

# Interfacing Inorganic Nanocrystals with Biological Systems Using a Coordinating Polymer Coating



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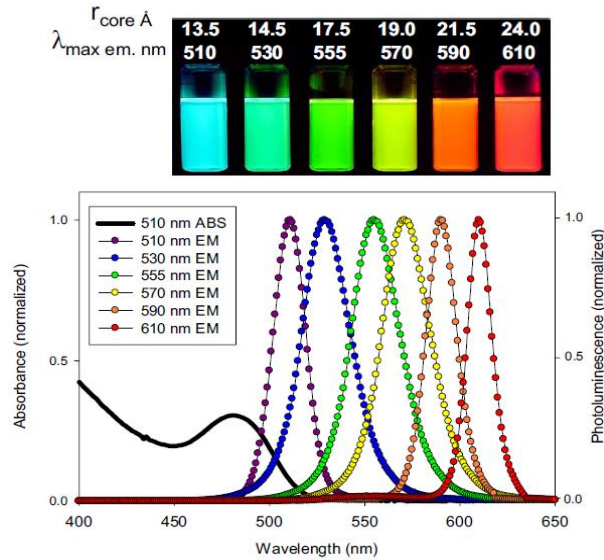
NIH/NCI, Frederick, MD



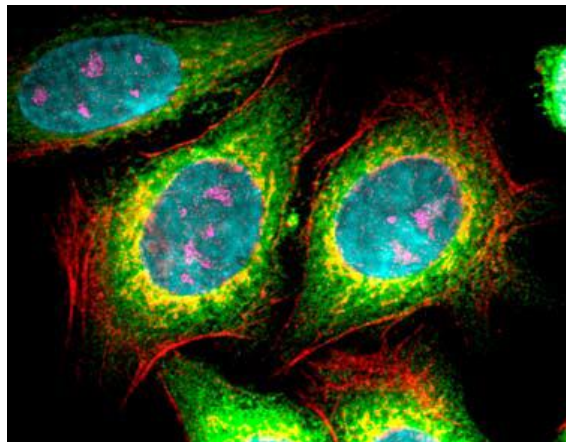
THE FLORIDA STATE UNIVERSITY

***The 16th U.S.-Korea Forum on Nanotechnology***

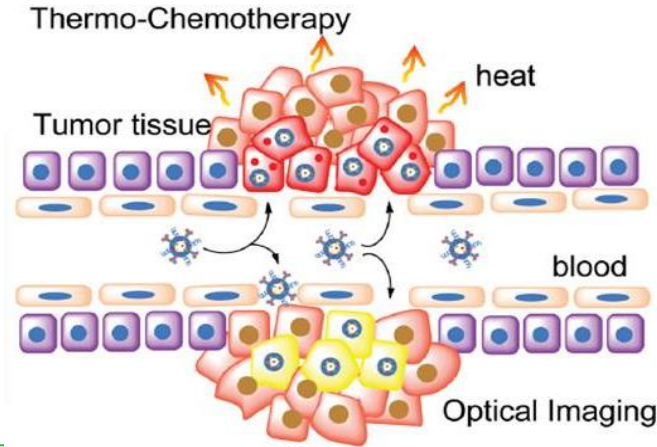
# Potential Applications of Colloidal Nanocrystals



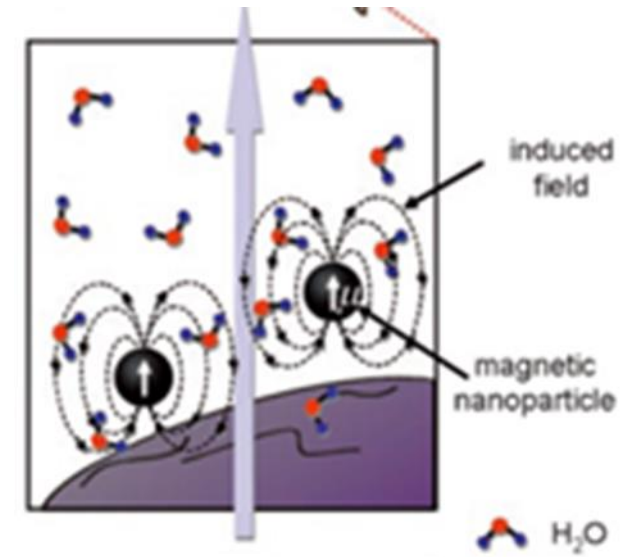
*Nat. Mater* 2005,4, 435



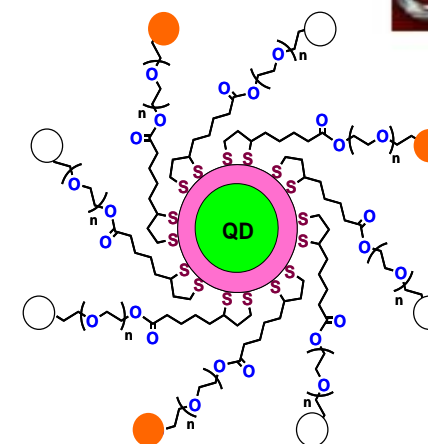
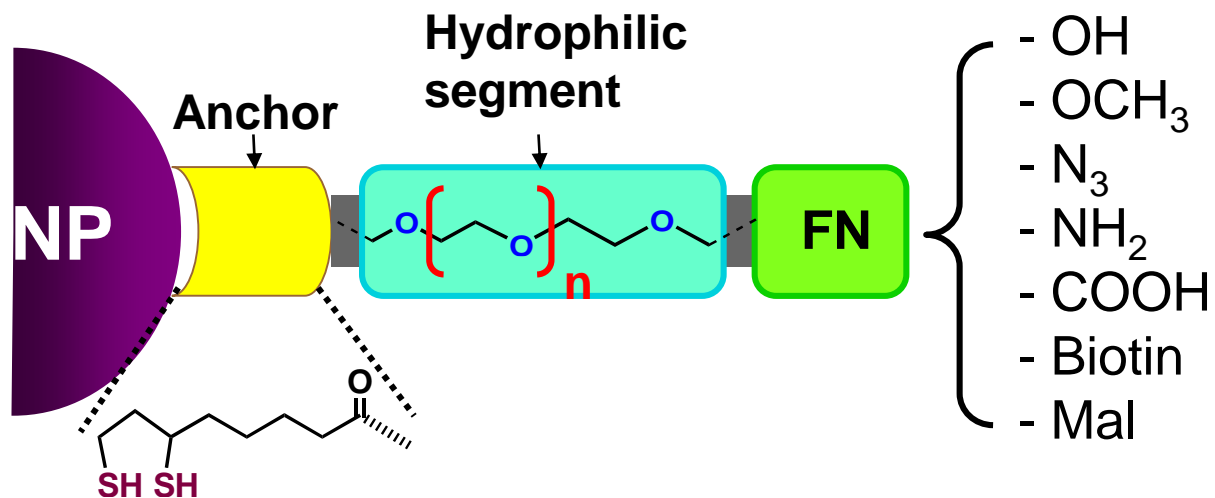
From Invitrogen



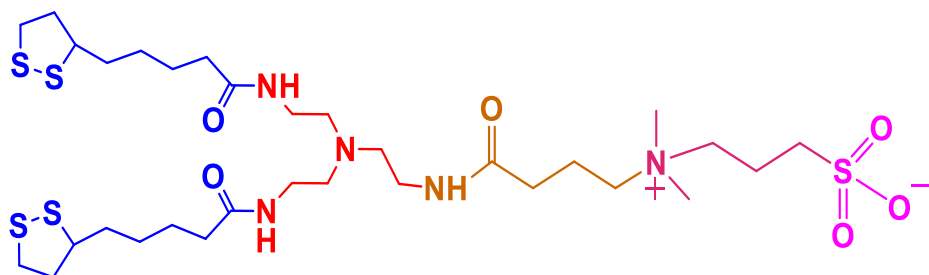
Zhang et al., *Adv. Mater.* 2013, 25: 3869



