

Molecular Imaging of Colonic Adenomas with Fluorescent Tilmanocept

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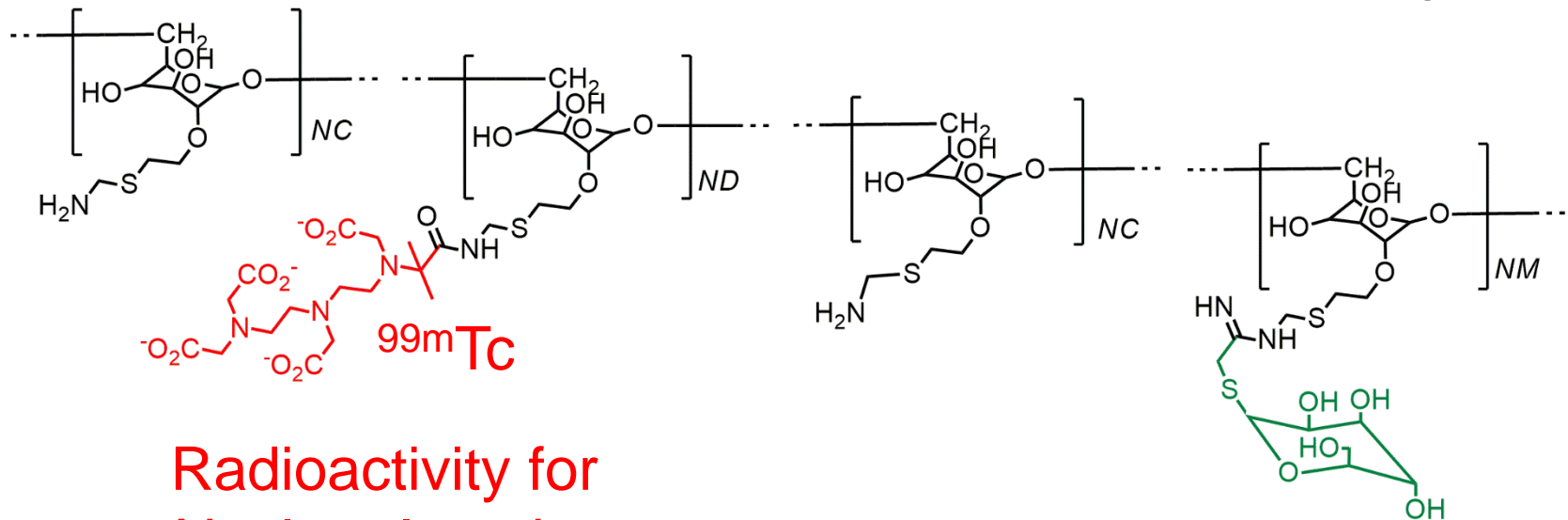
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and
Kyoto University*

Contrast-Enhancement Motivation

- Lesion detection is one of the major challenges
- Miss rates for polyps run in the region of 25%
- Factors that can affect visualization of polyps
 - Adequate prep and cleansing
 - Lesions hiding behind folds
 - Flat, pale lesions
 - Time constraints

Chemical Structure of Tc-99m-Tilmanocept

FDA-approved for Sentinel Lymph Node Mapping



Radioactivity for
Nuclear Imaging

Mannose Binds to the
Receptor CD206

- Vera et al. *J Nucl Med* 2001
- Wallace et al. *Ann Surg Oncol* 2007
- Wallace et al. *Ann Surg Oncol* 2013

CD206 Cellular Distribution

- Fixed Macrophages
 - liver, marrow, lymph nodes
- M2 Macrophages
 - invade cancers & adenomas
- Dendritic Cells
 - resides in colon, lymph nodes
 - invade cancers & adenomas
- Microglial Cells
 - brain
- Mesangial Cells
 - kidneys

Strategy for Fluorescence-Enhanced Colonoscopy via Molecular Imaging

- ▶ Attach fluorescent tag to tilmanocept
- ▶ Target CD206 in adenomas to enhance detection

