Molecular Optical Imaging with Quantum Dot Fluorescence Probes

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University of Ulsan College of Medicine, Seoul, Korea

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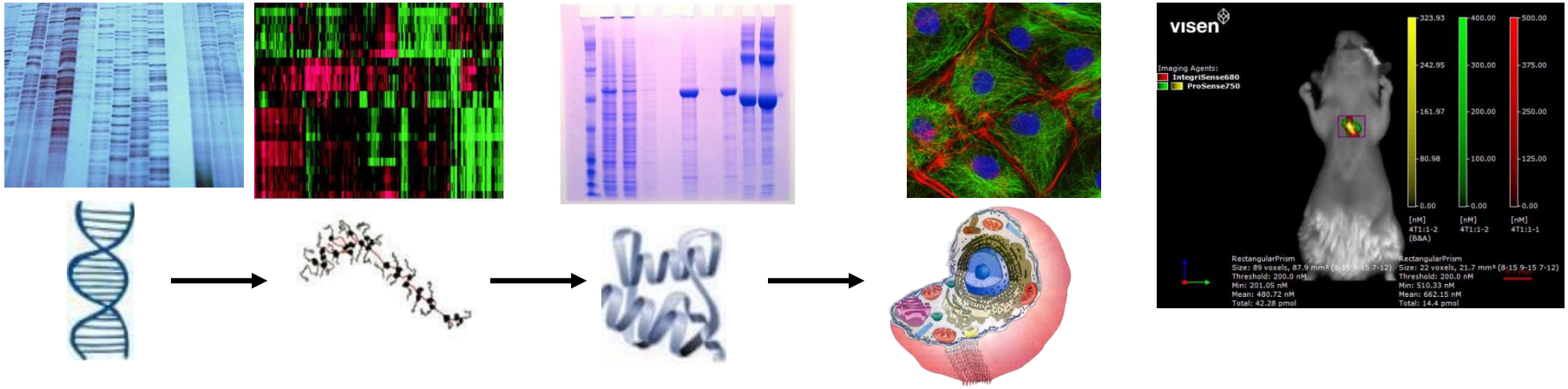
ASAN Medical Center

Imaging Science



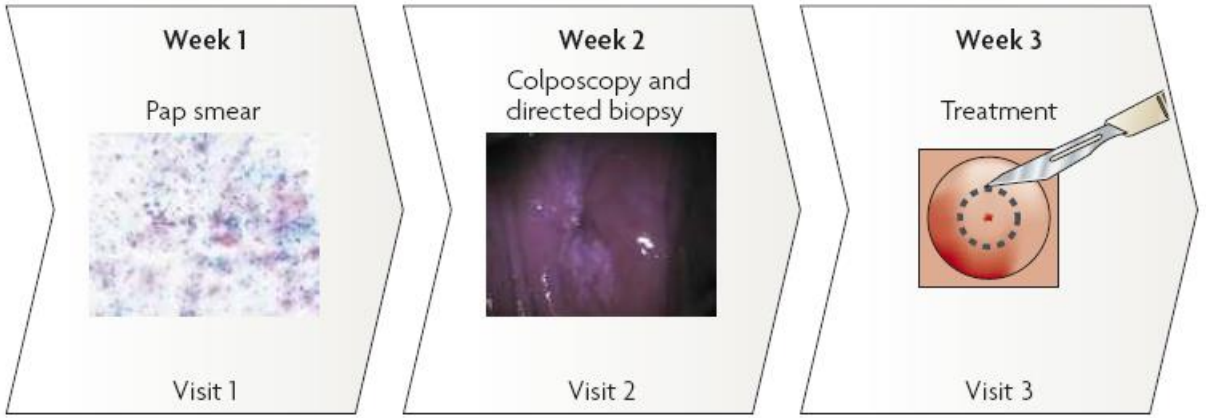
Linked Systems, Agents, Application Development = Enhanced data

Preclinical and Clinical Application of Optical Imaging

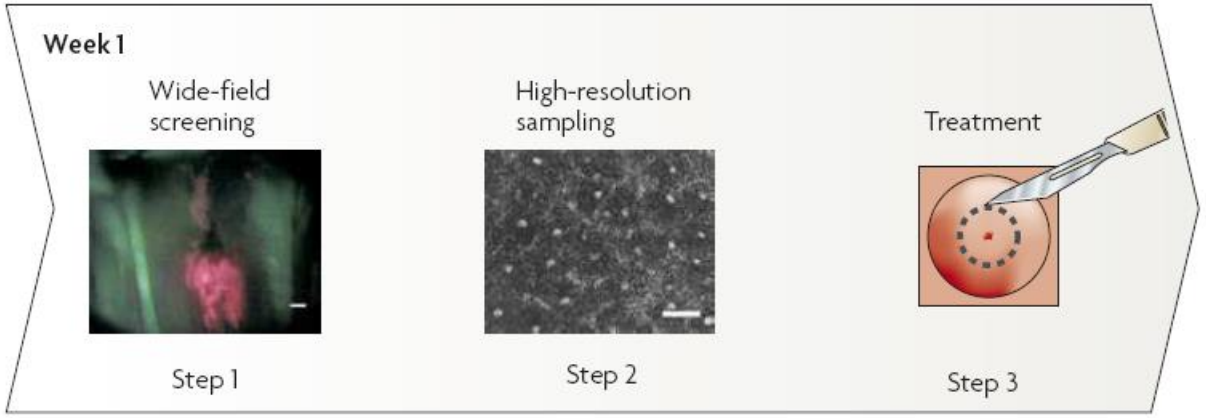
- Preclinical Drug Evaluation
  - Monitor Tumor growth and metastasis
  - Determine Drug Targeting
  - Monitor Enzyme Activity
  - Host-tumor interactions
- Clinical Application
  - Intraoperative Cancer detection
  - Endoscopy, Colposcopy, Cystoscopy, Bronchoscopy
    - Early detection and Pathologic evaluation of Lesions

Optical Imaging for Cervical Cancer Detection

Current

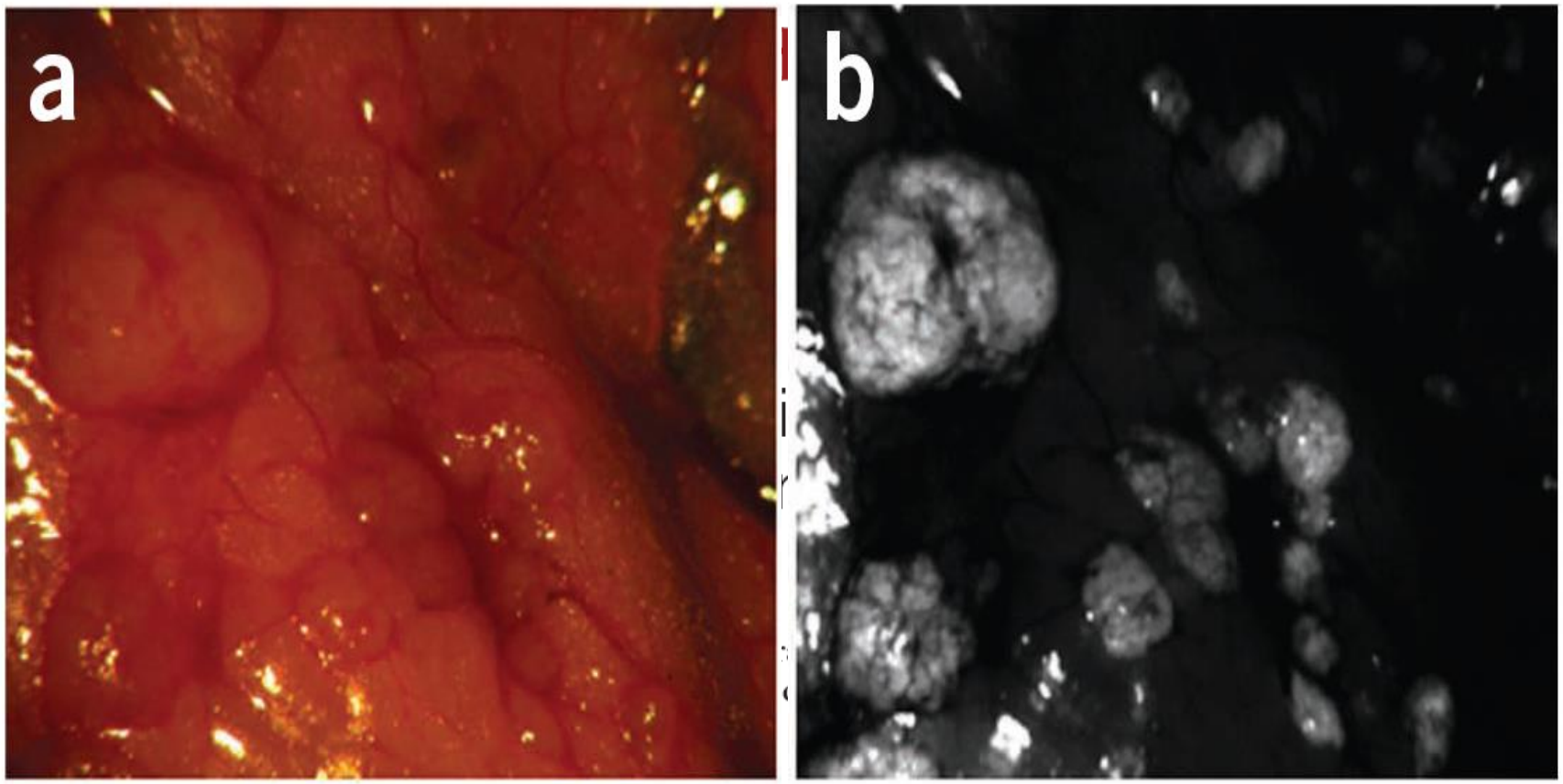


Future



Thekketk N, Richards-Kortum R. Nat Rev Cancer 2008;8:725-731

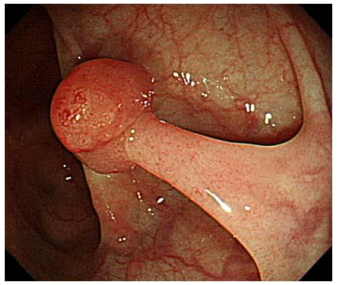
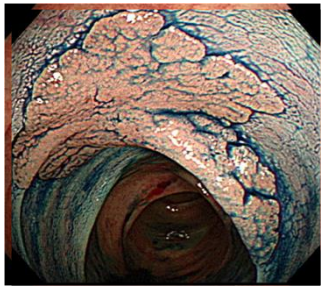
Fluorescence Imaging In Operation
- Folate Receptor Imaging (FITC) -

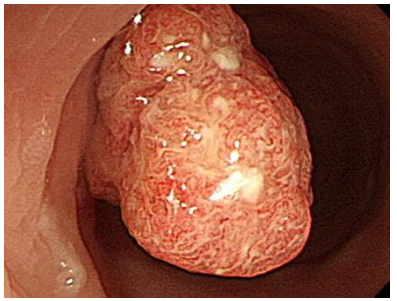


Gooitzen M van Dam et al. Nat Med 2011;17:1315

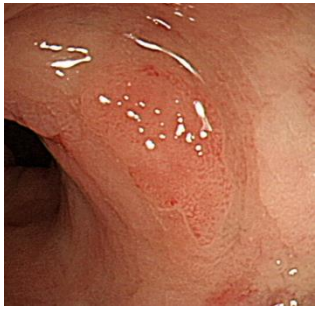
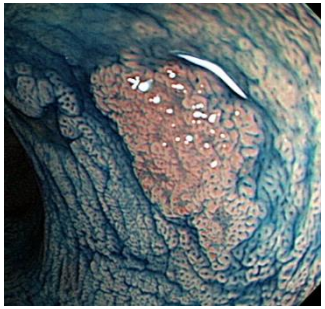
Clinical Problem in Endoscopy

