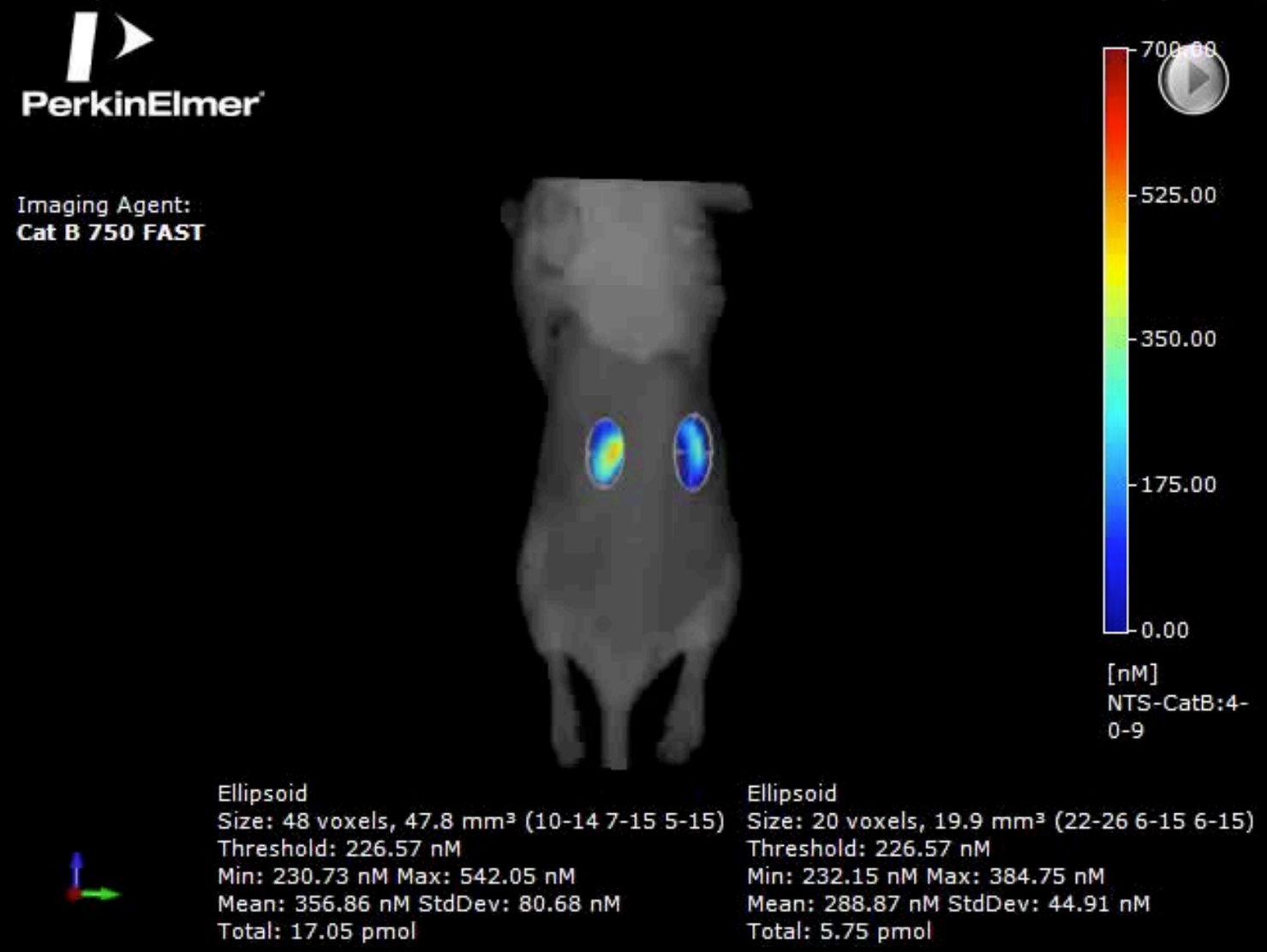
Noninvasive assessment of experimental glomerulonephritis using fluorescence molecular tomography



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LUPUS 2019
San Francisco, CA, USA
08 April 2019

Washington University in St. Louis
School of Medicine

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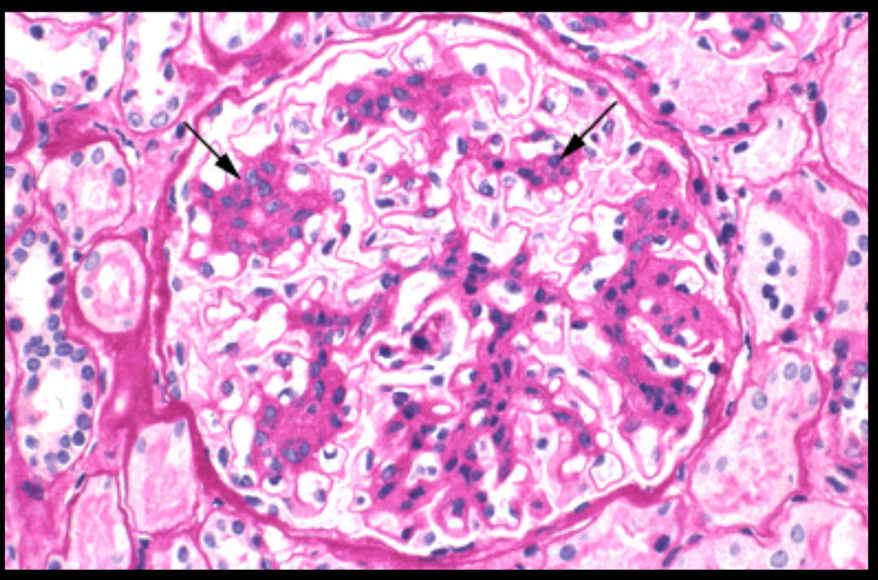
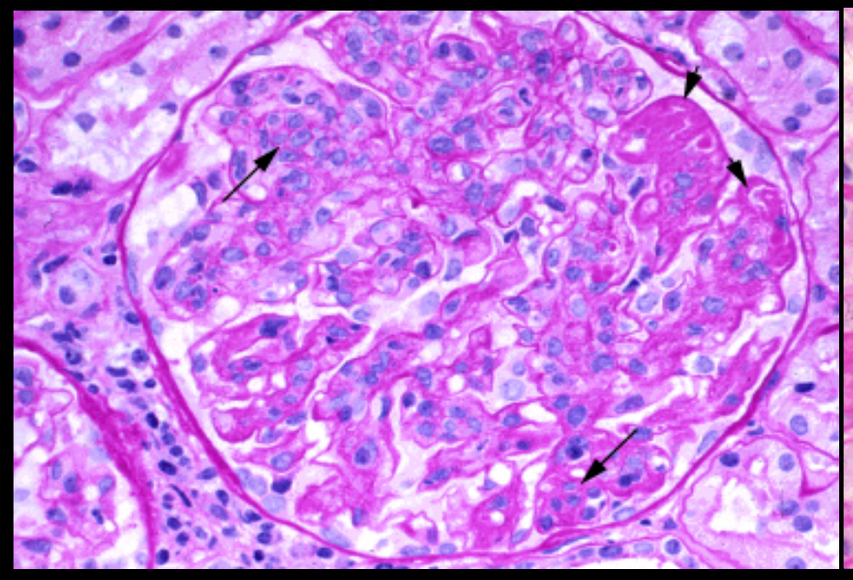
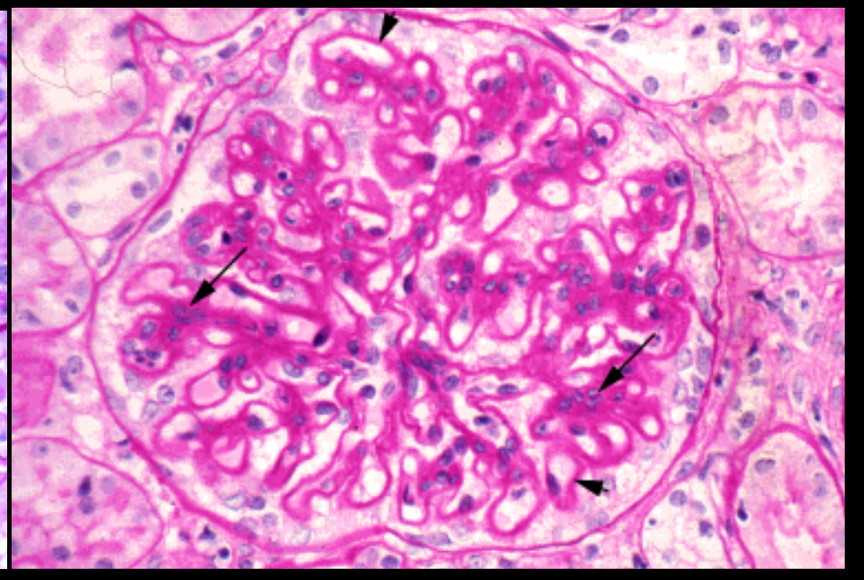
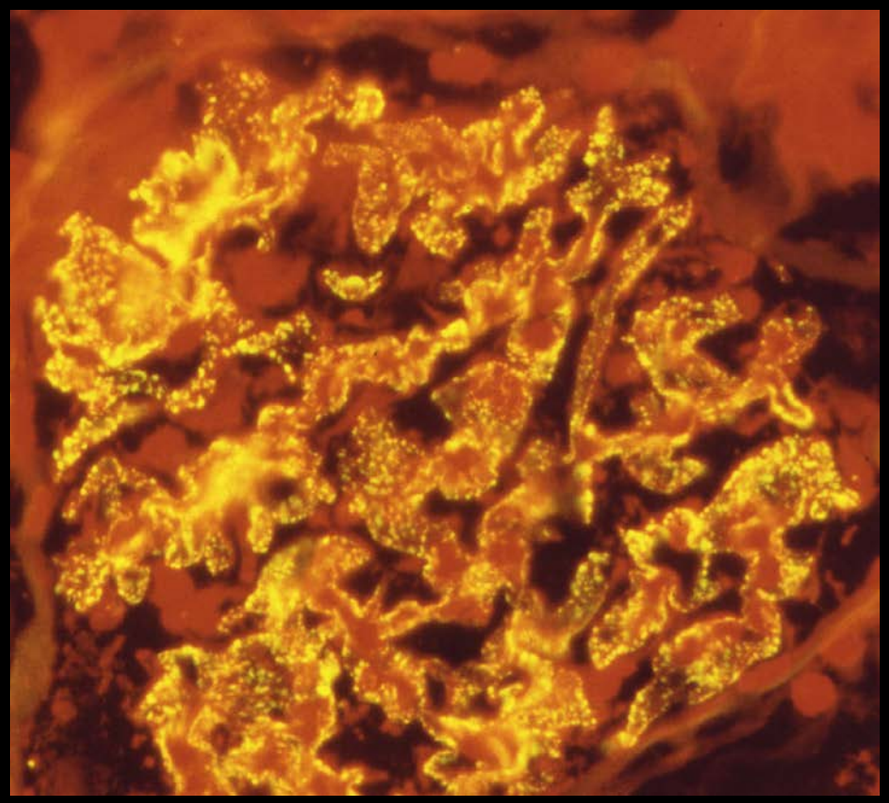
Traditional imaging modalities continue to provide mechanistic and diagnostic value in lupus nephritis