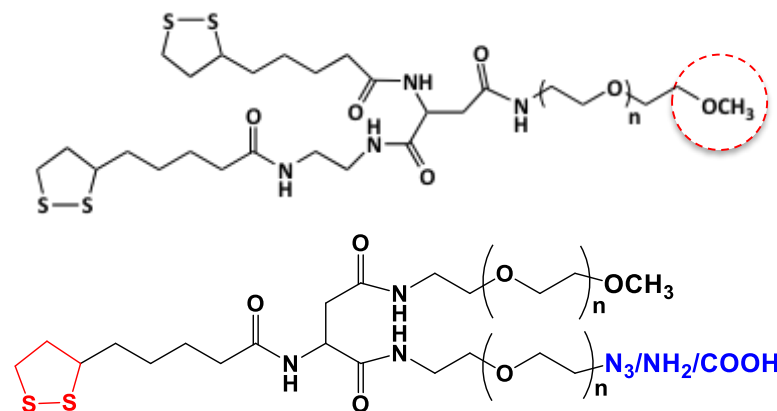
# QDs and AuNPs: Lipoic Acid Anchors



Susumu et al., *J. Am. Chem. Soc.* **2007**, 129, 13987; Mei et al., *J. Mat. Chem.* **2008**, 18, 4949



Zhan, Palui, ... Mattoussi *J. Am. Chem. Soc.* **2013**, 135, 13786 -13795

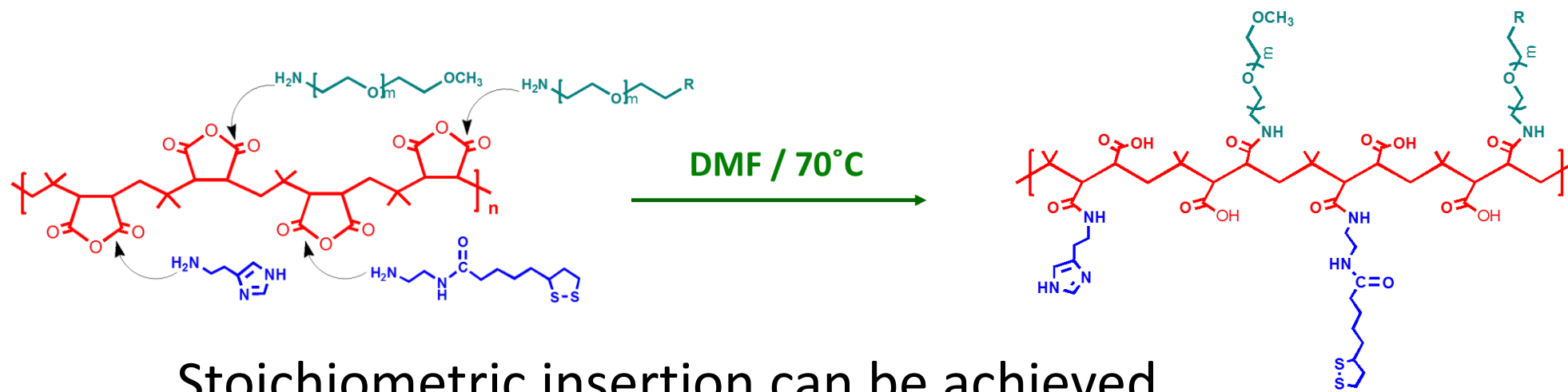


Zhan, Palui, ... Mattoussi, *J. Am. Chem. Soc.* **2015**, 137, 16084-16097

# Lipoic Acid/Histidine-Modified Polymer for QDs

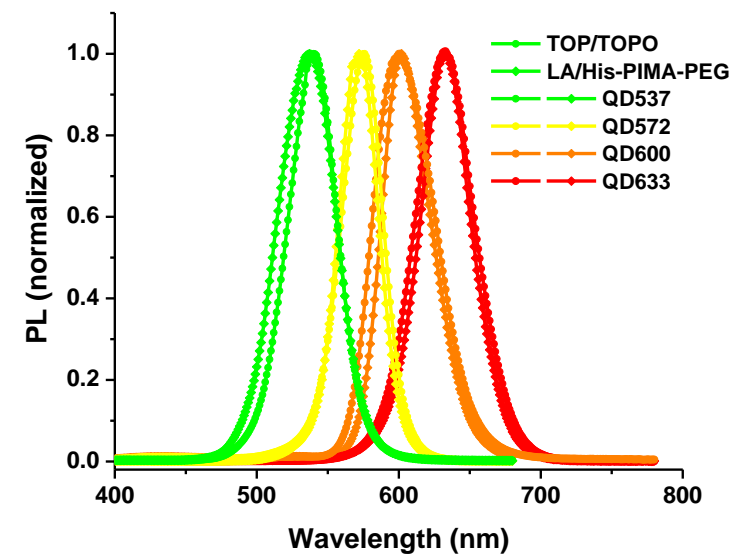
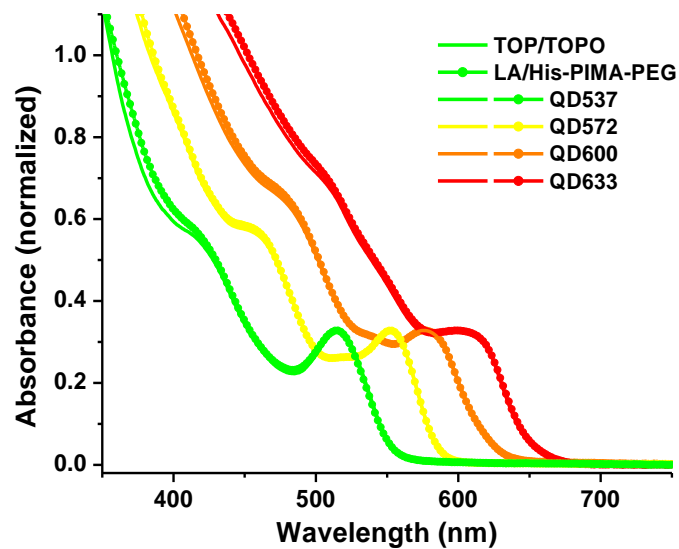
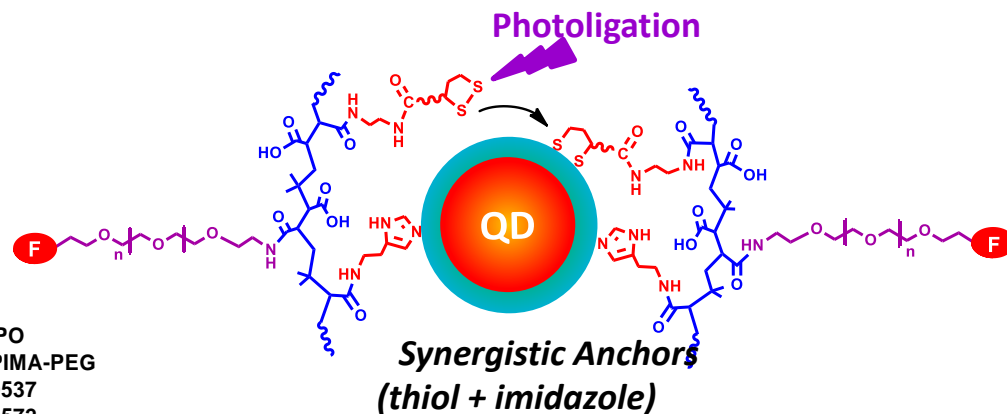


Wang, Kapur, Ji, Safi, Palui, Palomo, Dawson, and Mattoussi,  
*J. Am. Chem. Soc.* **2015**, *137*, 5438–5451



Ligand	(molar fractions)	Nominal numbers per chain <sup>a</sup>				Experimental numbers per chain <sup>b</sup>		
LA-PIMA-PEG	(x:z = 30:70)	LA: 12	PEG: 27		LA: ~13	PEG: ~27		
His-PIMA-PEG	(y:z = 30:70)	His: 12	PEG: 27		His: ~10	PEG: ~27		
His-PIMA-PEG	(y:z = 50:50)	His: 20	PEG: 20		His: ~17	PEG: ~19		
LA/His-PIMA-PEG	(x:y:z = 20:30:50)	LA: 8	His: 12	PEG: 20	LA: ~10	His: ~12	PEG: ~18	
LA/His-PIMA-PEG-R	(x:y:z:z' = 20:30:45:5)	LA: 8	His: 12	PEG: 18	R: 2	---		