- Precancerous lesions – Flat lesion



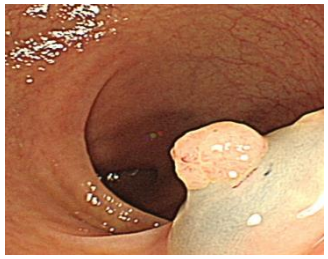
- Colitic Cancer Detection in IBD

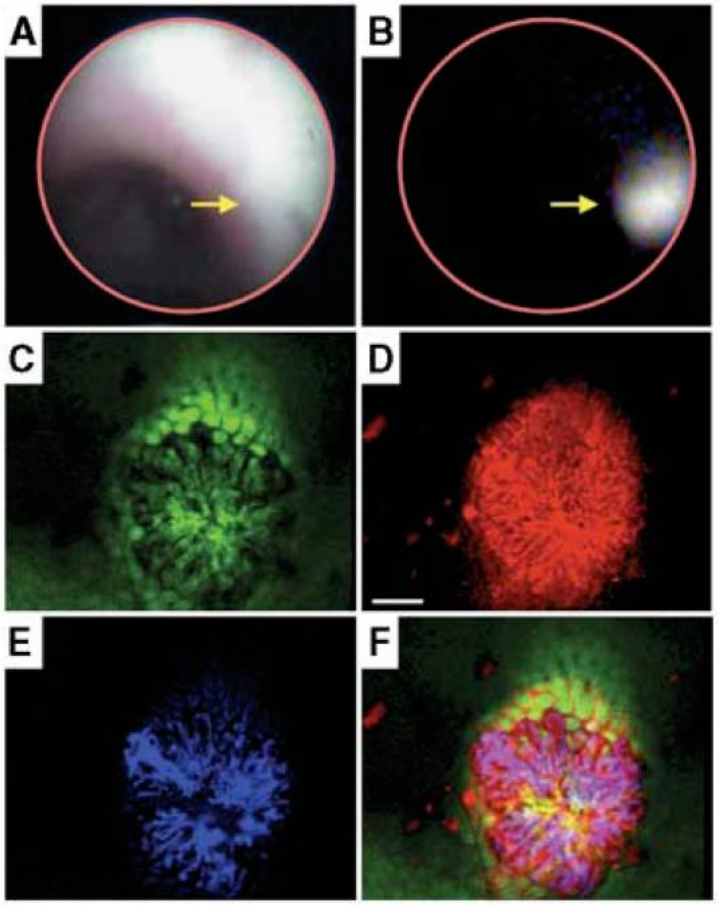



* Missing Rate : 15-25%

More Sensitive Method Needed

Molecular Imaging (MI)

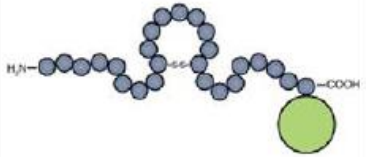
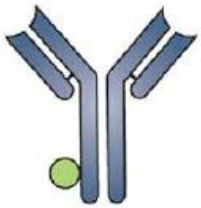
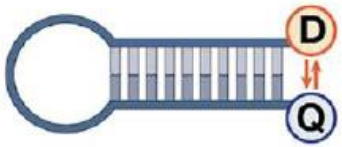
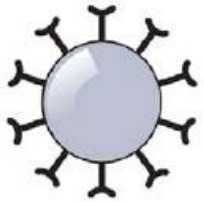




- MI: Visualization, and measurement of biological process at the molecular and cellular levels in humans and other living systems.
  - 2D, or 3D, Quantification
  - Nuclear medicine, MRI, Optical Imaging, US

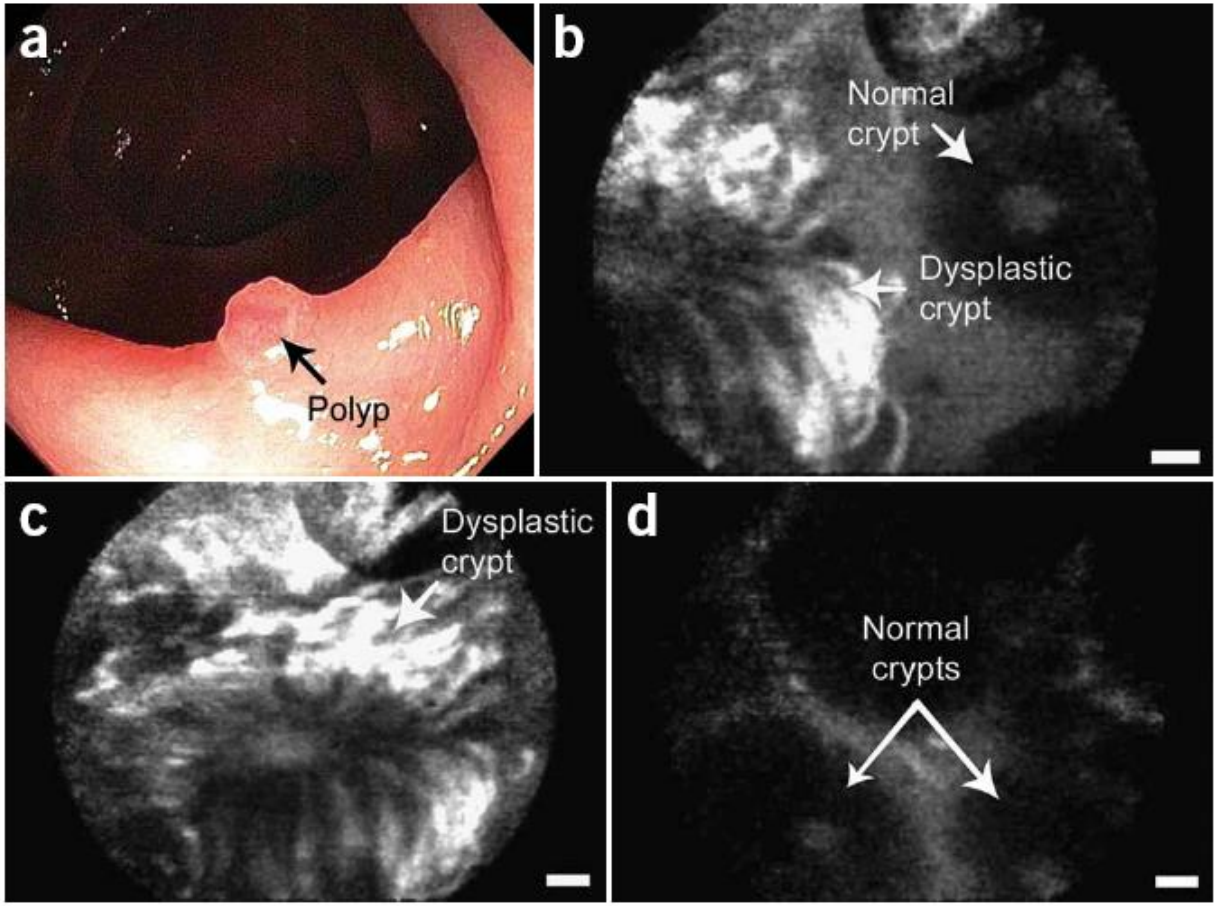
Science 2006;312:1168-1171

Comparison of different Molecular Probe Classes

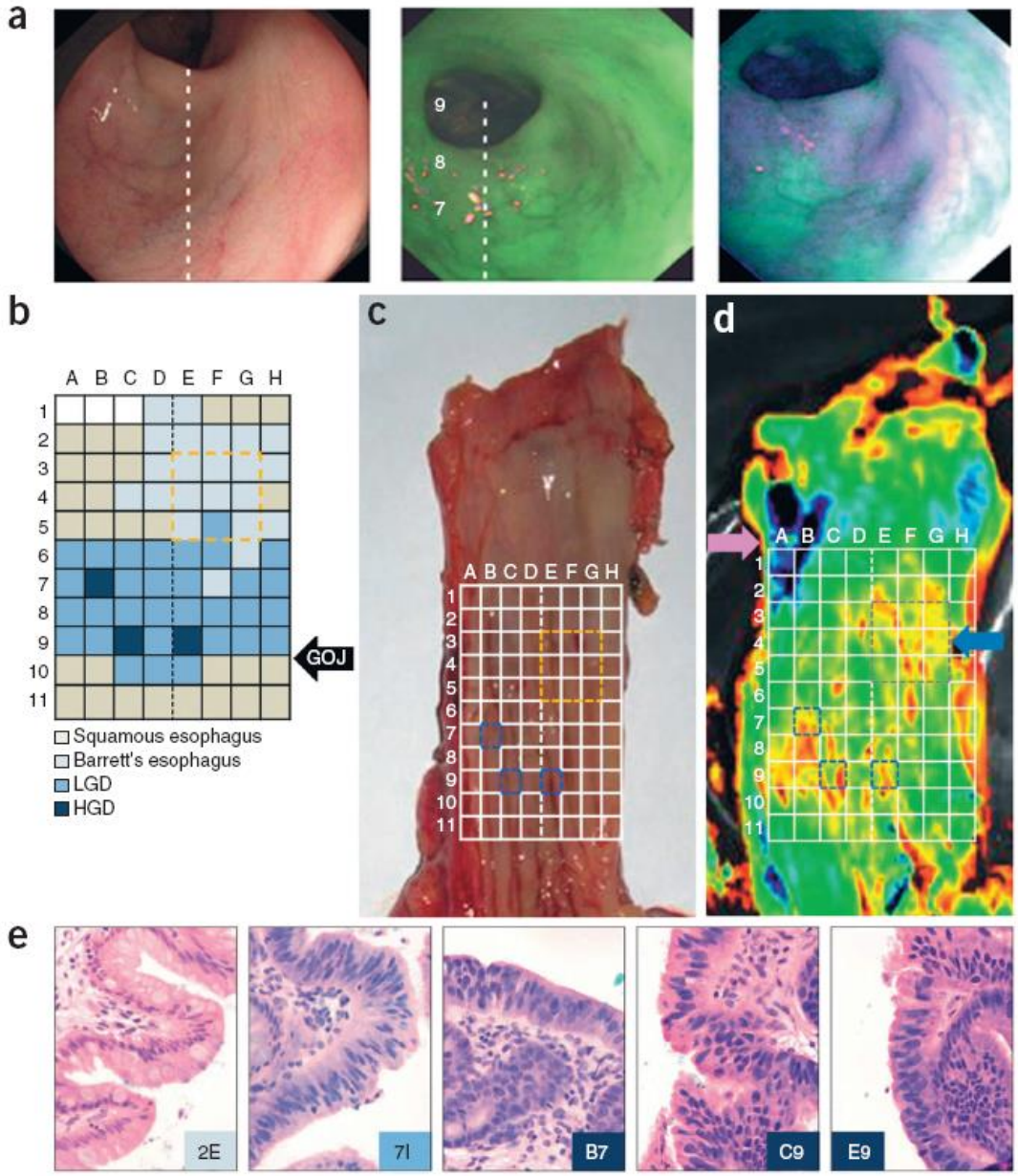
Type	Peptide	Antibody	Activatible probe	Nanoparticle
				
Advantages	• Easy delivery to target structure • Low immunogenicity • Low cost	• High specificity • Defined target • Defined and approved therapeutic ab may be labeled	• Specific activation • Optimized signal-to-noise ratio	• Loading with multiple proteins for multivalent targeting • Strong fluorescence
Disadvantages	• Variable affinity	• Potential immunogenicity	• Internalization frequently required for activation • Undefined safety profile	• Potential toxicity of non-biocompatible core • Renal clearance

Goetz M, Wang TD. Gastroenterology 2010;138:828-33

In vivo Confocal Fluorescence Images of Colon Tumors



Hsiung PL, Wang TD, et al. Nat Med 2008;14:454-8

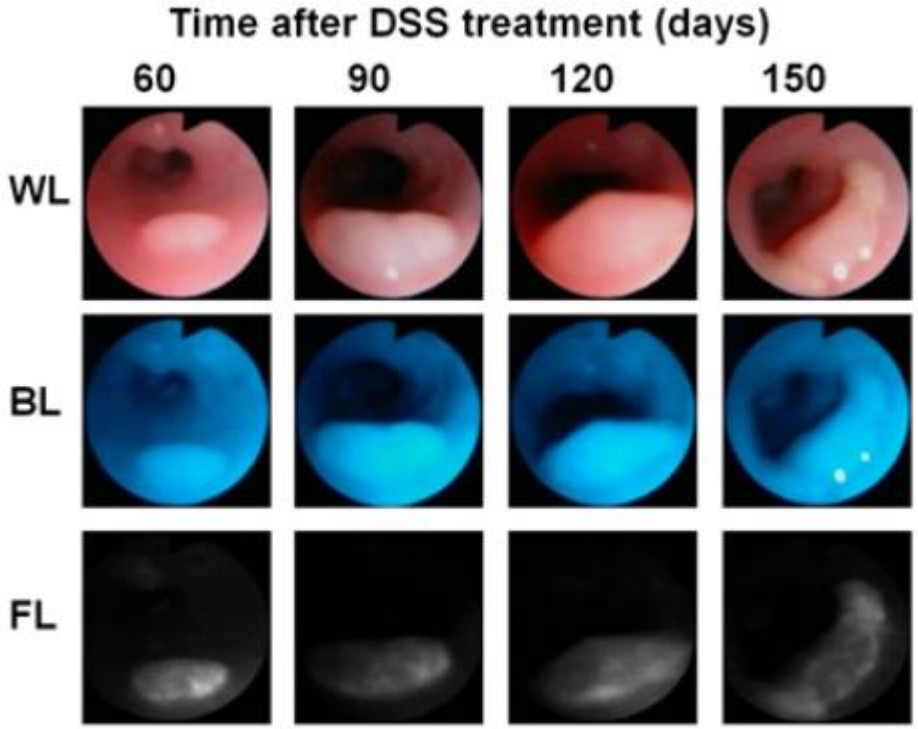


Lectin Probe for Barrett's Esophagus

Bird-Lieberman EL, Fitzgerald RC
Nat Med 2012;18:315

Fluorescence endoscopic detection of murine colitis-associated colon cancer by topically applied enzymatically rapid-activatable probe

