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PMID: 33443161

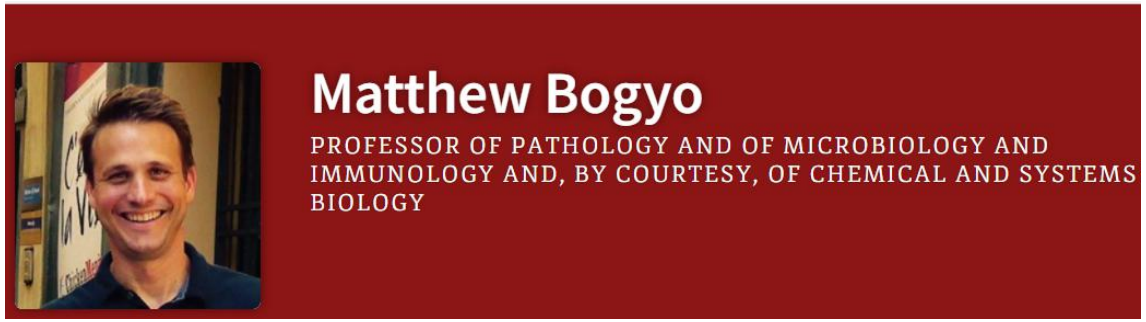
Medical Sciences

A protease-activated, near-infrared fluorescent probe for early endoscopic detection of premalignant gastrointestinal lesions

Reporter: Bao Fang

Date: 2021-12-31

Introduction



B.S., Bates College, Chemistry (1993)
Ph.D., MIT, Biochemistry (1997)

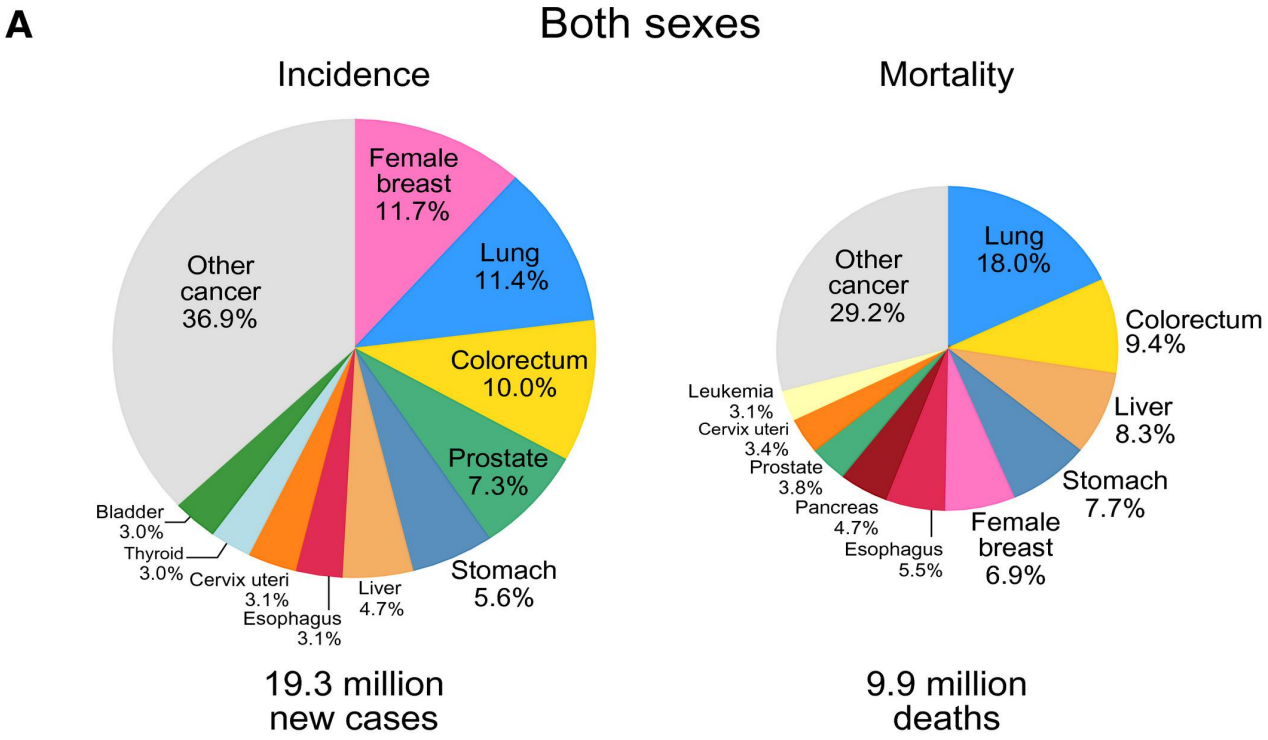
1) Design and synthesis of novel chemical probes for serine and cysteine hydrolases.
2) Understanding the role of hydrolases in bacterial athogenesis and the human parasites, plasmodium falciparum and oxoplasma gondii.
3) Defining the specific functional roles of proteases during the process of tumorogenesis.
4) In vivo imaging of protease activity.

