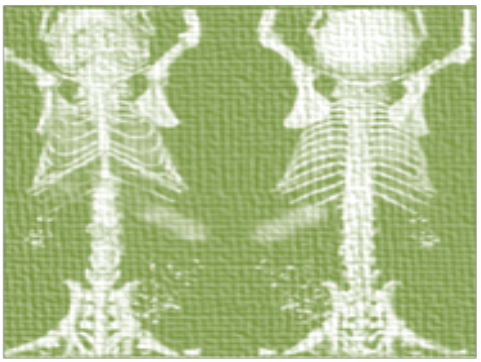
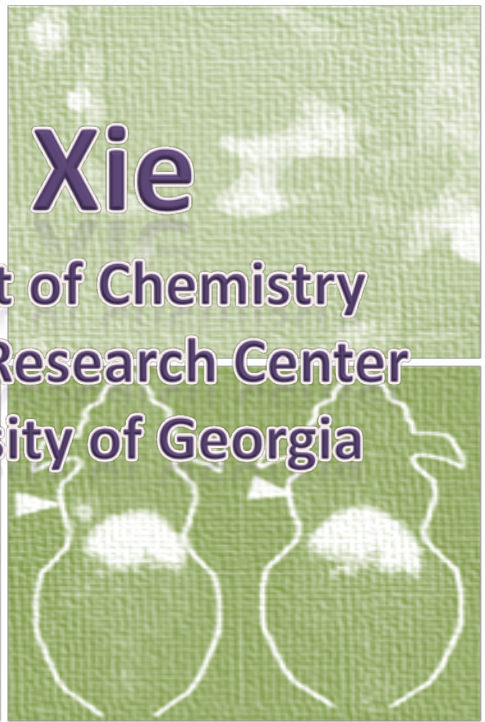
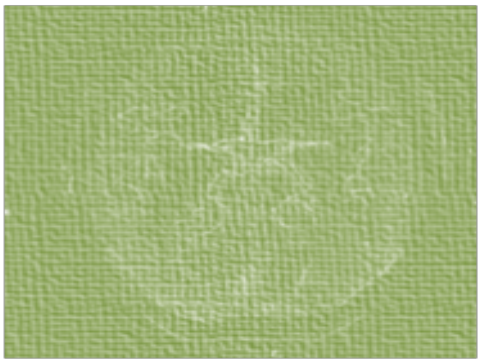
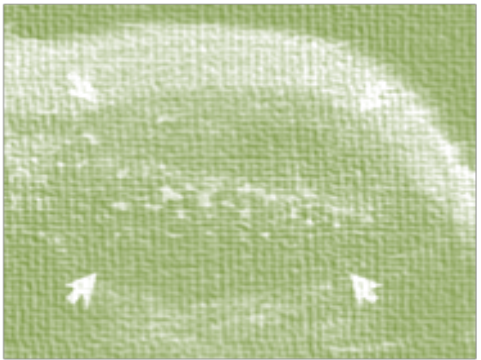
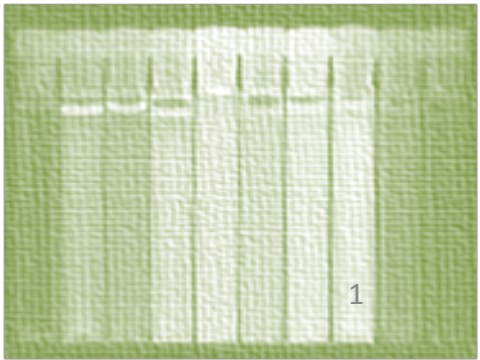
Surface Modified Ferritin Nanocages for Imaging and Drug Delivery







