# Supporting Information

# Protease-Modulated Cellular Uptake of Quantum Dots

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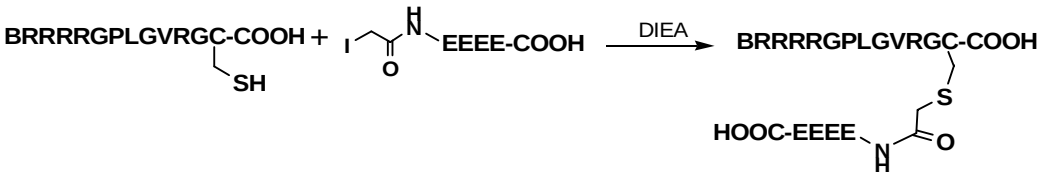
## Experimental Section

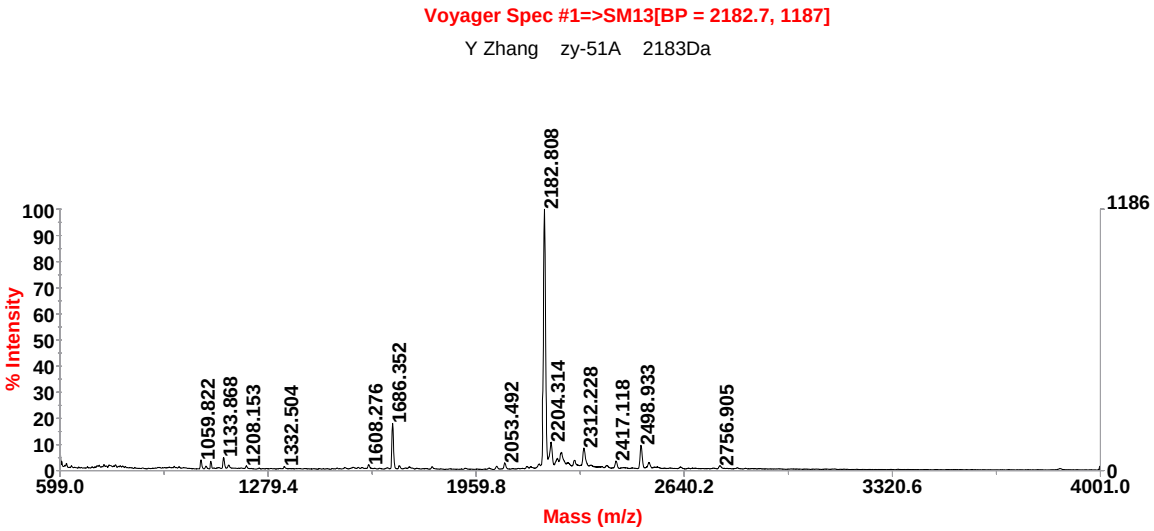
**Chemicals**: All the Fmoc amino acids and resins for solid phase synthesis were from Bachem or Novabiochem. Other chemicals were from Sigma-Aldrich. Quantum dots conjugated with streptavidin were obtained from Quantum Dots Invitrogen Nanocrystal Technologies.

**Synthesis of peptides**: All the biotinylated peptides without side chain coupling were synthesized by standard Fmoc solid-phase synthesis on 2-chlorotrityl resin using TBTU/HOBt/DIEA as coupling reagents. All the crude products were purified by reverse phase HPLC using acetonitrile and water as the eluent. MALDI-MS were used for structure confirmation of the products.