Makoto Mitsunaga,[1] Nobuyuki Kosaka,[1] Peter L Choyke,[1] Matthew R Young,[2] Christopher R Dextras,[2] Shakir M Saud,[2,3] Nancy H Colburn,[2] Masayo Sakabe,[4] Tetsuo Nagano,[4] Daisuke Asanuma,[5] Yasuteru Urano,[5] Hisataka Kobayashi[1]



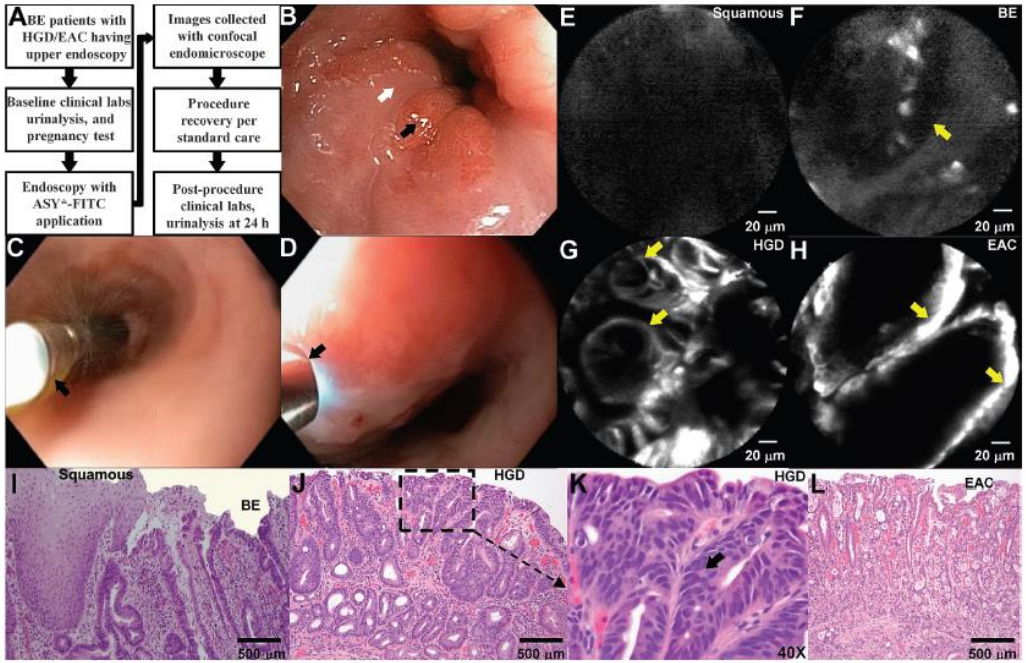
Gut 2013

RESEARCH ARTICLE

CANCER IMAGING

Targeted Imaging of Esophageal Neoplasia with a Fluorescently Labeled Peptide: First-in-Human Results

Matthew B. Sturm,[1]* Bishnu P. Joshi,[1]* Shaoying Lu,[2]* Cyrus Piraka,[1] Supang Khondee,[1] Badih Joseph Elmunzer,[1] Richard S. Kwon,[1] David G. Beer,[3] Henry D. Appelman,[4] Danielle Kim Turgeon,[1] Thomas D. Wang[1,5,6†]



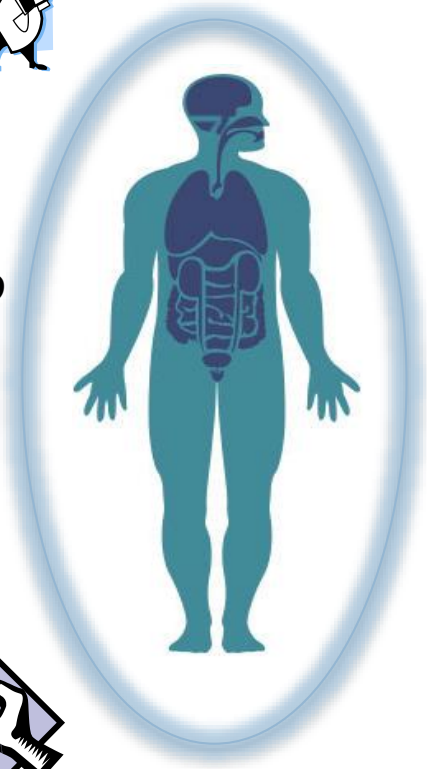
Science Transl Med 2013; 5: 1

e-MIT (Endoscopic Molecular Imaging Team)

1st Division
Asan Medical Center

Seung-Jae Myung, MD, PhD

- Colon disease research



2nd Division
GIST

Euiheon Chung, PhD
In Vivo Imaging

- Fluorescence Endoscopy

3rd Division
POSTEC

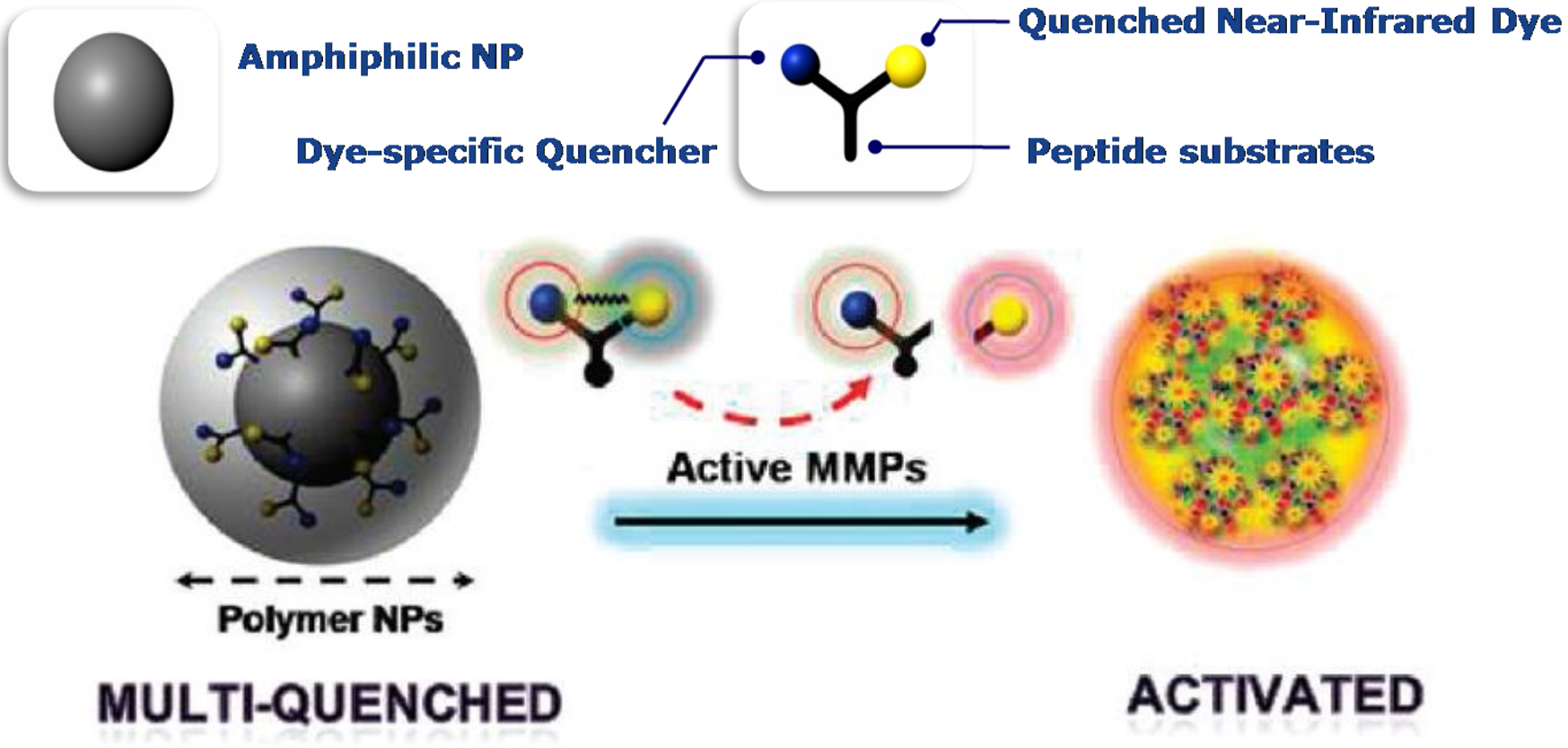
Sungjee Kim, PhD
Chemistry- Quantum dot

- Multitarget Probe Dev.