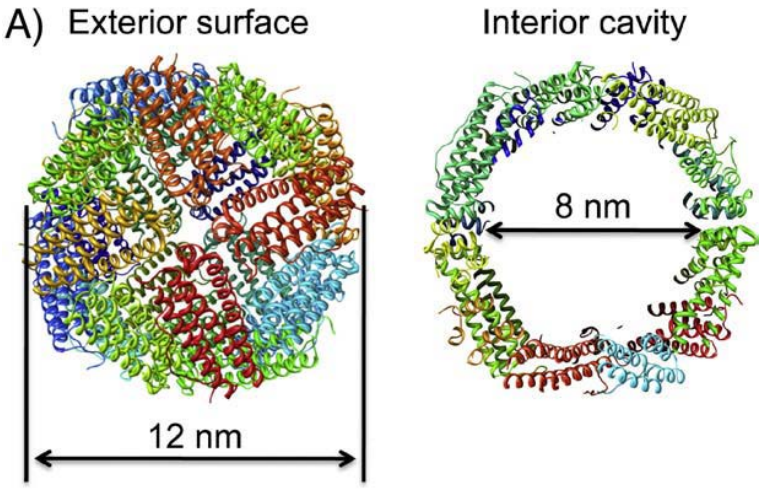


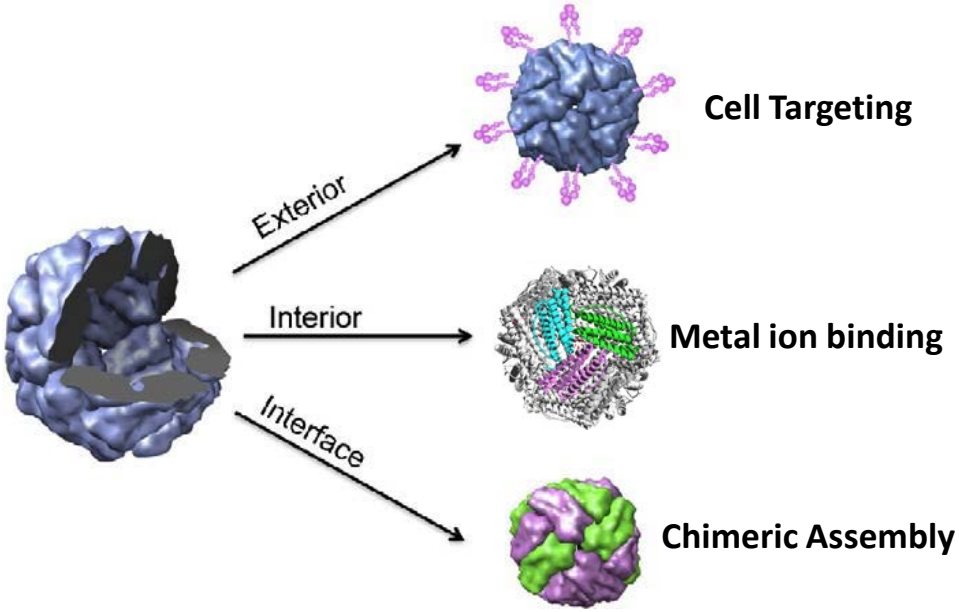


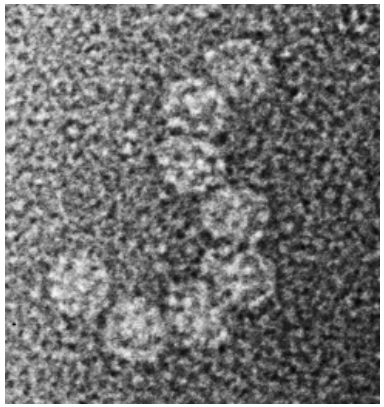
Jin Xie

Department of Chemistry
Bio-Imaging Research Center
The University of Georgia

Apoferritin Nanocages



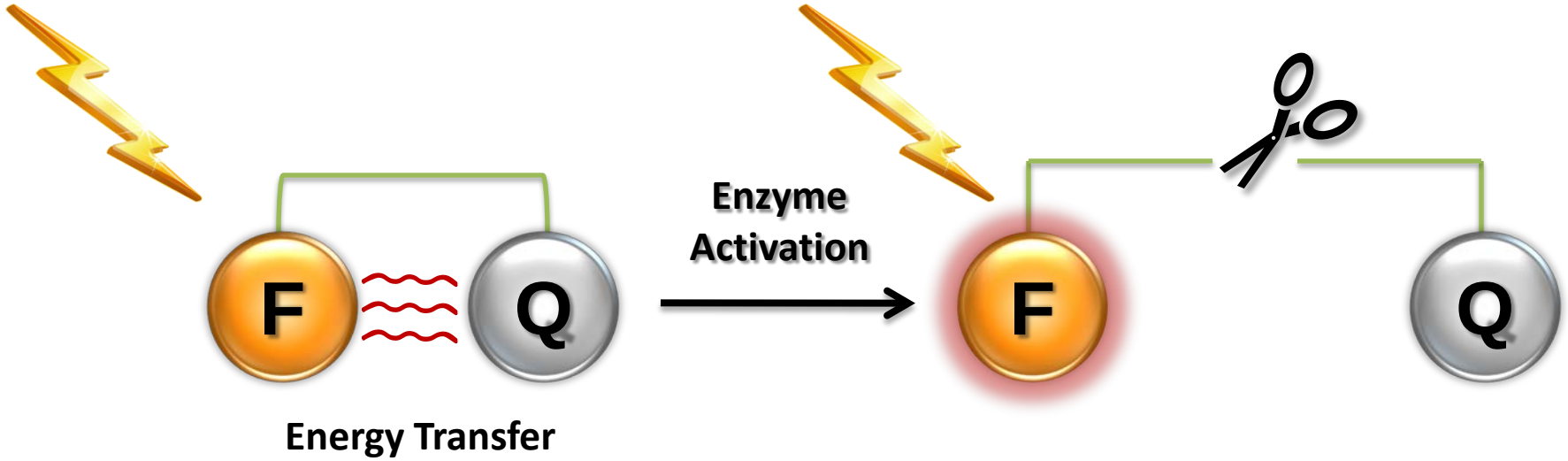




Unique self-assembled nanostructures

- Self-assembled by 24 subunits
- Large cavity, 8 nm inner diameter
- Rigid under physiological environments
- Decomposed at pH=2 but reversible

Activatable Imaging Probes



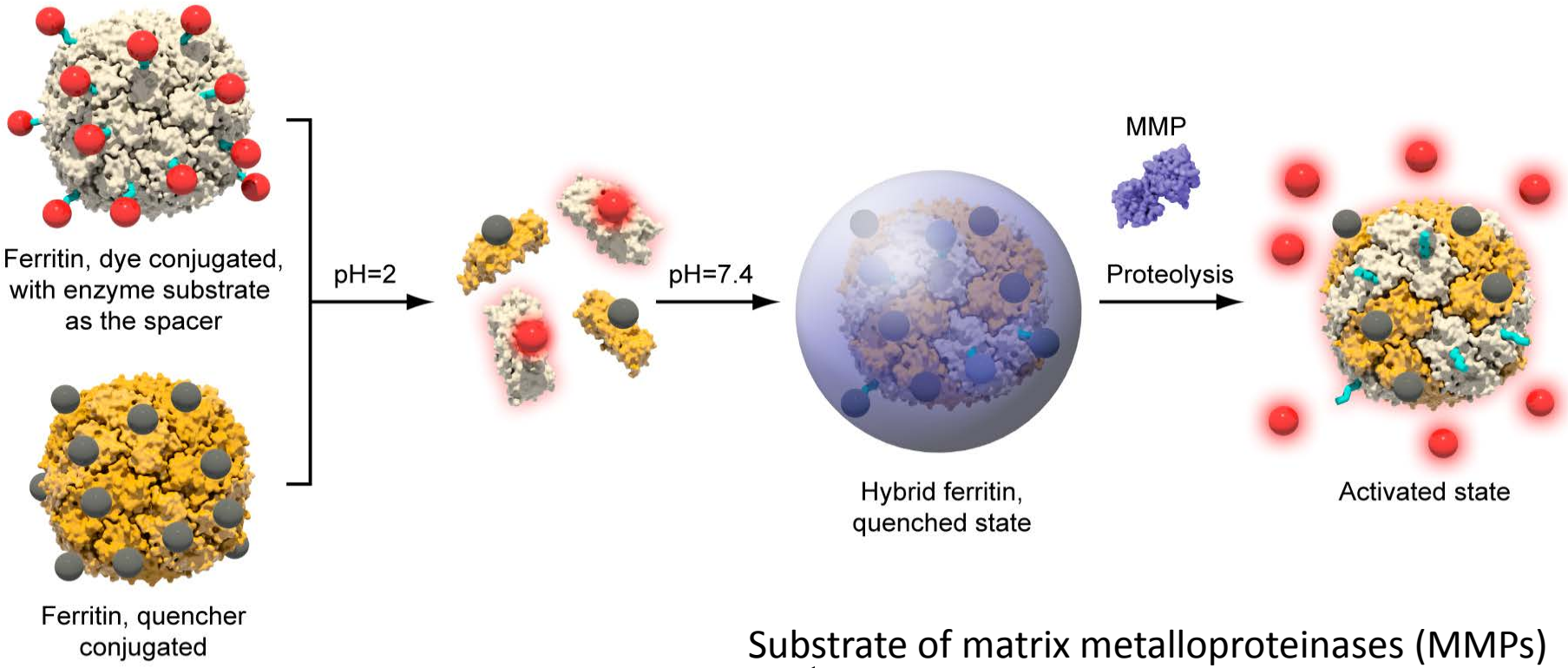
Quenching mechanisms:

- Self-quenching
- Small molecule quencher
- Gold nanoparticles

Advantages:

- Low background
- High sensitivity
- High specificity

Ferritin-Based Activatable Nanoprobes

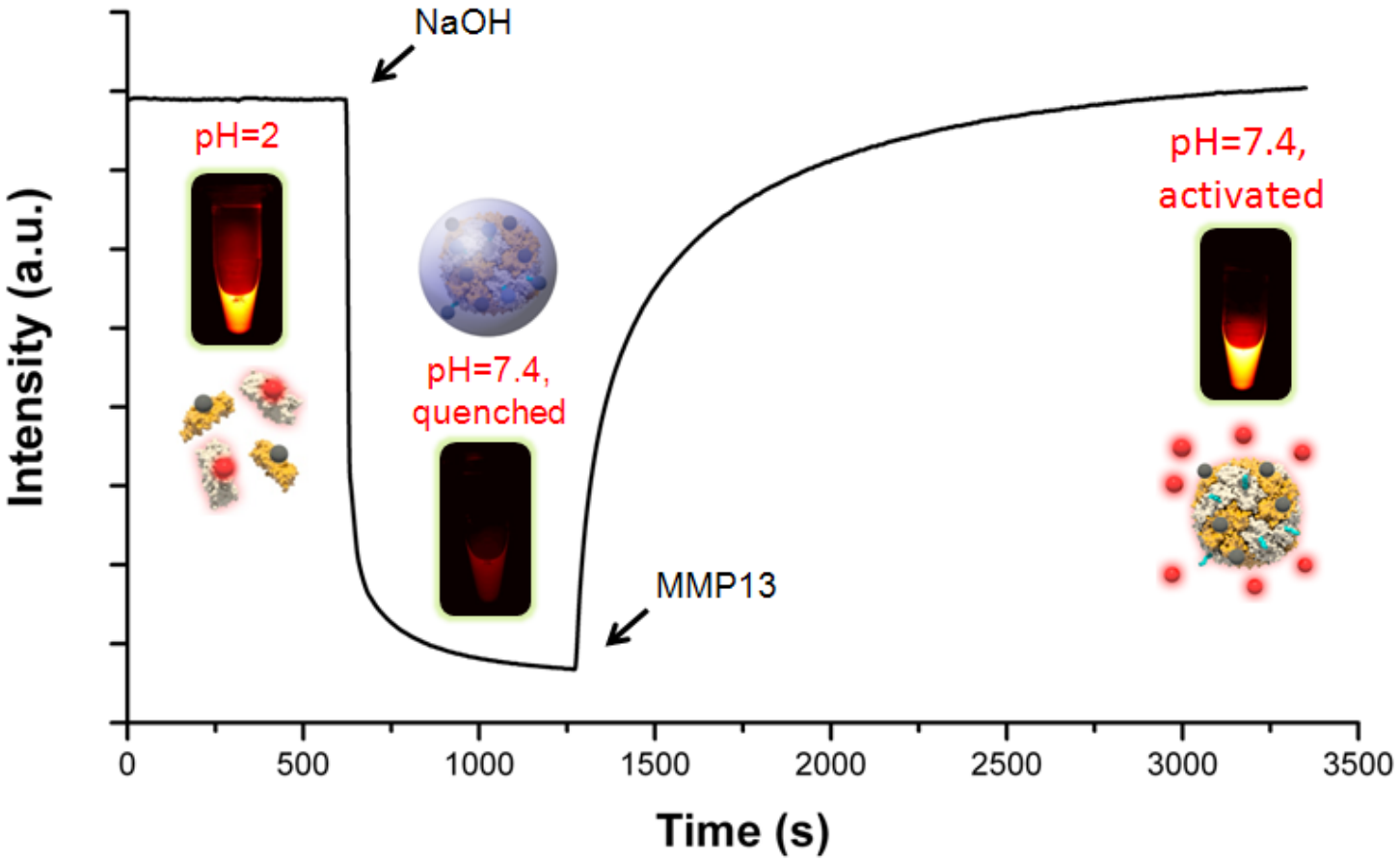


Substrate of matrix metalloproteinases (MMPs)