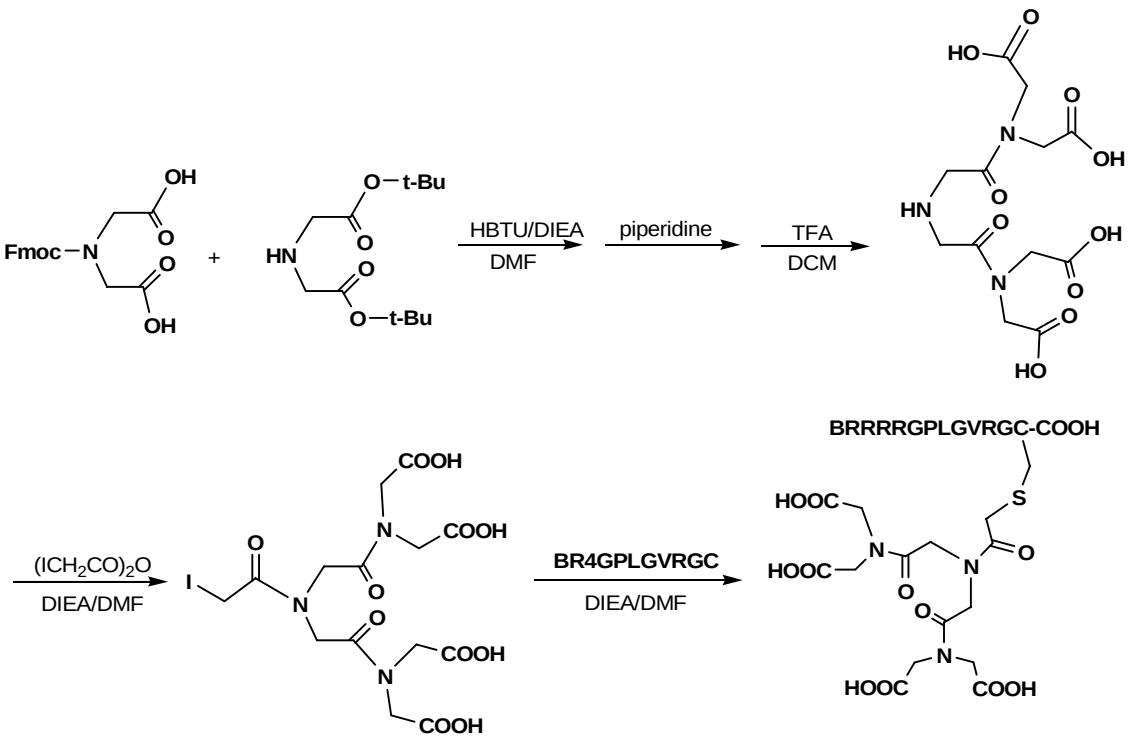
Synthesis of BR4GPLGVRGC(E4):