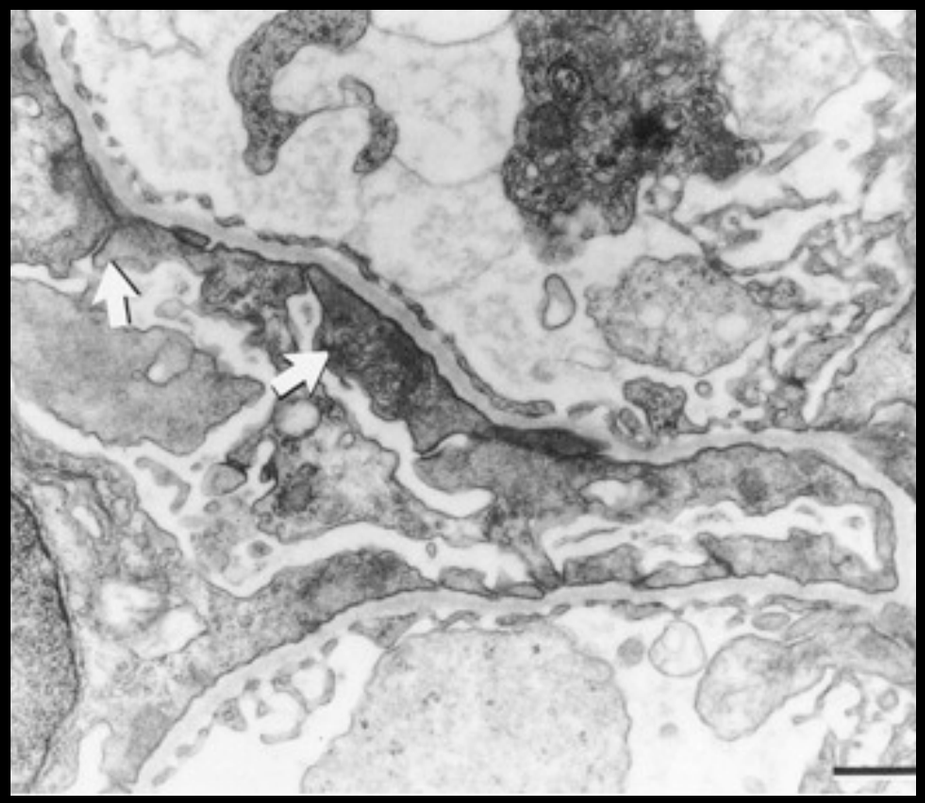
Light, immunofluorescence, and electron microscopy commonly used











Traditional imaging modalities continue to provide mechanistic and diagnostic value in lupus nephritis

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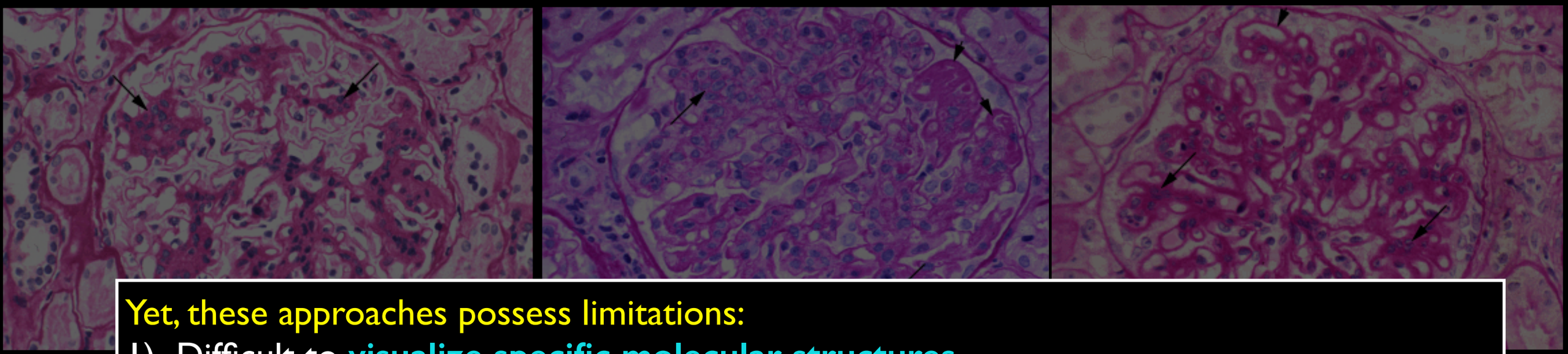
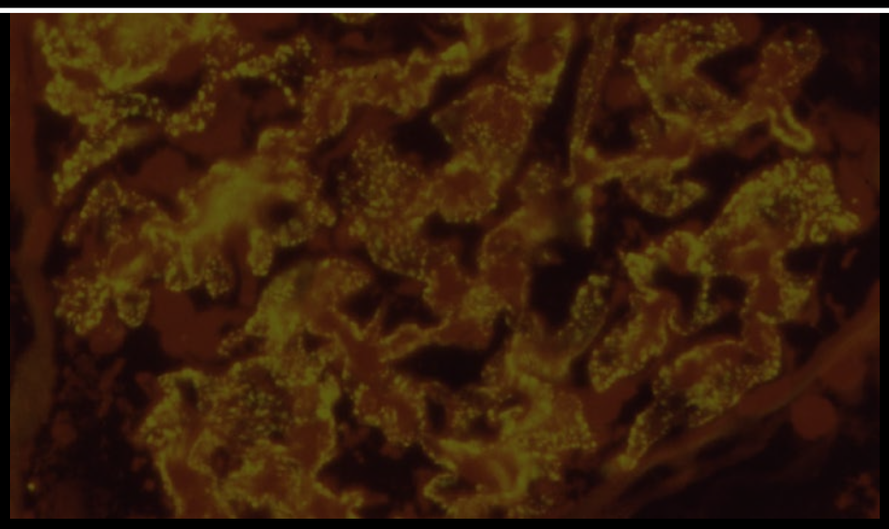
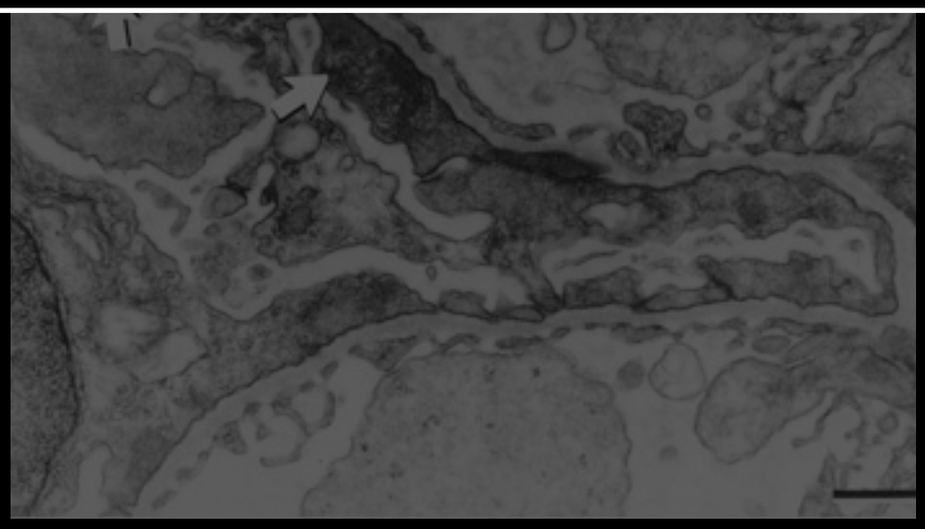