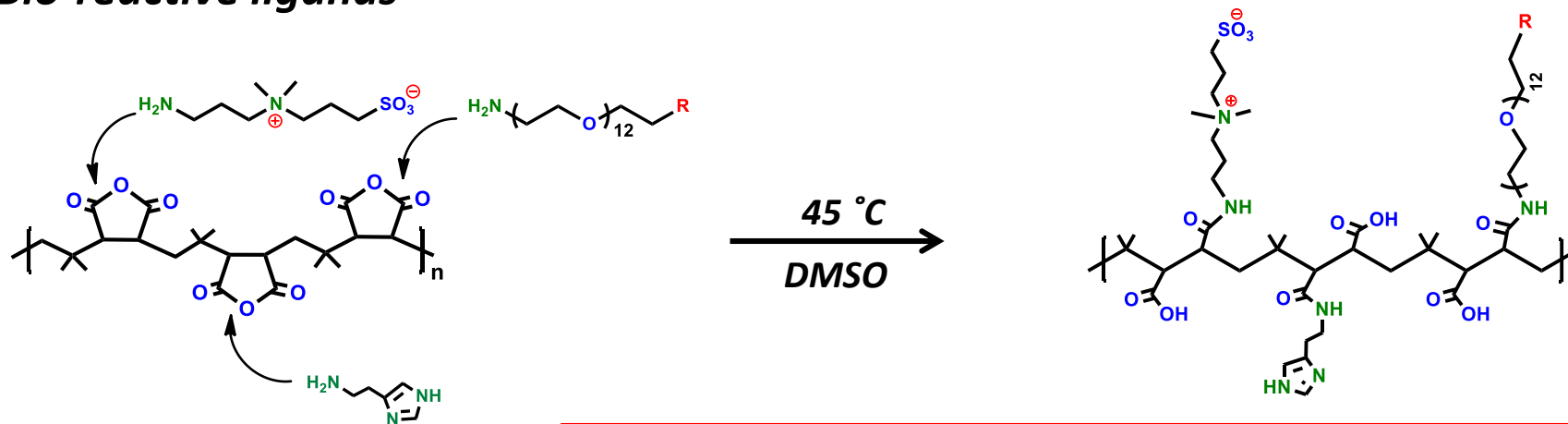
# Photoligation of LA-containing Polymer Ligands



# The Zwitterion Motif: an Alternative to PEG



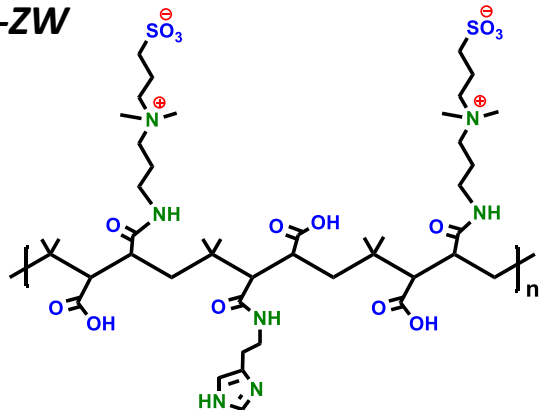
## Bio-reactive ligands



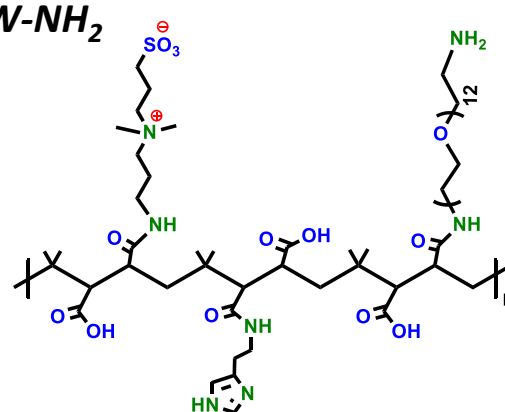
Wang, Ji, Kapur, Zhang, ... Mattoussi, *J. Am. Chem. Soc.* **2015**, 137, 14158-14172

## Representative ligands

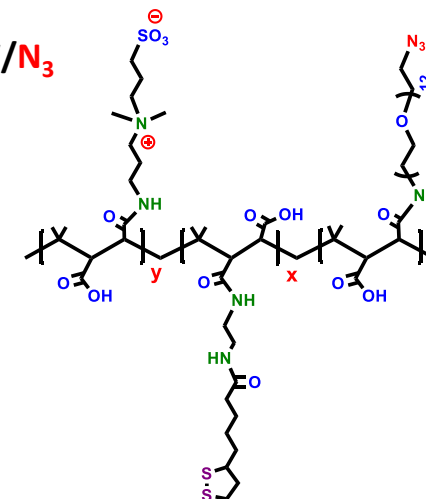
His-PIMA-ZW



His-PIMA-ZW-NH<sub>2</sub>



LA-PIMA-ZW/N<sub>3</sub>

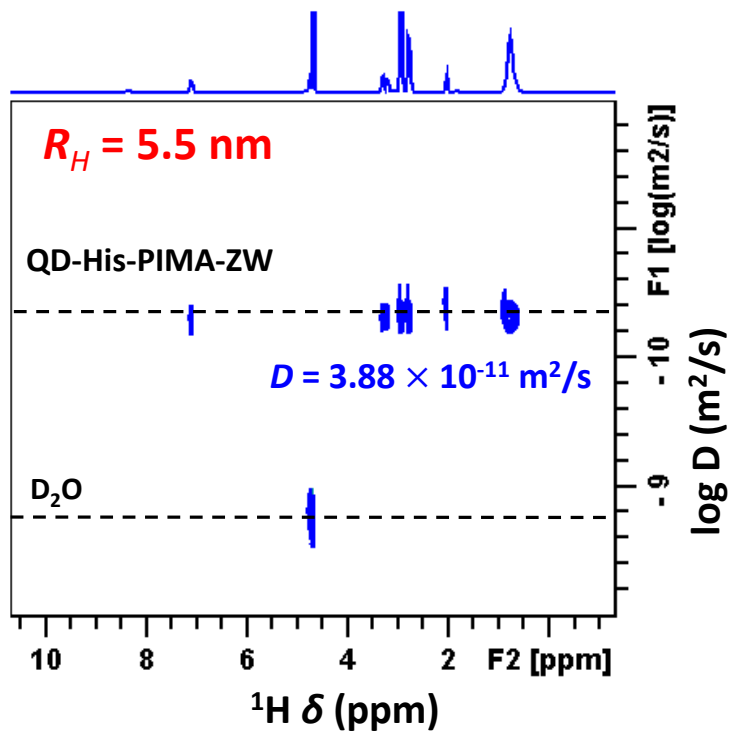


Wang, Kapur, Ji, Zeng, Mishra and Mattoussi, *Bioconjugate Chem.* **2016**, 27, 2024-2036