Ki-Hyun Kim, PhD
Optical Imaging

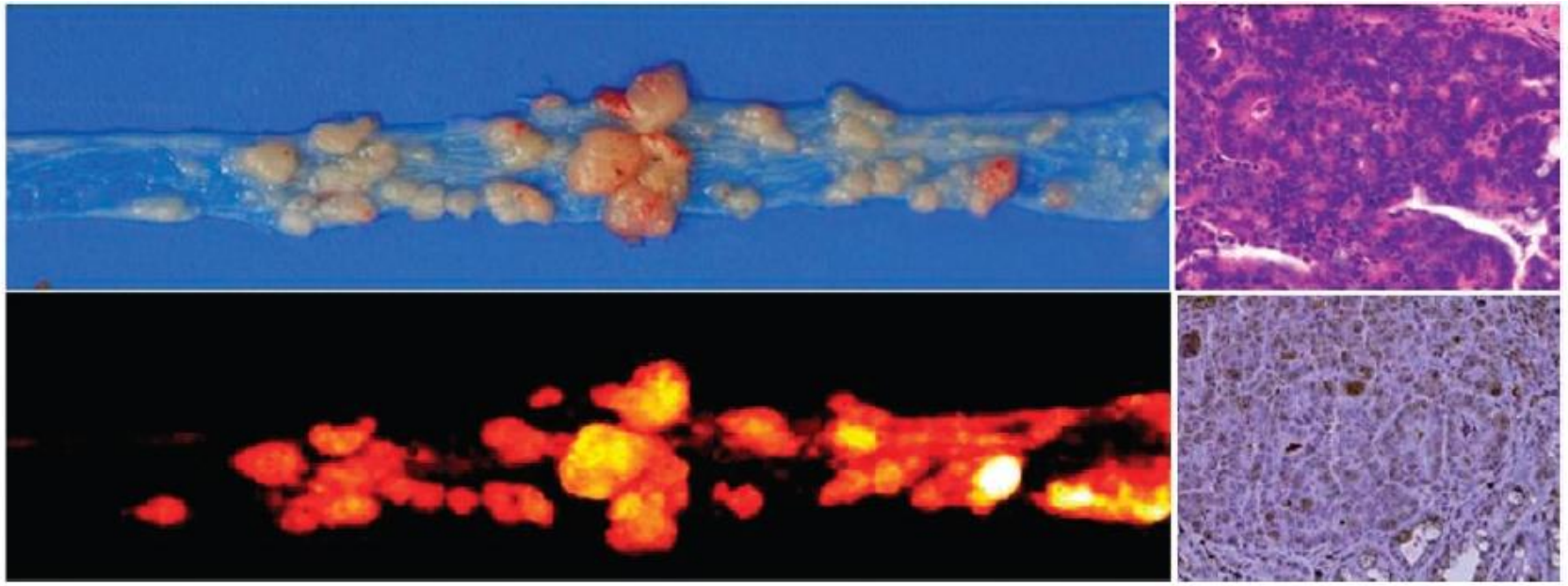
- 2 photon-OCT

Polymeric-Nanoparticle based MMP Probe



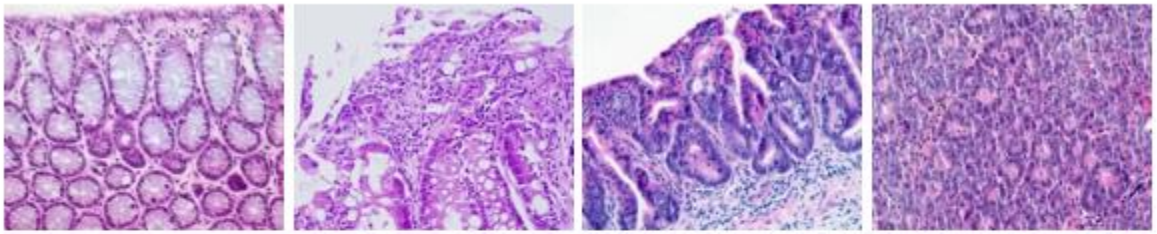
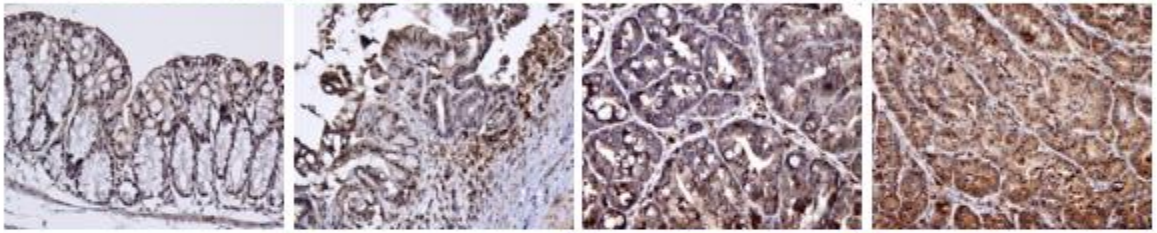
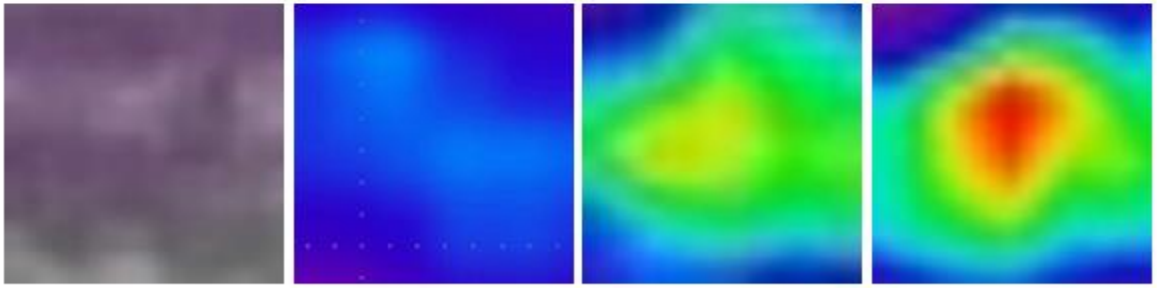
Lee S, Myung SJ, Kim K et al. Nano Letter 2009; 9: 4412-6

Polymeric Naoparticle-Based Activatable Near-Infrared Nanosensor for Protease Determination In Vivo



Lee S, Myung SJ, Kim K et al. Nano Letter 2009; 9: 4412-6

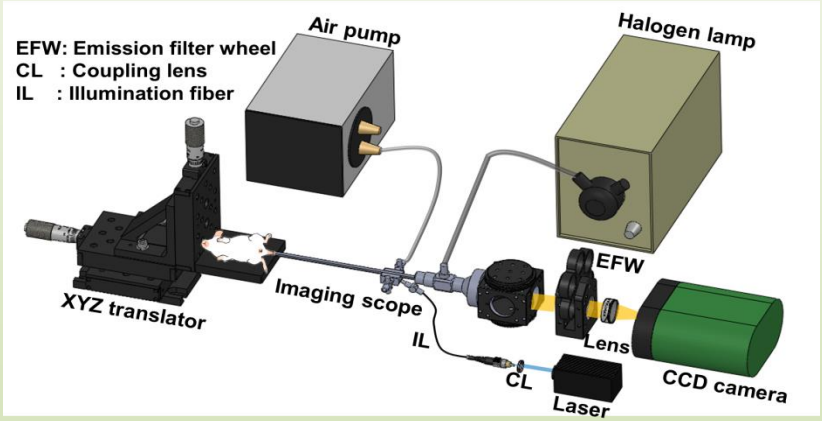
Histology and NIRF Findings in AOM/DSS Treated Mice

	Normal	Inflammation	Adenoma	Adenocarcinoma	p-value
Histology* (H&E stain)					
IHC*					
NIRF image†					
Signal intensity† (total photon count/mm^2)	181.3±58.0	451.0±80.1	1,039.2±408.0	3,585.0±1,251.6	<0.001
TBR		2.5±0.4	5.7±2.3	19.8±6.9	<0.001

Yoon SM, Myung SJ, et al. Gut and Liver 2010; 4:488-97

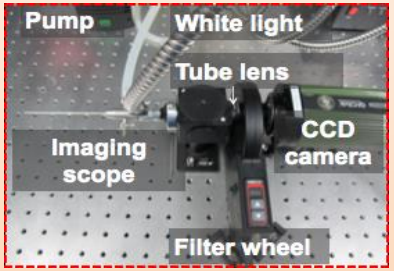
Multichannel Fluorescence Endoscopy

Fluorescence Enoscopy System

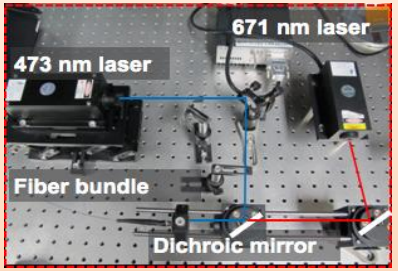


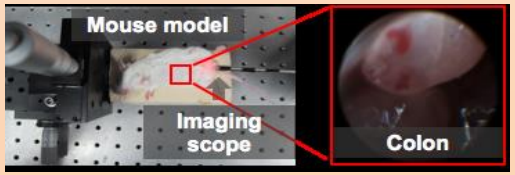
In vivo experiment

Detection part

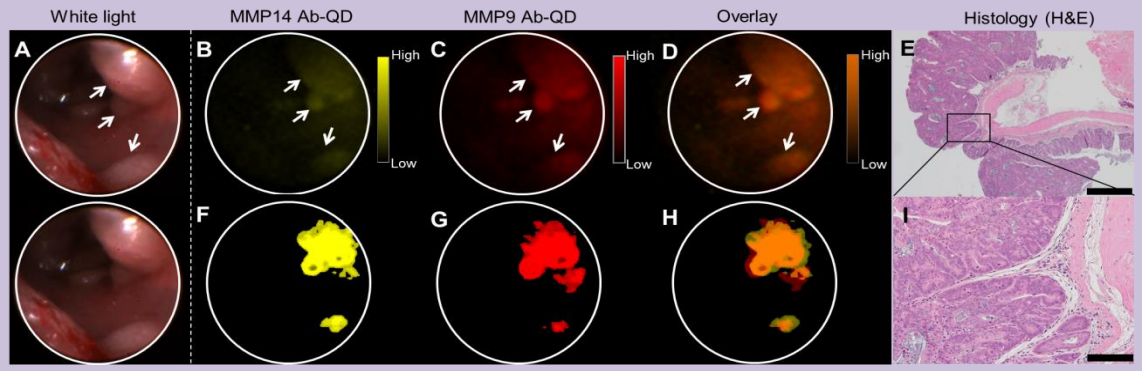


Excitation part



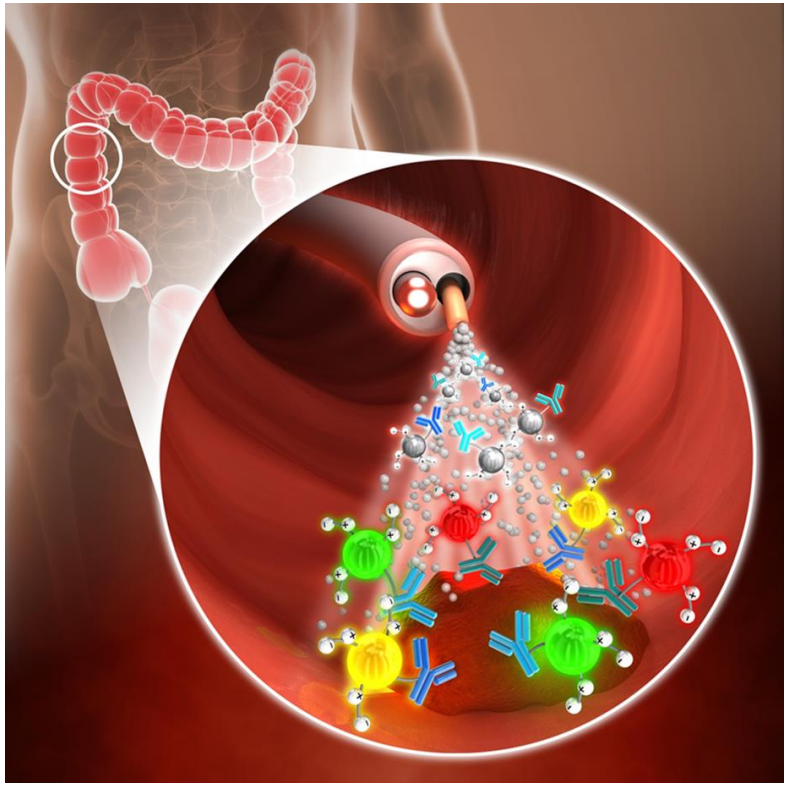


In vivo Colon Cancer Animal Model



Oh KS, Chung EH, Kim SJ, Kim KH, Myung SJ et al., *Biomedical Optics express*, Vol. 5, Issue 5, pp. 1677-1689 (2014)

Spraying Quantum Dot Conjugates in the Colon of Live Animals Enabled Rapid and Multiplex Cancer Diagnosis Using Endoscopy

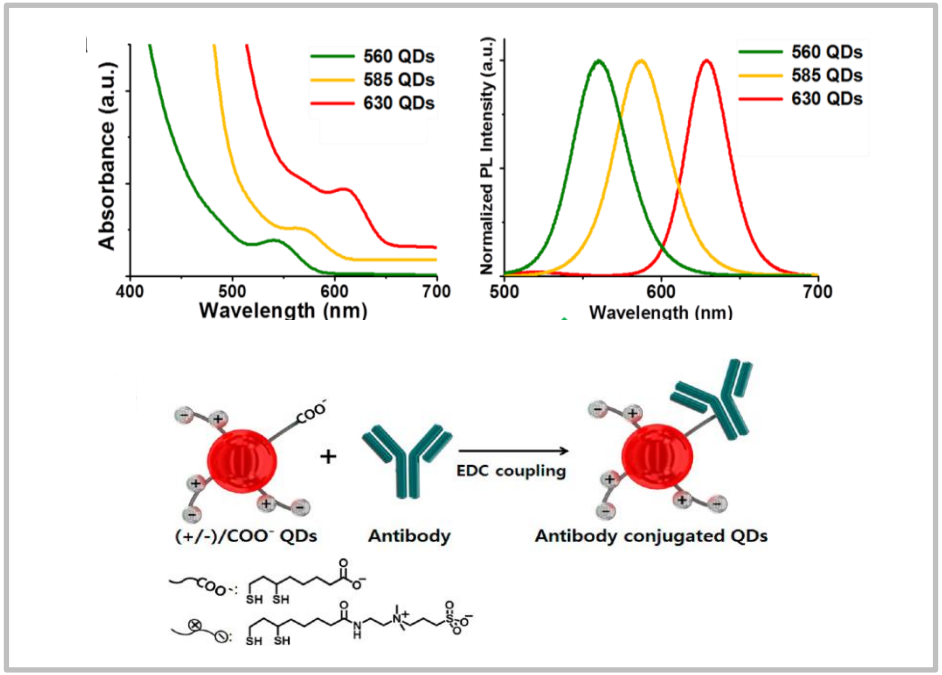


Park Y, Ryu YM, Kim KH, Kim S, Myung SJ. ACS Nano 2014; 8: 8896

Experimental Procedure

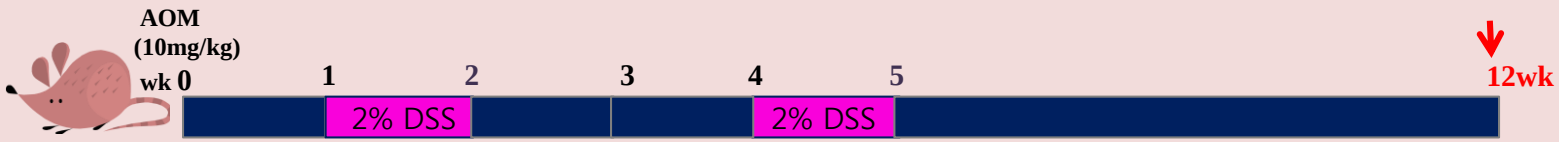
Ab conjugated Quantum-dot

-CEA (carcinoembryonic antigen)
-MMP14 (matrix metalloproteinase 14)
-MMP9 (matrix metalloproteinase9)