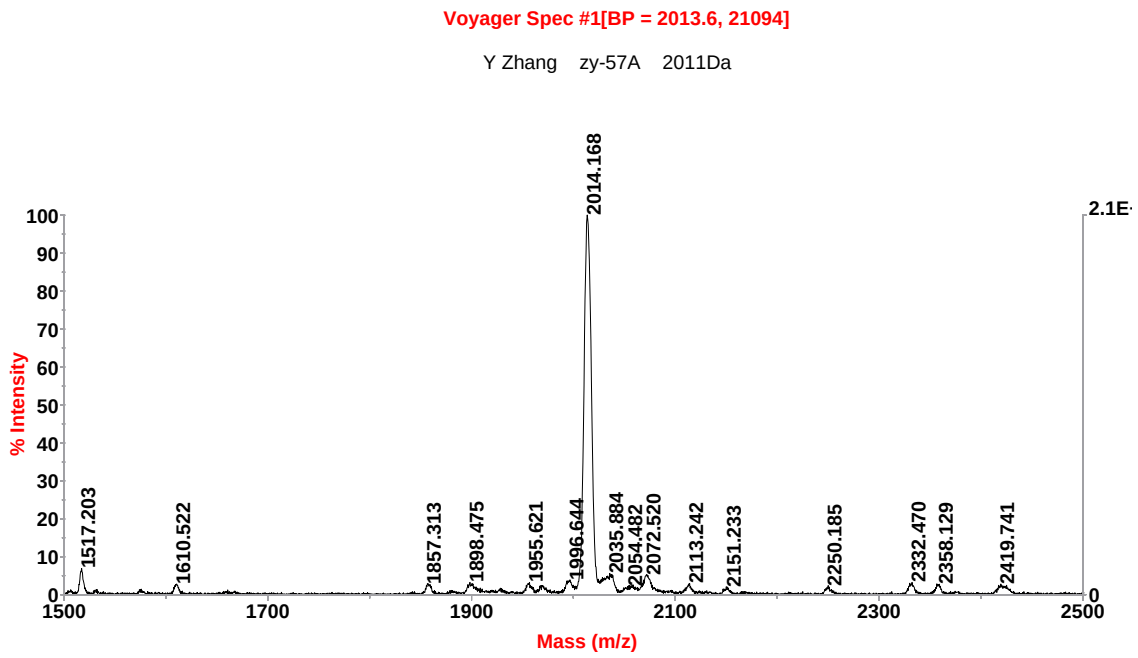

Calc. MS ($M^+$): 2182, and found ($M+H^+$): 2182.8.



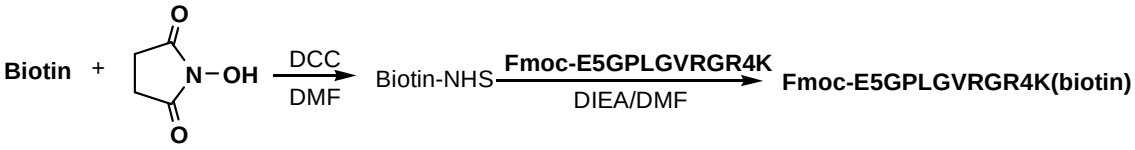

Synthesis of BR4GPLGVRGC(IDA(IDA)$_2$):



