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

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

Fluorescent-Tilmanocept

Endoscopic Molecular Imaging

Fluorescent Dye for Endoscopic Imaging

- Emerson et al. Radiology 2012

Mannose Binds to the Receptor CD206
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

colorized intensity map

six lesions “of interest” found
Fluorescence Imaging
Common Features

Mouse One

Ileum & Cecum

Background

Dendritic Cells

Proximal End

Distal End

colorized intensity map

background intensity 25 kilocounts per second

Fluorescence Imaging

Common Features

Mouse One

Ileum & Cecum

Background

Dendritic Cells

Proximal End

Distal End

colorized intensity map

background intensity 25 kilocounts per second
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.

Fluorescence Detection

Fluorescence Intensity (kcps)

Mouse

- Adenoma
- Non-Adenomatous
- Peyer's Patch
- Hyperplasia
- High Grade Dysplasia
- Prominent Histiocytes

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 Collaborators

Napoleone Ferrara, MD
Molecular Biologist

Samir Gupta, MD, MSCS
Gastroenterologist

David J Hall PhD
Medical Physicist
UCSD Collaborators

Carl Hoh, MD
Nuclear Medicine

Mark Valasek, MD
Pathologist

David R Vera, PhD
Radiochemist
Kyoto University Collaborators

Yoshiro Itatani, MD, PhD
Surgeon

Makoto Taketo, MD, PhD
Immunologist
Thank You
&
Questions