Medical Education: Charite-Universitatsmedizin (2006)
Postdoctoral :Stanford Medical School (2015)

1)Development of new imaging tools in neoplasia of the GI-tract.
2)Guided resection of medulloblastoma using integrated optical tools for multimodality imaging.
3)Precision Medicine in Inflammatory Bowel Disease

Introduction

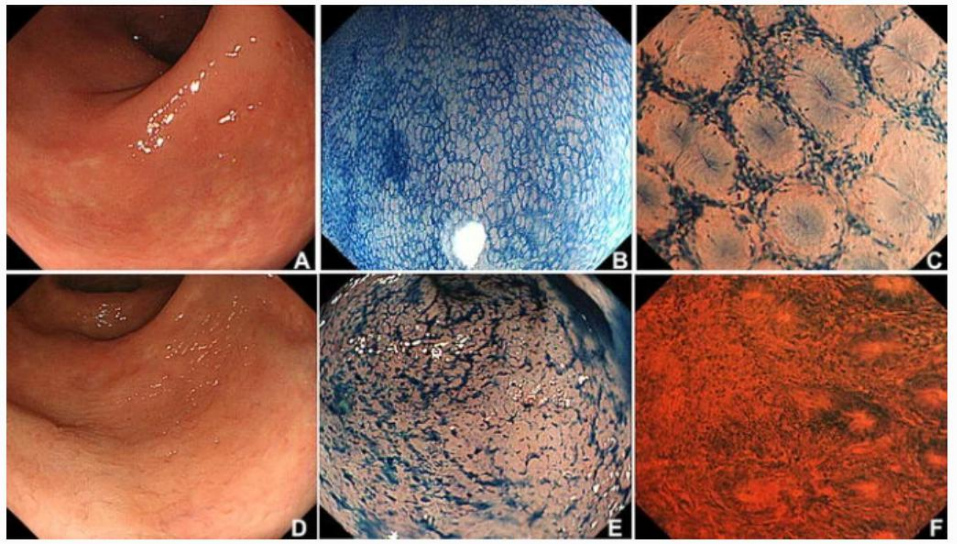
Global Cancer Statistics 2020



CA Cancer J Clin. 2021;71(3):209-249

常用筛选方式

- Faecal Immunochemical Test
- Colonoscopy

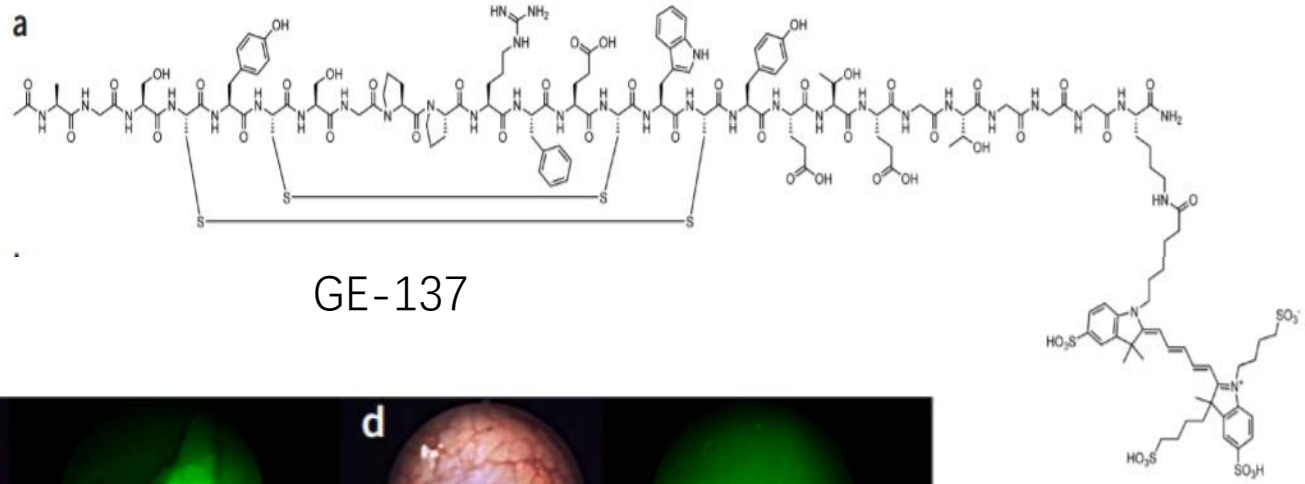


Representative series. Group A: **a** conventional endoscopy, **b** chromoendoscopy, **c** endocytoscopy. Group B: **d** conventional endoscopy, **e** chromoendoscopy, **f** endocytoscopy

J Gastroenterol. 2015;50(11):1087-1093.