Fluorescence-Capable Endoscope

An Example

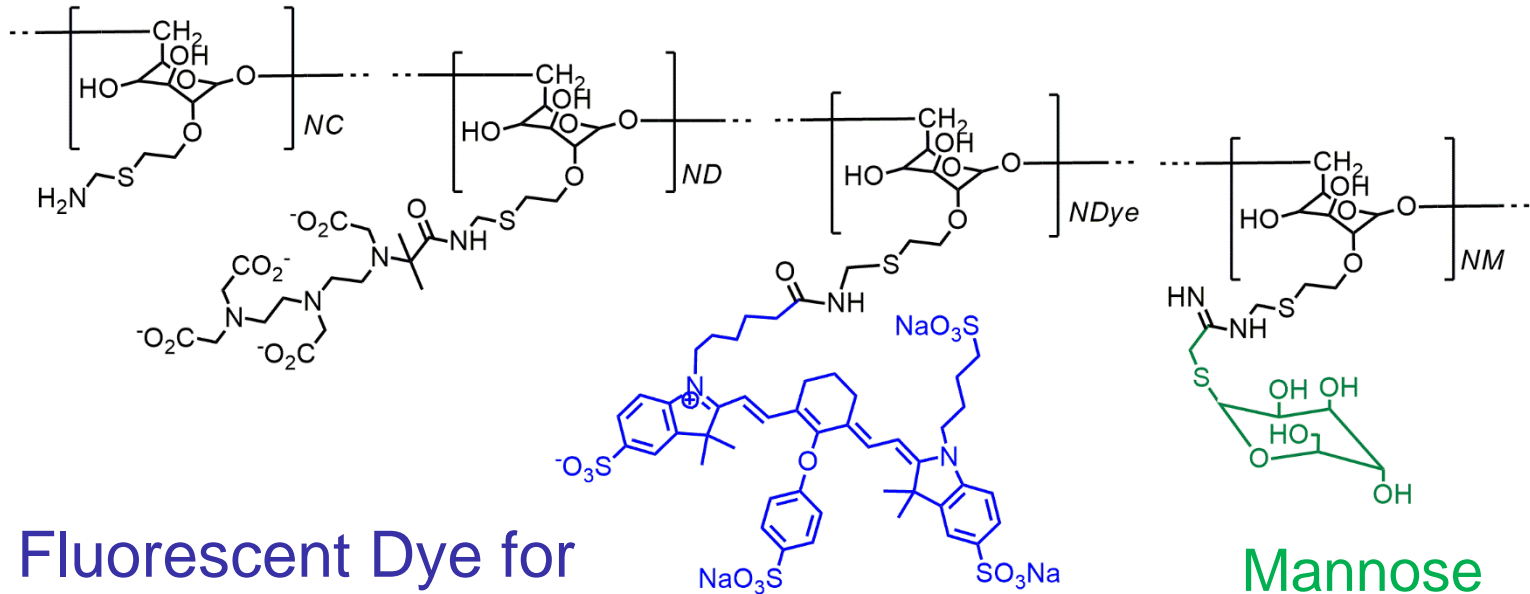
(CF-H260AZI)
Olympus Medical Systems Corp



Aihara H, et al. *Gastro Res Pract* 2012

Fluorescent-Tilmanocept

Endoscopic Molecular Imaging



Fluorescent Dye for Endoscopic Imaging

Mannose
Binds to the
Receptor CD206

- Emerson *et al.* *Radiology* 2012
- Qin *et al.* *J Biomed Opt* 2013
- Hosseini *et al.* *J Surg Res* 2014