- Cy5.5-Gly-Pro-Leu-Gly-Val-Arg-Gly-Cys (dye-substrate)
- Black hole quencher-3 (BHQ-3, quencher)

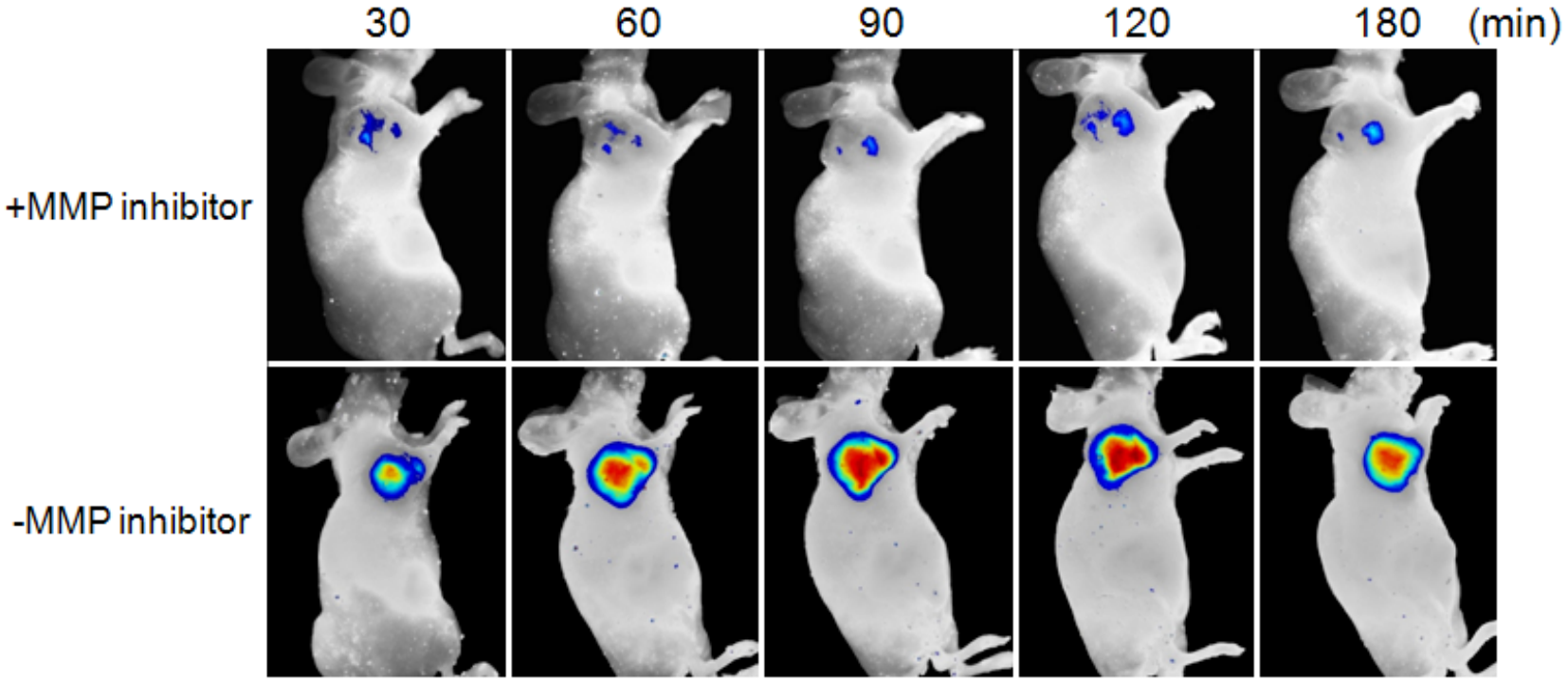
Lin X, Xie J et al. *Angew Chem Int Ed*, 2011.

Real-Time Quenching and Activation



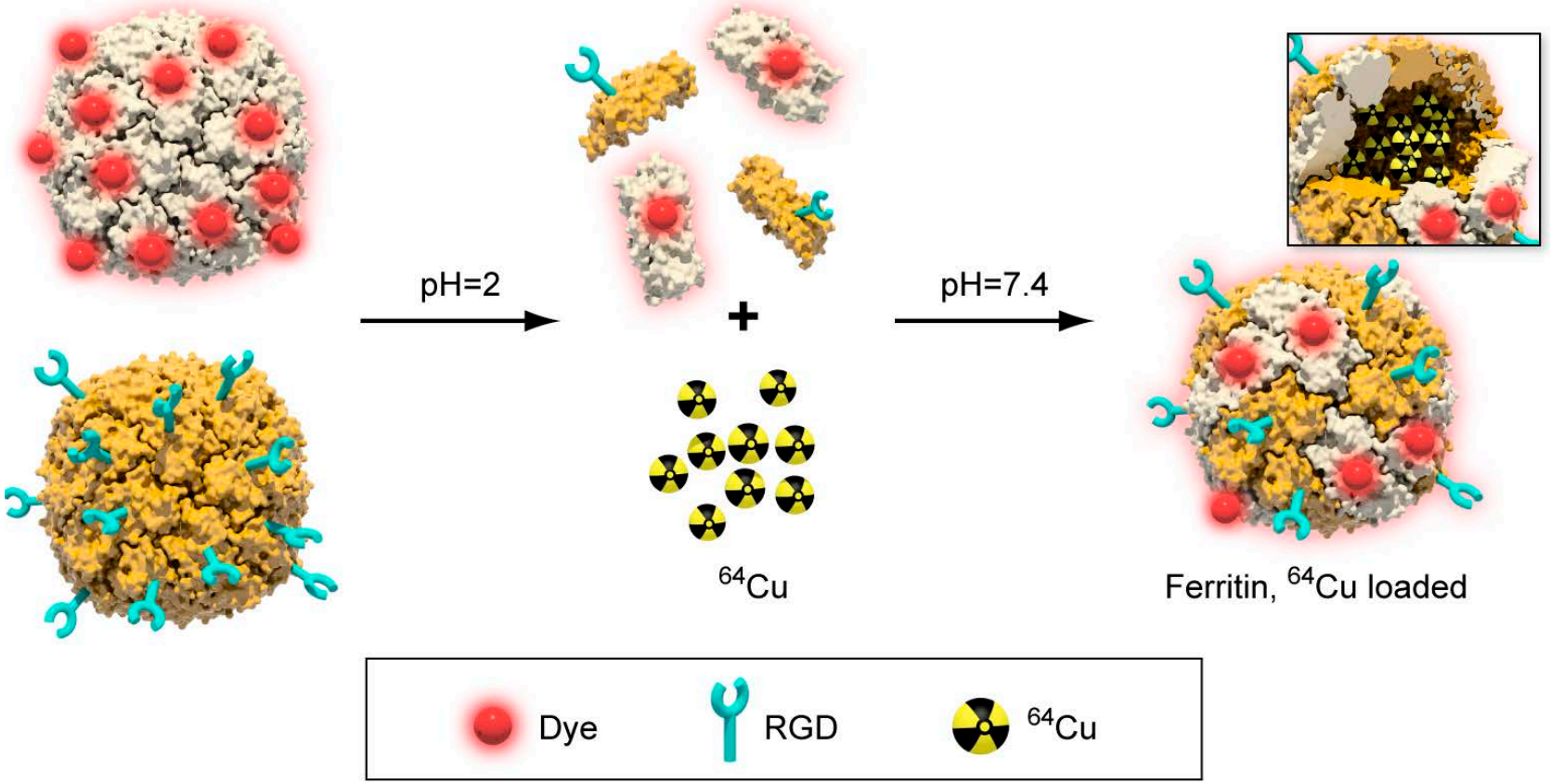
Lin X, Xie J et al. *Angew Chem Int Ed*, 2011.

In Vivo Studies in 22B SC Models



Lin X, Xie J et al. *Angew Chem Int Ed*, 2011.

