

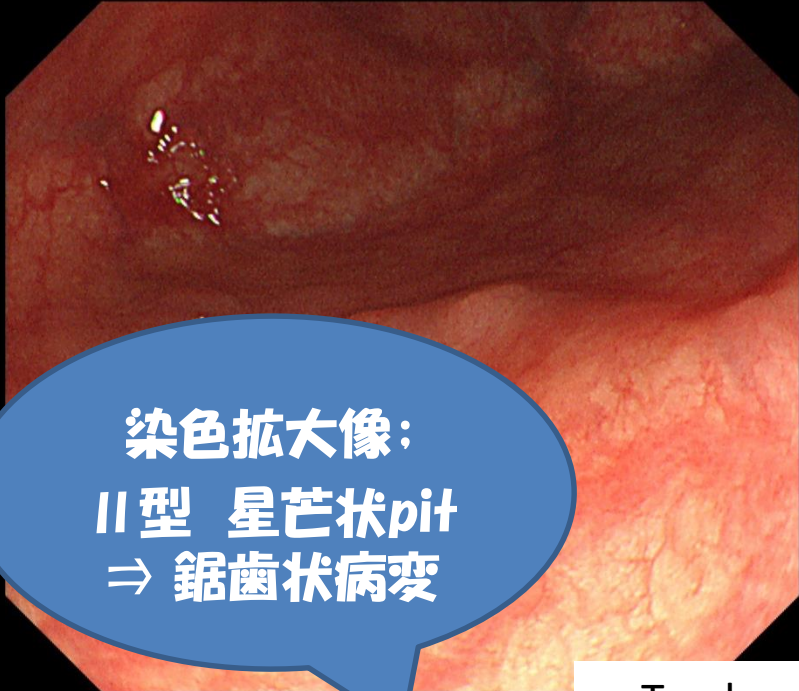
【症例】80代、女性

【現病歴】健診で便潜血陽性を指摘され、大腸内視鏡検査が施行された。その際、肛門縁から60 cmの横行結腸に25 mm大の laterally spreading tumorが認められた。拡大内視鏡観察でII型 pit構造が認められ、鋸歯状病変としてESDにて一括切除された。

【既往歴】肺血栓塞栓症

【家族歴】妹および長男 癌 (詳細不明)

【問題点】組織診断

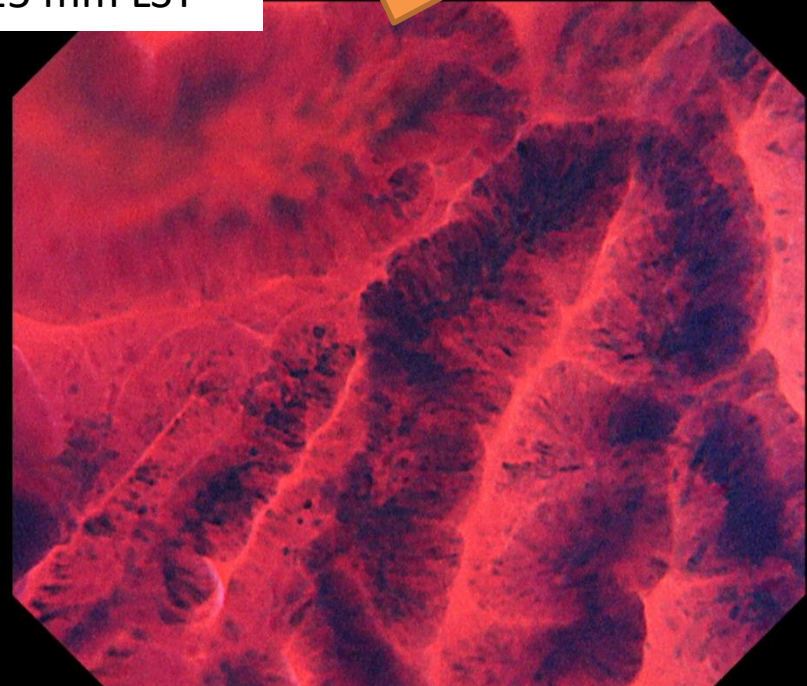
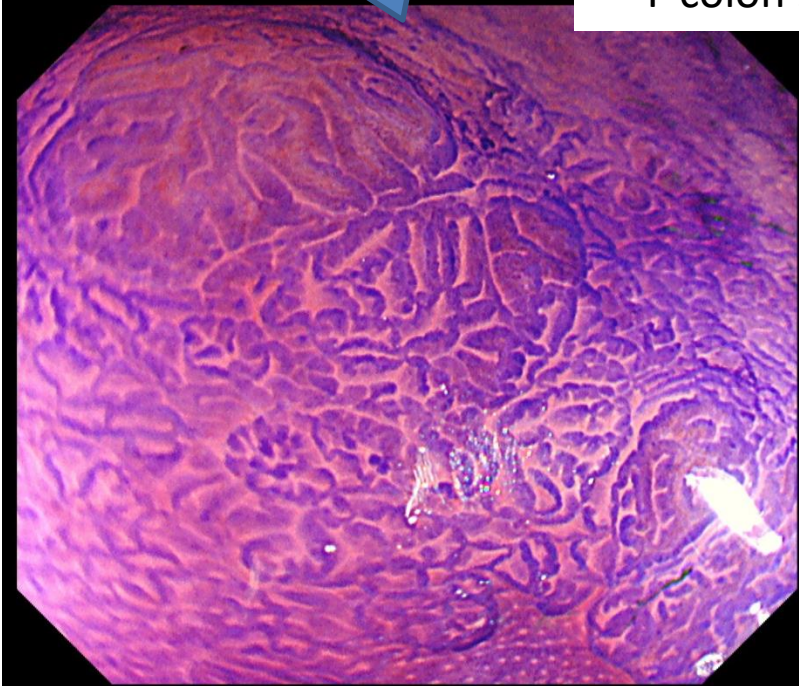