Yet, these approaches possess limitations:

1) Difficult to **visualize specific molecular structures**
   ➔Limits mechanistic interpretation of pathologic processes
2) Only **visualize a fraction** of sampled renal tissue due to sectioning (~4 μm)
   ➔Observe from available sections of tissue, and infer pathology in-between sections of tissue
3) Kidney biopsies are **invasive** and interrogate a **minute fraction of tissue**





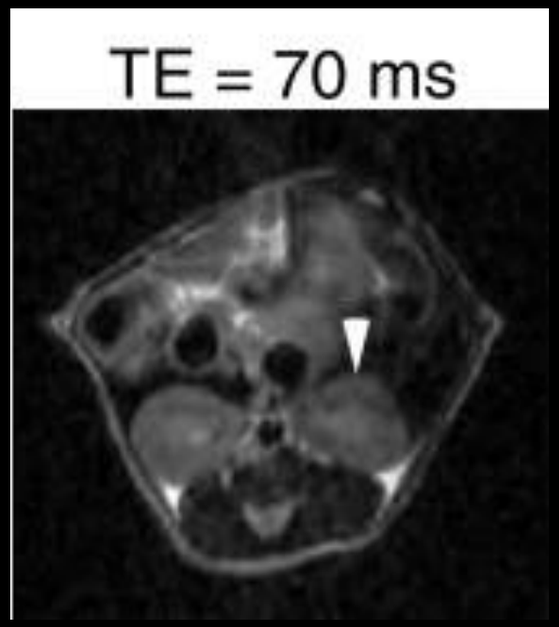
Can glomerulonephritis be detected noninvasively?

Traditional laboratory (i.e. proteinuria) and imaging modalities (i.e. ultrasound, CT, MRI, PET) cannot specifically assess changes due to GN

Targeted contrast probes with MRI

Superparamagnetic iron oxide nanoparticles linked to CR2

Wild-type



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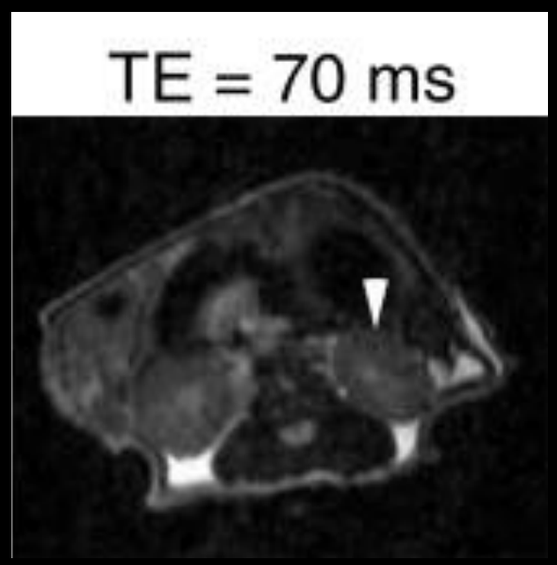
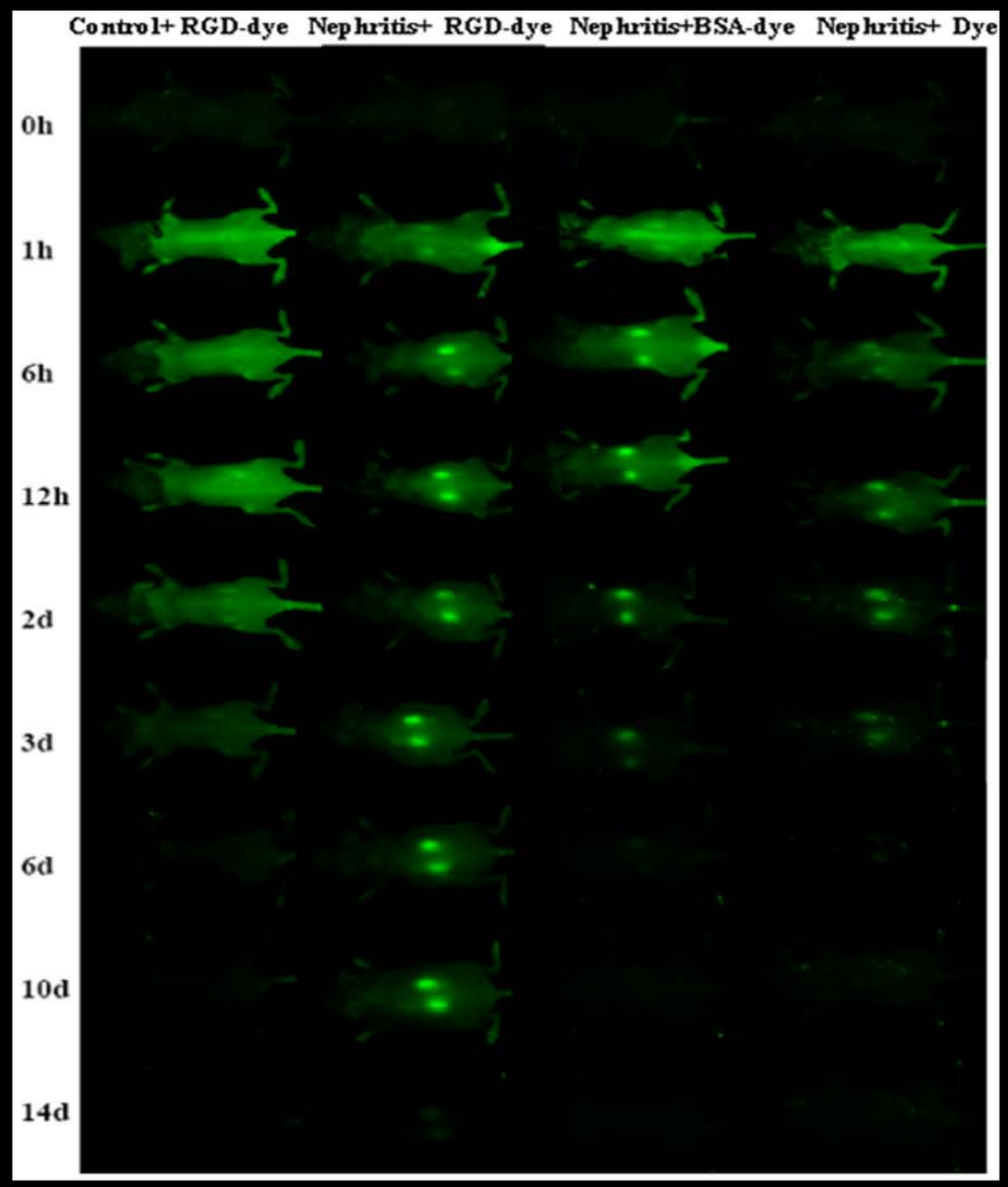


Serkova, NJ, *et al.*, *Radiology*, **255**:517 (2010)

Near-infrared probes to markers of GN activity

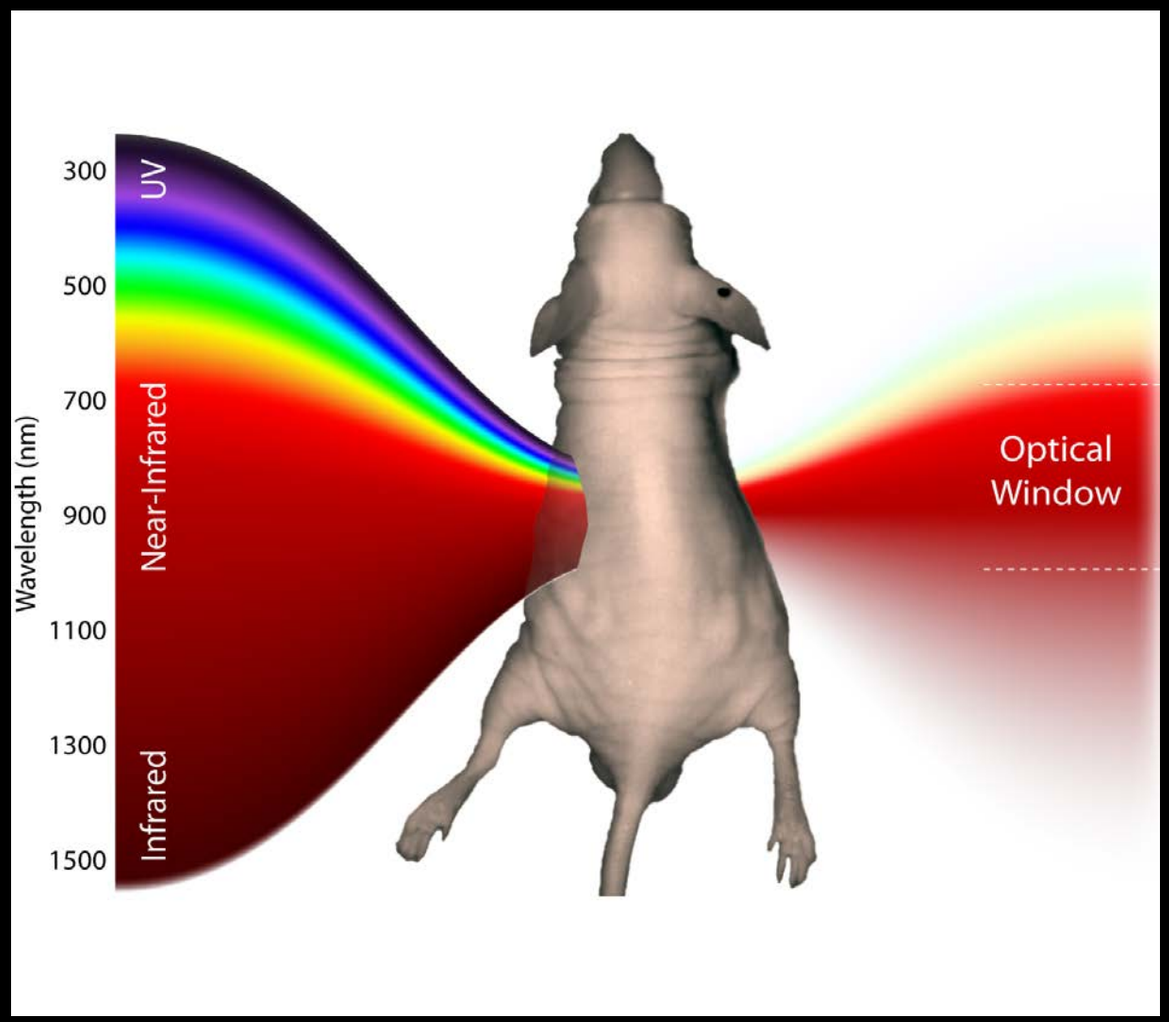
NIR dye attached to RGD motifs that target αvβ integrins