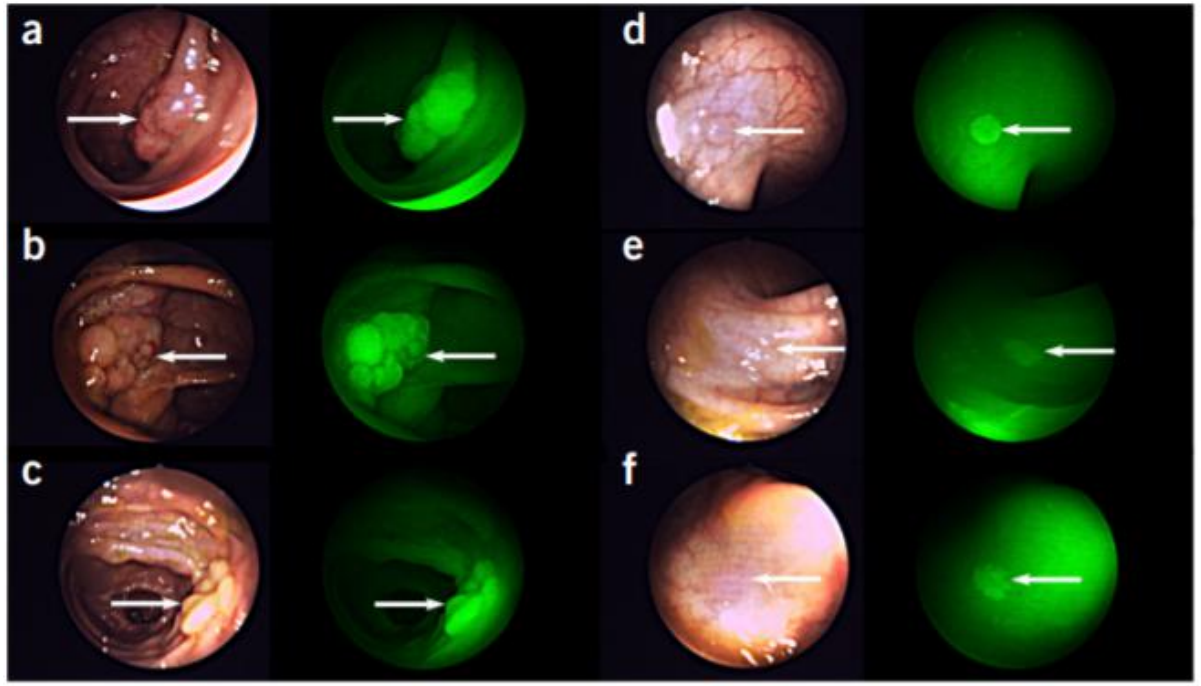
Introduction

GE-137是一种水溶性的26氨基酸环状肽，可用花菁染料进行标记，与细胞膜上的c-Met具有高亲和力



GE-137

GE-137的安全性、药代动力学已得到验证，但由于正常组织中也有c-Met的表达，导致肿瘤与正常组织背景比(TBR) 相对较低。



TBR：1.51

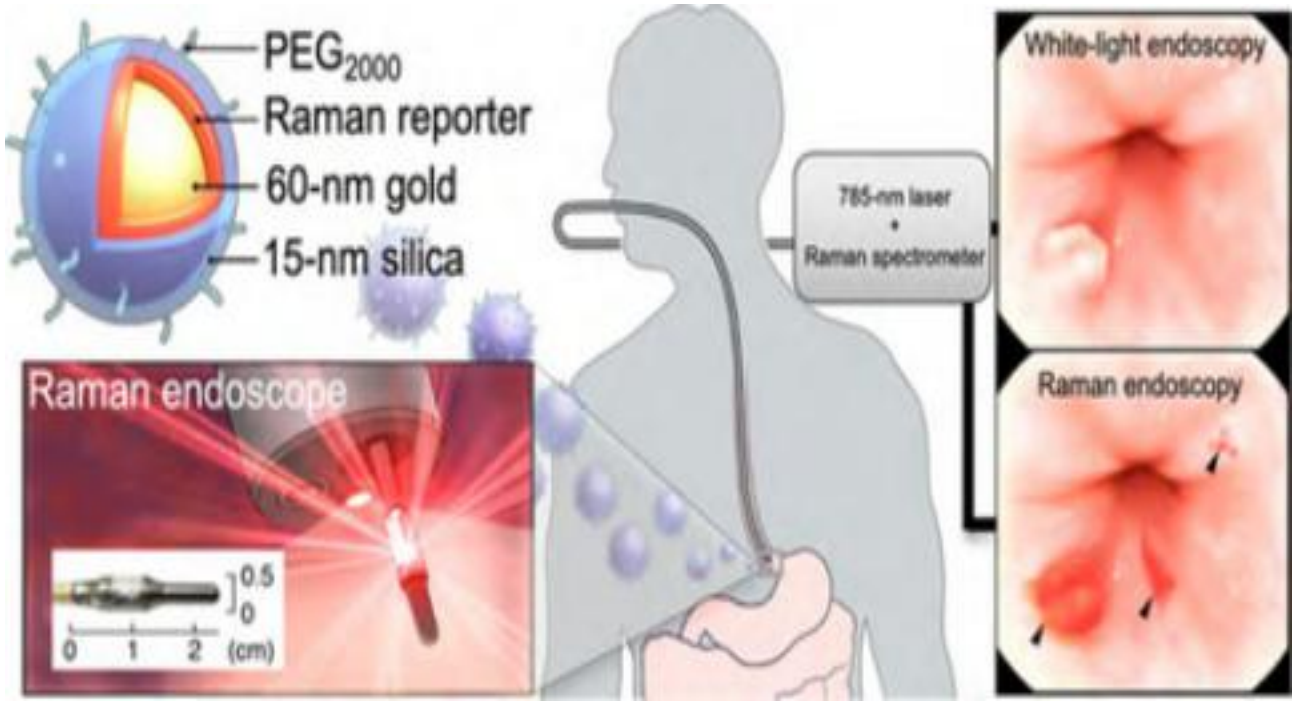
Nat Med. 2015;21(8):955-961.

Introduction

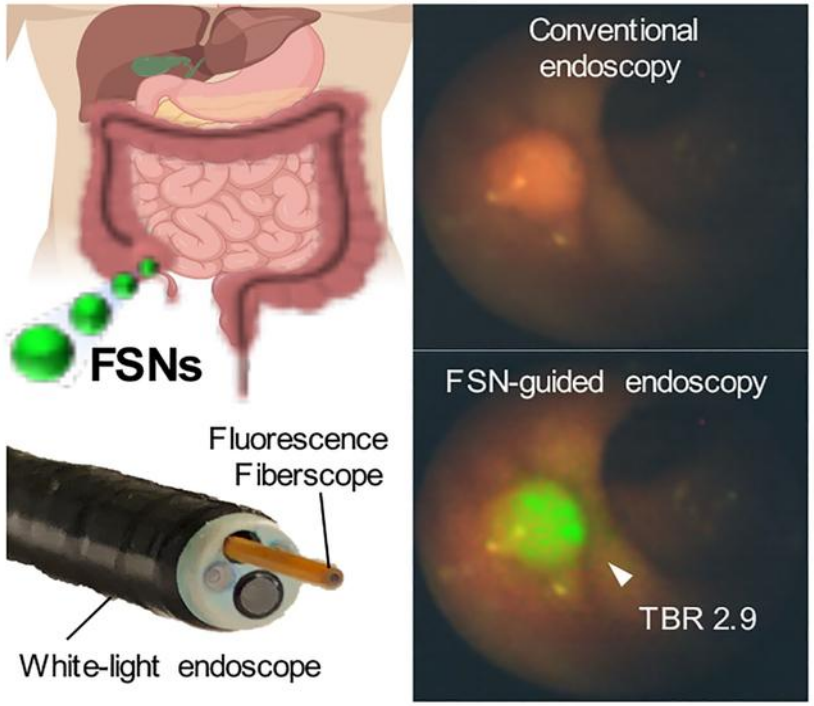
白光内窥镜：5-7mm

基于光学活性、近红外荧光 (NIRF) 纳米颗粒的造影剂能够在静脉给药后通过内窥镜检测癌前病变

表面增强共振拉曼散射纳米颗粒（SERRS-NP） （0.5-1.0mm)