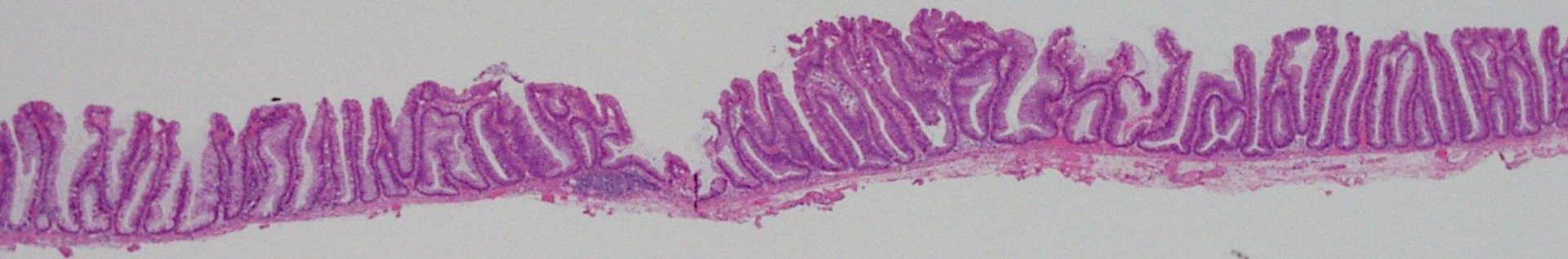
染色拡大像：
II型 星芒状pit
⇒ 鋸齒状病変

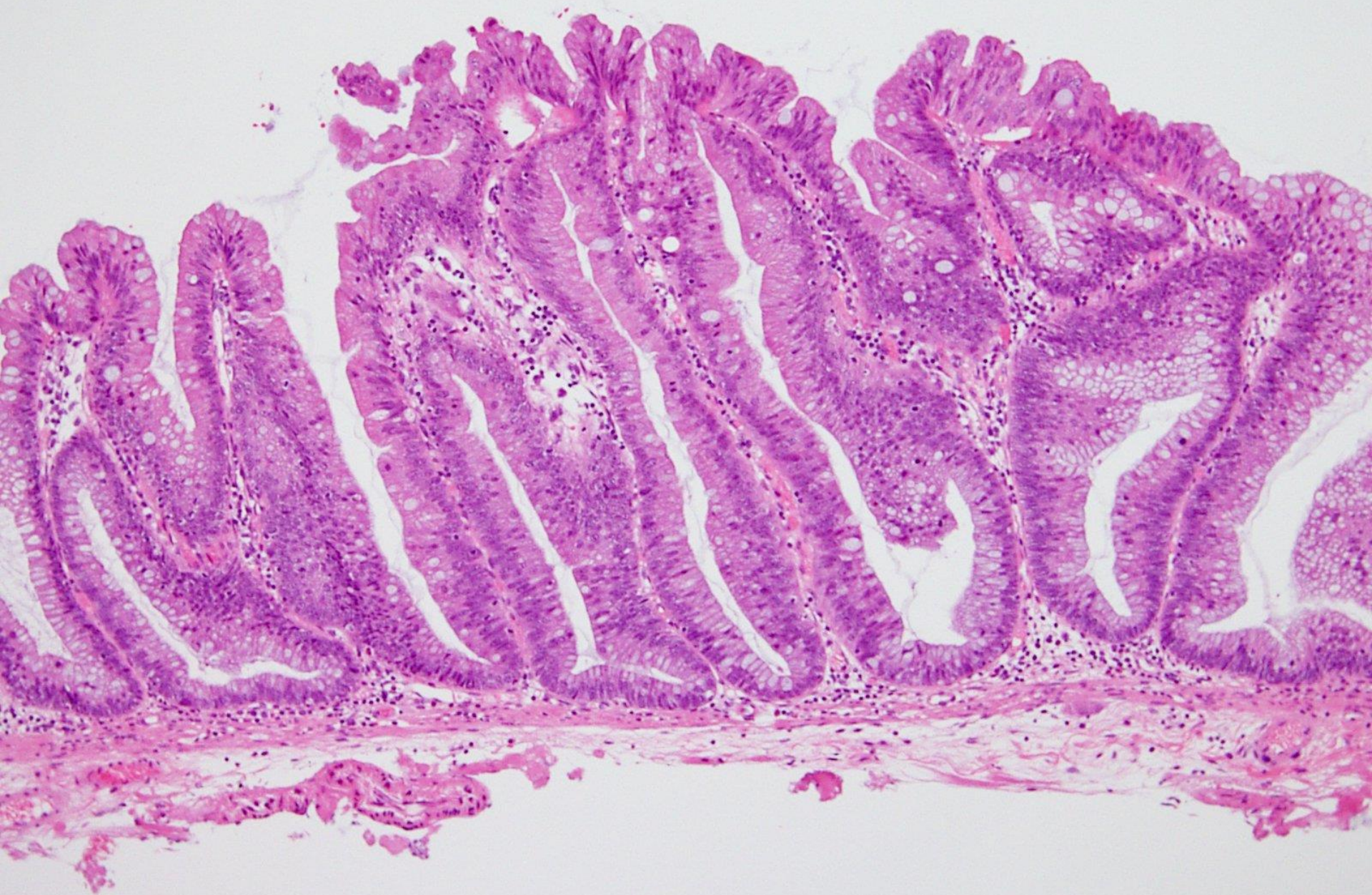


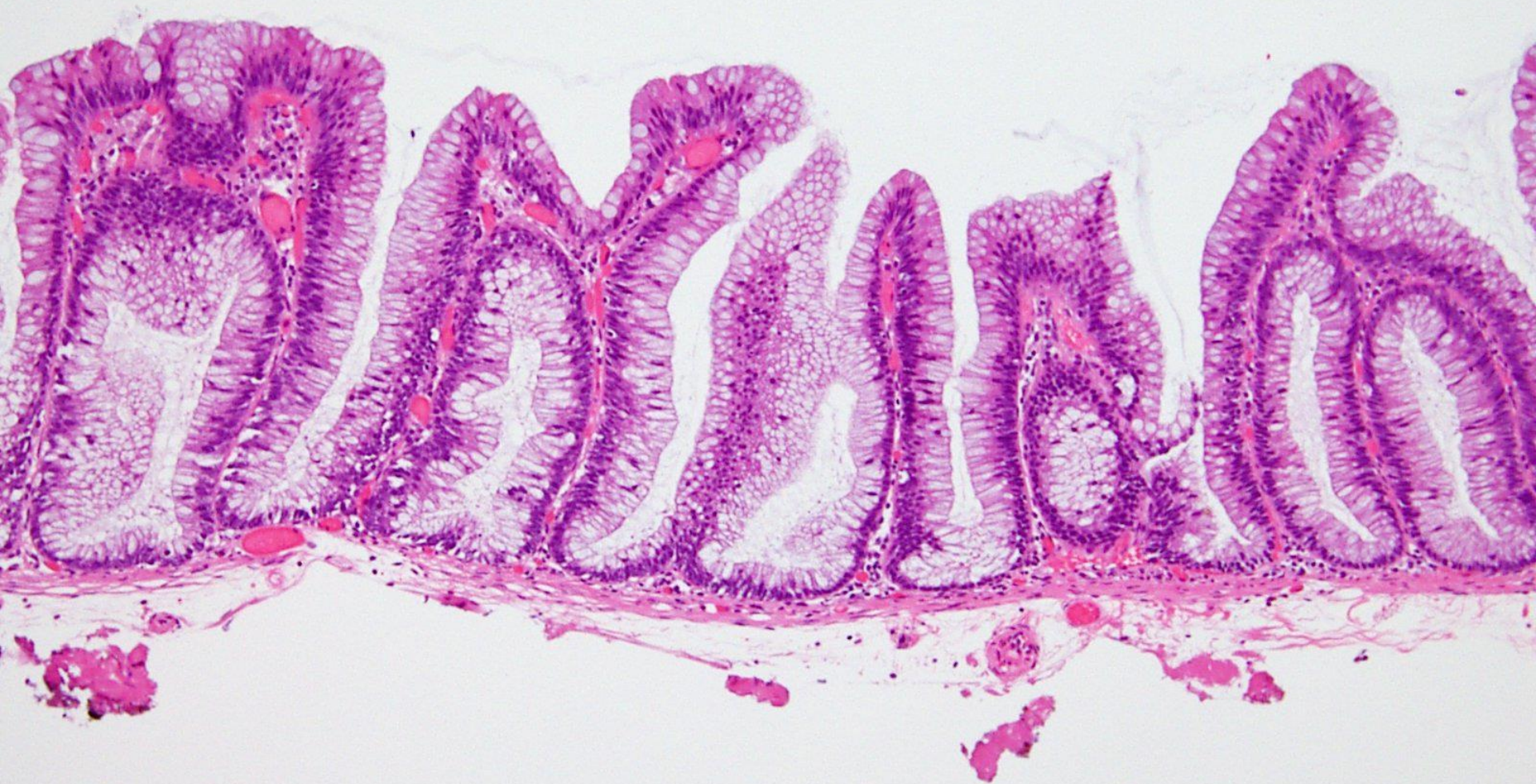
Endocyte Scope：