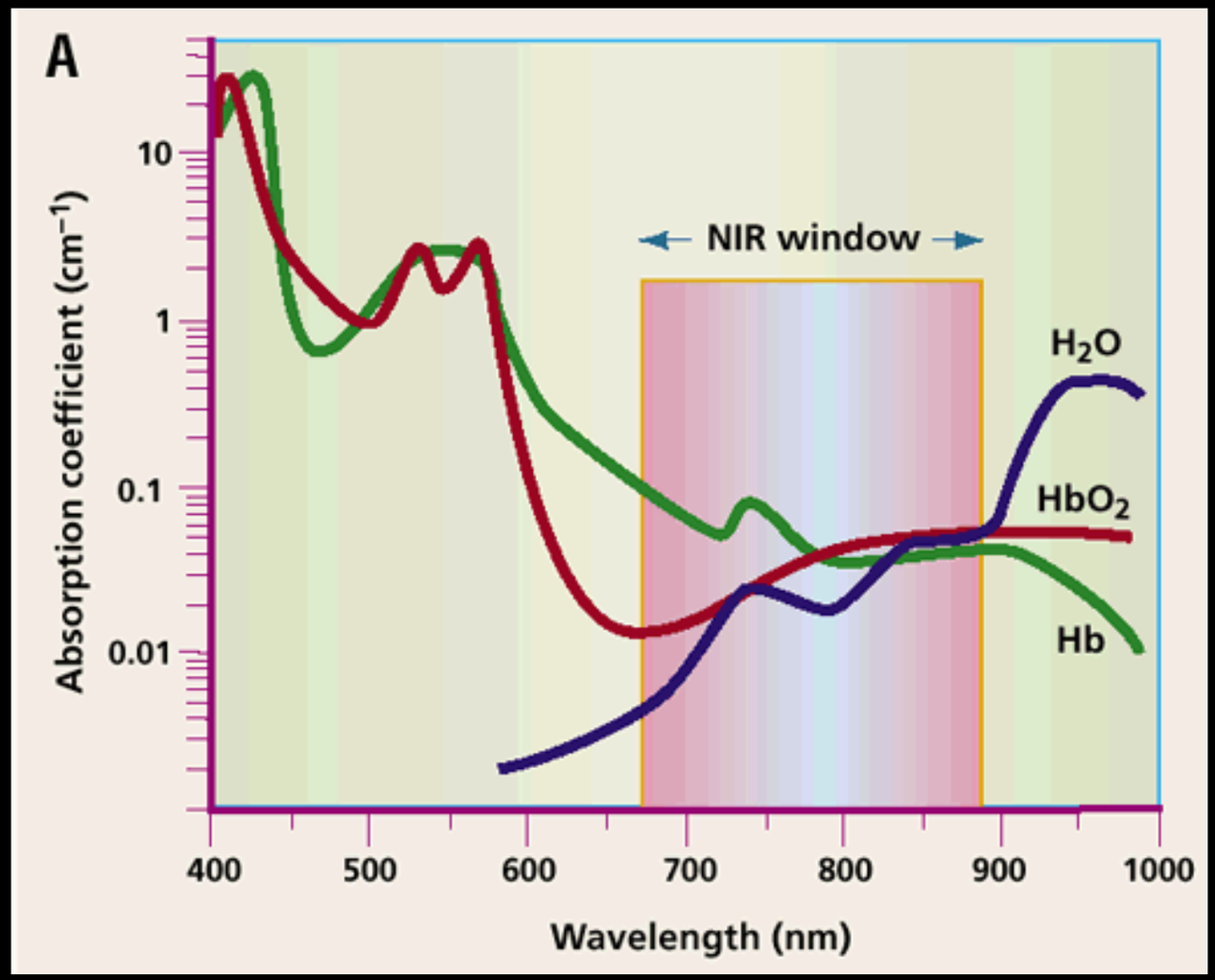


Du *et al.*, *PLoS One*, **7**:e43941 (2012)

Near-infrared wavelengths optimal for *in vivo* imaging

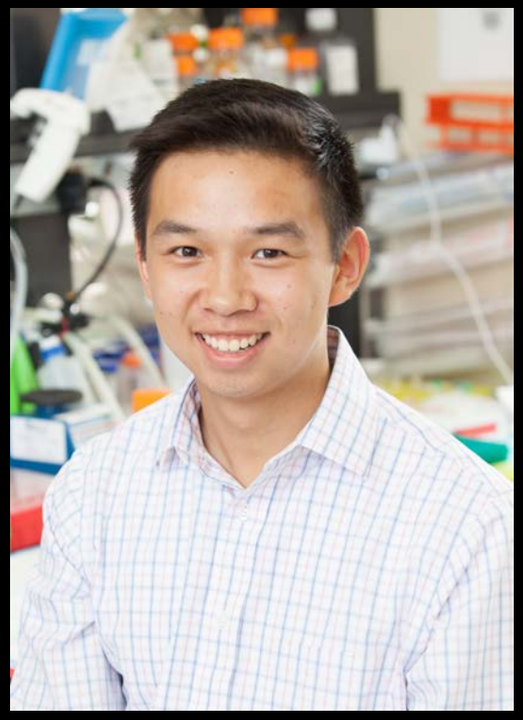
NIR minimally scattered and absorbed by biologic tissue





Weissleder, R, *Nat. Biotechnol.*, **17**:375 (2001)

NIR enables for deep tissue imaging (up to several cm depending on power source)



Matthew Cheung, BA
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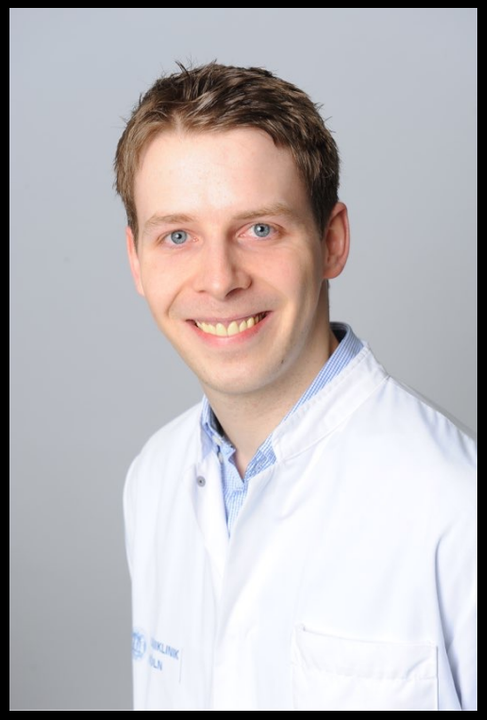