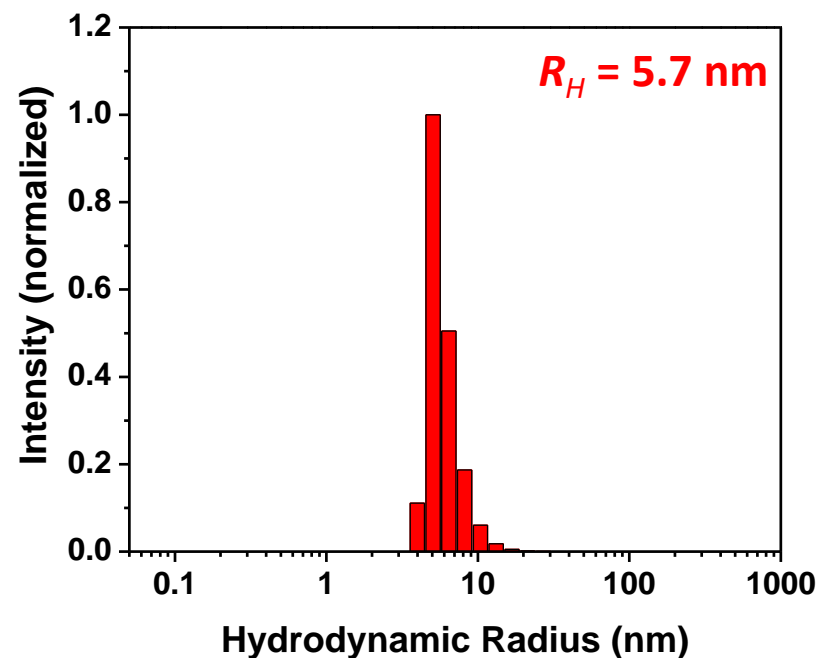
# His-PIMA-ZW: Compact Coating



His-PIMA-ZW => Compact size QDs

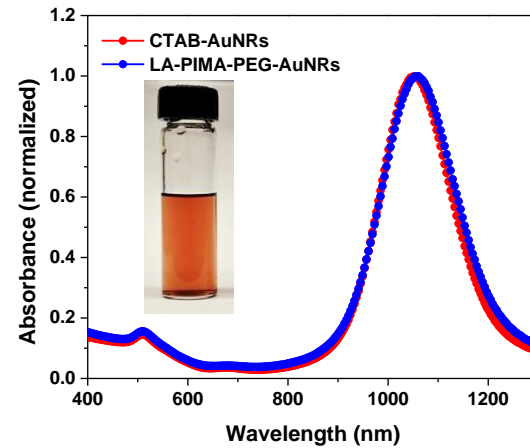
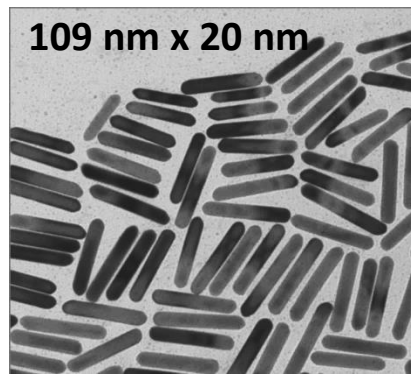


Diffusion Ordered Spectroscopy (DOSY)

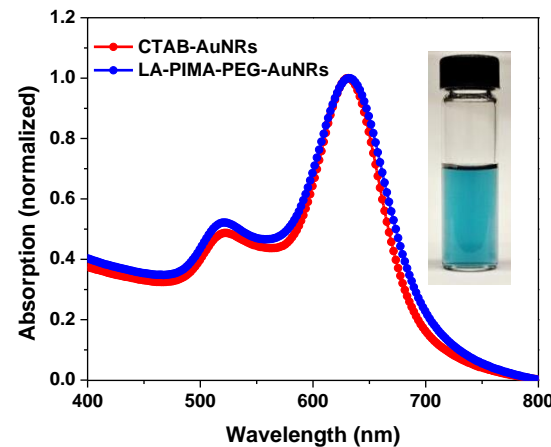
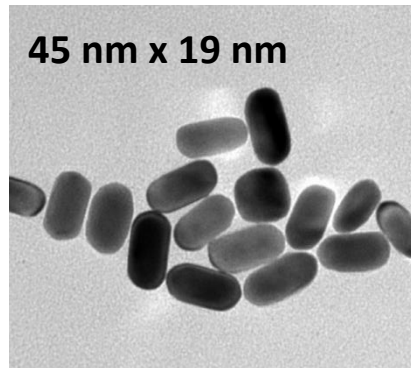


Dynamic Light Scattering

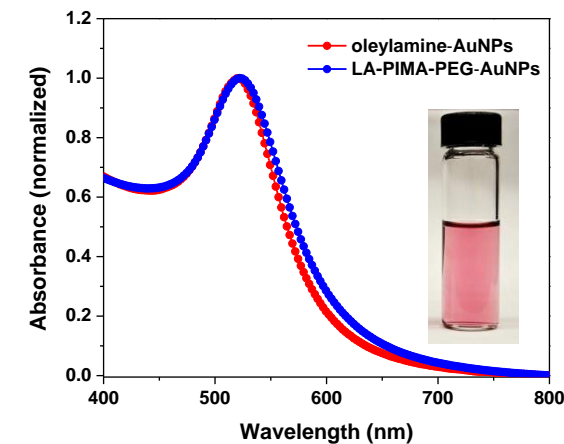
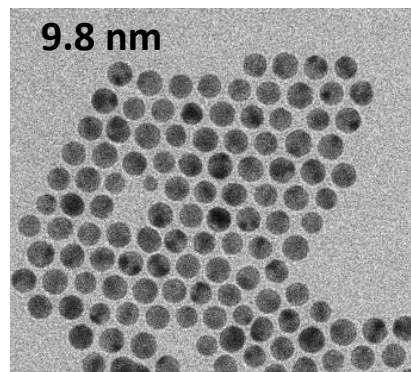
$$R_H \text{ extracted using Stokes - Einstein Eq.: } D = \frac{k_B T}{6\pi\eta R_H}$$



# Functionalization of Au-Nanostructures



Gold nano-structures with a PEGylated (or ZW) polymer coating



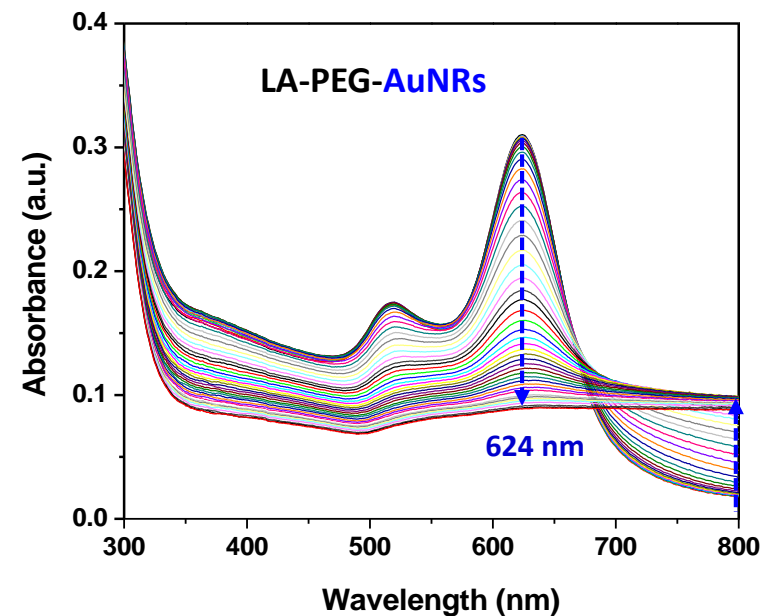
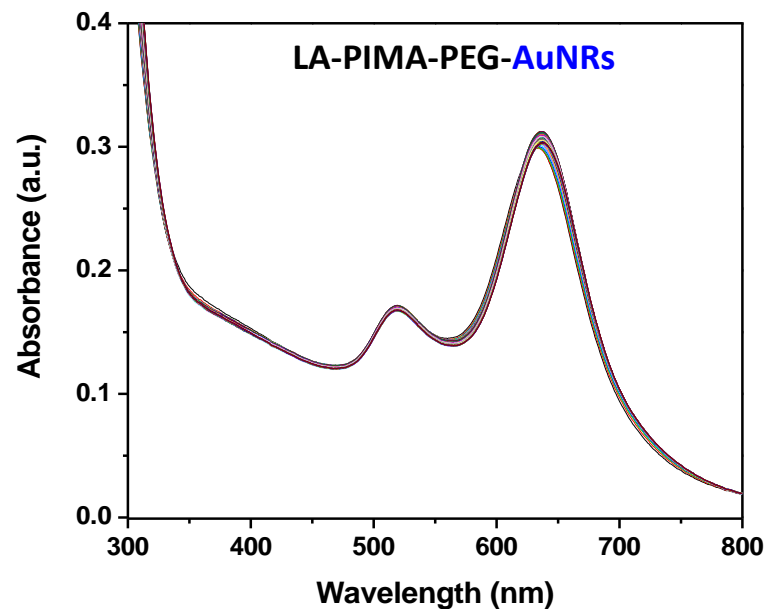
Wang, Ji, Du, Mattoussi, *J. Phys. Chem. C* **2017**, 121, 22901-22913.