核が基底膜に染まってる、
大小不同なし

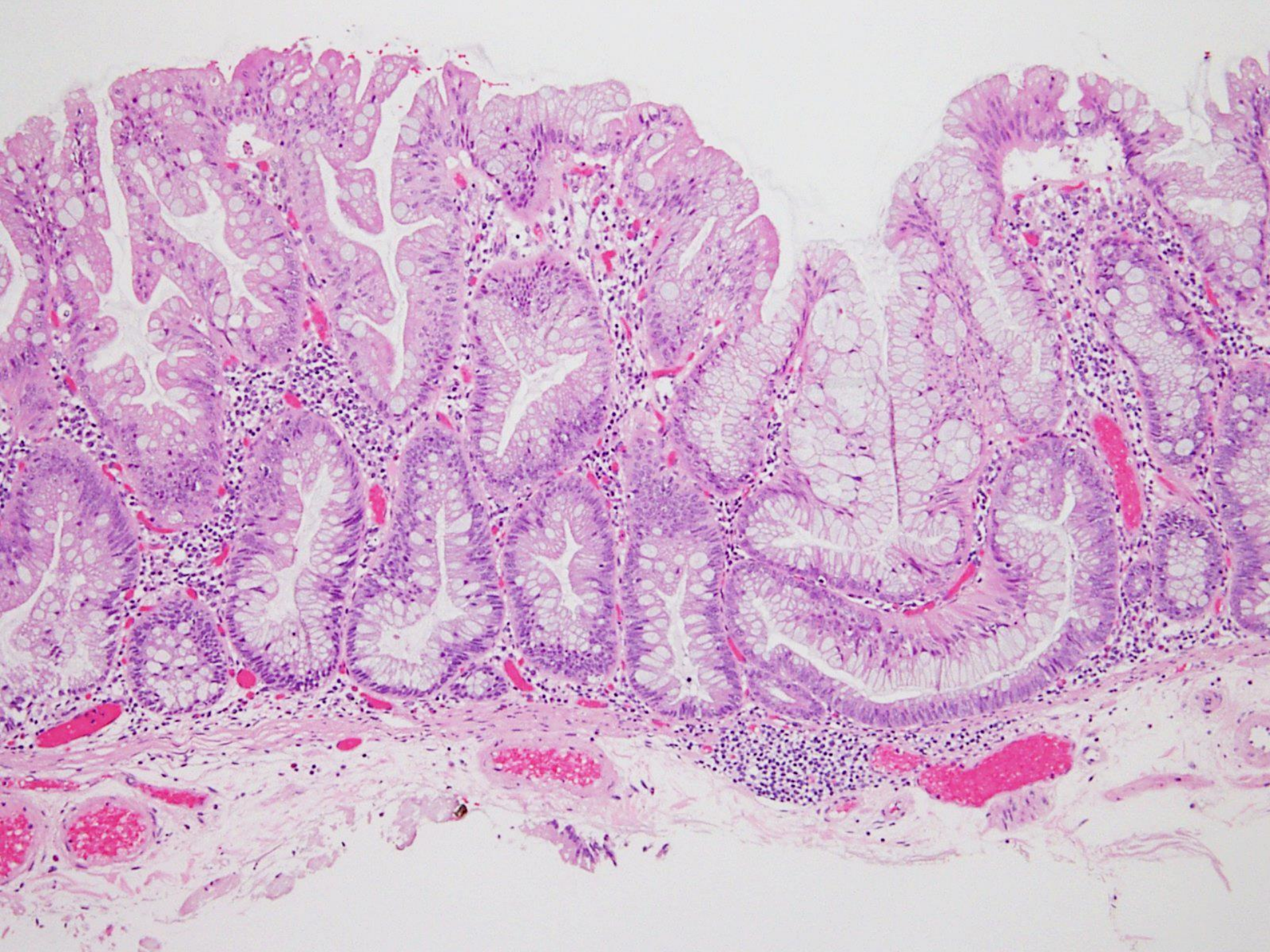
T-colon 25 mm LST

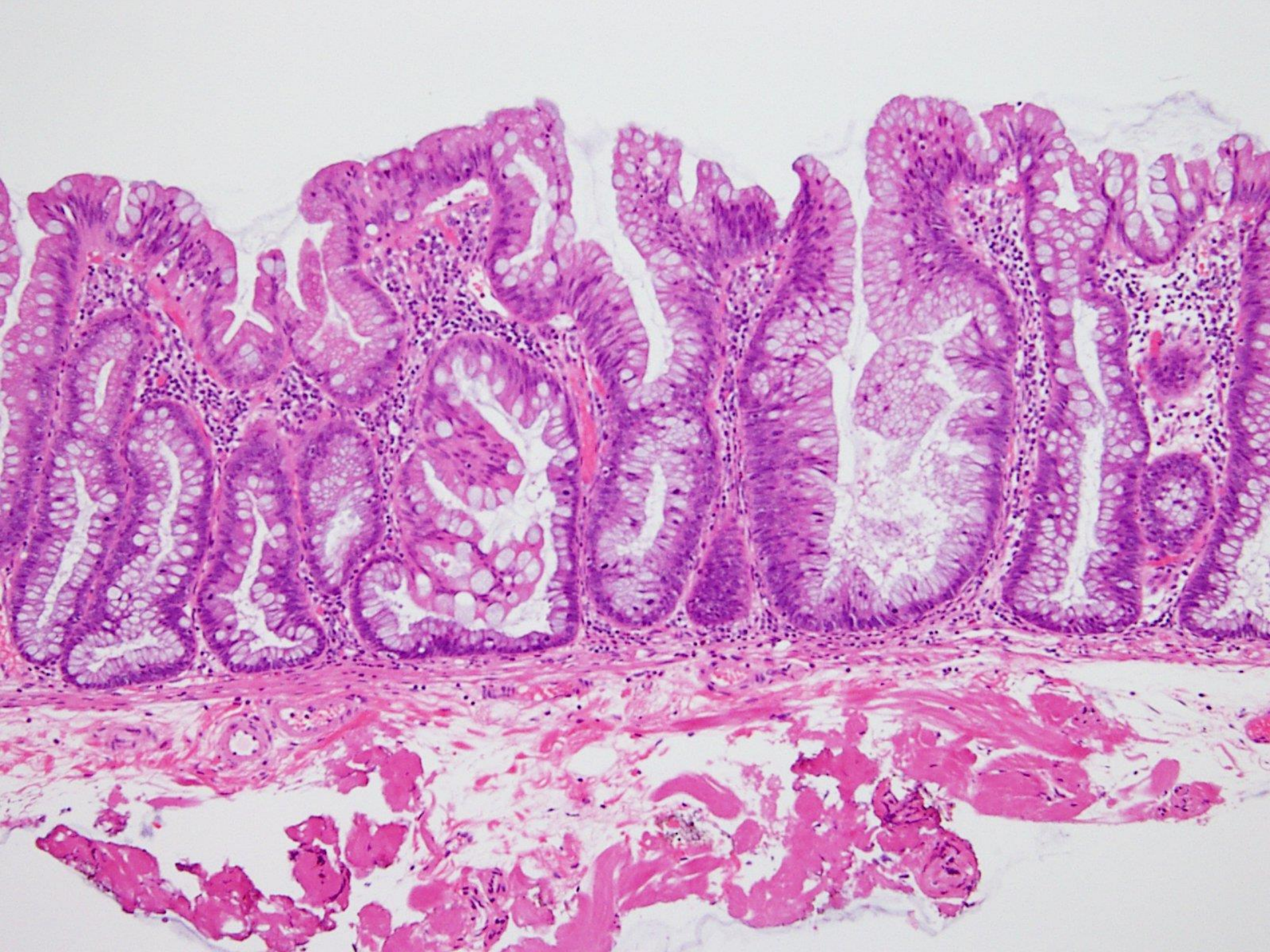


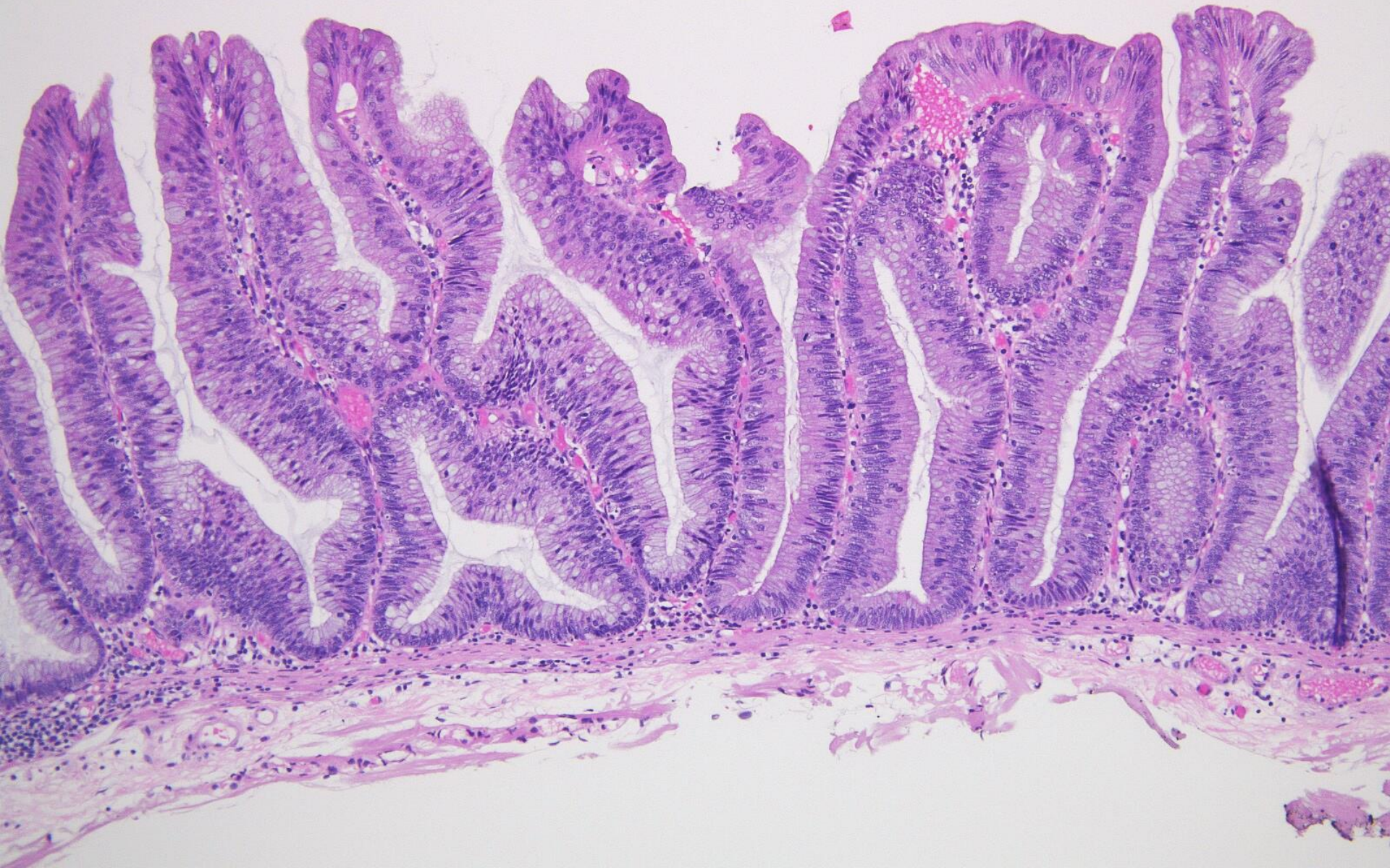