近红外荧光二氧化硅纳米粒子 (FSN)(0.5mm)

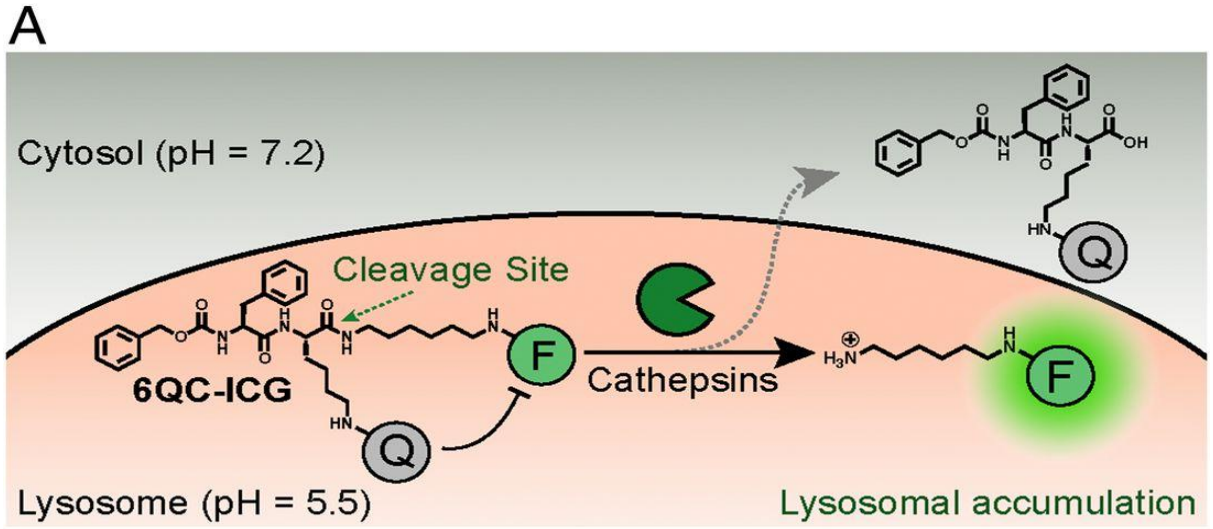


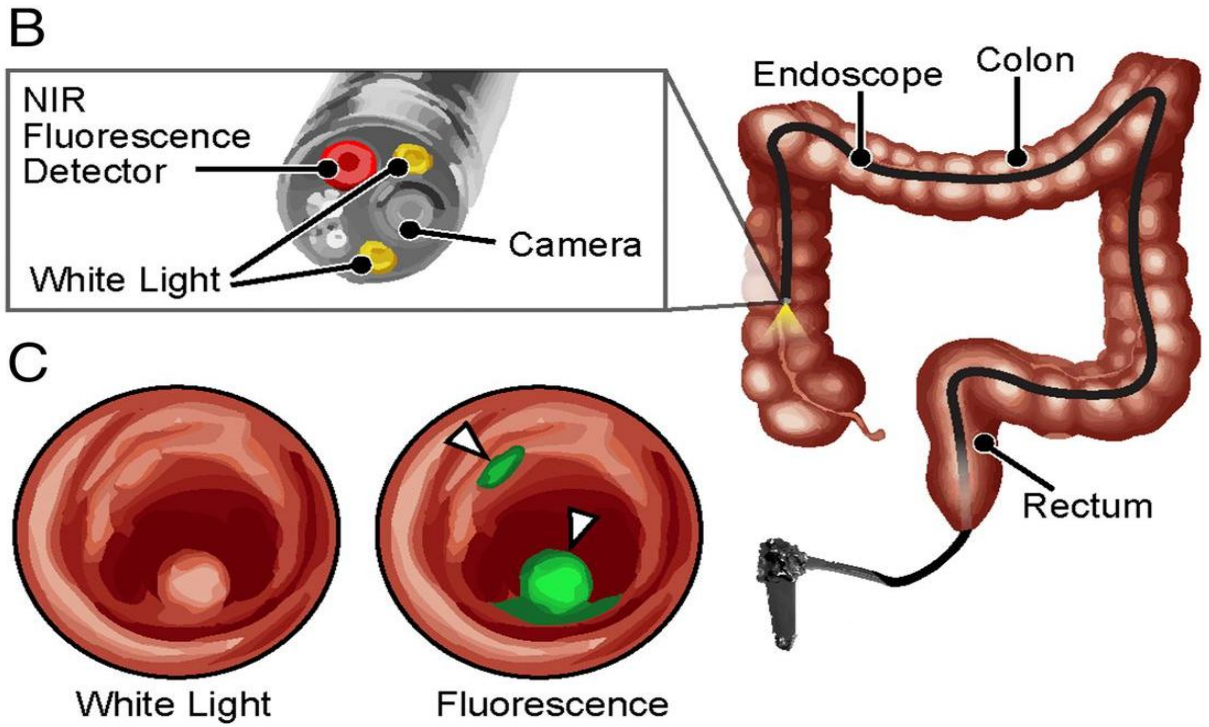
? 纳米颗粒的长期毒性问题

ACS Nano. 2019;13(2):1354-1364.

Adv Funct Mater. 2019;29(51):1904992.