# DTT Stability Test: Polymer vs Monomer PEG-Coating



## Au Nanorods

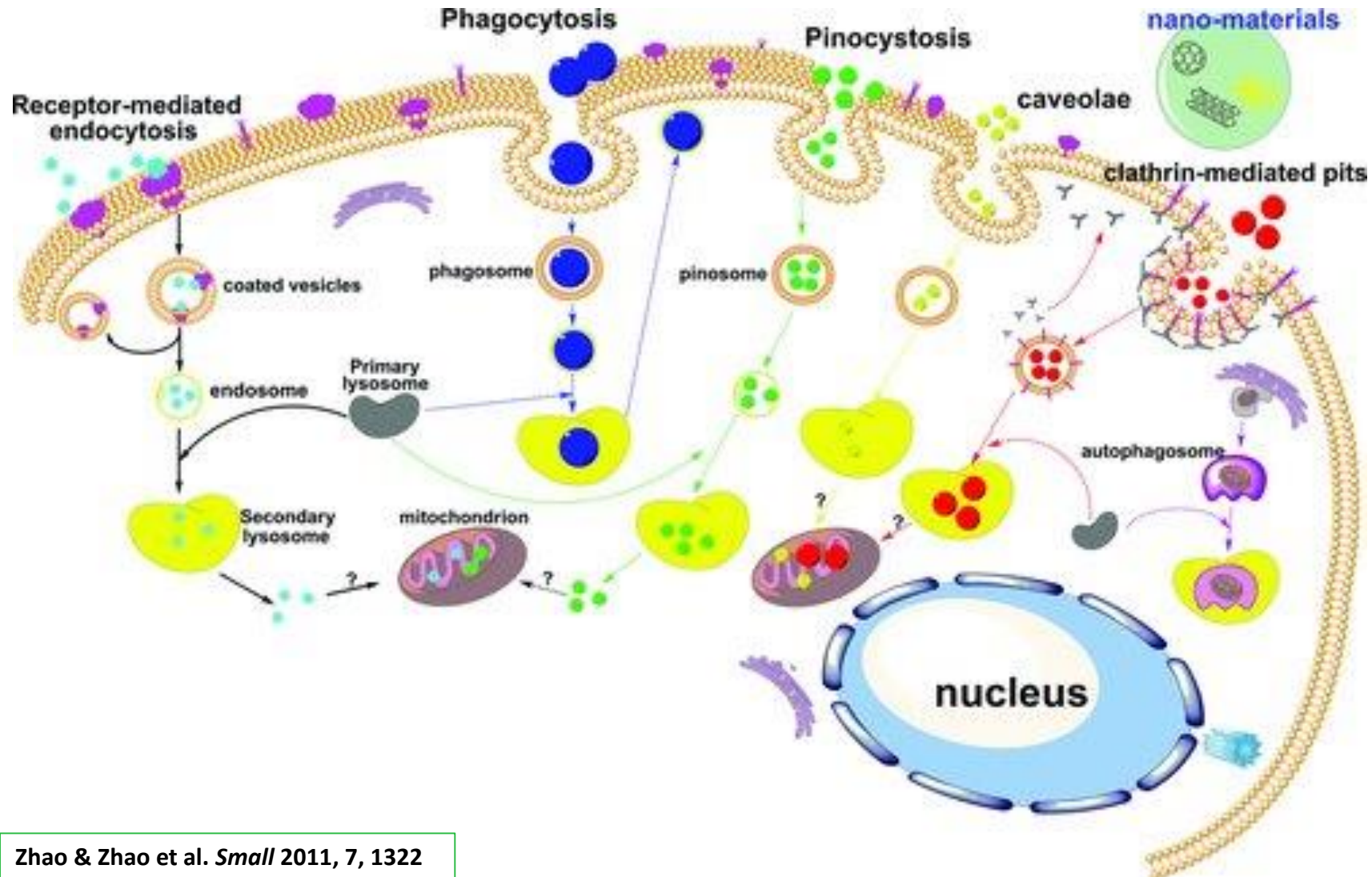


Wang, Ji, Du, Mattoussi, *J. Phys. Chem. C* **2017**, 121, 22901-22913.

Similar results were collected for AuNPs.

Similar differences between polymer and monomer were found with the zwitterion motif.

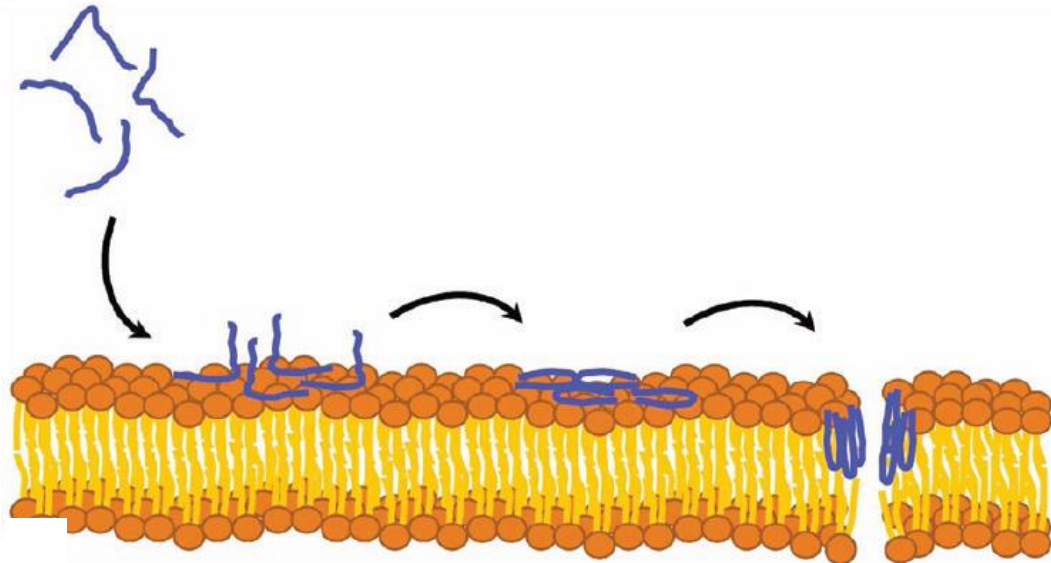
# Cellular Uptake of Nanoparticles: The Endocytosis Problem