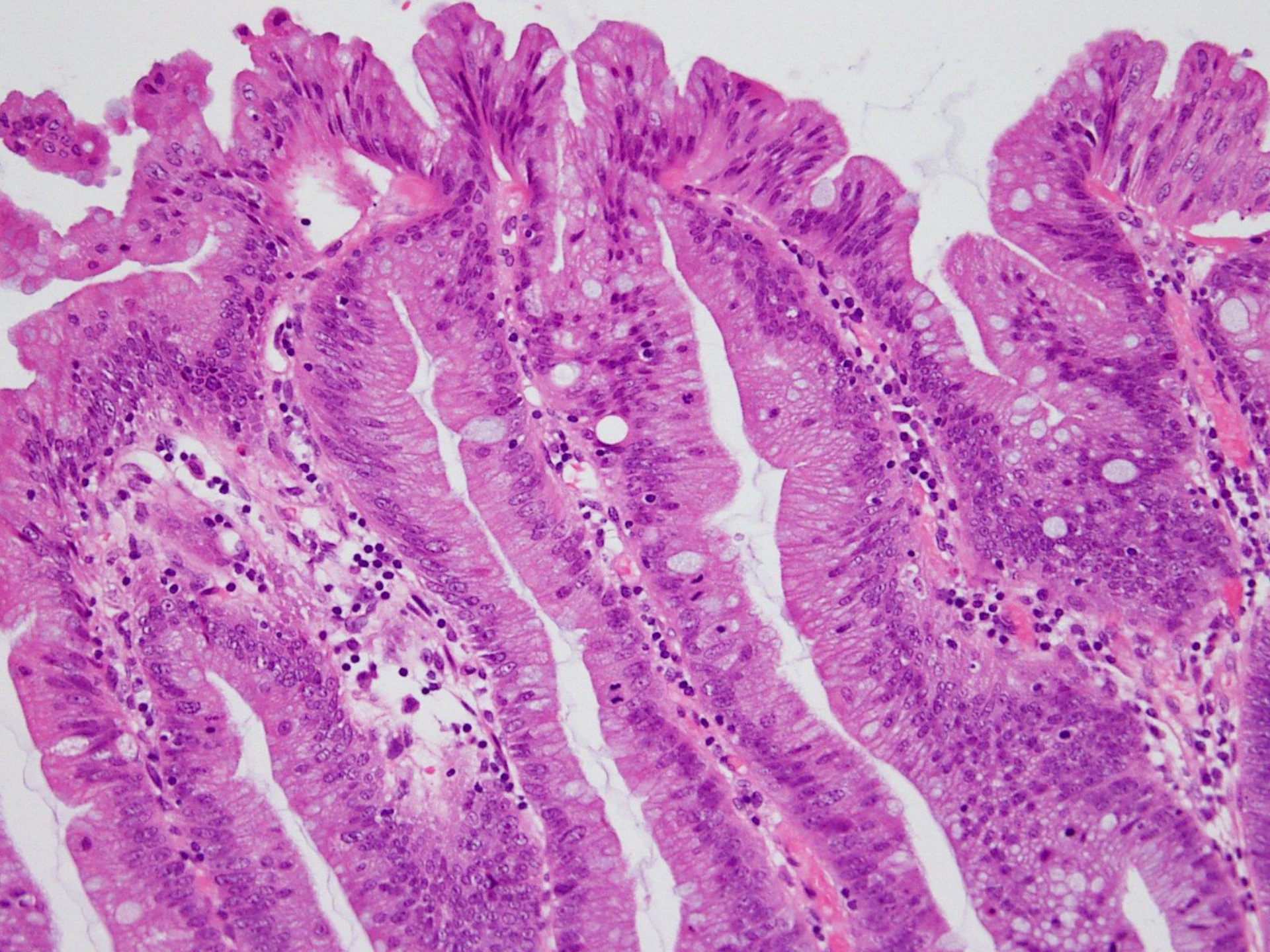












Speaker's Diagnosis;

Serrated lesion, NOS

よくわかりません...

どれか。。。

- Hyperplastic polyp
 - microvesicular type
 - goblet cell type
 - mucin poor type
- Sessile serrate adenoma/polyp **BRAF**
- Sessile serrated adenoma with cytological dysplasia **BRAF**
- Serrated tubulovillous adenoma **KRAS**
- Traditional serrated adenoma **BRAF** > **KRAS**
 - Filiform TSA **BRAF** > **KRAS**
 - Flat TSA
 - Mucin-rich variant of TSA **BRAF**
- Superficially serrated adenoma **KRAS**