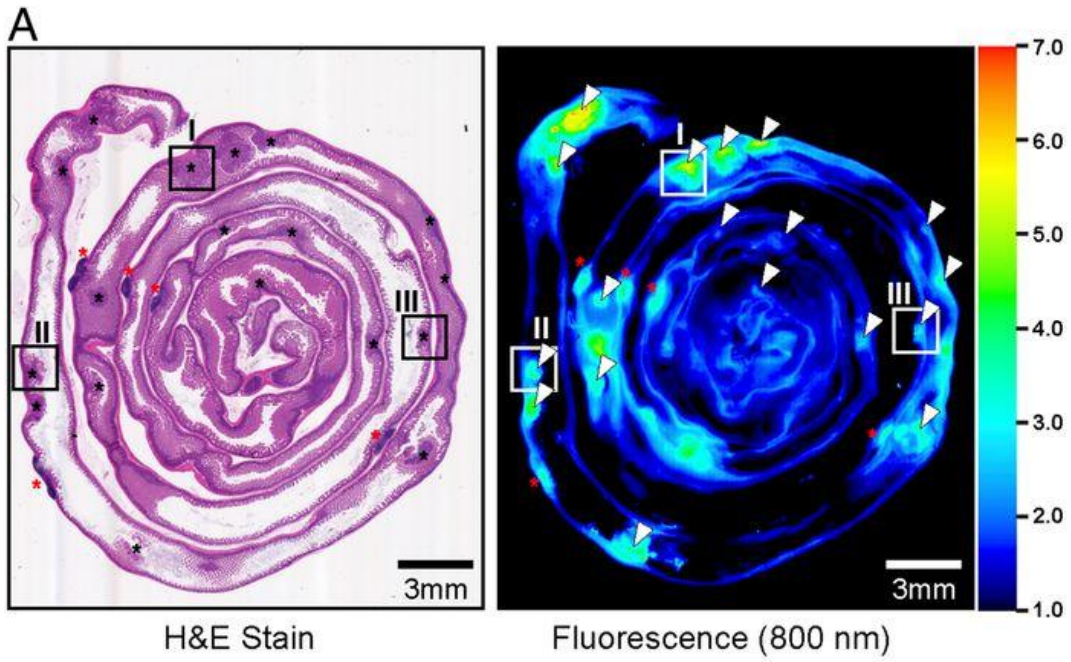
Introduction

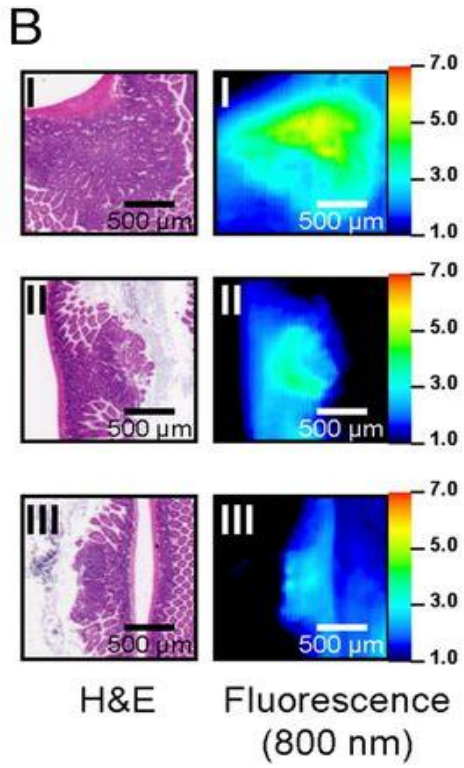


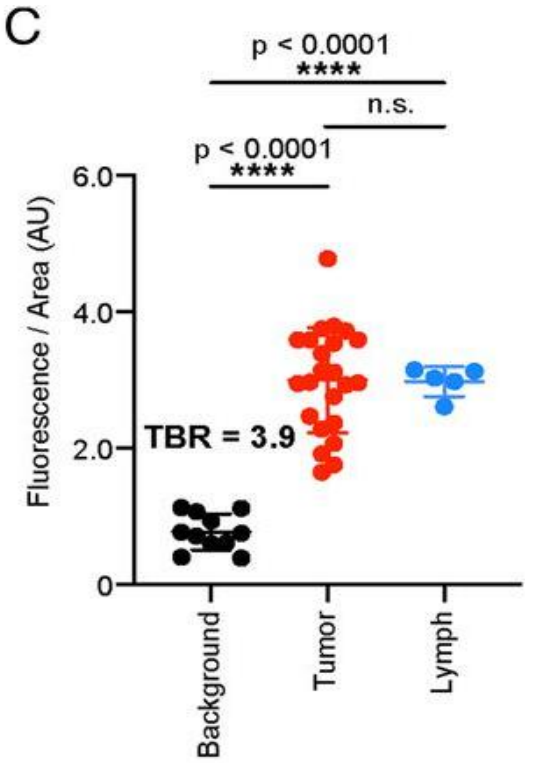


6QC-ICG 由近红外染料 (ICG) 组成，该染料通过肽底物与光学猝灭剂 (QC-1) 偶联，该底物可被多个半胱氨酸组织蛋白酶有效切割

Detection of Intestinal Lesions in Apc$^{min/+}$ Mouse Model of Colorectal Carcinogenesis.