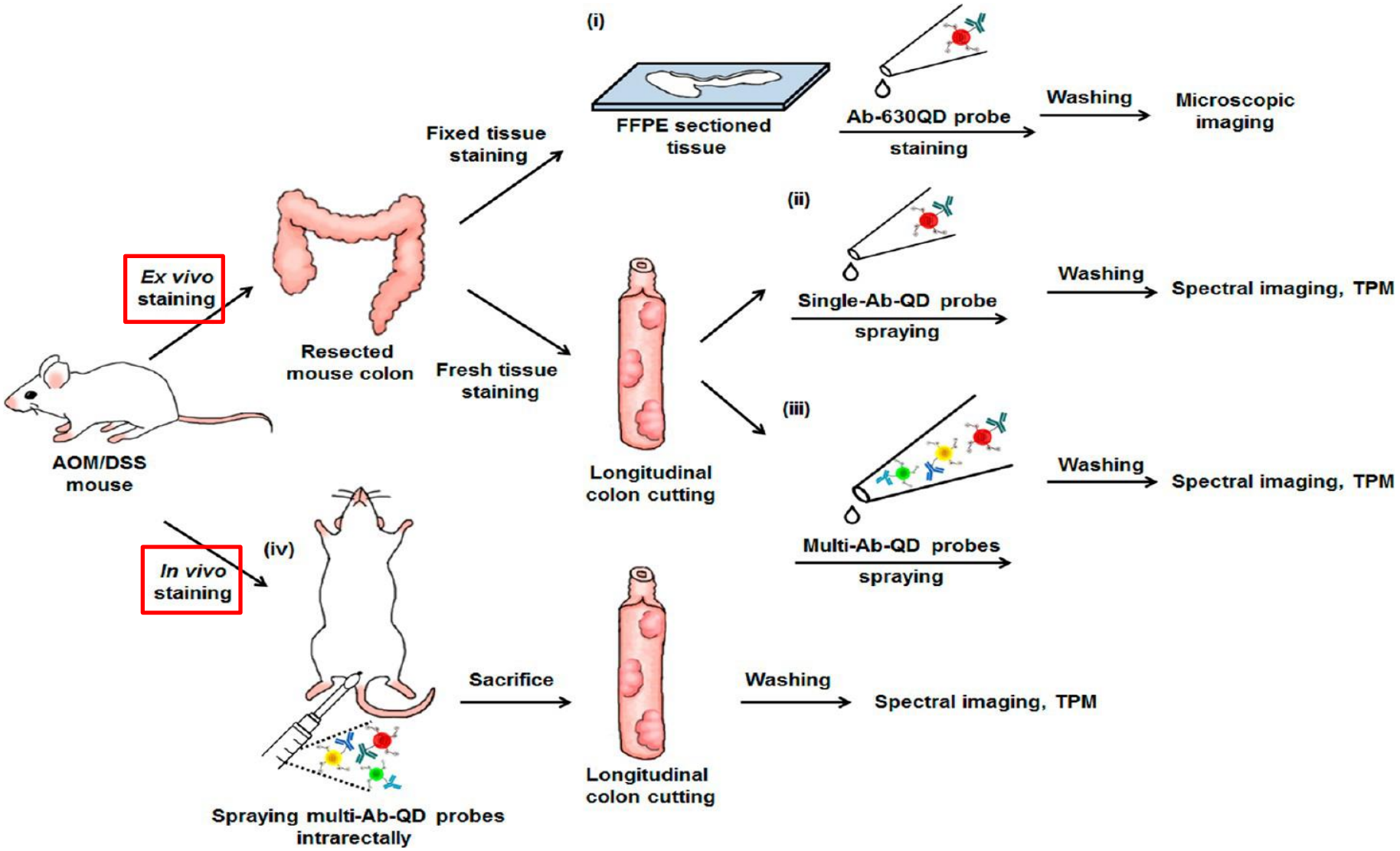


Mouse model

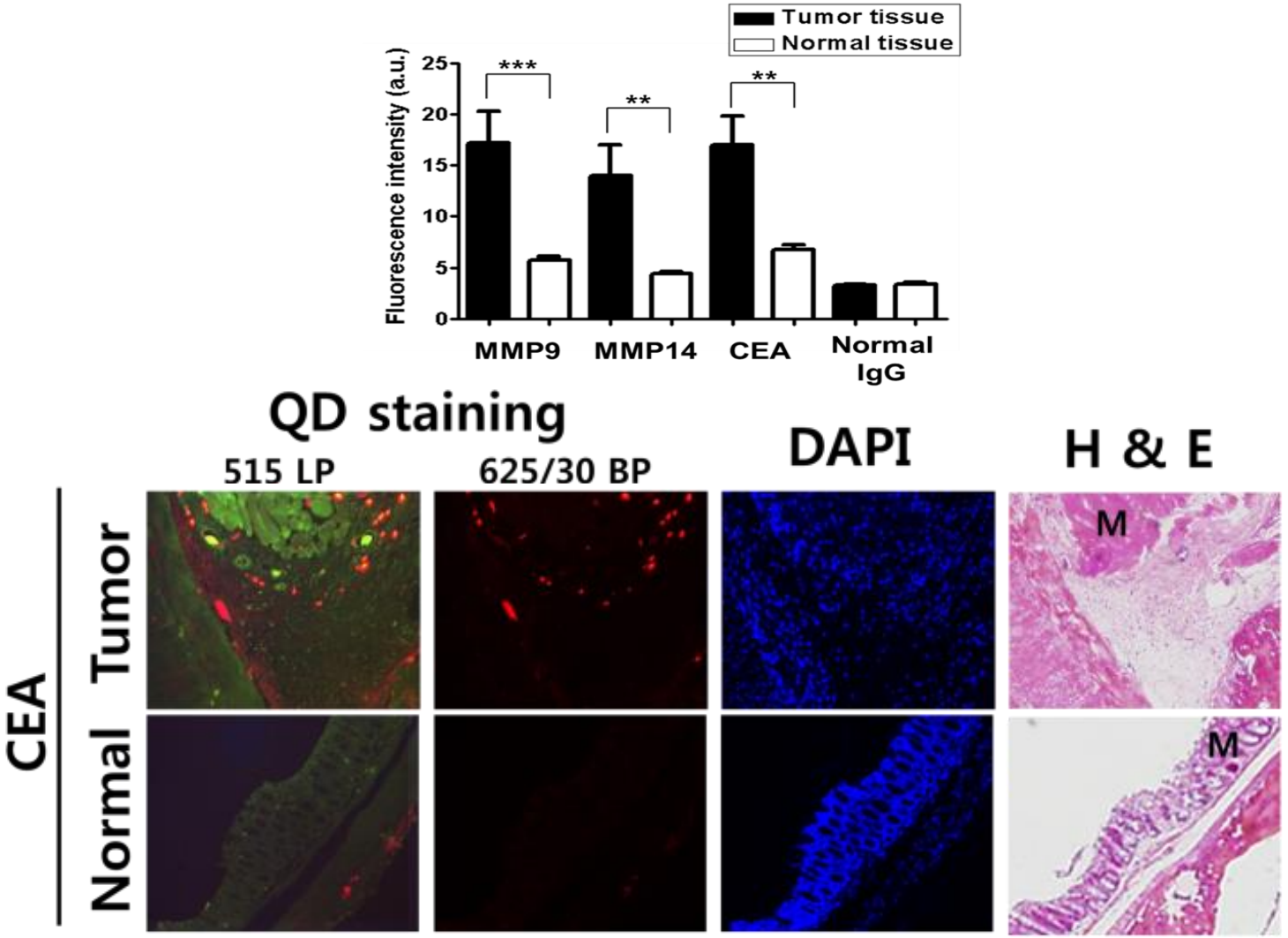
AOM/DSS model; Colitis-Associated Cancer model **:** AOM (Azoxymethane) : Carcinogen
DSS (Dextran sulfate sodium): Induce inflammation



Experimental Procedure

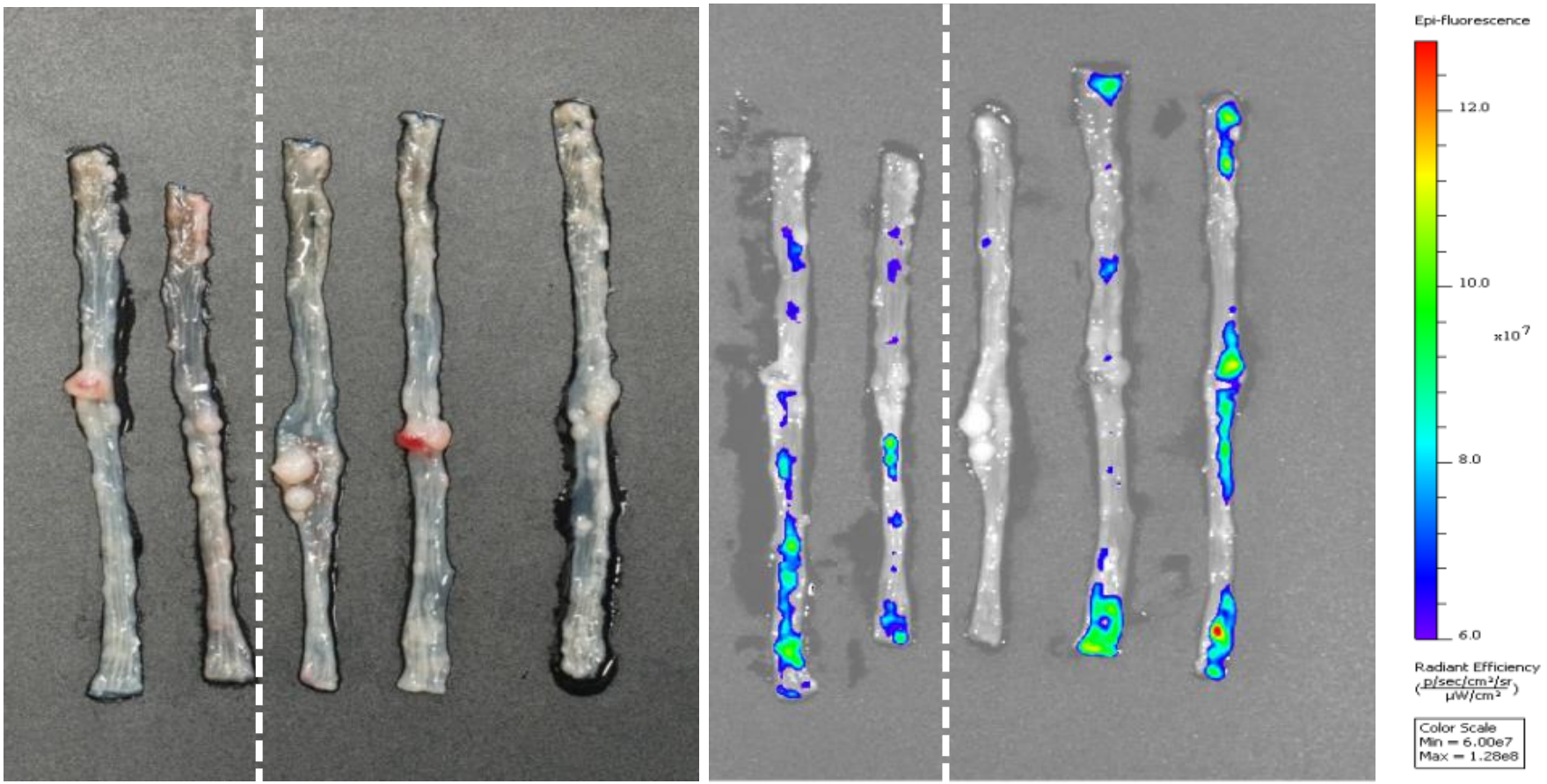


Fluorescence miroscope image on sectioned AOM/DSS colon tissues



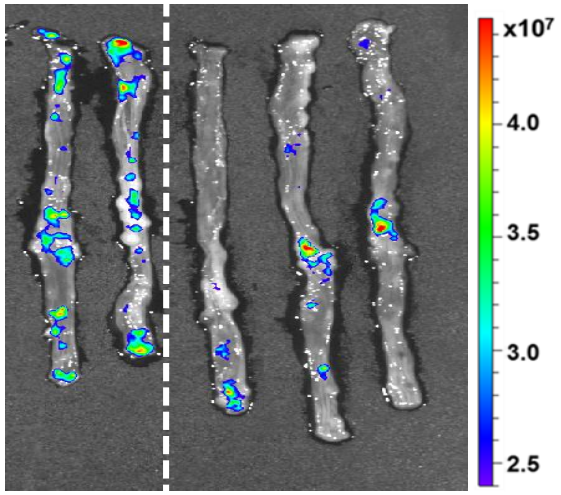
Park Y, Ryu YM, Kim KH, Kim S, Myung SJ. ACS Nano 2014; 8: 8896