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WashU

Walter Akers, DVM, PhD
St. Jude's

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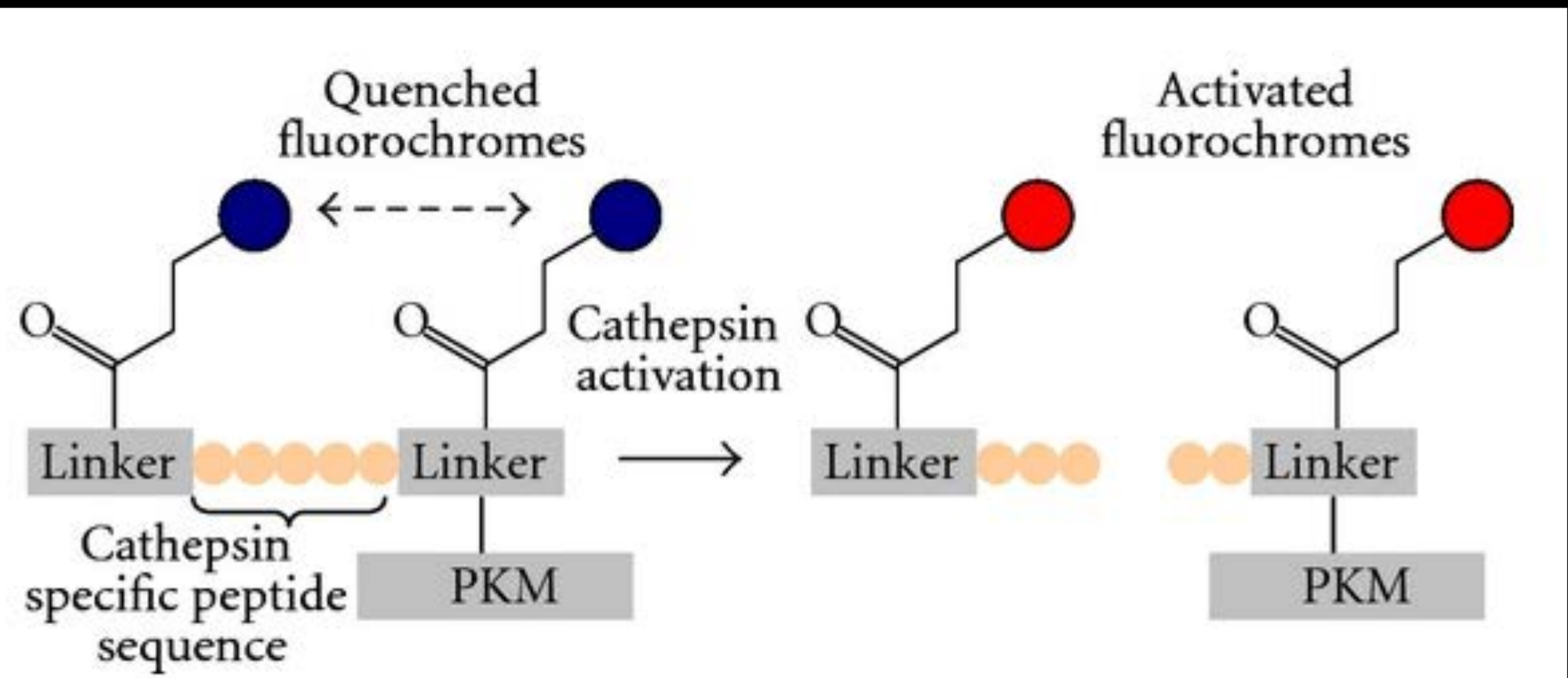
Activatable NIR probes can detect enzymatic activity within tissue

For example, cathepsin B produced by inflammatory macrophages can activate quenched probes generating a detectable signal



Lin SA, *et al.*, *Int J Mol Imaging*, **2012**:Article ID 189254 (2012)

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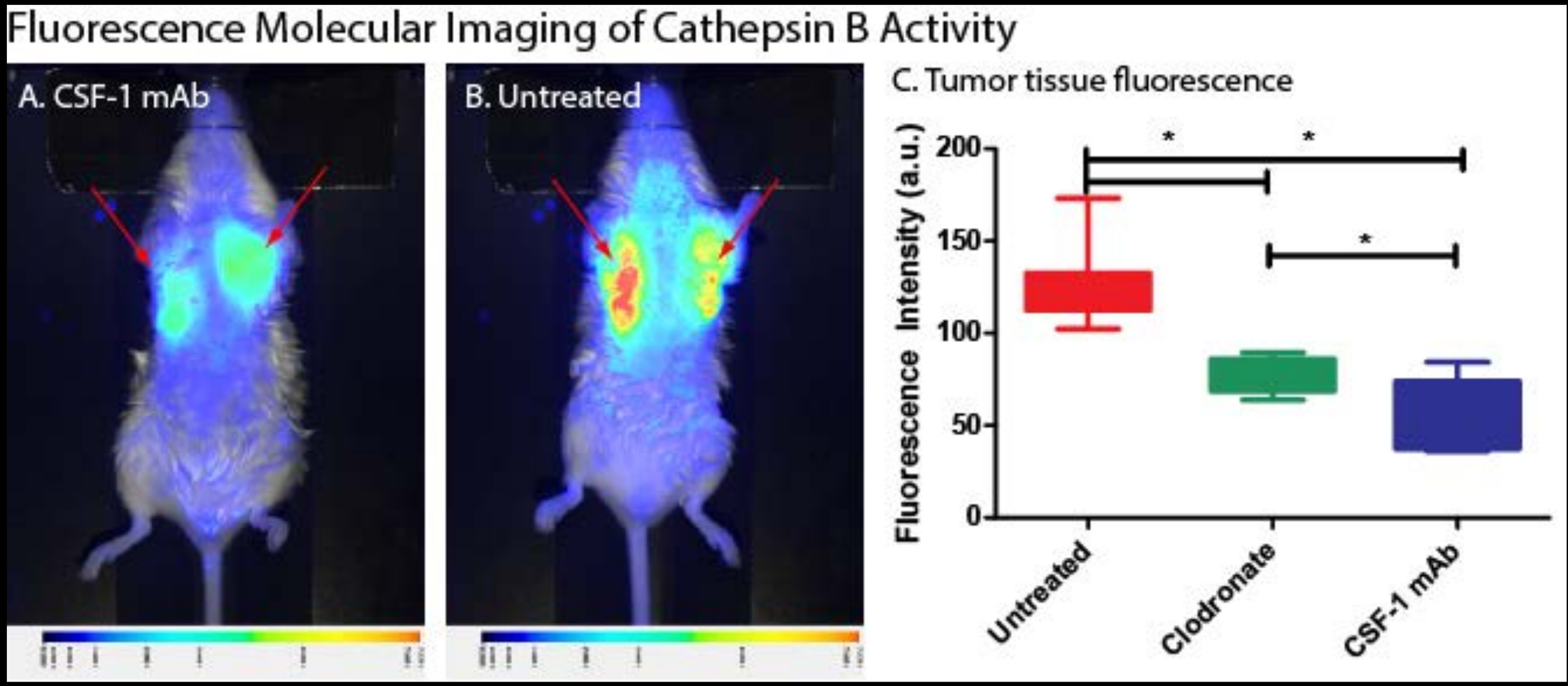

Walter Akers

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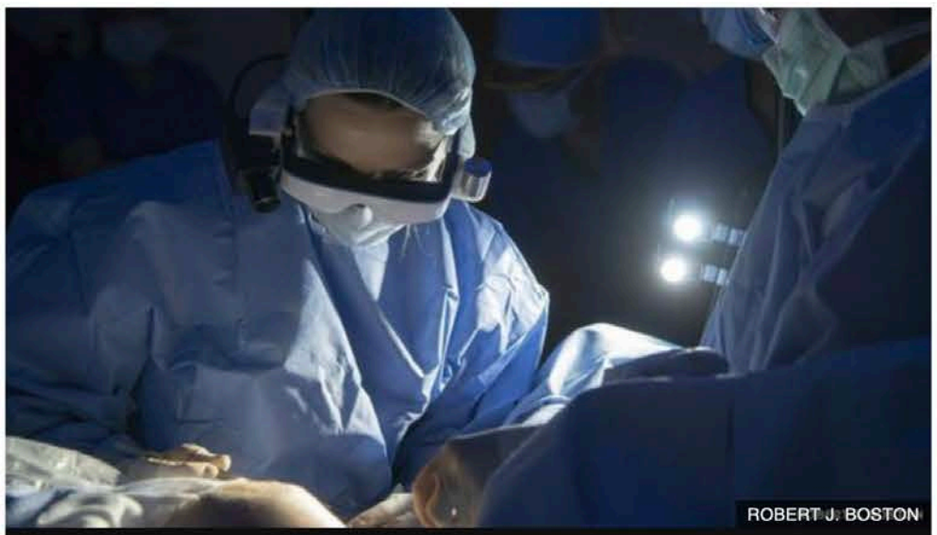
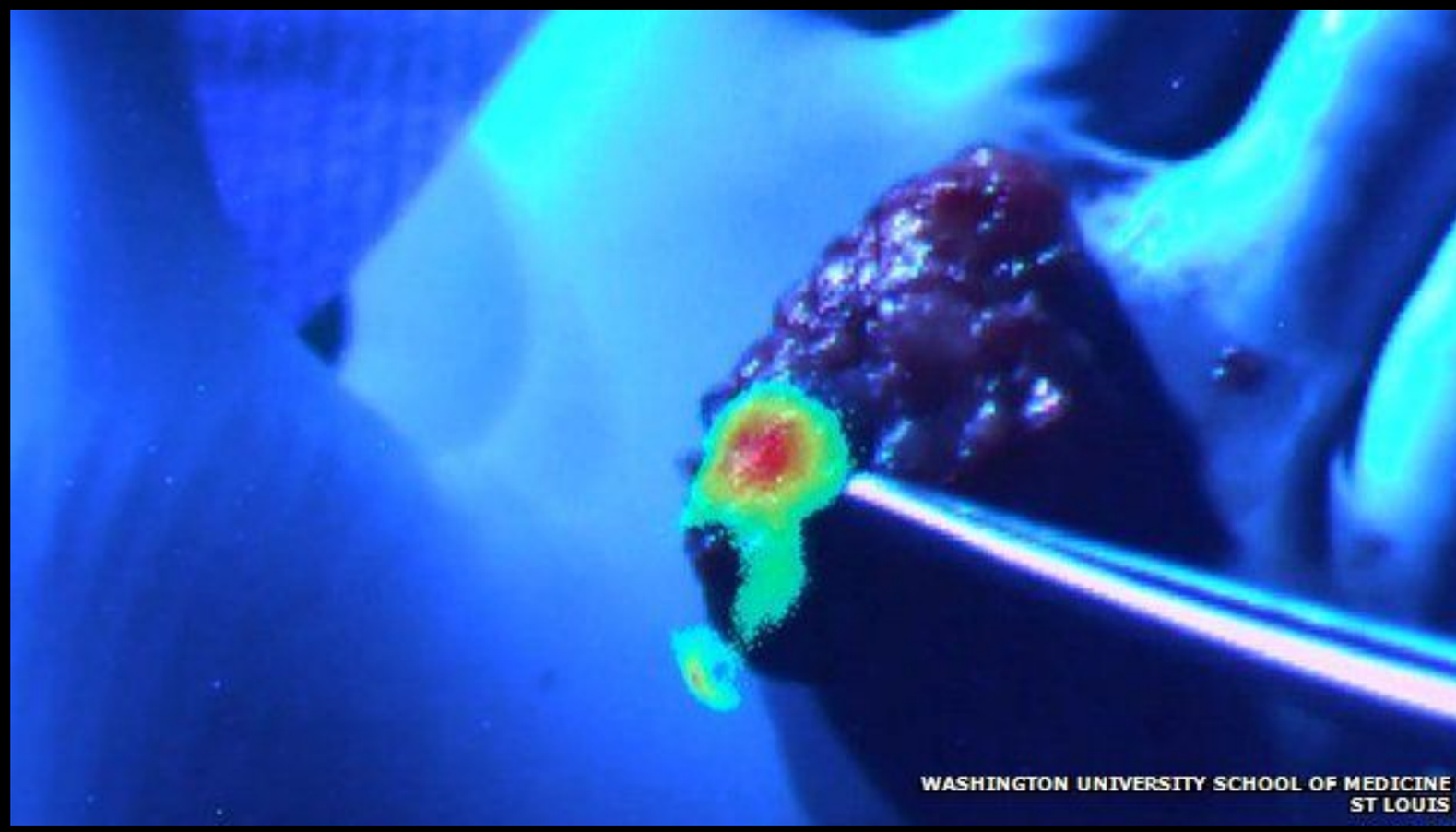
Health

