriers that can target specific subcellular organelles for therapy.

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