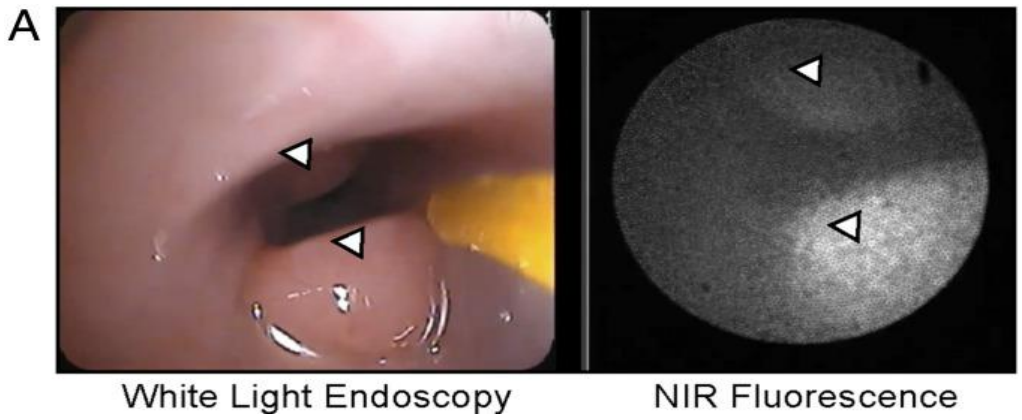


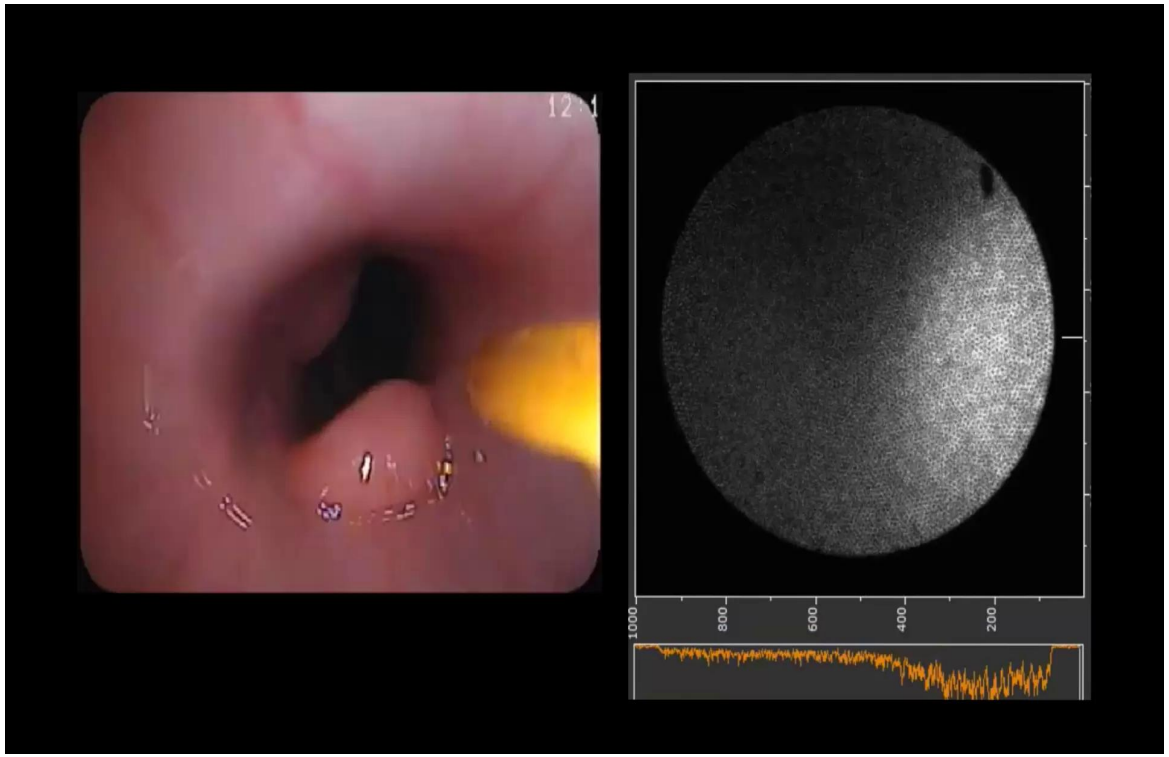


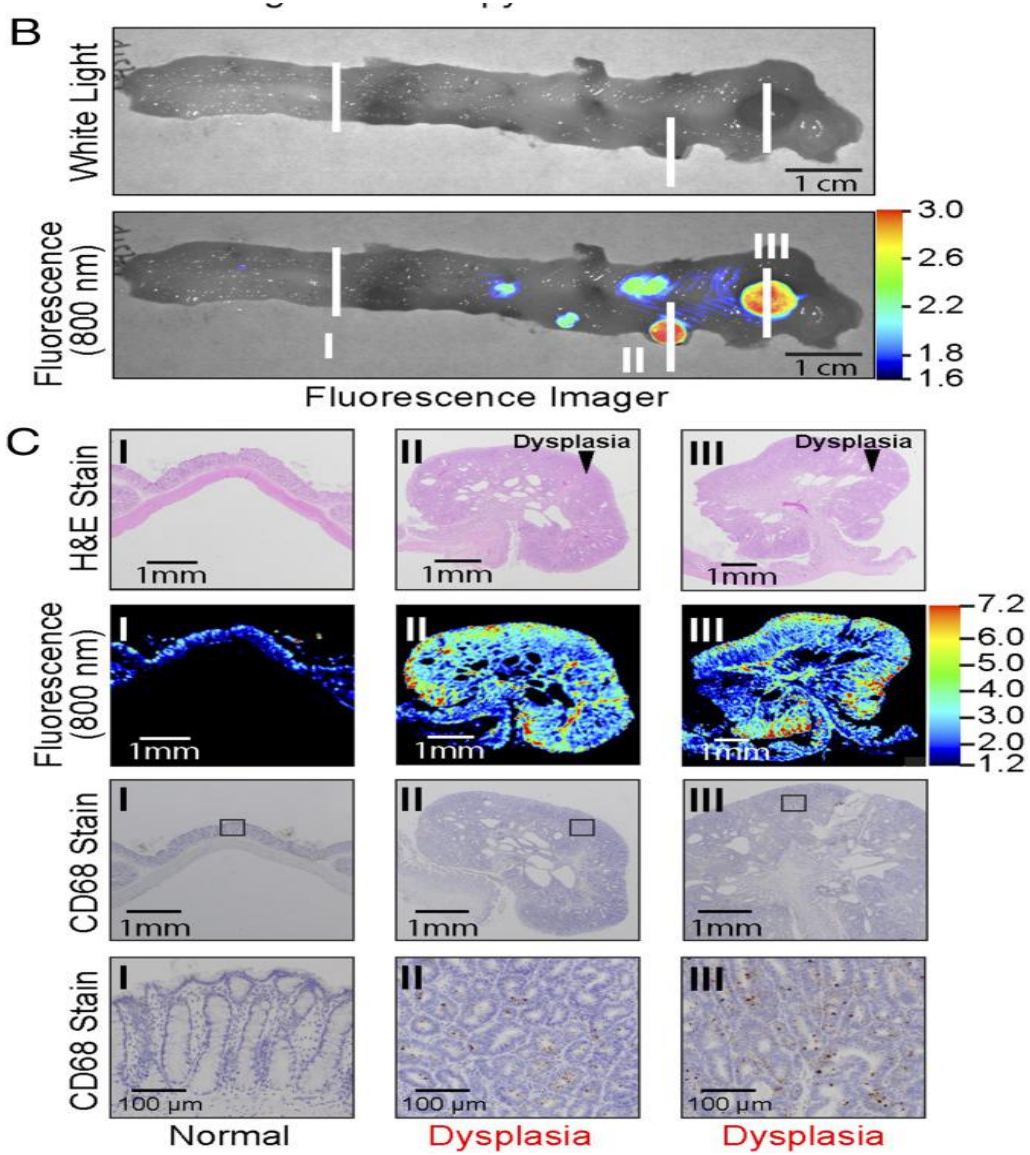


黑色星号表示肿瘤;
红色星号表示淋巴组织。