Goggles help surgeons ‘see’ tumours

13 April 2014 Share



The newly developed goggles allow surgeons to 'see' the cancer cells they need to remove



Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae

Yuqian Ma,[1,5] Jin Bao,[1,2,5,*] Yuanwei Zhang,[3,5] Zhanjun Li,[3] Xiangyu Zhou,[1] Changlin Wan,[1] Ling Huang,[3] Yang Zhao,[3] Gang Han,[3,*] and Tian Xue[1,2,4,6,*]

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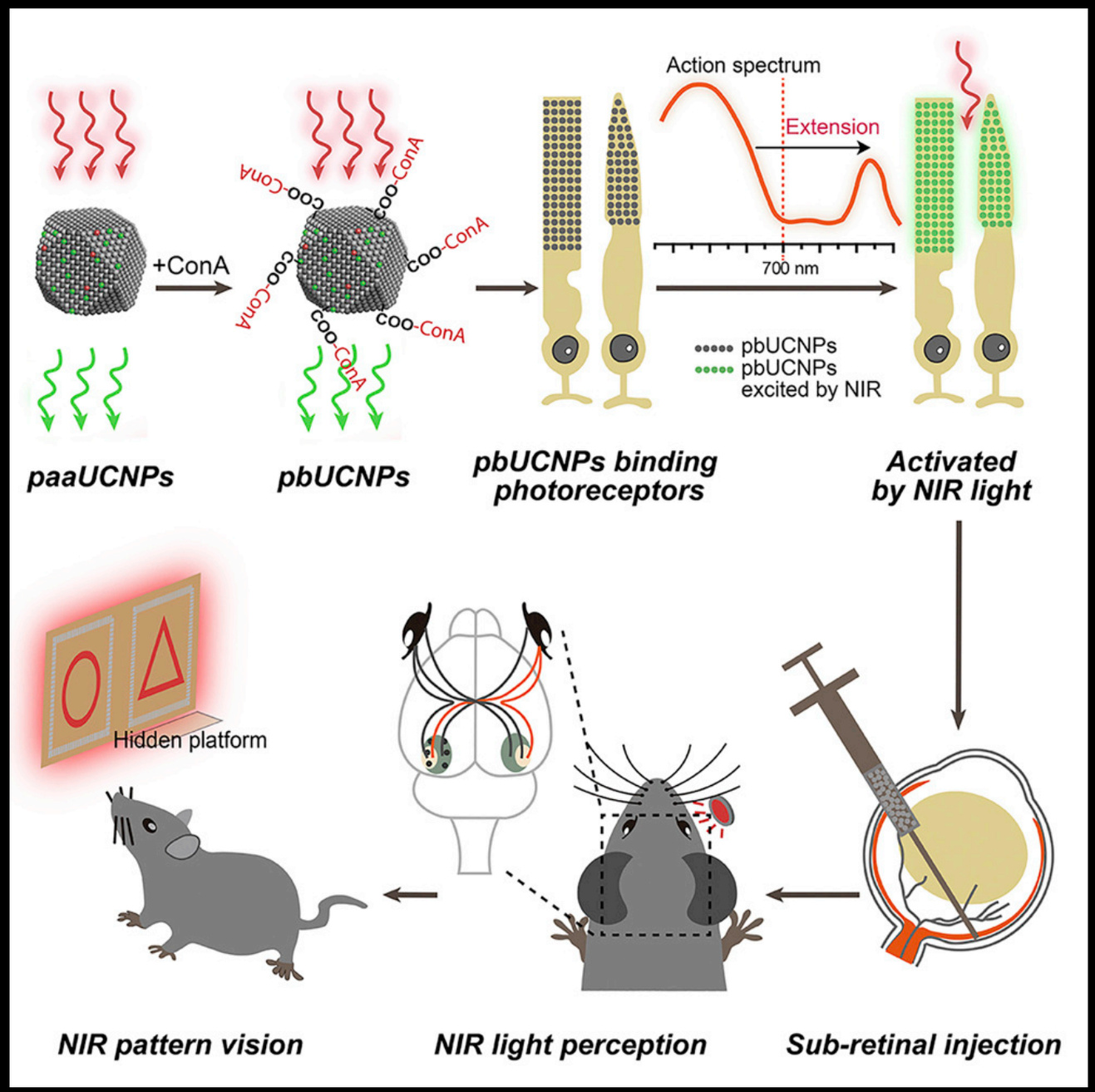
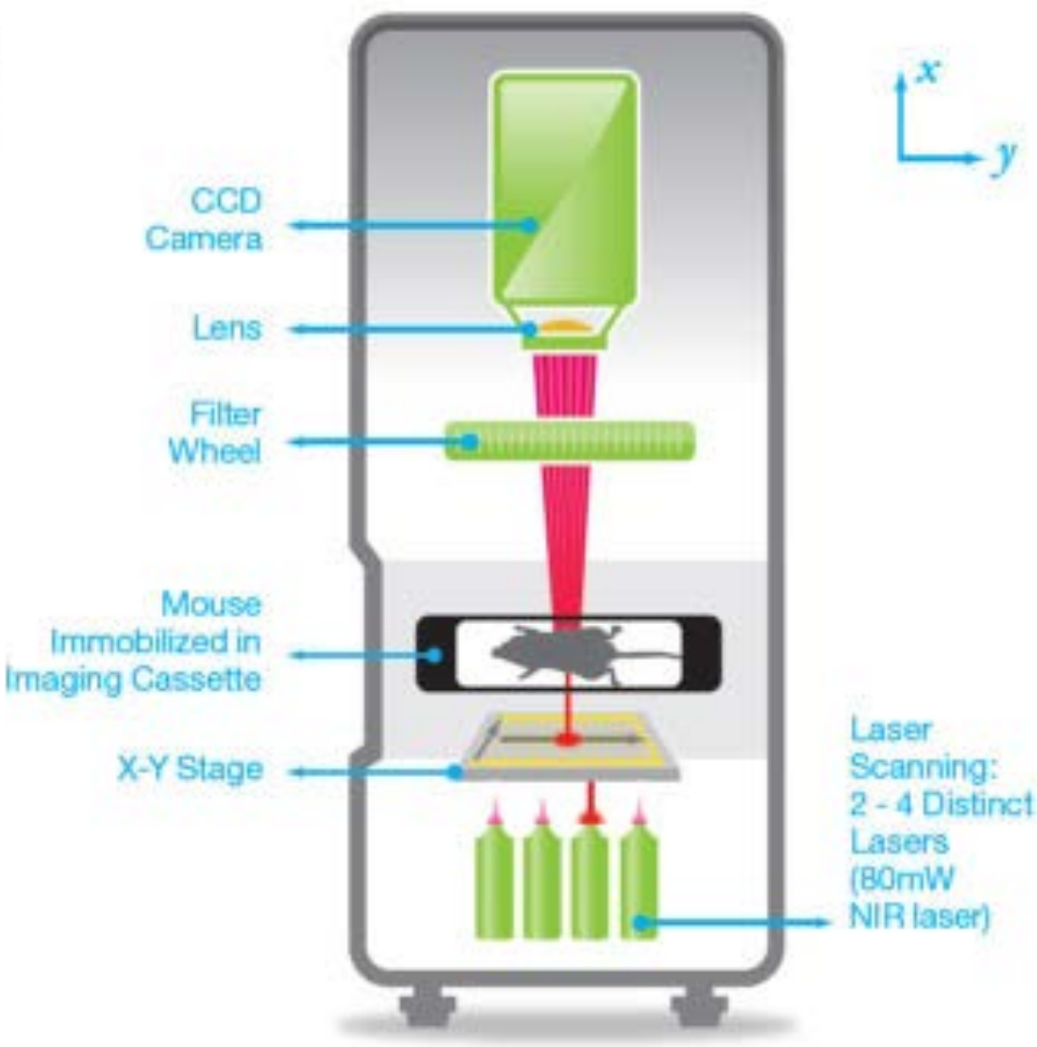
Cell 177, 243–255, April 4, 2019