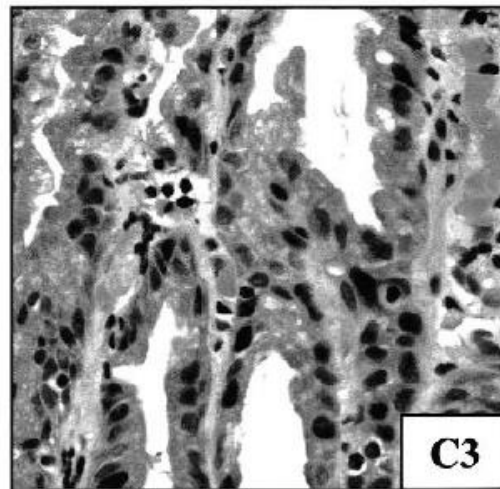
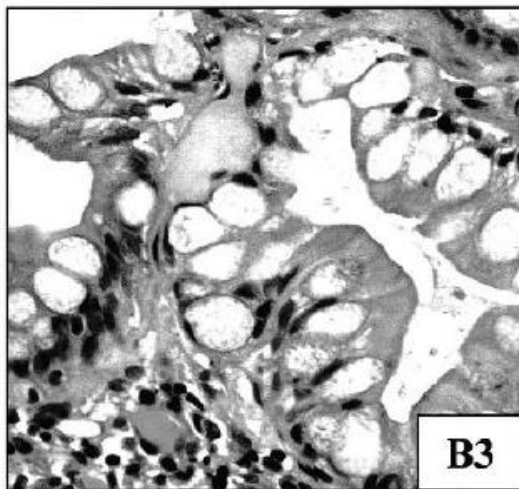
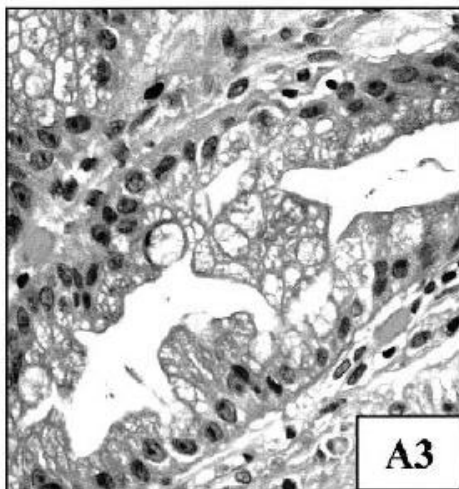
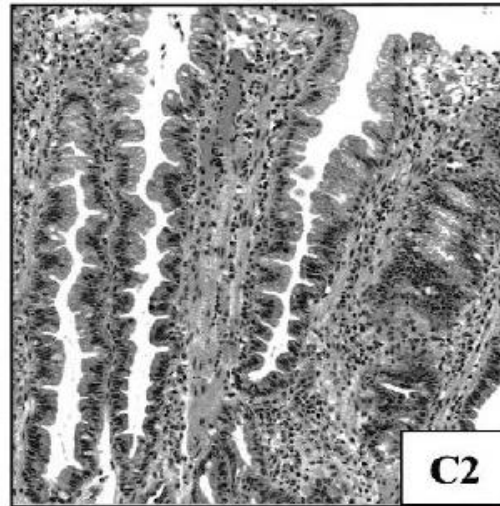
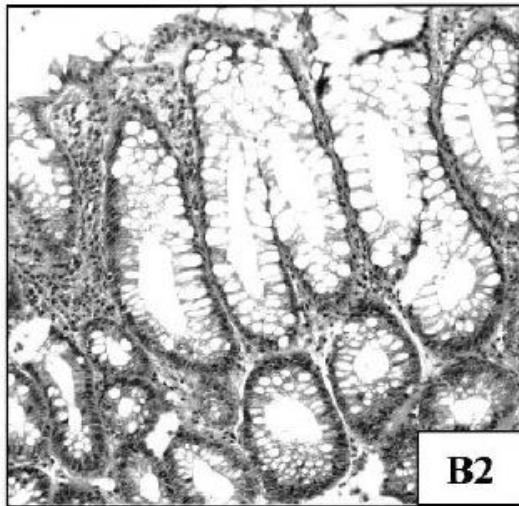
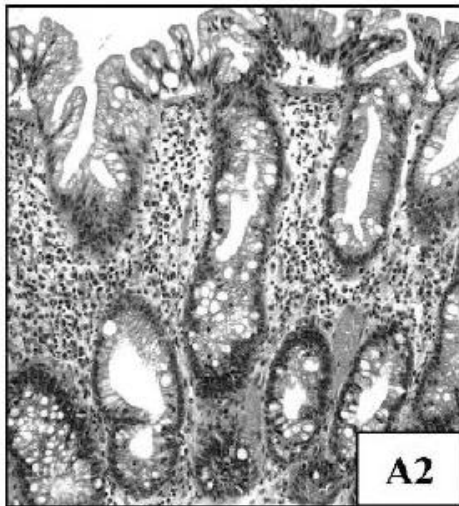
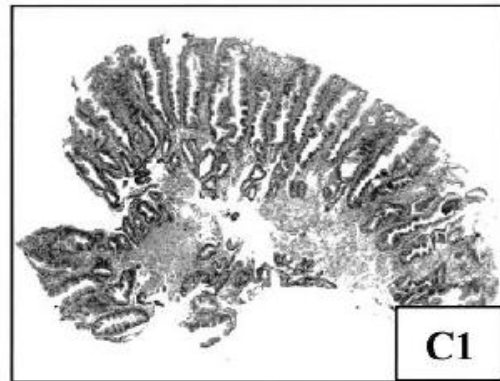
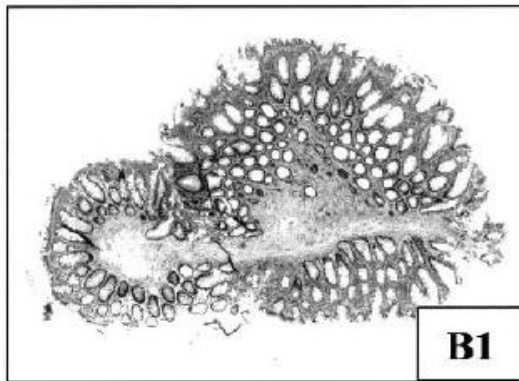
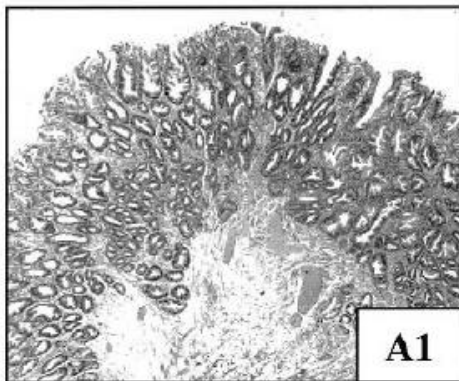
Hyperplastic polyp