白色箭头对应于 H&E Stain中的黑色星号

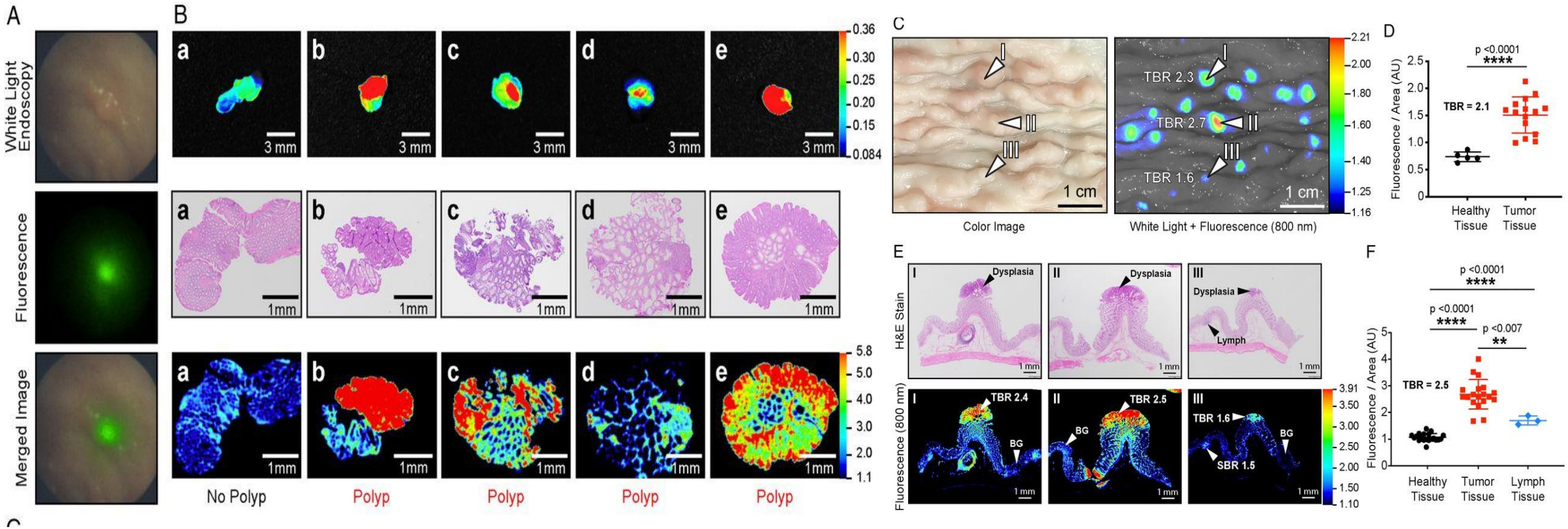
Endoscopic Detection of Colorectal Lesions in Apc$^{Pirc/+}$ Rat Model of Colon Carcinogenesis.