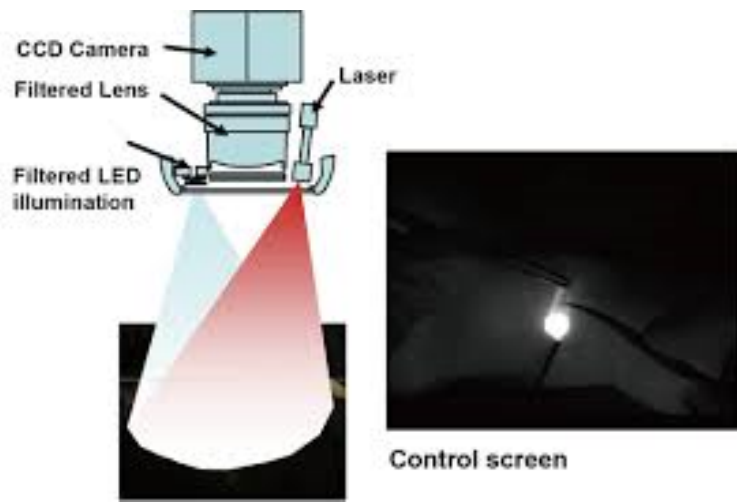
Proposed Implementation Fluorescence-Enhanced Colonoscopy

- ▶ Inject fluorescent-tilmanocept through I.V. line at least 15 minutes before colonoscopy
- ▶ Perform colonoscopy
 - Switch colonoscope between brightfield and fluorescence modes to identify and remove or biopsy suspicious lesions
- ▶ Histopathology

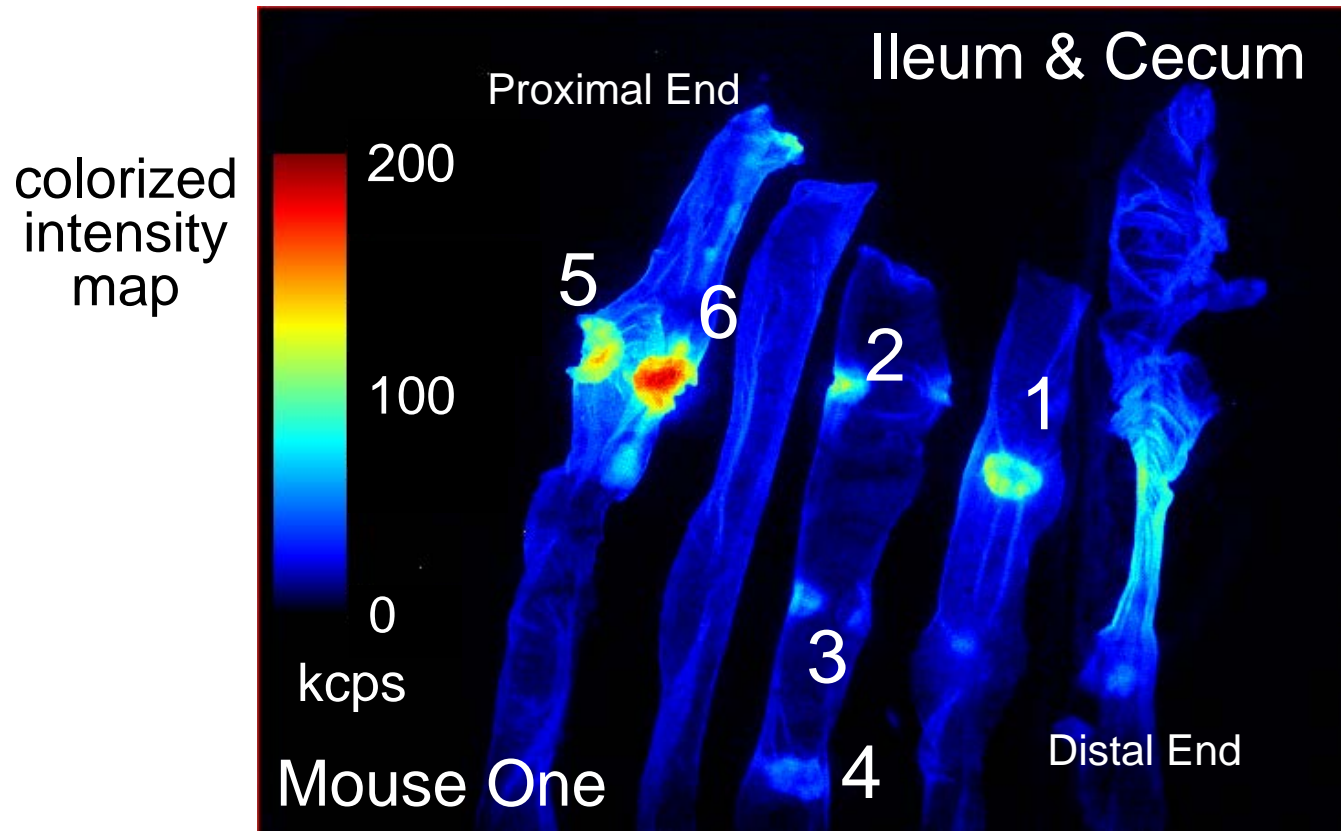
We Tested the Ability to Image Adenomas in ACP Mice