# Uptake Promoted by SVS-1 Peptide



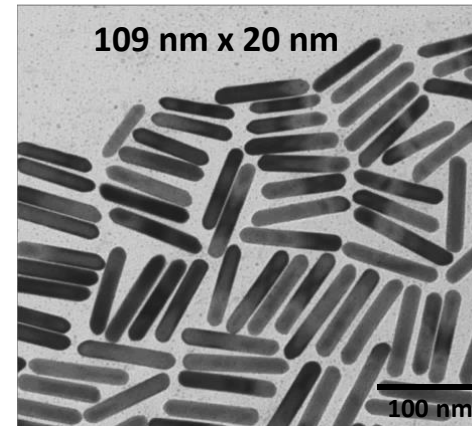
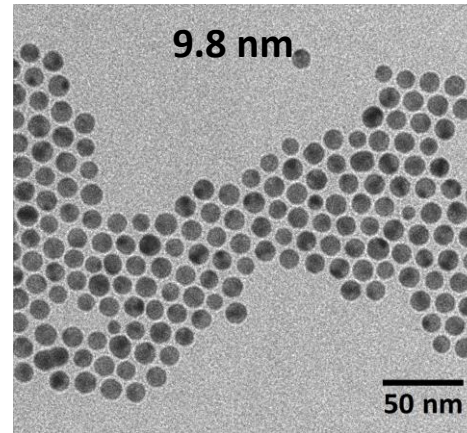
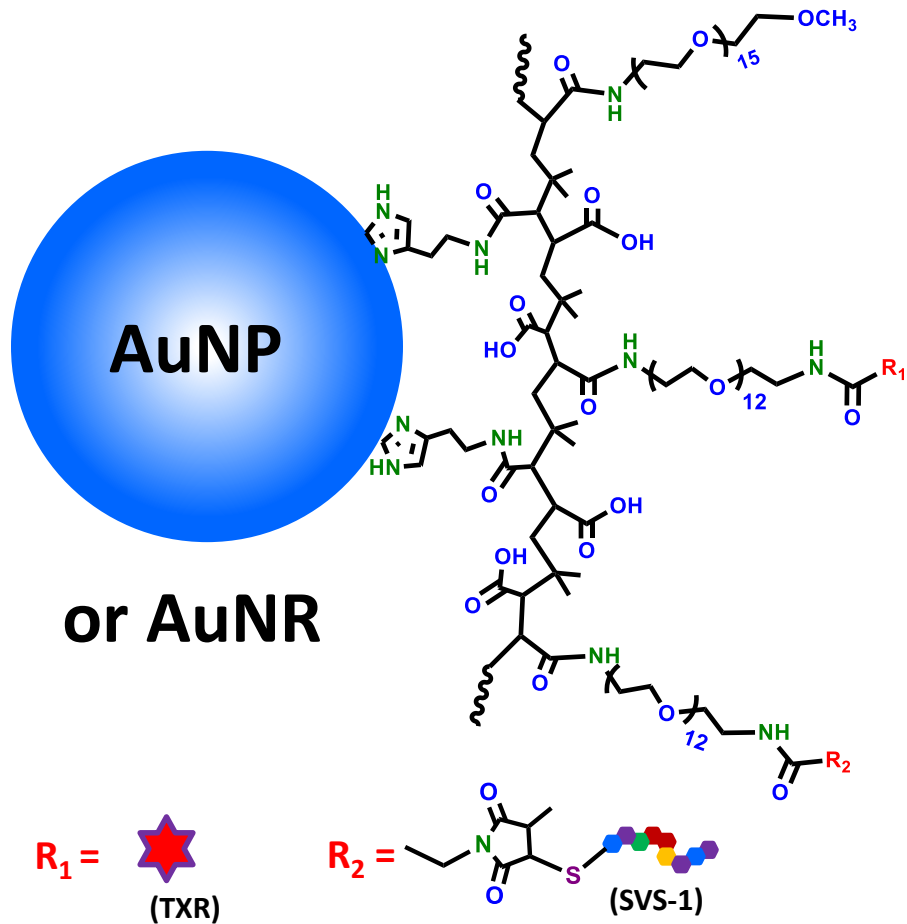
- **Cationic, amphiphilic peptide with anti-cancer activity**
- Peptide: “**CGG-KVKVKVKVDPPTKVKVKVK-NH<sub>2</sub>**”
- Preferentially folds at the negatively charged surface of cells, adopting an amphiphilic  **$\beta$ -hairpin structure** capable of **disrupting cell membranes**.