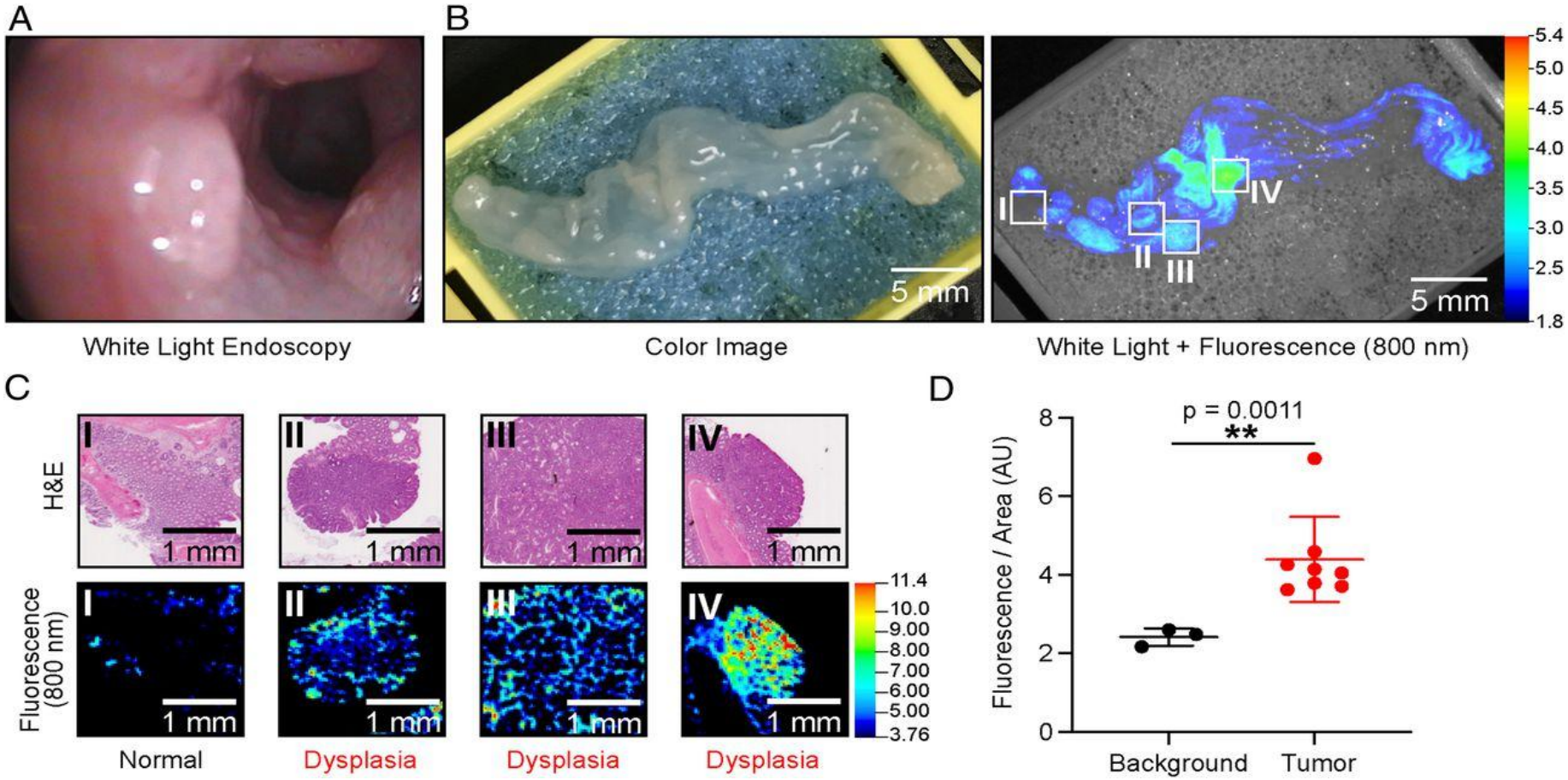


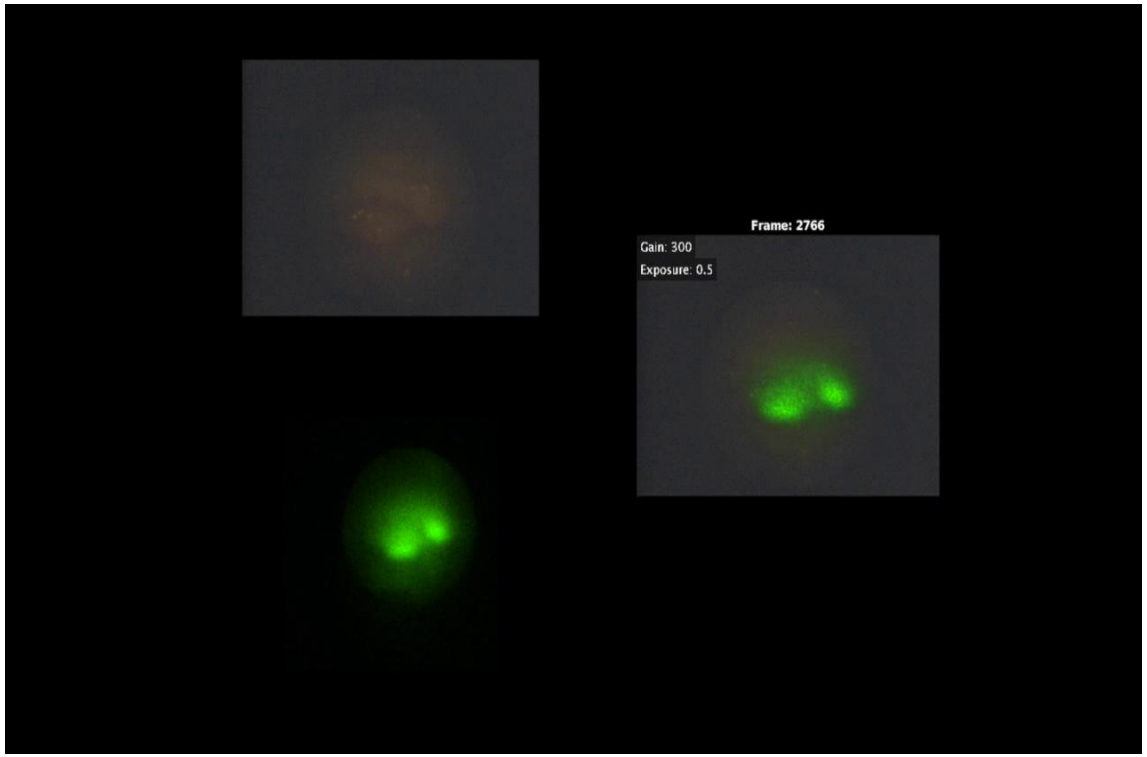
Evaluation of NIRF-Guided Endoscopy in the APC$^{1311/+}$ Porcine Model Using 6QC-ICG.



低荧光信号(TBR < 1.2）对应于正常组织
高荧光信号 (TBR > 2.1) 对应于发育不良的存在

Evaluating 6QC-ICG in a Combined Model of GPR15 Knockout and Azoxymethane-Dextran Sulfate Sodium Mouse Model of Inflammation-Induced Carcinogenesis.



Result

Movie in pig