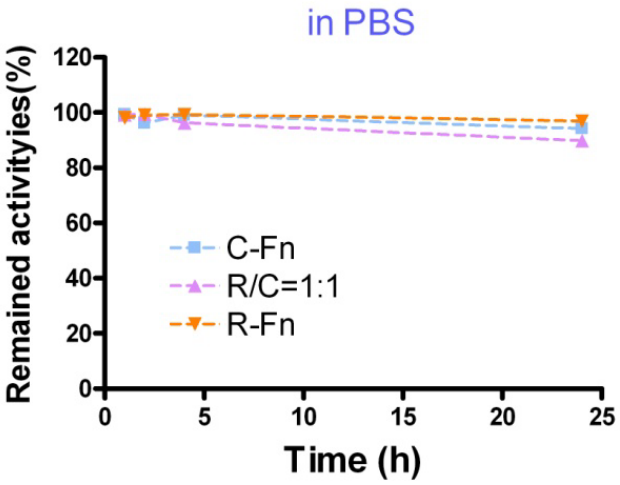
Ferritin-Based Multimodal Imaging Probes

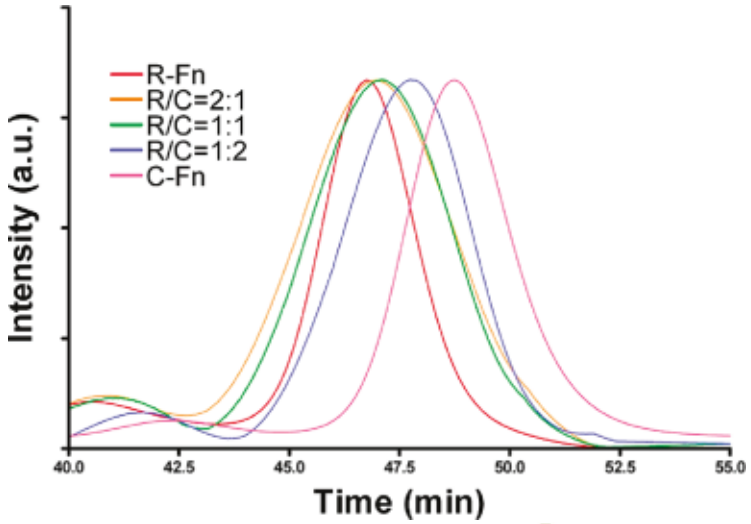


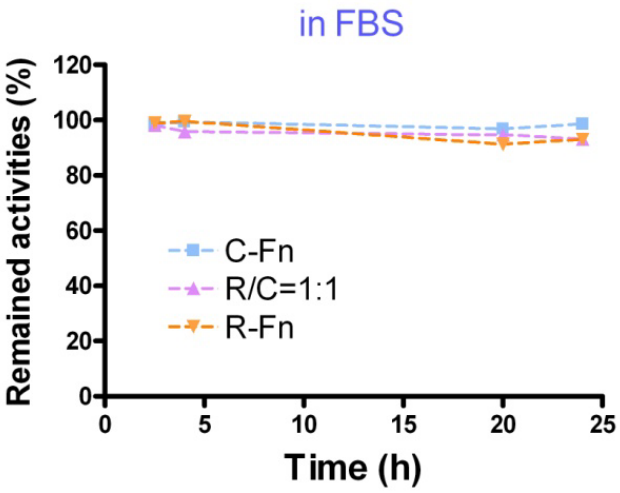
- **Two surfaces: exterior surface and interior surface**
- **Chemical and genetic modifications**
- **Metal cations can be encapsulated into the interiors**

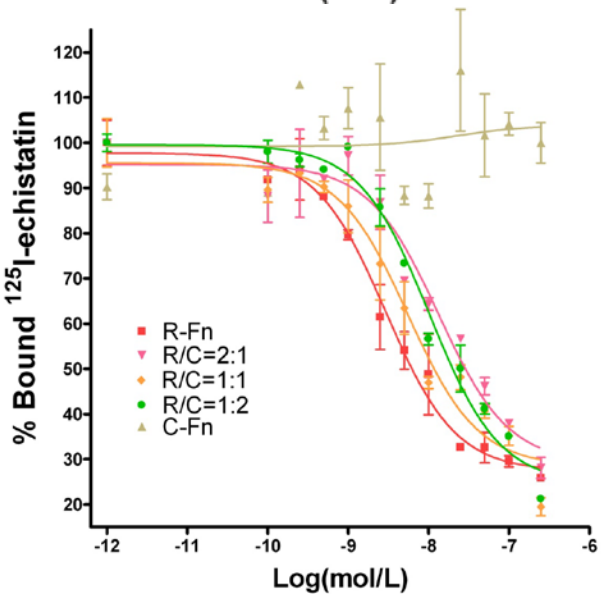
Xie J and et al. *Nano Letters*, **2011** *11*, 814-9