- ▶ Six ACP mice were used (adenoma model)
- ▶ Injected fluorescent-tilmanocept
- ▶ Euthanized after 30 minutes
- ▶ Exposed ileum and cecum
- ▶ Imaged with a hand-held fluorescence imager
- ▶ Under white-light identified and excised suspicious lesions
- ▶ Recorded fluorescence intensity of each lesion
- ▶ Histopathology

Fluobeam800 Fluorescence Imager Imaging at Near Infra-Red Wavelengths

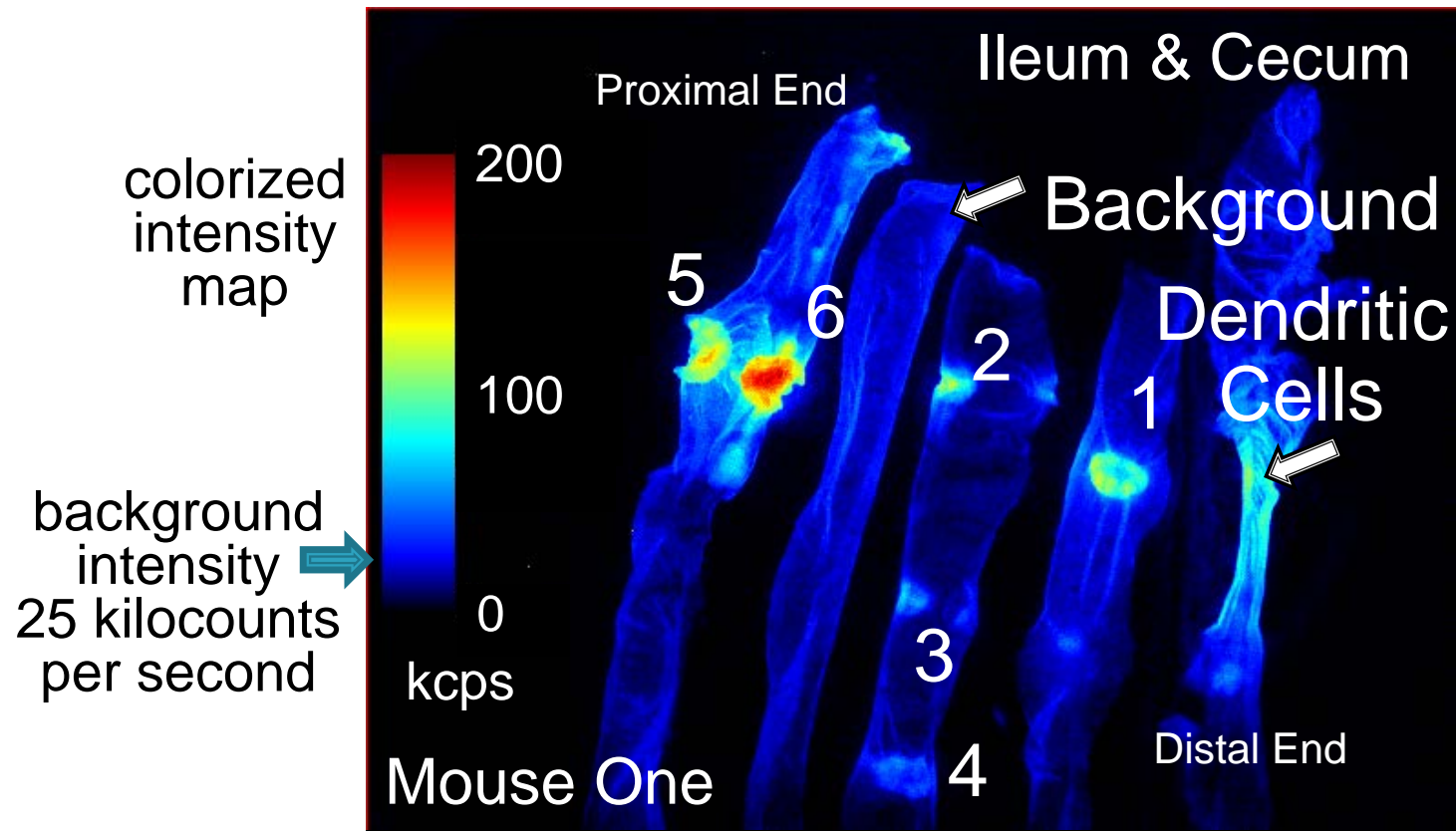


Example: Mouse One Fluorescence Image



six lesions “of interest” found

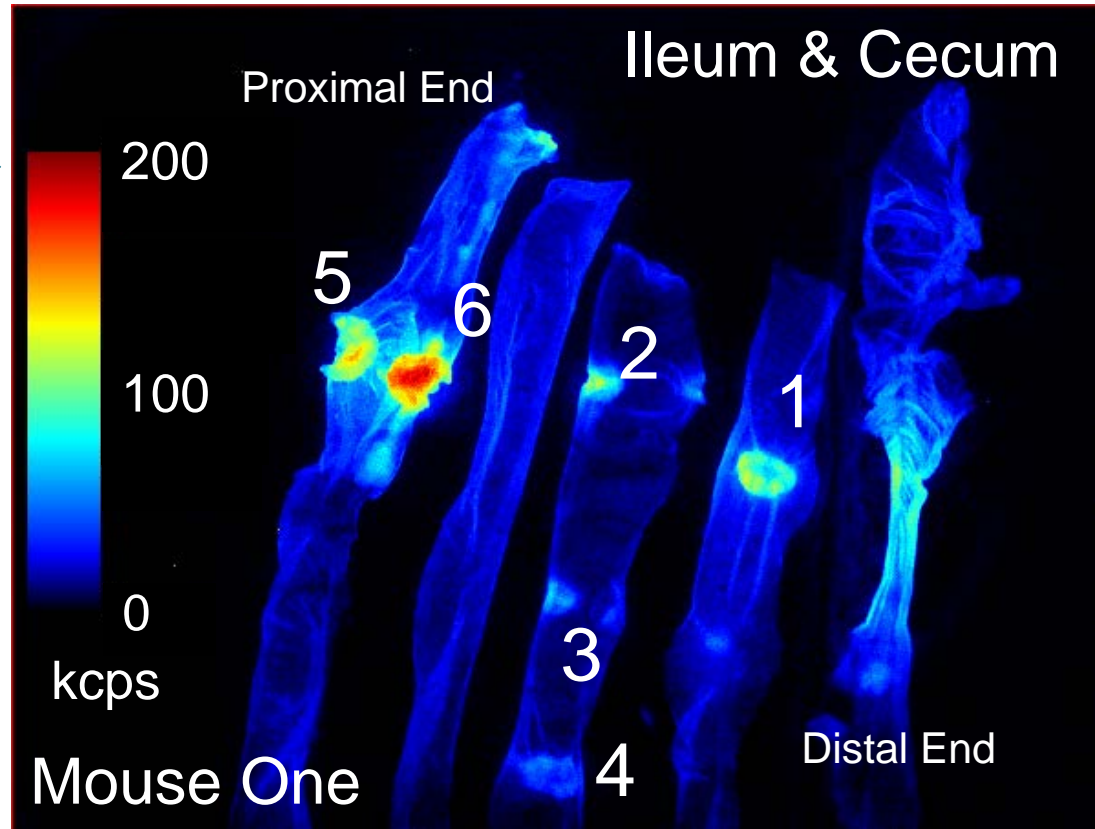
Fluorescence Imaging Common Features



Fluorescence Imaging

Lesion #6 fluorescence intensity: 195 kilocounts per second

lesion #6
intensity →