Imaging: AB-QD probe ex vivo staining

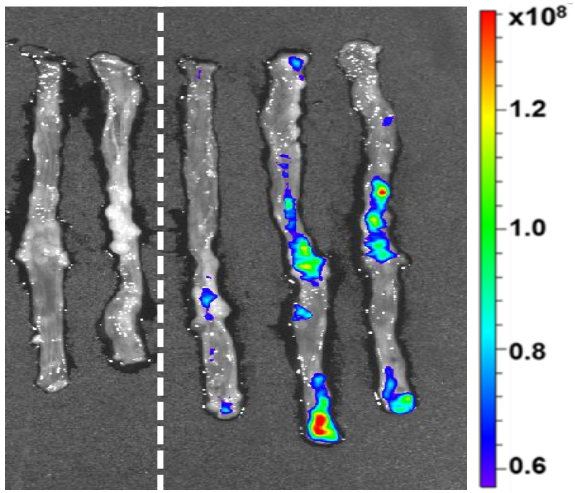


Park Y, Ryu YM, Kim KH, Kim S, Myung SJ. ACS Nano 2014; 8: 8896

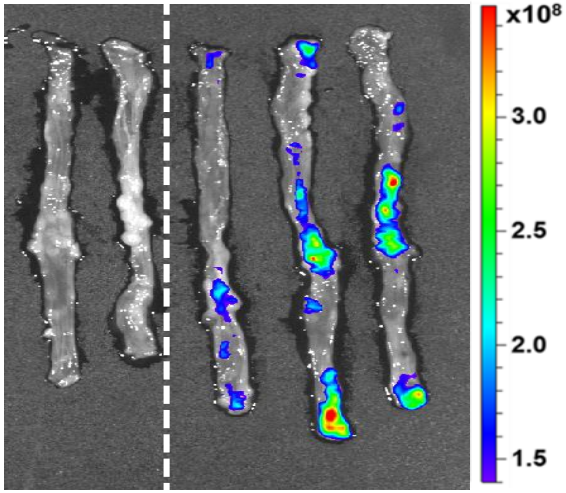
Multi-QD probe ex vivo staining



IgG-QD CEA-QD



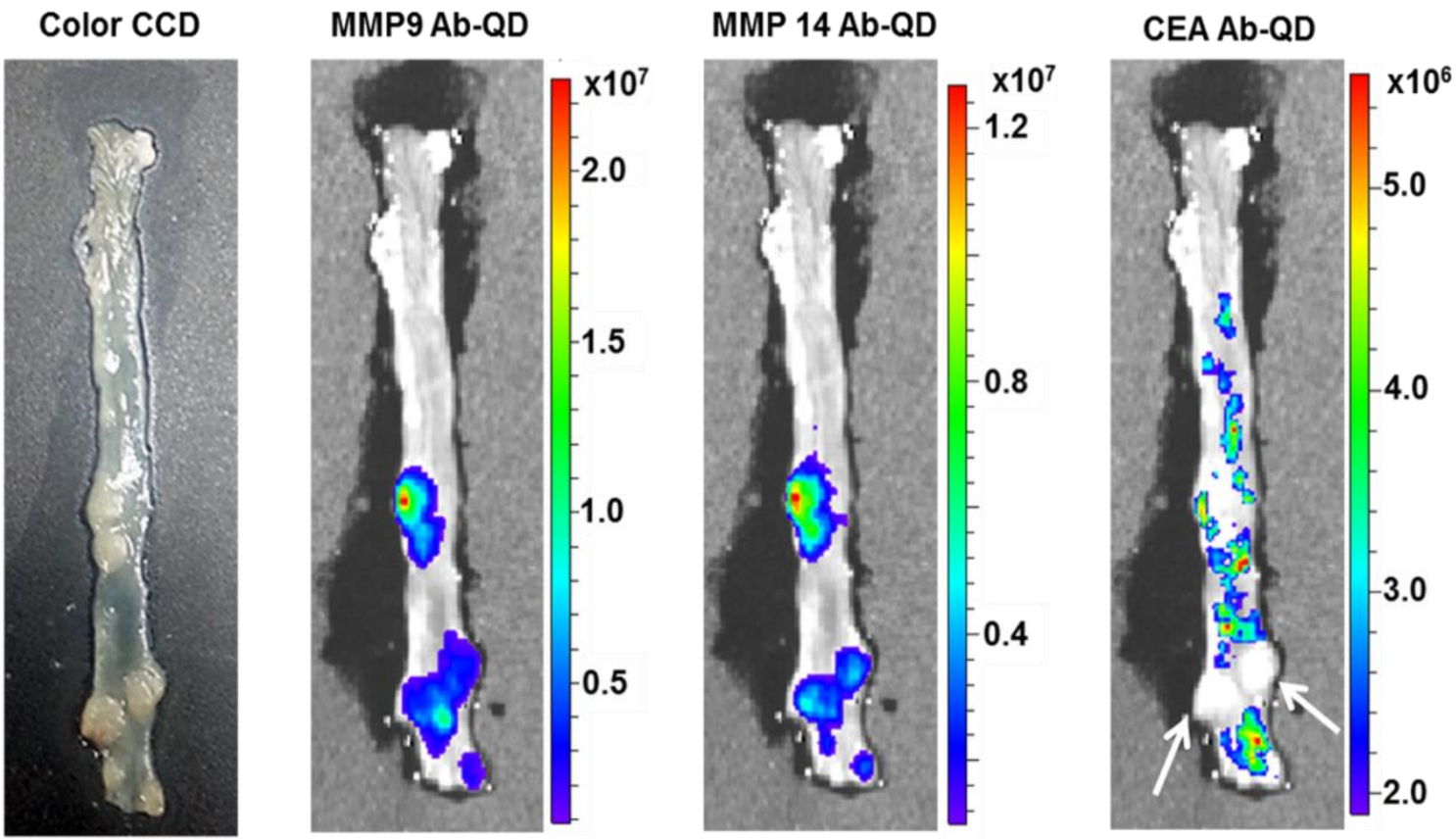
IgG-QD MMP14-QD



IgG-QD MMP9-QD

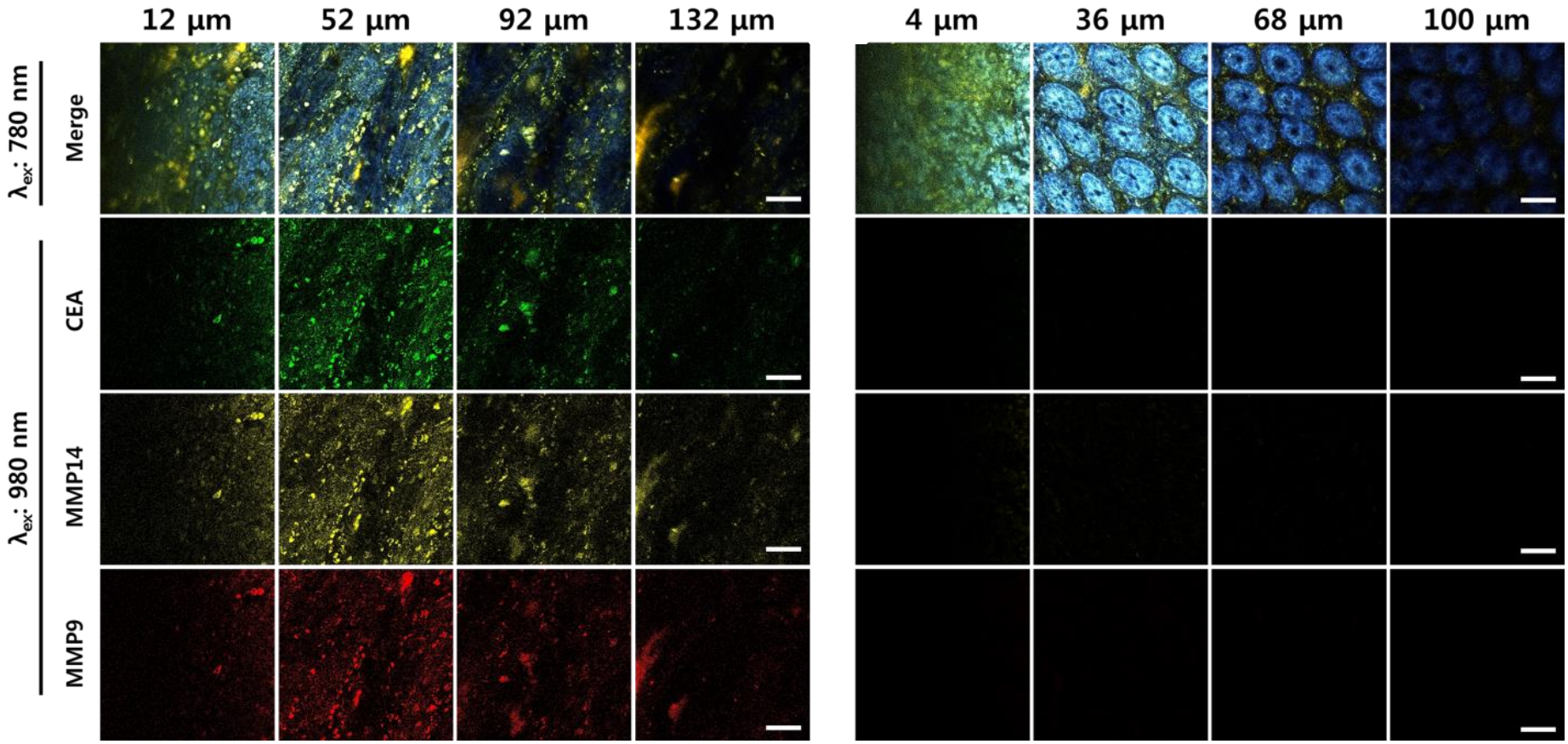
ACS Nano 2014; 8: 8896

Ab-QD probe in vivo staining



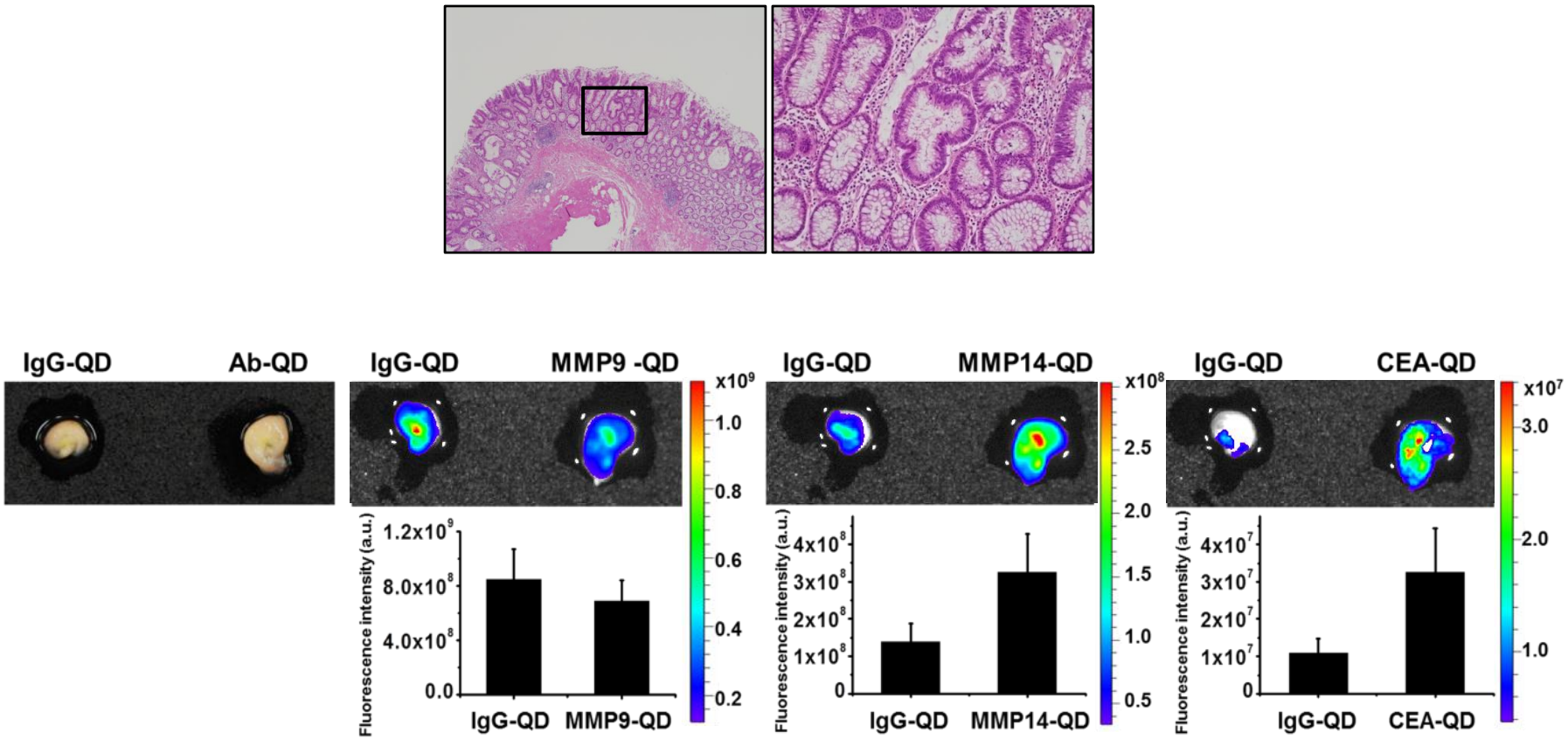
Park Y, Ryu YM, Kim KH, Kim S, Myung SJ. ACS Nano 2014; 8: 8896

Two-photon microscopic imaging



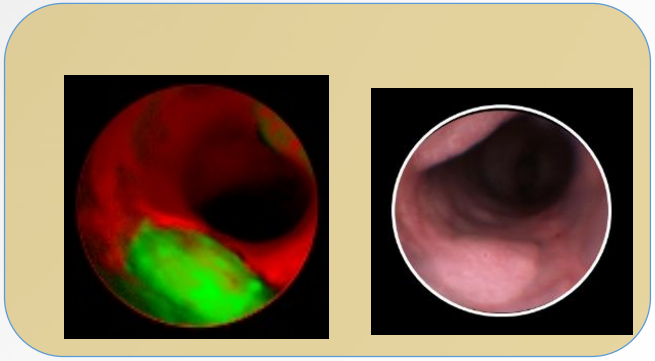
