Supporting Information

Supplementary Information:

1. Sensor Particle Calibration:
The pH sensitivity of these particles (Figure 2) was determined based upon the ratio between the peak sensor intensity (fluorescein: 520nm at 488nm excitation) and the peak reference intensity (rhodamine: 575nm at 540nm excitation) in a series of sodium phosphate buffers from pH 5.0 to 8.5.

2. Confocal Microscopy:
All fluorescence microscopy was conducted using separate excitation lines for green (488nm) and red (543nm) of an Argon ion laser using a 63X 0.9 NA water immersion objective. In each instance, emission was collected sequentially for green (500-545nm) and red (555-615nm) channels as well as a bright field image, which were subsequently background corrected, analyzed and overlaid in MATLAB 6.12 and Adobe Photoshop 7.0. For each cell experiment a minimum of ten cells were individually imaged to ensure a representative image is shown.

3. Cell Handling Protocols:
RBL-2H3 cells were maintained in monolayer cultures and harvested with trypsin-EDTA (Life Technologies, Rockville, MD) 3–5 days after passage, as described.[1] Prior to harvesting, cells were labeled with AlexaFluor®488-labeled Cholera Toxin B (5 mg/ml, 37ºC) for half an hour and then washed to remove the unbound cholera toxin. The cells were resuspended in 1mg/ml BSA in BSS (BSA-BSS) at a density of $5x10^6$ cells/ml and then incubated with $1.6x10^{11}$/ml of 70 nm sensor (Figure 4) or analogue (Figure 3) particles for 1 hour at 37ºC. To induce endocytosis, cells were treated with Phorbol dibutyrate (5µg/ml, 20 min, 37ºC) during the incubation with particles. The cells were then washed thrice with BSA-BSS and plated in 35-mm Petri dishes with coverglass bottom (0.16–0.19 mm; MatTek, Ashland, MA) at $1.25x10^5$ cells/ml and visualized by confocal microscopy.

[1] L. Pierini, D. A. Holowka, B. Baird. *Journal of Cell Biology,* **1996,** *134***,** 1427–1439