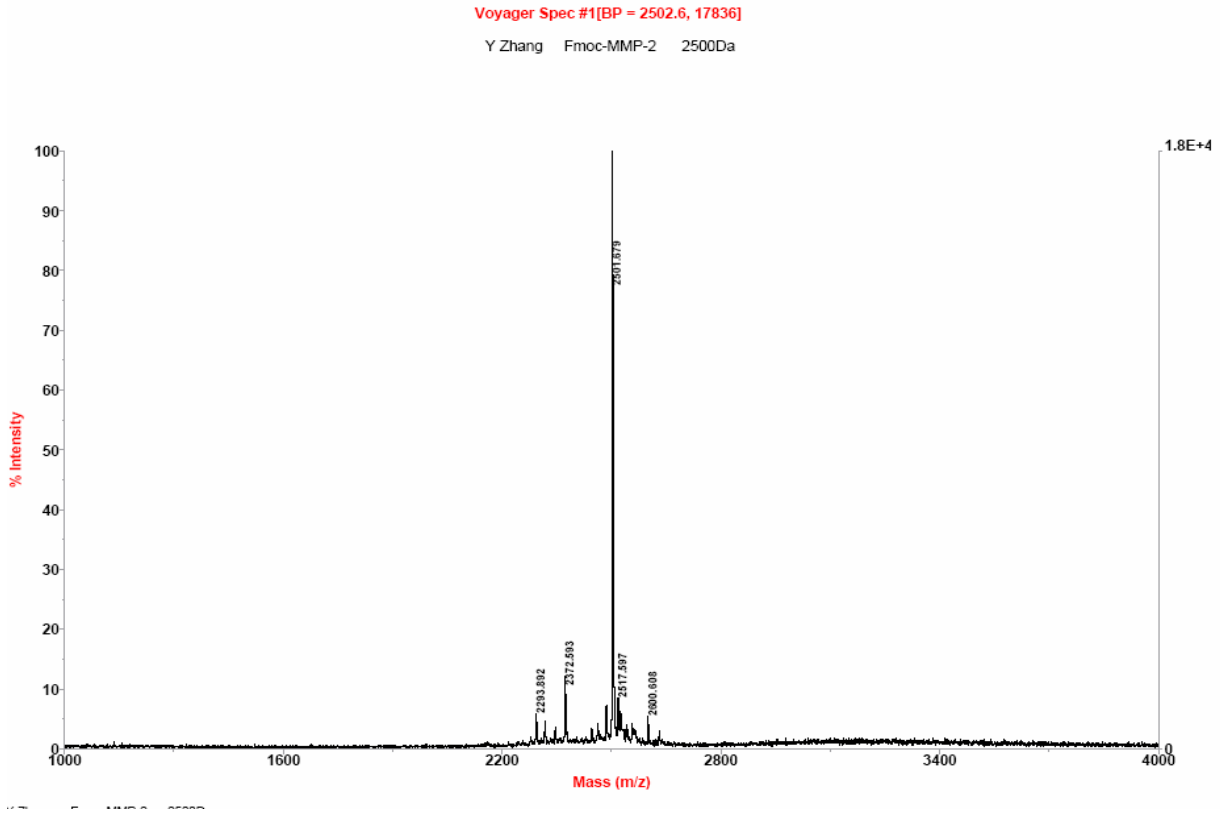

Calc. MS ($M^+$): 2012.2, and found ($M+H^+$): 2014.2.




Synthesis of Fmoc-E5GPLGVRGR4K(Biotin):

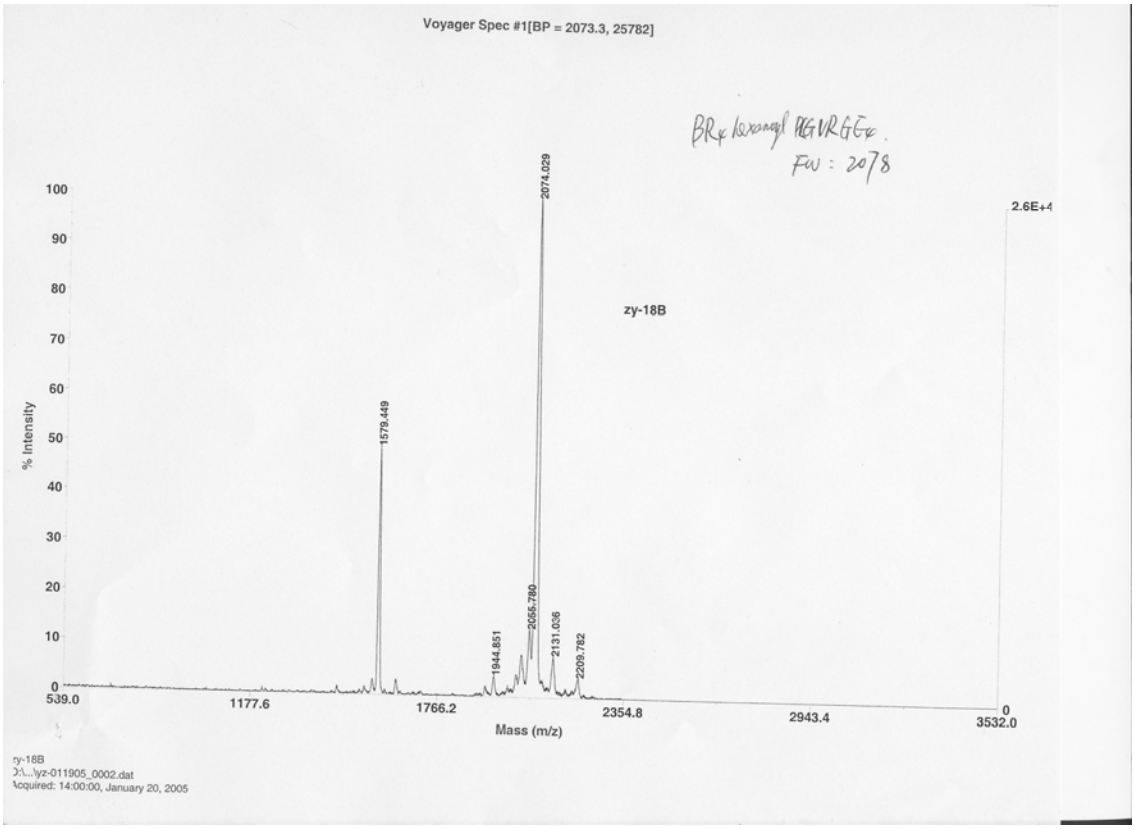



Fmoc-E5GPLGVRGR4K(Biotin): Calc. 2501.8, found 2501.7.