195 kilocounts
per second

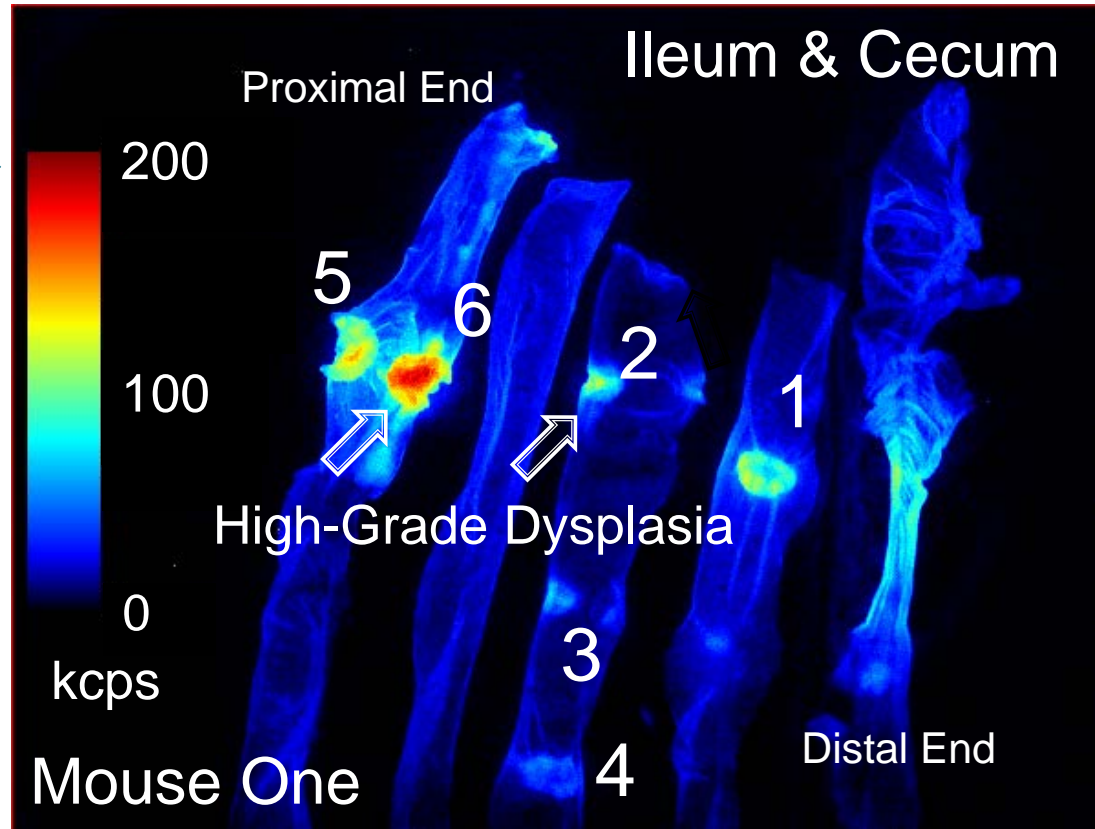


Adenomas: All Numbered Locations

Histopathology

Lesions #2 & #6: High Grade Dysplasia

Lesion #6
intensity →
195 kilocounts
per second

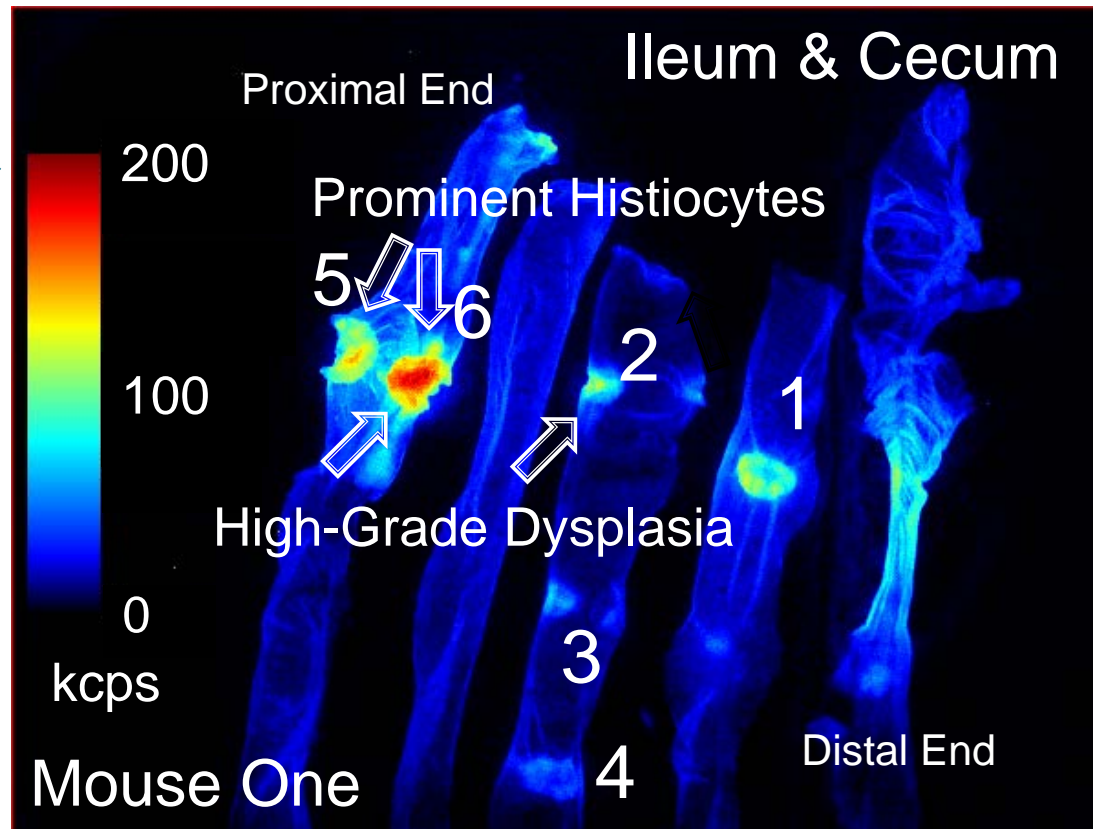


Adenomas: All Numbered Locations

Histopathology

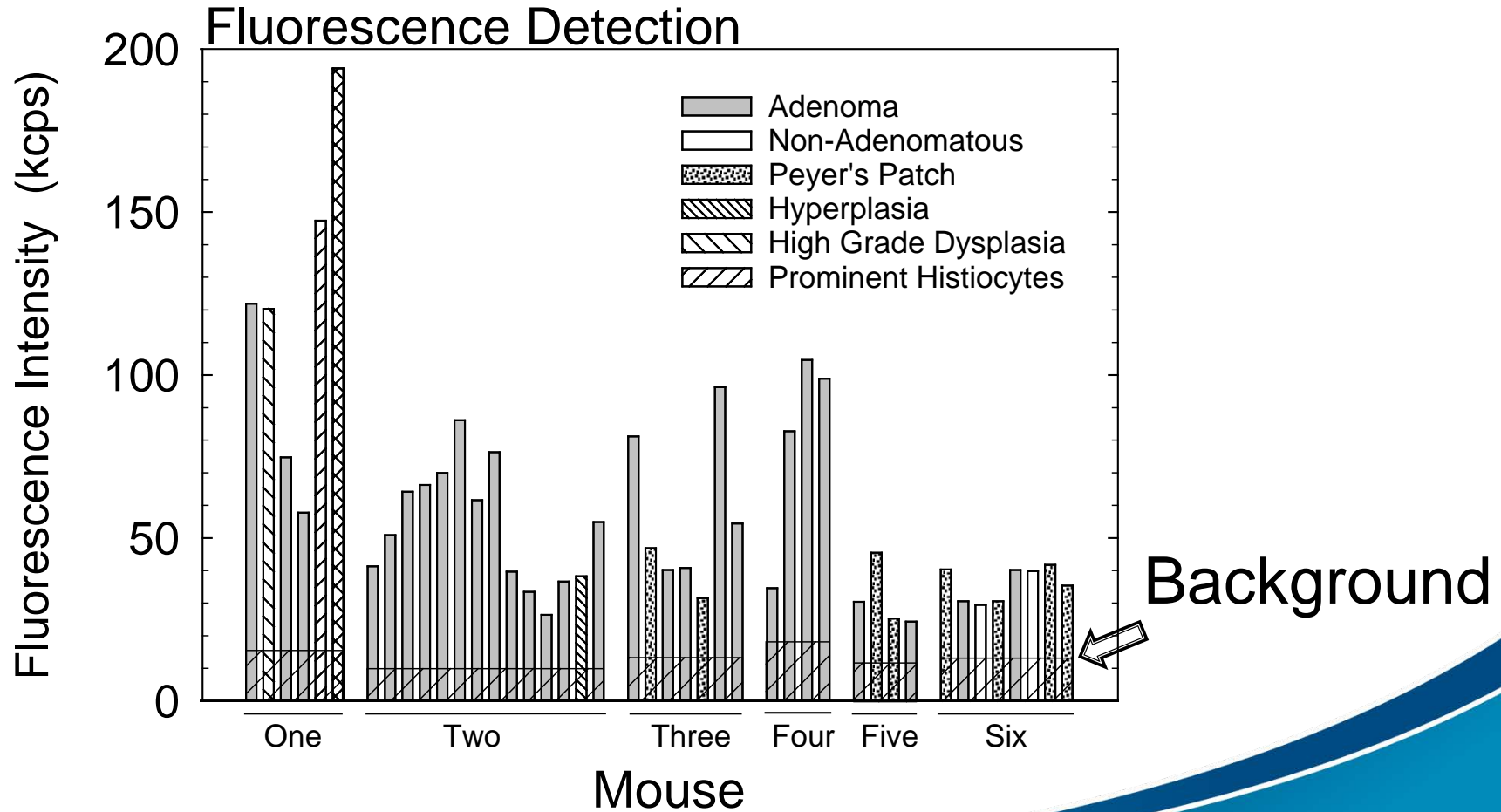
Lesions #5 & #6: Prominent Histiocytes

Lesion #6
intensity →
195 kilocounts
per second



Adenomas: All Numbered Locations

All adenomas had a FL signal higher than background



Current Status

- ▶ Demonstrated fluorescence imaging after i.v. injection
- ▶ High adenoma detection rate
- ▶ Successfully completed biosafety study

Future Plans

- ▶ Obtain fluorescence-capable colonoscope
 - Seeking equipment partner or
 - Modify a standard colonoscope
- ▶ Start Phase 1 clinical trial

UCSD Colaborators

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David R Vera, PhD
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Surgeon



Makoto Taketo, MD, PhD
Immunologist



Thank You
&
Questions