Sinthuvanich *et al.* *J. Am. Chem. Soc.* **2012**, 134, 6210

Medina *et al.*, *J. Controlled Release* **2015**, 209 317–326

# Cell Uptake Studies: Case of AuNR/NP-SVS-1 Conj.



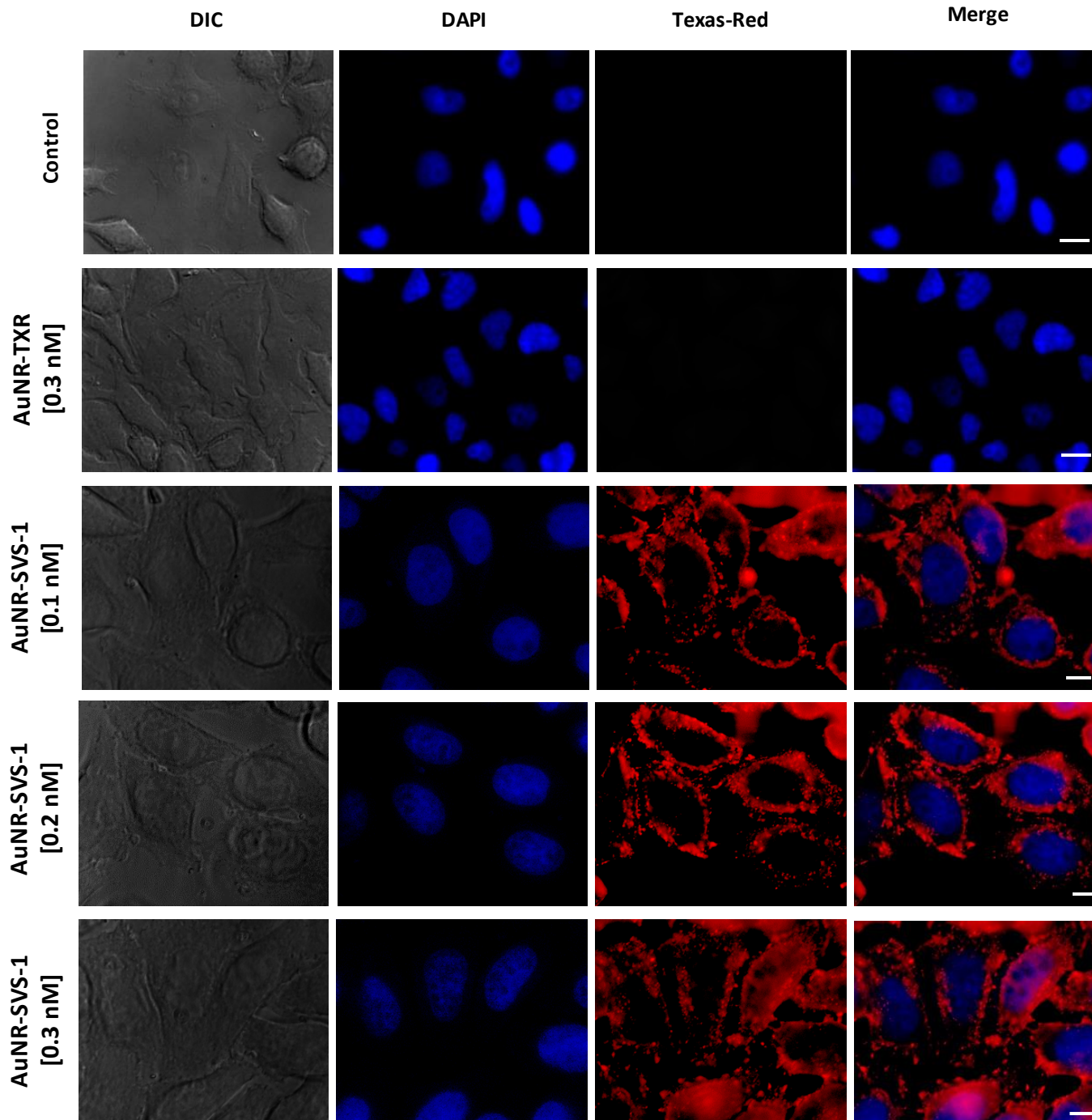
Proof of Imidazole-to-AuNC coordination

Aldeek, Safi, Zhan, Palui, Mattoussi, *ACS Nano* 2013, 11, 10197

S. Medina et al., *J. Controlled Release* 2015, 209 317–326

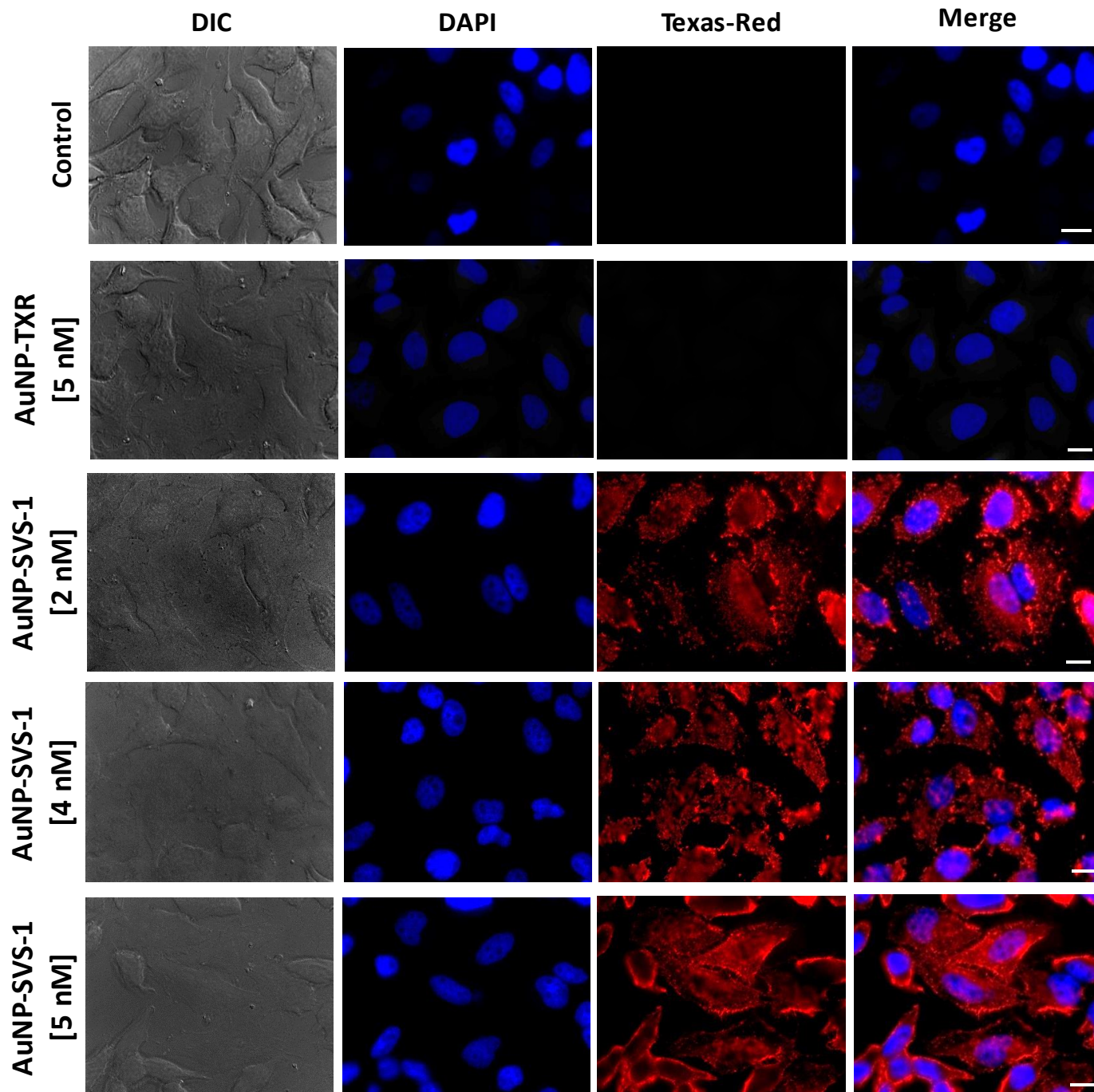
**SVS-1: CGG-KVKVKVKV<sup>D</sup>PPTKVKVKVK-NH<sub>2</sub>**

1. NHS-Texas Red/NHS-maleimide
2. SVS-1 peptide (thiol-maleimide)



- SVS-1-mediated delivery of AuNR- conjugates into HeLa cells.
- Here, Texas-Red dye coupled to AuNR- conjugates allowed visualization of the AuNR-SVS-1 distribution inside cells.
- Scale bar ~ 10  $\mu\text{m}$ .

Kapur, Medina, Wang, ... , Mattoussi,  
*ACS Omega* **2018**, 3, 12754–12762



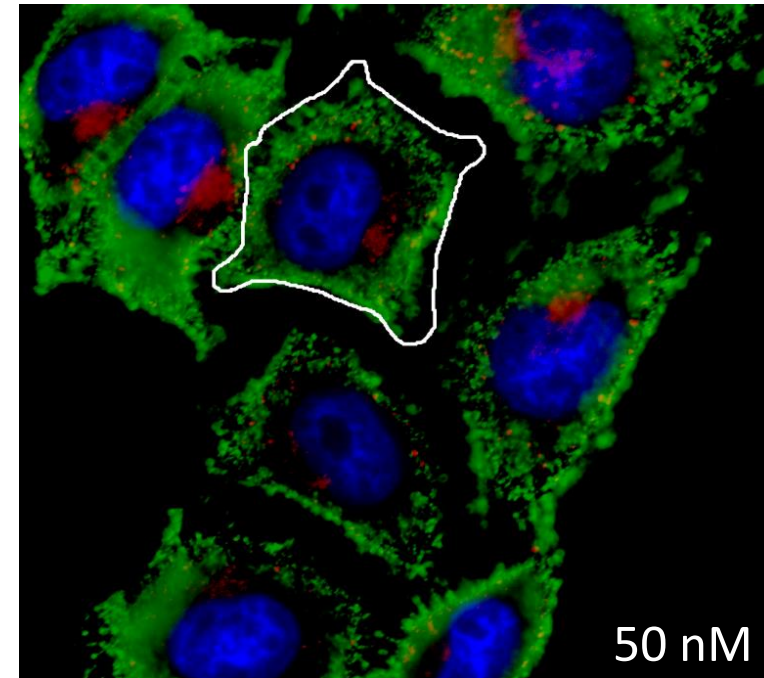
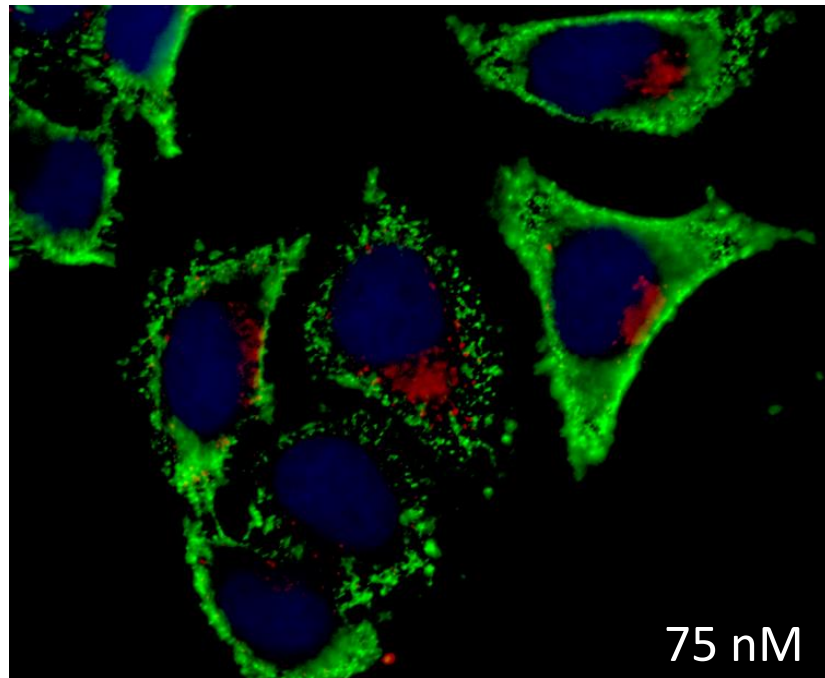
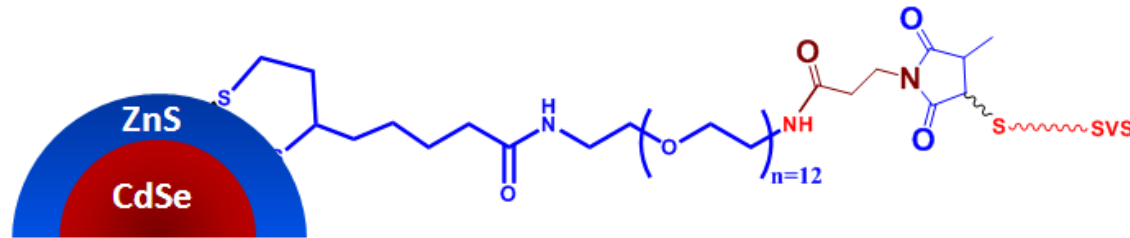
**SVS-1-mediated delivery of AuNP–conjugates into HeLa cells.**