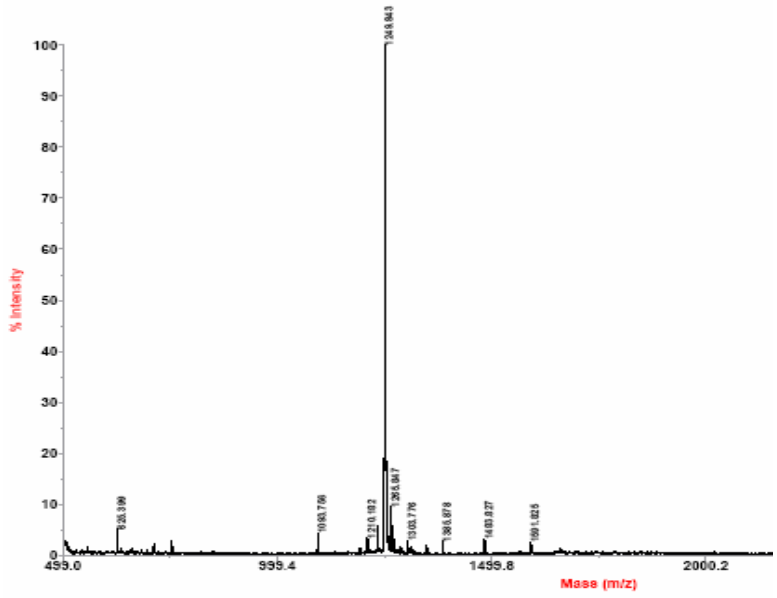


**Mass spectra of the peptide substrate BR4XPLGVRGE4 and its MMP-2 hydrolyzed product BR4XPLG**

BR4XPLGVRGE4: Calc. MS ($M^+$): 2077; found ($M^+$): 2074.




BR4XPLG: Calc. MS ($M^+$): 1248.7; found ($M^+$): 1248.8.



**Conjugation of peptides to quantum dots**: Quantum dots coated with 5-10 streptavidin were used for further modification by biotinylated peptides. Biotinylated peptides (100 equivalents) in pH 8.0 borate buffer were incubated with quantum dots at room temperature for 30 min. Filtration through 100K NanoSep filter to remove excess unbound free peptide in the solution is optional since there was no detectable difference between filtered and unfiltered samples. Therefore in our experiments, QD conjugates were used directly after incubation without further purification.

**Microplate assay:** COS-7 cells were cultured in 96-well clear-bottom tissue culture plate (Corning) in DMEM supplemented with 10% fetal bovine serum for 48 hours at 37 degree with 5% carbon dioxide until 100% confluency. Quantum dots with maximum emission at 655 nm were conjugated with corresponding peptides. Cells were washed carefully with HBSS before incubated with QD conjugates. Each sample was tested in four wells in parallel comparison. The concentration of the QD conjugate was typically at 10 nM, and the total volume of the incubation solution in each well was 50 μL. After 1 hr incubation at room temperature, cells were washed with care by HBSS. Fluorescence intensity was measured on a Tecan micro-plate reader with excitation at 450 nm and the gain at 120.

**Fluorescent microscope imaging:**

HT-1080 cells (from ATCC) were cultured in glass-bottom dishes (MatTek Cultureware) in MEM supplemented with 10% fetal bovine serum to a confluency of 50%. Cells were washed three times with HBSS before incubated with QD conjugates in HBSS at a

concentration of 5 nM at room temperature for 1 hr. After incubation, cells were washed five times with HBSS to remove free QD conjugates in the incubation solution, and immersed in HBSS for imaging with a fluorescence microscope. Fluorescence images were acquired with an exciter D420/40, an emitter D660/40 and a beamsplitter 470dcxr (from Chroma). Exposure time for all the fluorescent images was set at 100 ms.