Imaging instrumentation: FMT4000

Fluorescence molecular tomography (FMT)



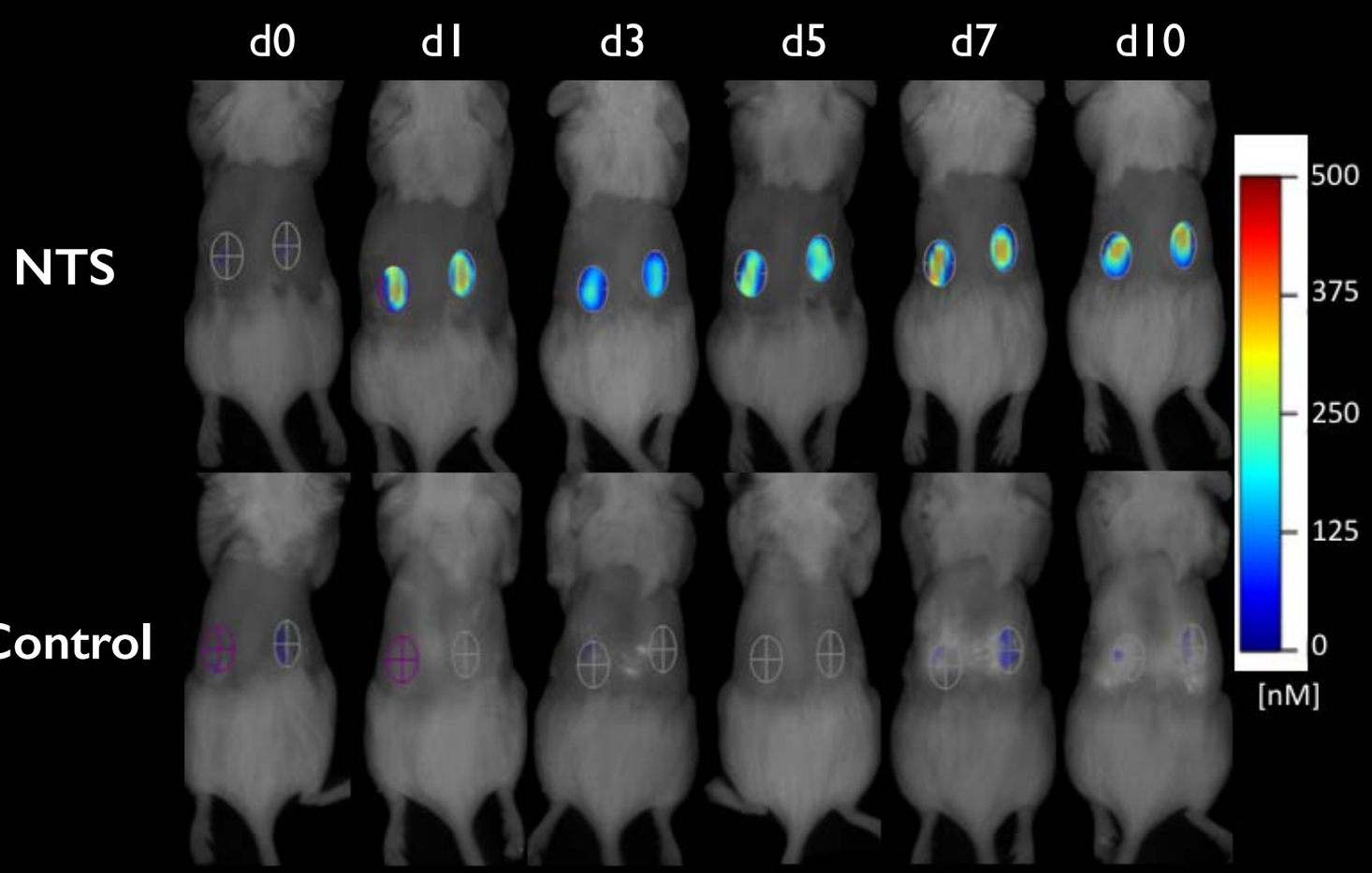
- FMT: form of optical imaging, detects fluorescence signals (intensity, lifetime) quantitatively and in 3D
- Light source and detector in transillumination geometry: generates paired absorption and fluorescence data maps throughout the mouse
- Possesses high sensitivity for probe (femtomole)
- Can generate whole body tomography reconstruction

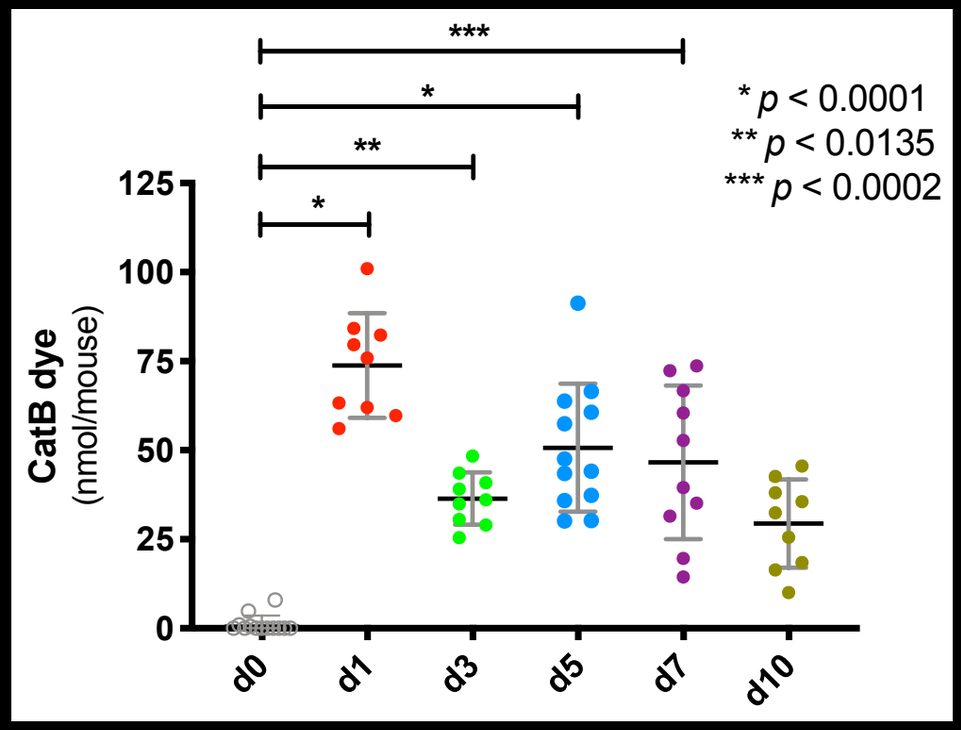
Optical imaging of experimental glomerulonephritis

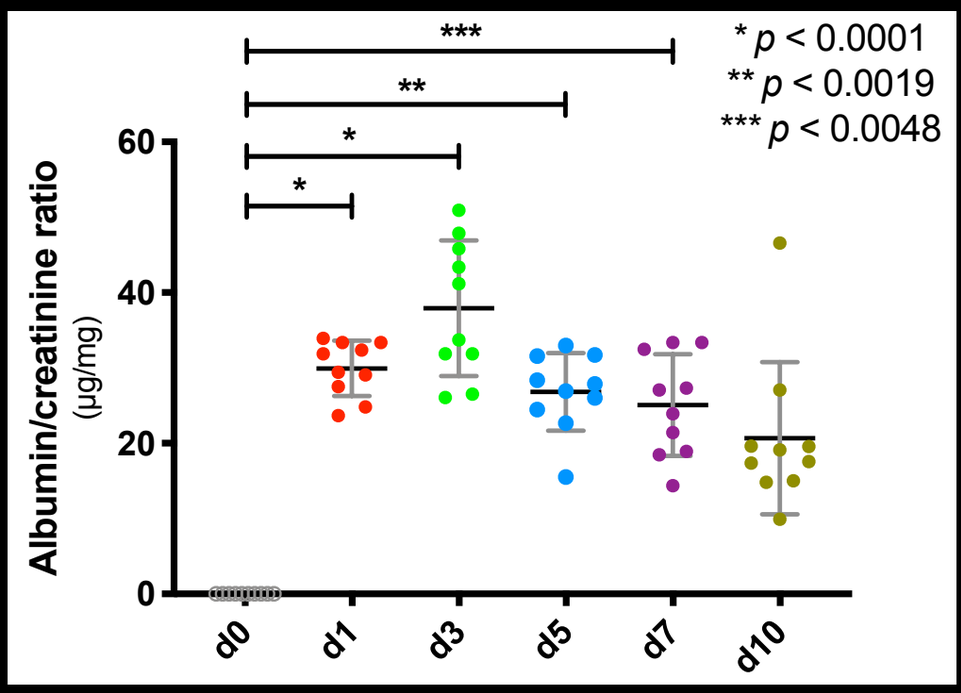
Cathepsin B-mediated activation of a NIR dye detectable and quantifiable