Park Y, Ryu YM, Kim KH, Kim S, Myung SJ. ACS Nano 2014; 8: 8896

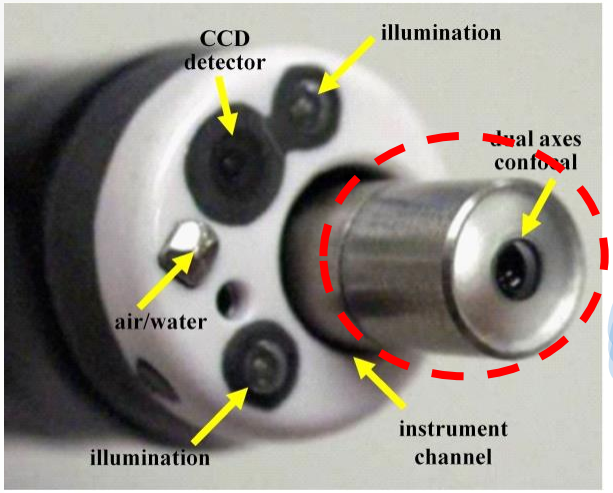
Human colon tissue imaging



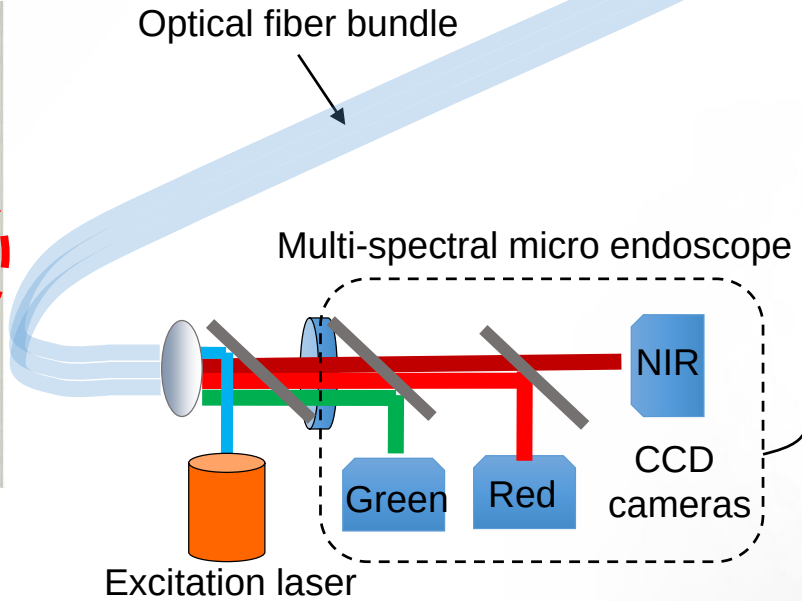
Park Y, Ryu YM, Kim KH, Kim S, Myung SJ. ACS Nano 2014; 8: 8896

Channel implantable multispectral micro-endoscope

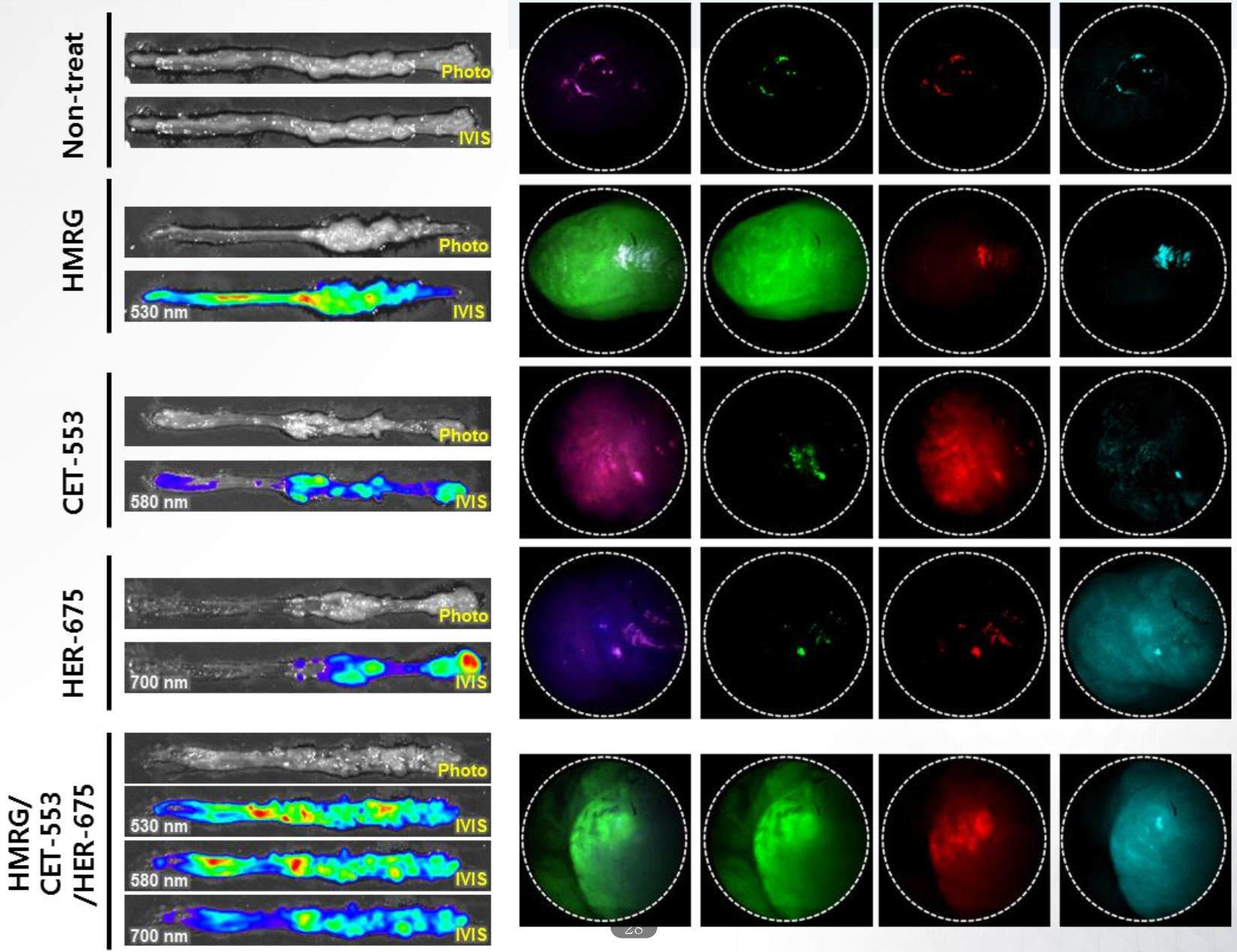




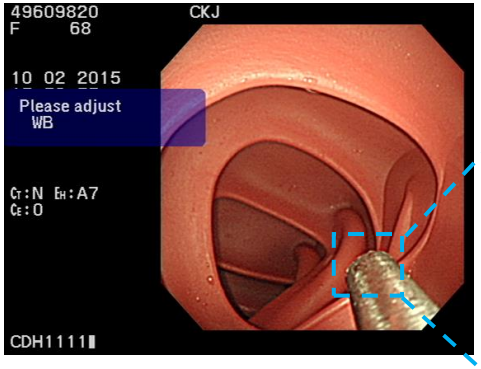
Endoscope-compatible instrument

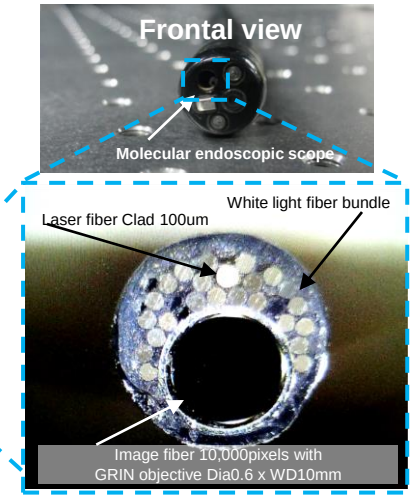


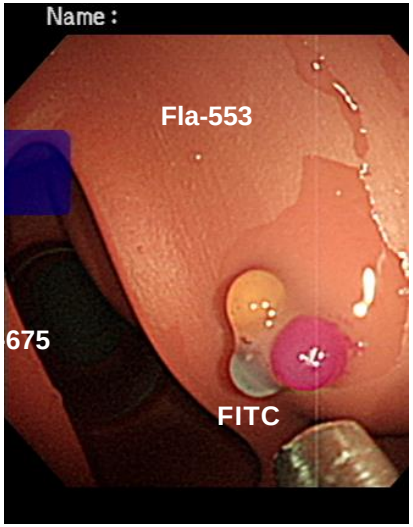
▶Injection with CET,HER(2 days before)
▶HMRG treatment (on 0day)
▶IVIS, Endoscopy imaging