In vitro binding assay and stability test



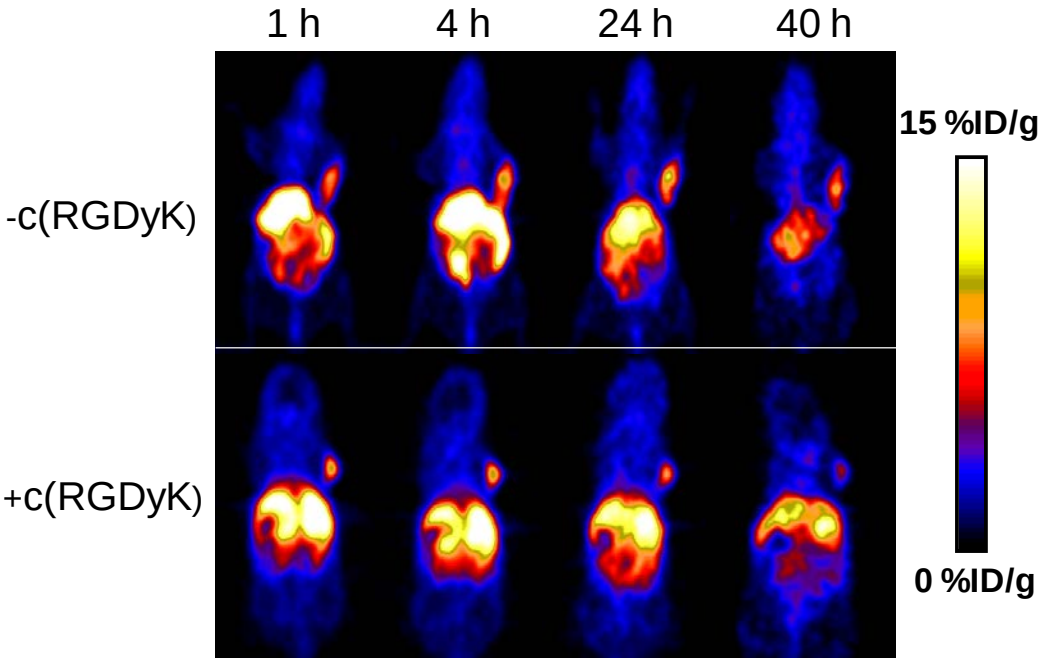


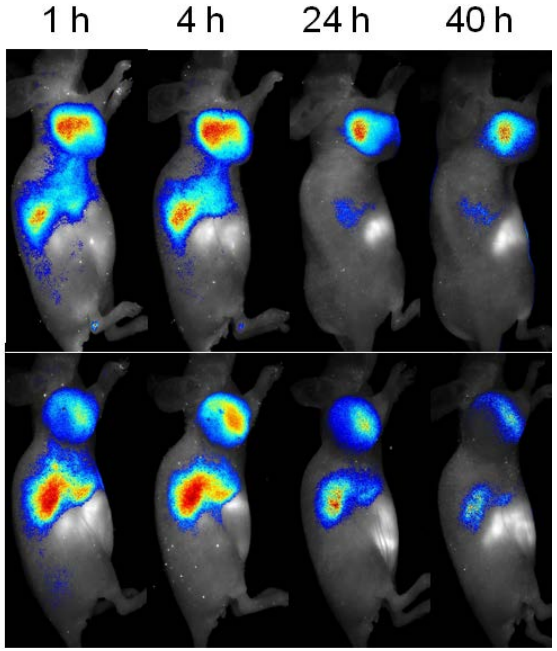


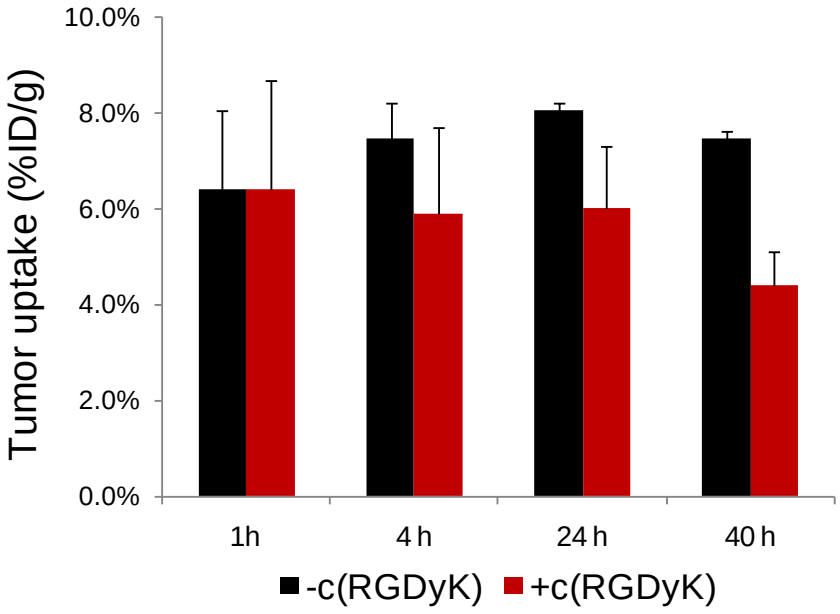


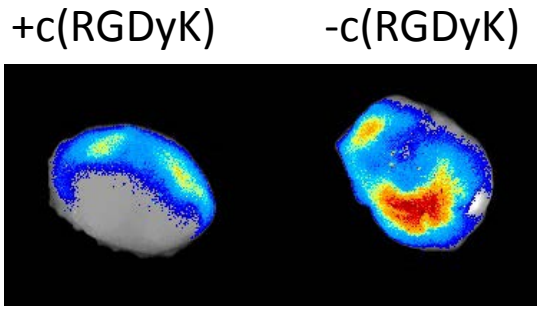
Lin X, Xie J and et al. *Nano Letters*, **2011** *11*, 814-9

In Vivo PET and NIRF Imaging





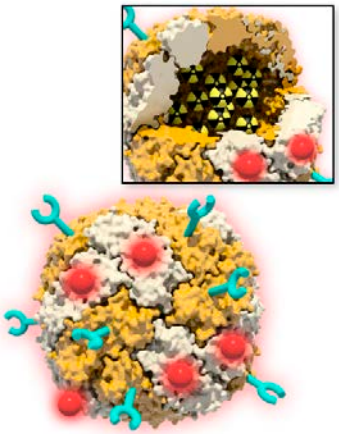




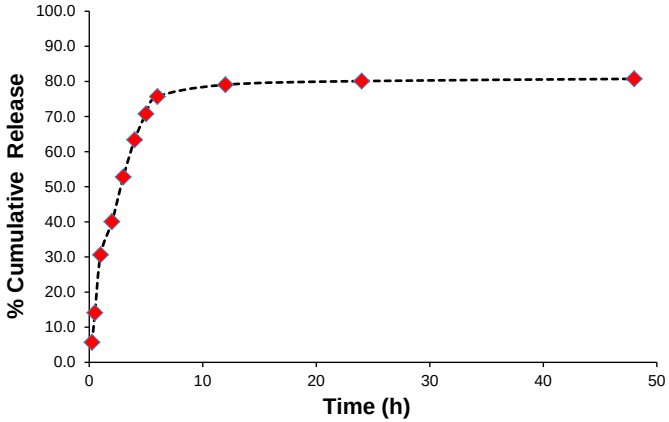
- Correlated PET and NIRF observations
- Tumor targeting was mediated by both EPR effect and RGD-integrin interaction

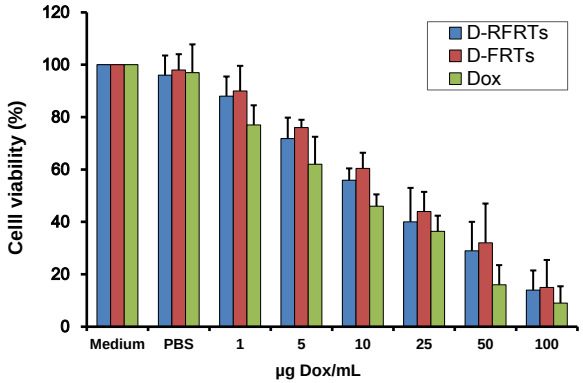
Lin X, Xie J and et al. *Nano Letters*, **2011** *11*, 814-9