Optical imaging of experimental glomerulonephritis

Cathepsin B-mediated activation of a NIR dye detectable and quantifiable

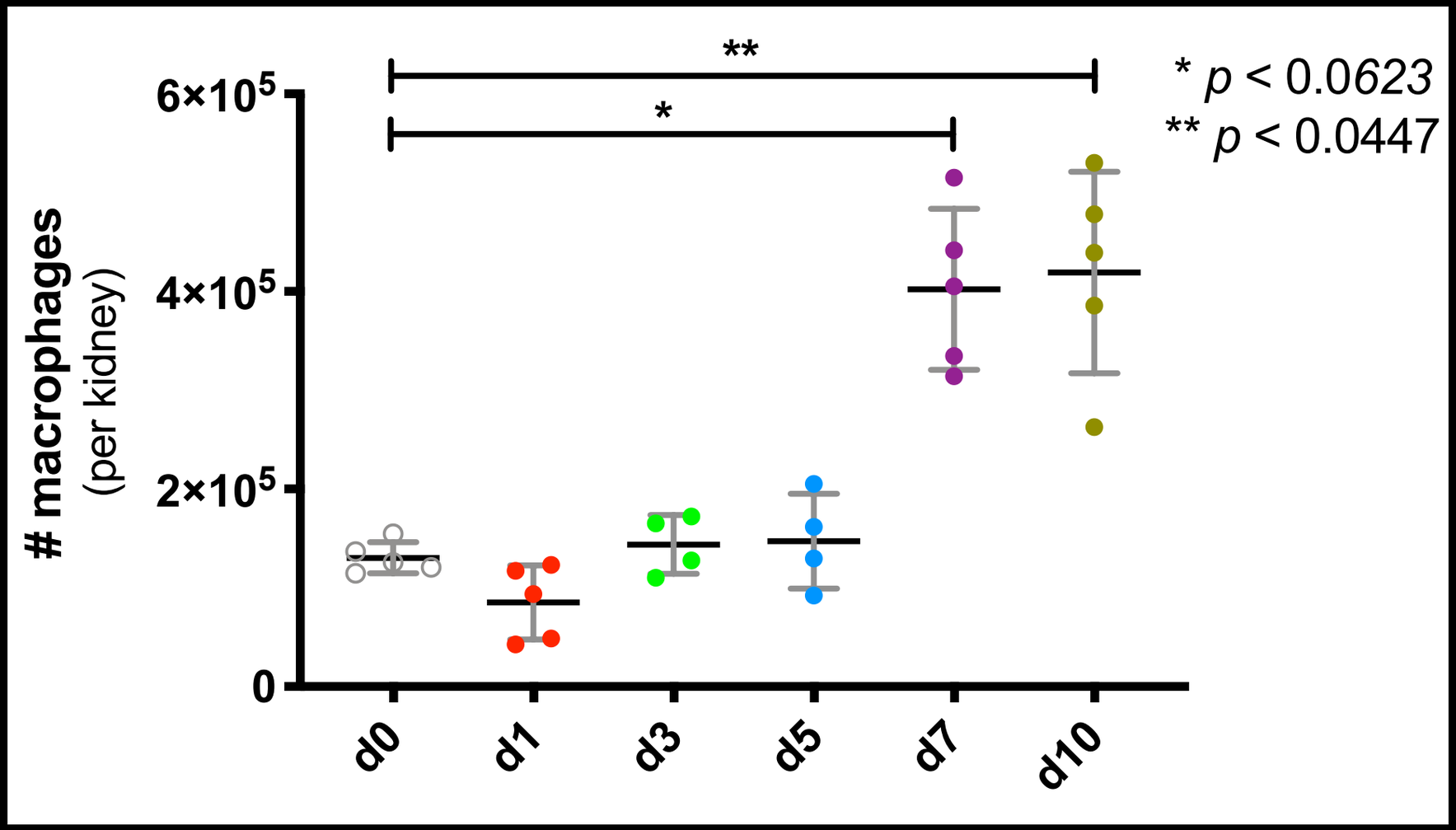






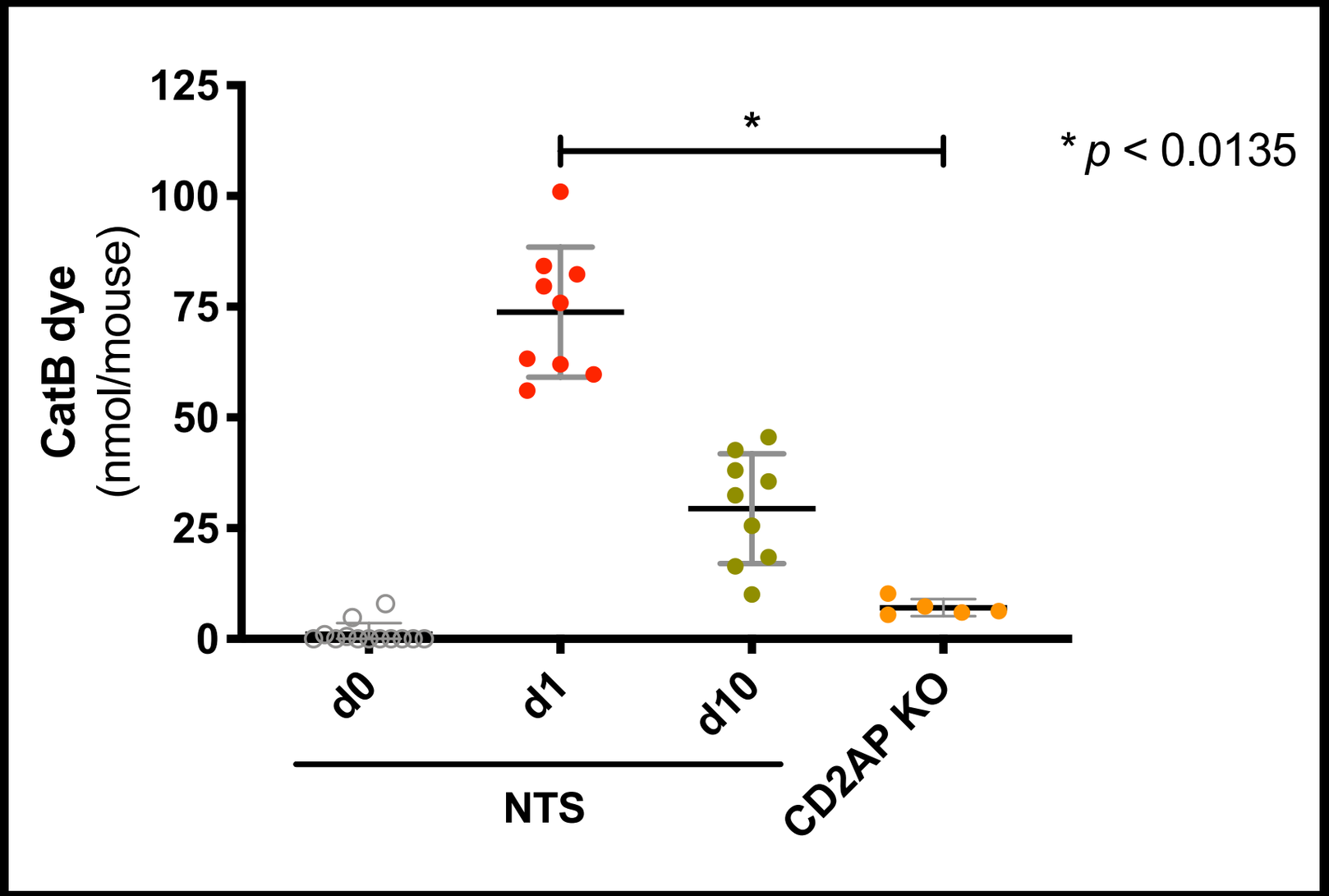
Optical imaging of experimental glomerulonephritis

Cathepsin B signal is not derived from macrophages



Optical imaging of experimental glomerulonephritis

Cathepsin B may be a specific signal for GN



Conclusions

- Cathepsin B activated probes can detect inflammatory changes in experimental glomerulonephritis
  - Other molecular targets uncovered through AMP?

- NIR-based platforms may have limited application for humans though due to signal attenuation
  - Can photoacoustics overcome this issue?

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Fast label-free multilayered histology-like imaging of human breast cancer by photoacoustic microscopy

Terence T. W. Wong,[1] Ruiying Zhang,[1] Pengfei Hai,[1] Chi Zhang,[1] Miguel A. Pleitez,[1] Rebecca L. Aft,[2,3]* Deborah V. Novack,[4,5]* Lihong V. Wang[1]*†

Wong *et al.*, *Sci. Adv.* 2017;**3**:e1602168 17 May 2017