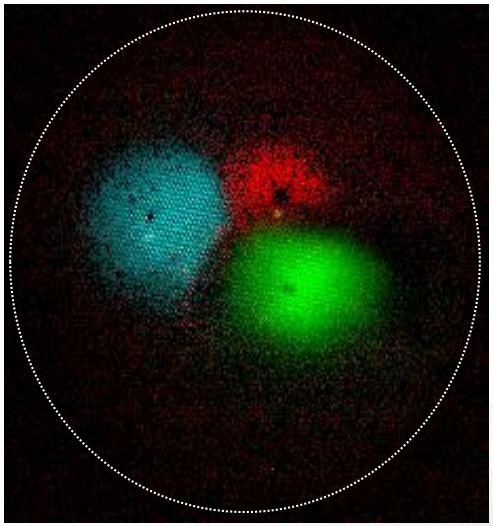


Channel implantable multispectral micro-endoscope
- Colonoscopy Simulator -

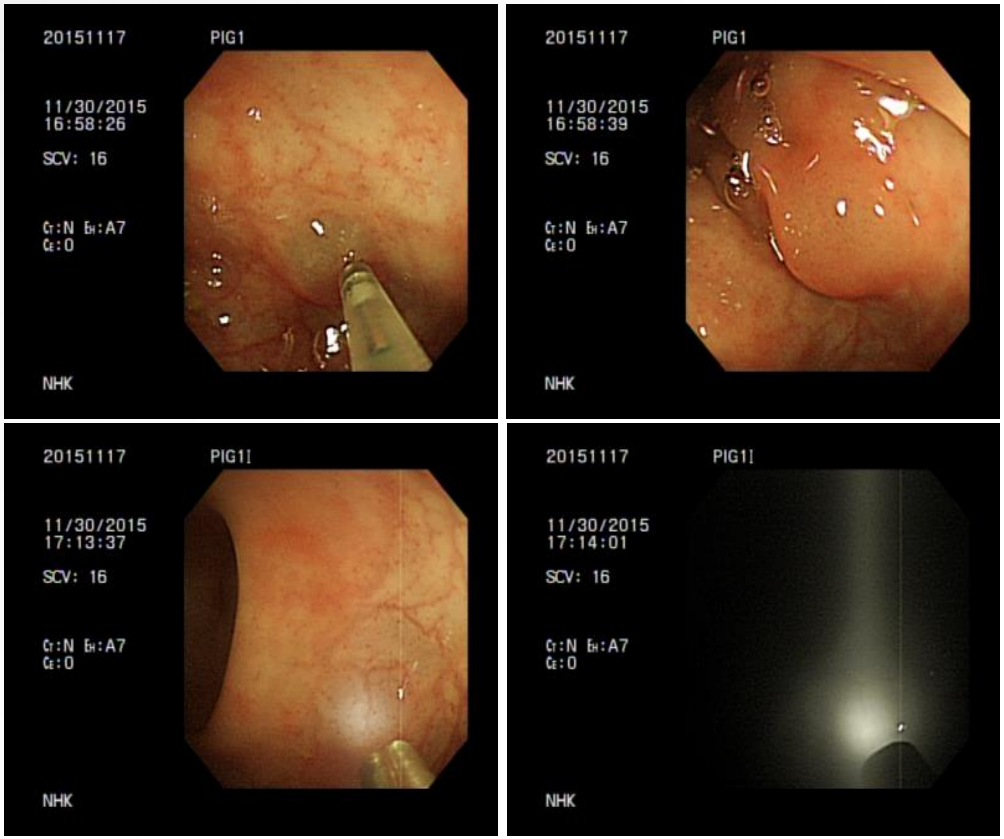


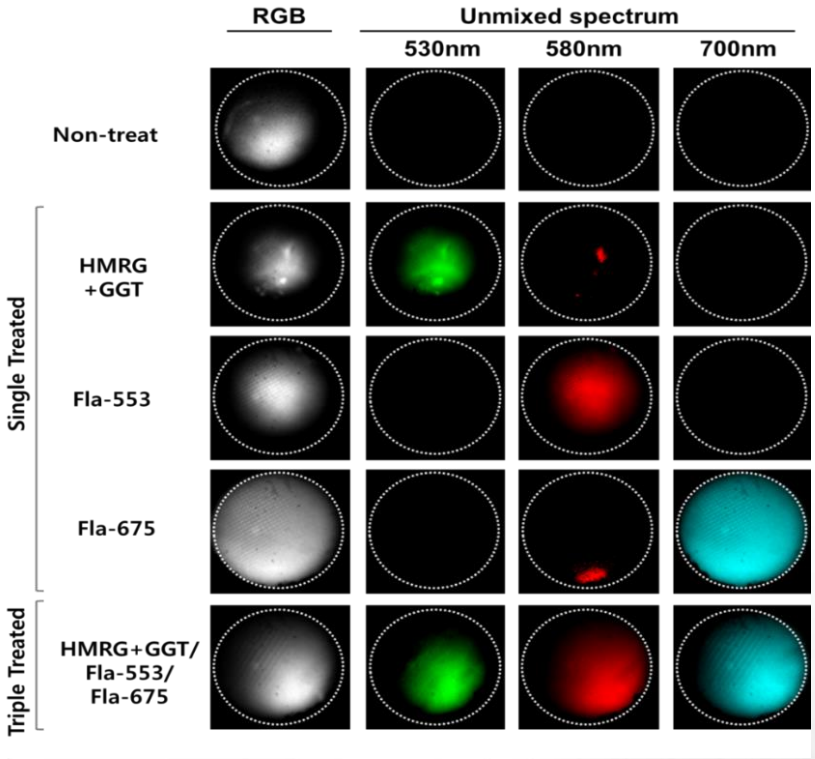






Channel implantable multispectral micro-endoscope
- Large Animal Experiment: Pig -





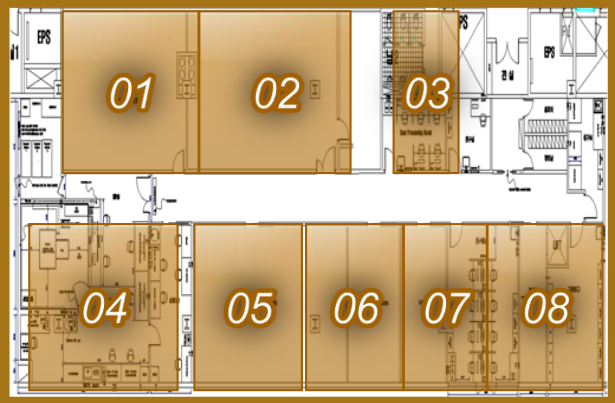
Bio-Imaging Center

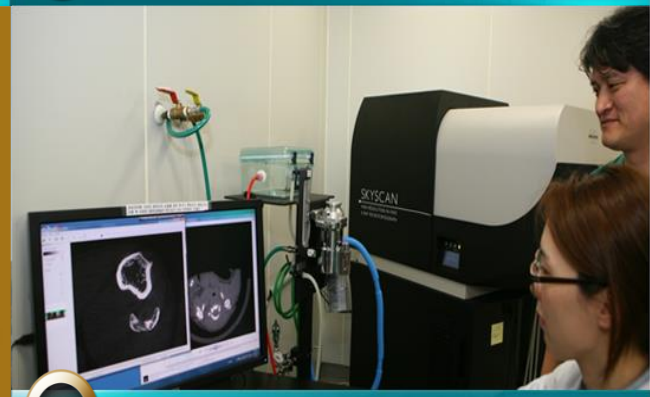
01 C-BiND office and meeting room

02 Micro PET/MRI

03 Office for researchers

04 9.4T MRI





05 Micro CT

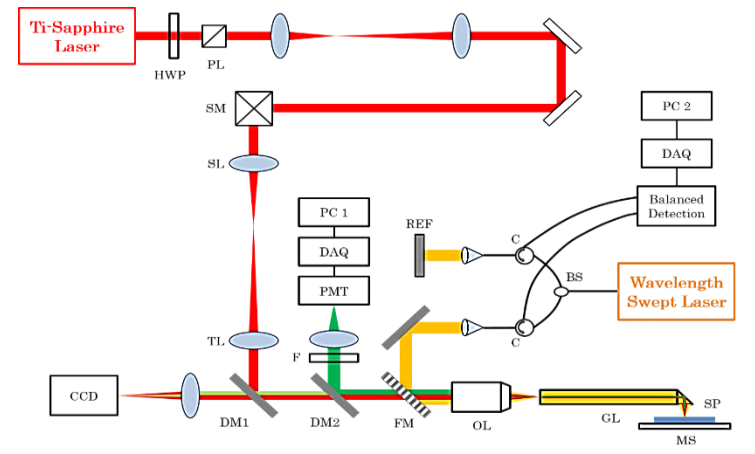
06 Optical/Cellular/Endoscopy

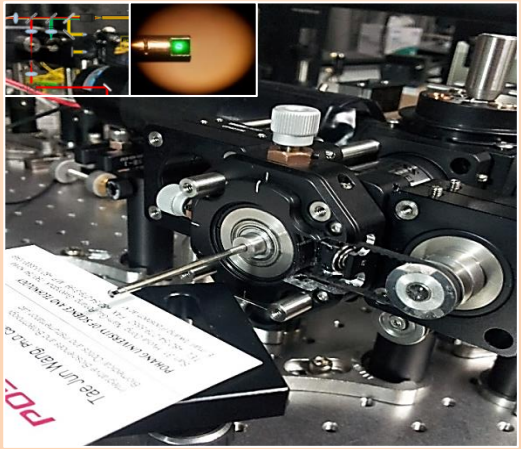
07 Probe development lab

08 Animal lift

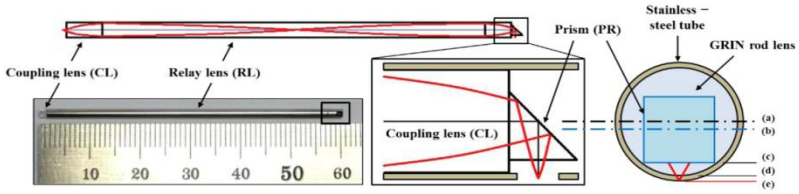
Two-photon Microscopy and Optical Coherence Tomography - Novel Endoscopy for Animal Experiment -

Two-photon Microscopy and Optical Choherence Tomography Endoscopy

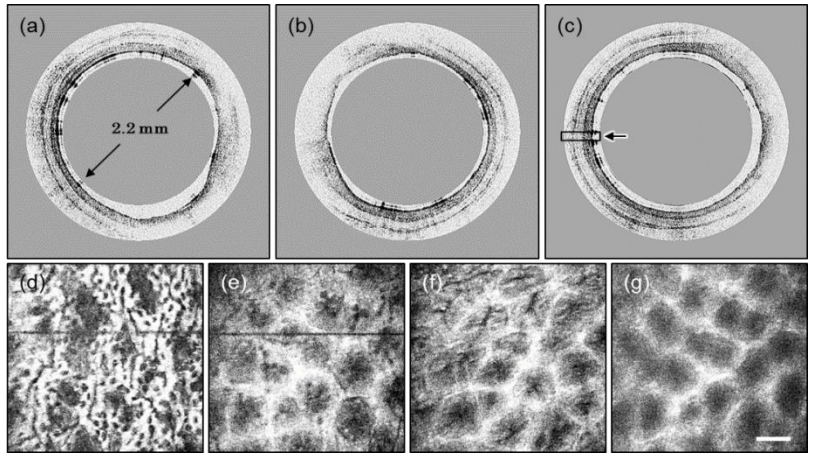




GRIN-Lens for TPM-OCT Endoscopy



TPM-OCT Endoscopy in Colon Cancer Animal Model



Wang TJ, Chung EH, Kim SJ, Myung SJ, Kim KH et al., *Optics Express* Vol. 22, issue 9 (2014)

Conclusion

- Nanotechnology has high potential for the application in Gastrointestinal Medicine.
- Molecular Imaging using Nanoparticle based probes will be effective for early detection of GI cancers.
- Fast reacting…. Specific….and Safe Nano-Probes are urgently needed !

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MYUNG's Lab in Asan Medical Center


Thank you for your Attention
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