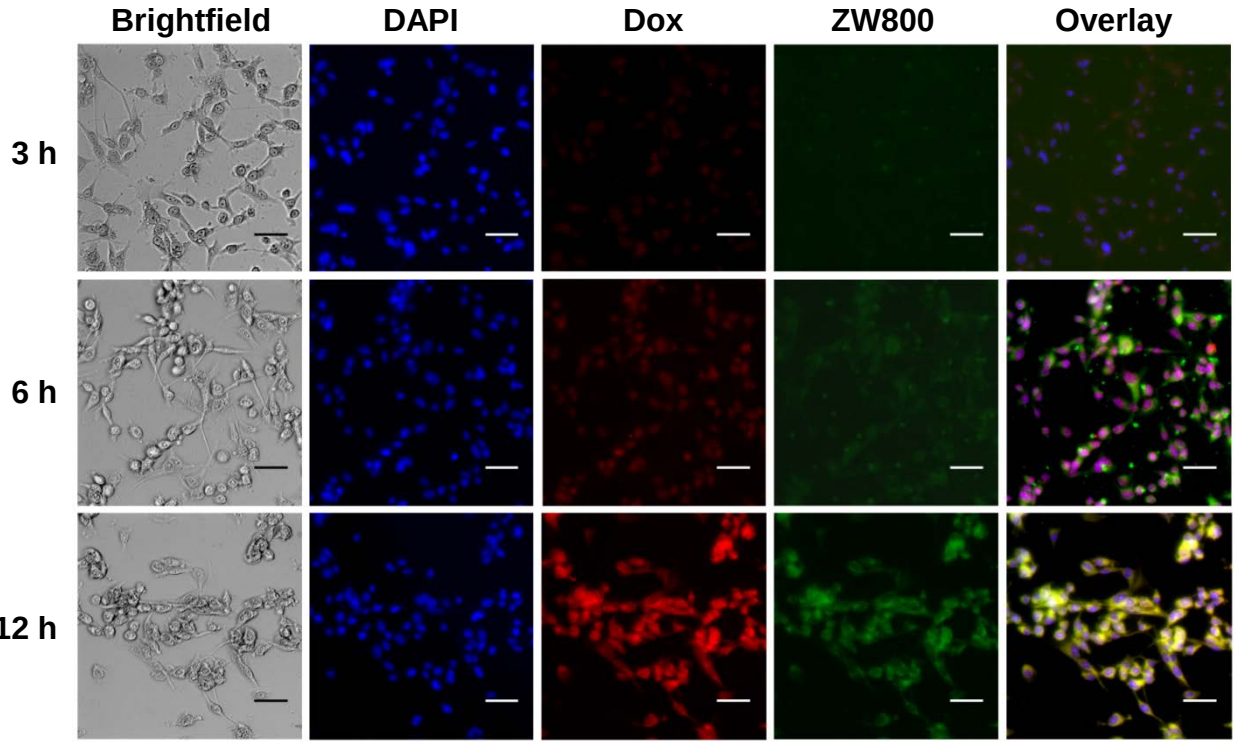
Doxorubicin-Loaded RGD-Ferritin NPs



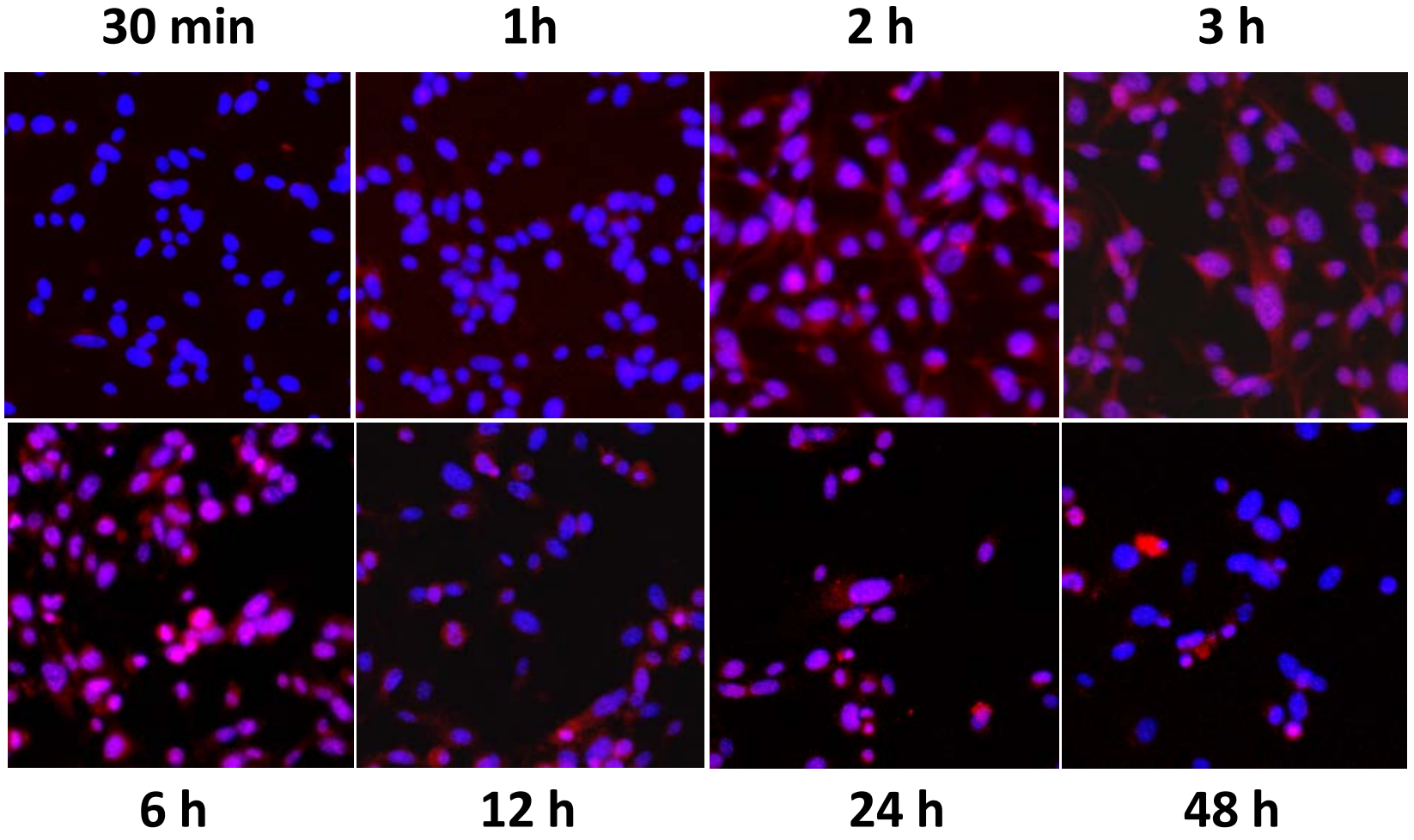
ZW800 RGD doxorubicin



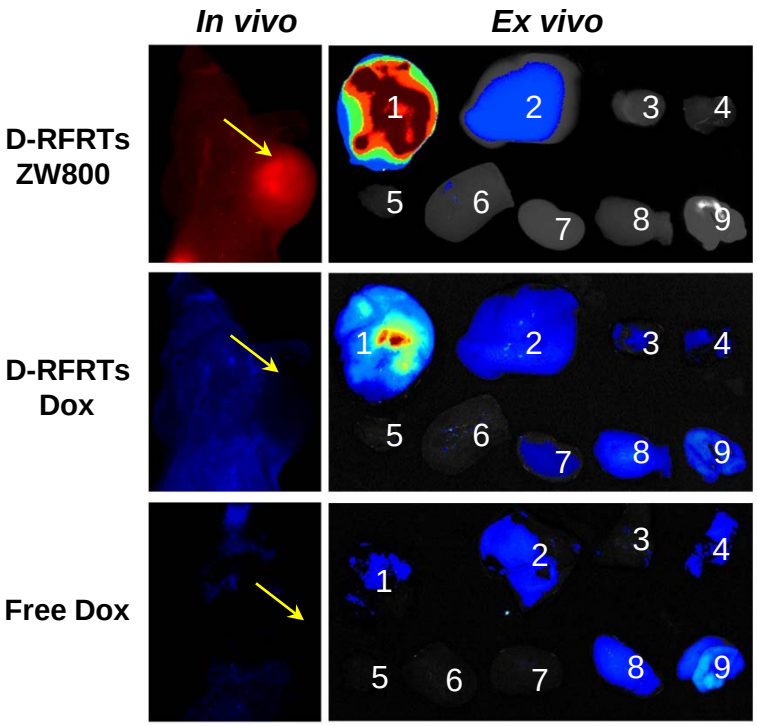


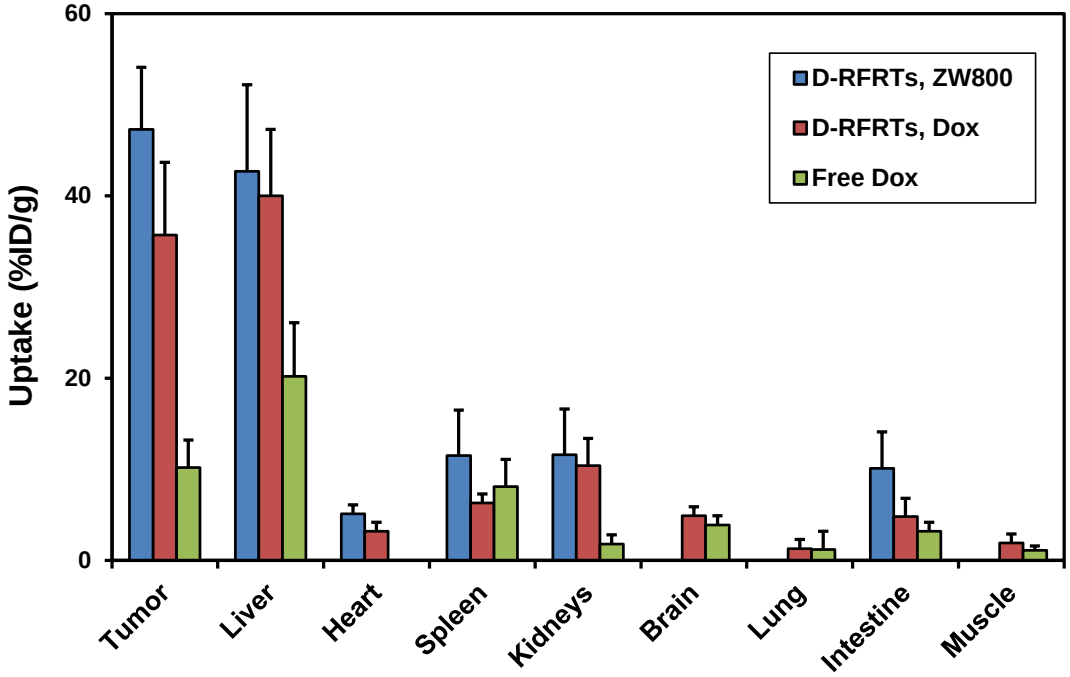


Doxorubicin-Loaded Apoferritin Nanoparticles

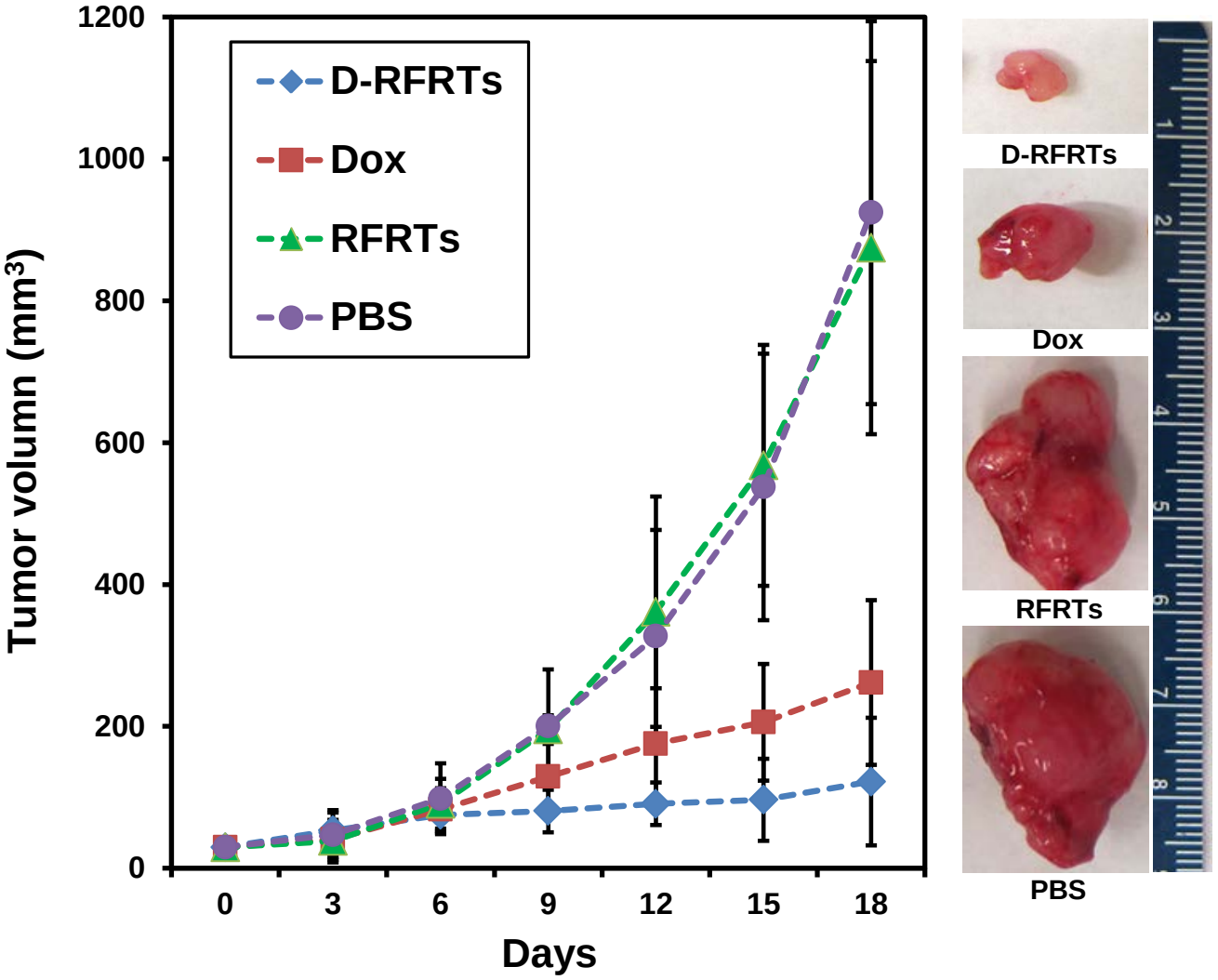


Biodistribution Studies

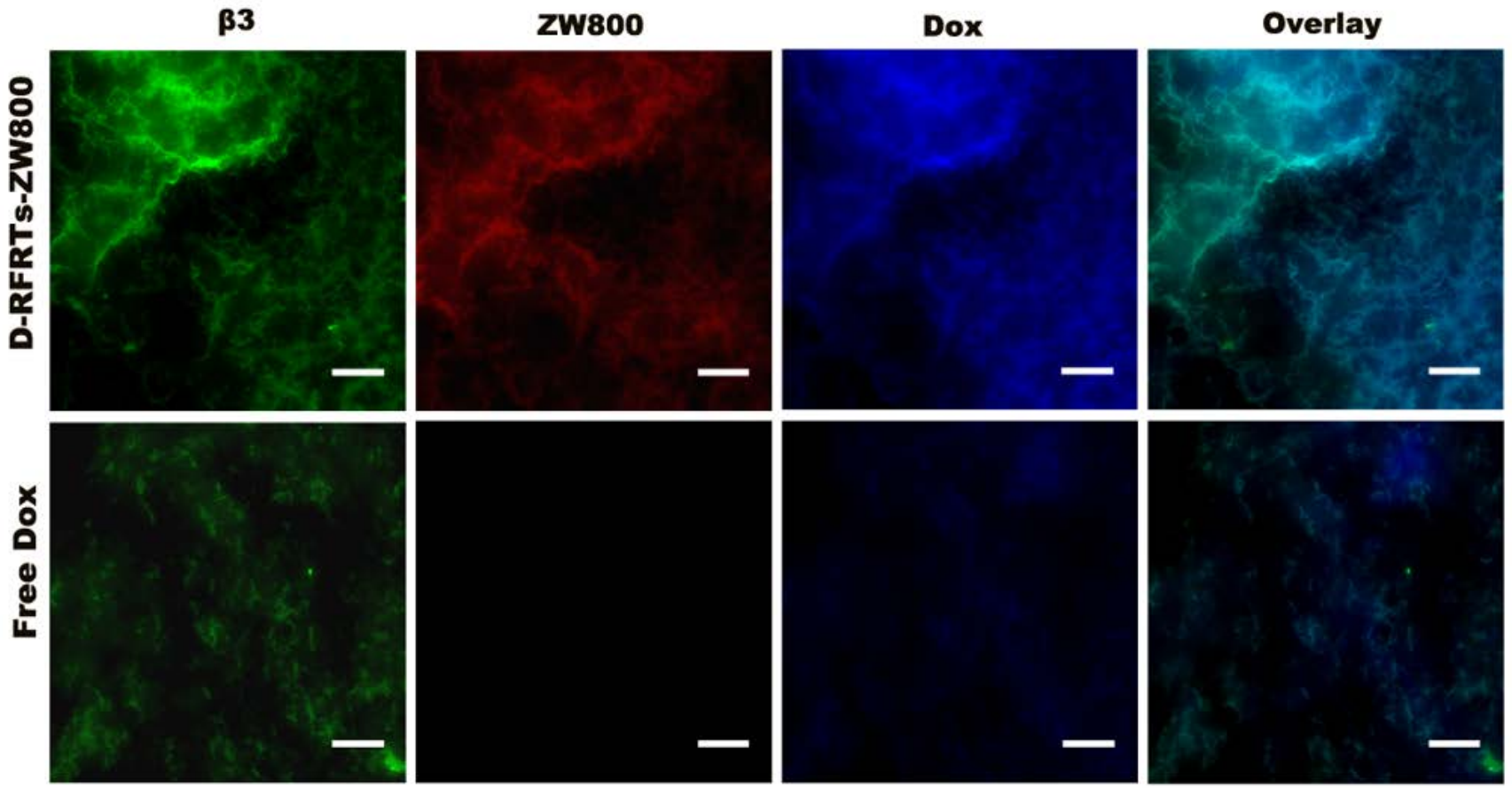




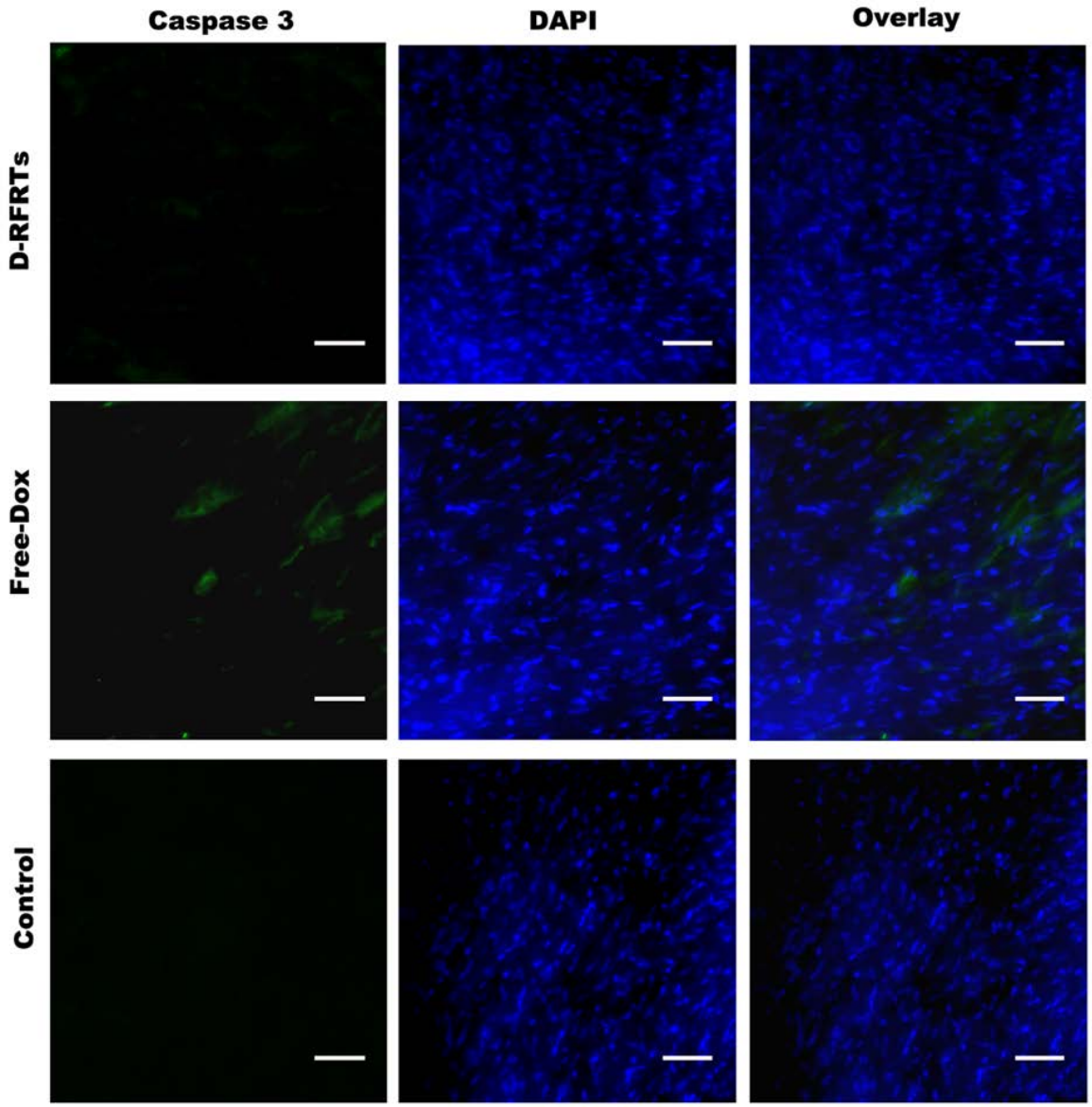
Therapeutic Study Results



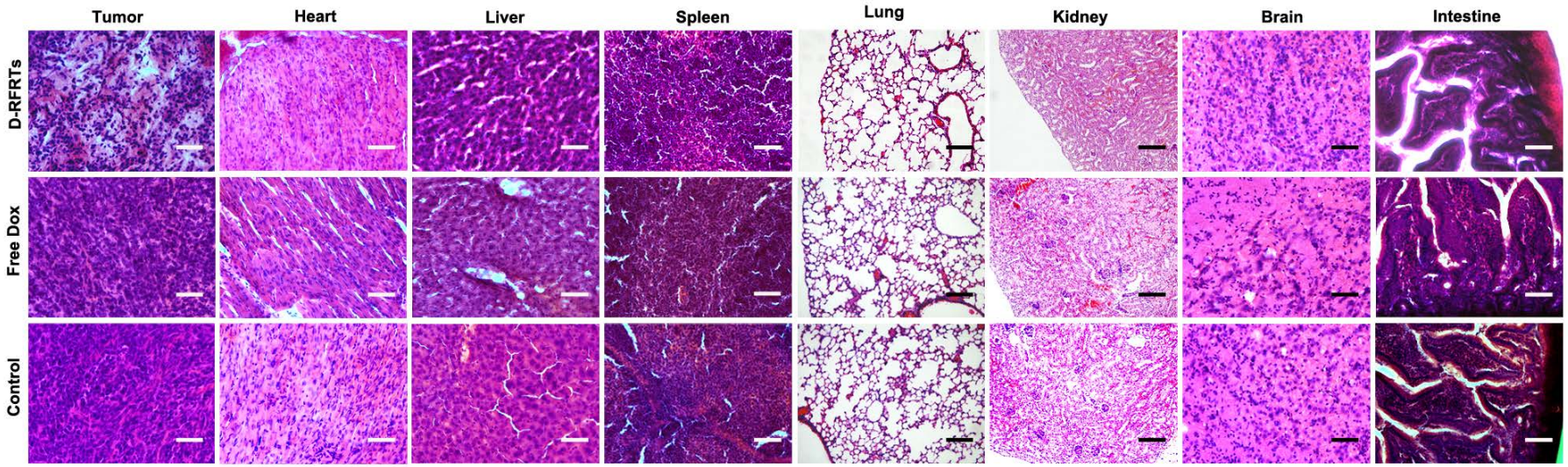
Immunostaining: Tumors



Immunostaining: the Heart