**10-nm NPs were used.**

**Scale bar = 10  $\mu$ m.**

Kapur, Medina, Wang, ... , Mattoussi,  
*ACS Omega* **2018**, 3, 12754–12762

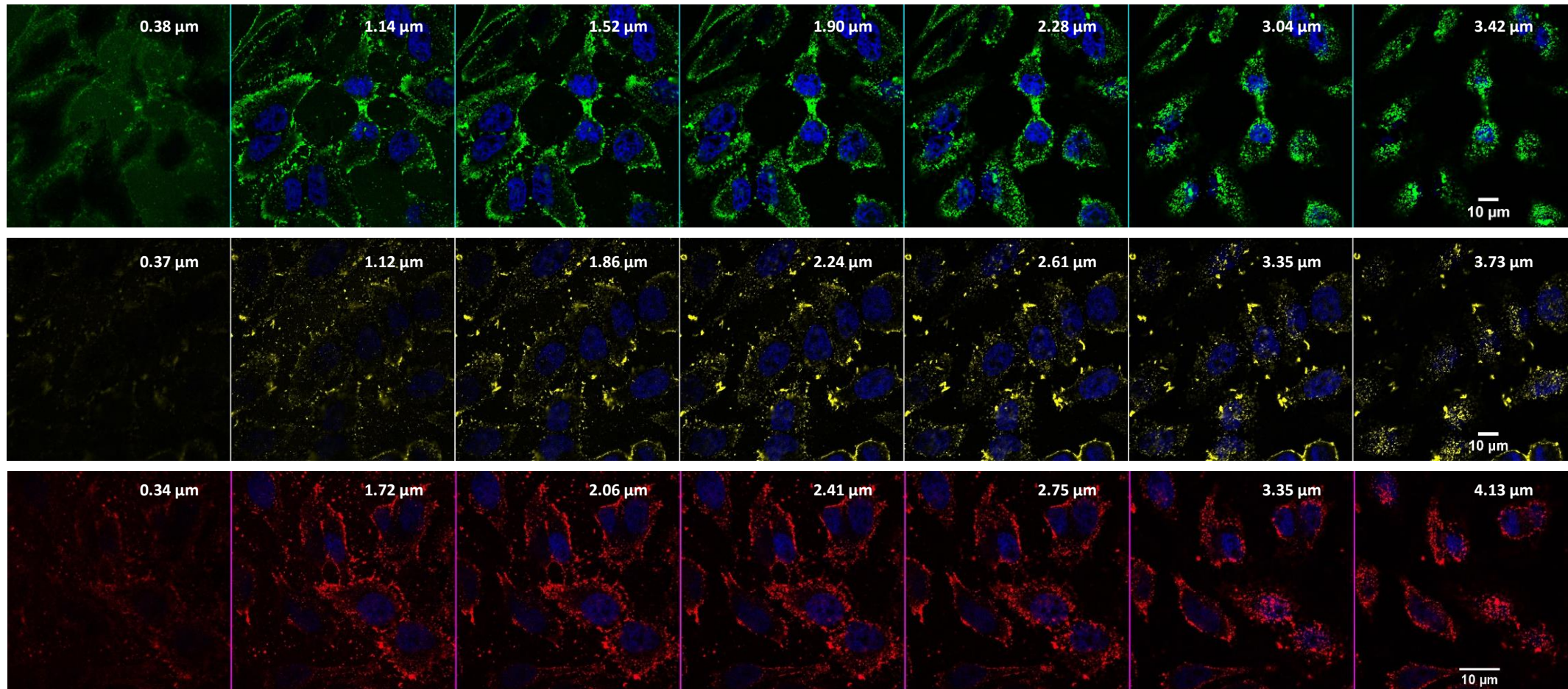
# Intracellular Uptake of QDs



# Confocal Images



Three color QD-peptide conjugates have been tested



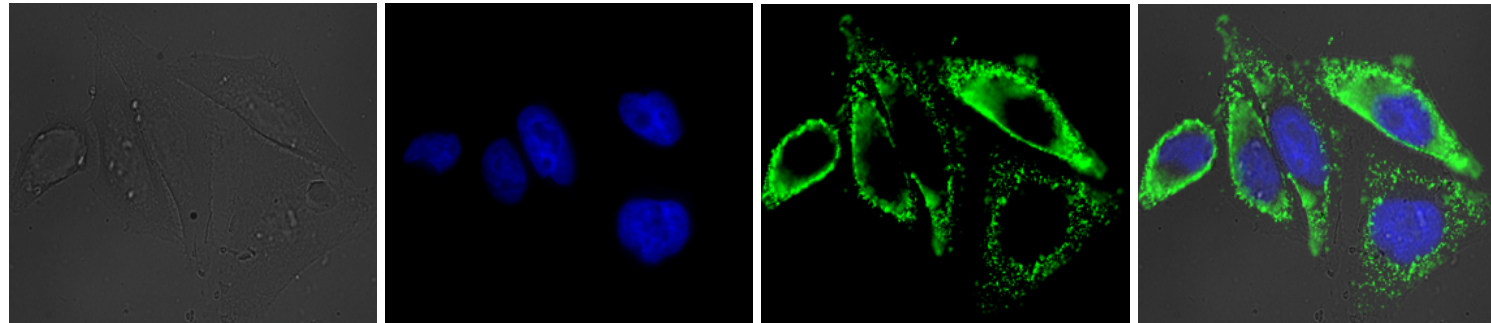
Kapur, Medina, Wang, Palui ... ACS Omega **2018**, 3, 17164–17172



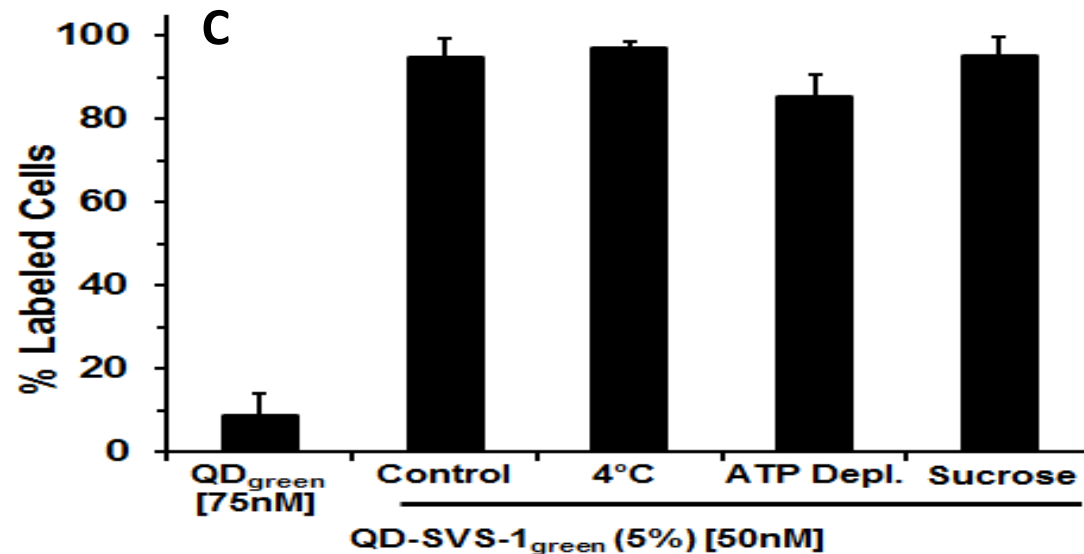
# Testing Uptake in the Presence of Inhibitors



1. Incubation at **4°C**
2. ATP depletion using **NaN<sub>3</sub>**
3. Clathrin mediated endocytosis inhibition using **Sucrose**



Kapur, Medina, Wang,  
Palui ... ACS Omega  
2018, 3, 17164–17172



[QD-SVS1]  
50 nM, 1hr, 4°C

# Acknowledgements

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Prof. Ken. Knappenberger (FSU Chem.)

Prof. Debi Fadool (FSU Bio.)

Prof. Daniel Hallinan (FSU Eng.)

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