H&E Staining Results



Conclusions

- Ferritin nanoparticles can be genetically and chemically modified, making them attractive nanoplatforms with potentials in imaging and drug delivery.

- Each ferritin nanoparticle is comprised of 24 subunits, which self-assemble into a nanostructure. The nanostructure is rigid in physiological environment but can be broken down in an acidic solution. The process is pH-dependent and reversible, affording a easy way of constructing hybrid nanostructures.

- In addition to iron, other transition metal isotopes, such as ^{64}Cu, can be encapsulated into ferritin interiors.

- Small molecule drugs, such as doxorubicin can be loaded onto ferritins with high efficiency.

Acknowledgements

Group members

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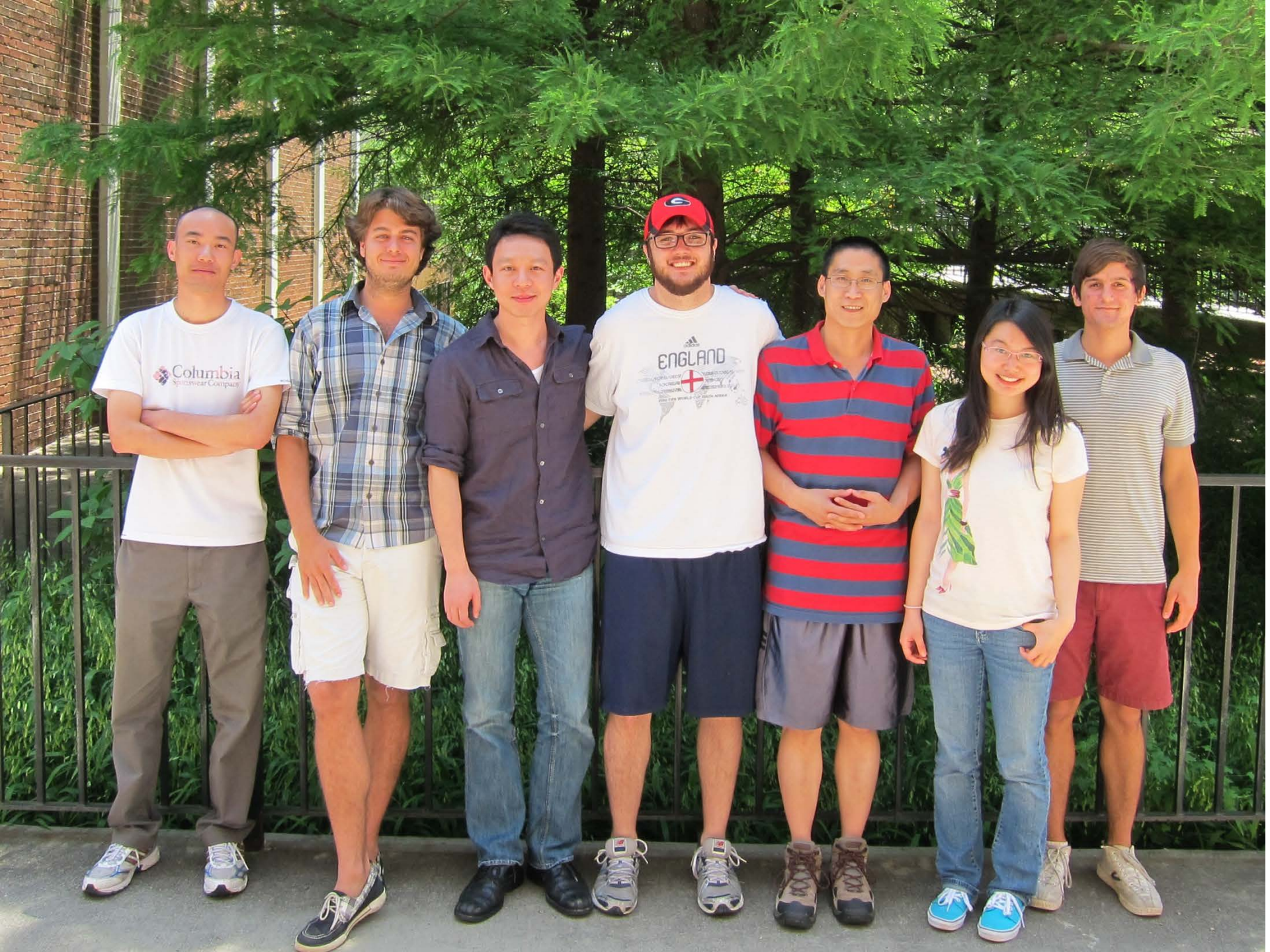
Qun Zhao
Luning Wang
Chunlian Wang
Xiaoyuan Chen
Fan Zhang
Yanglong Hou

NATIONAL INSTITUTES OF HEALTH

Pathway to Independence Award (K99/R00)

1785 The University of Georgia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Thanks!