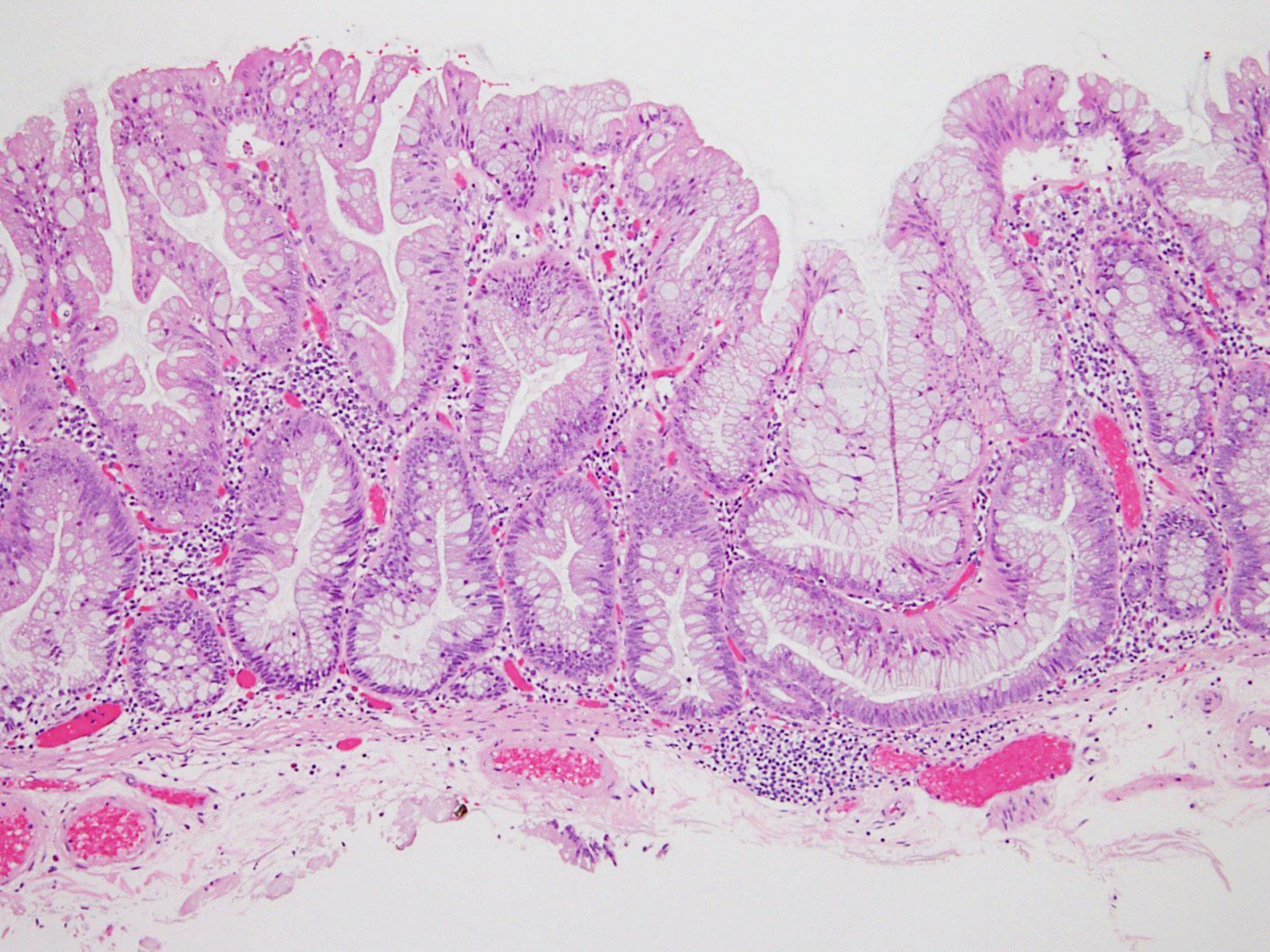
腺管の延長・拡張を伴い、管腔側腺管に上皮の鋸歯状増生がみられるのが特徴である。～
(大腸癌取扱い規約第9版)

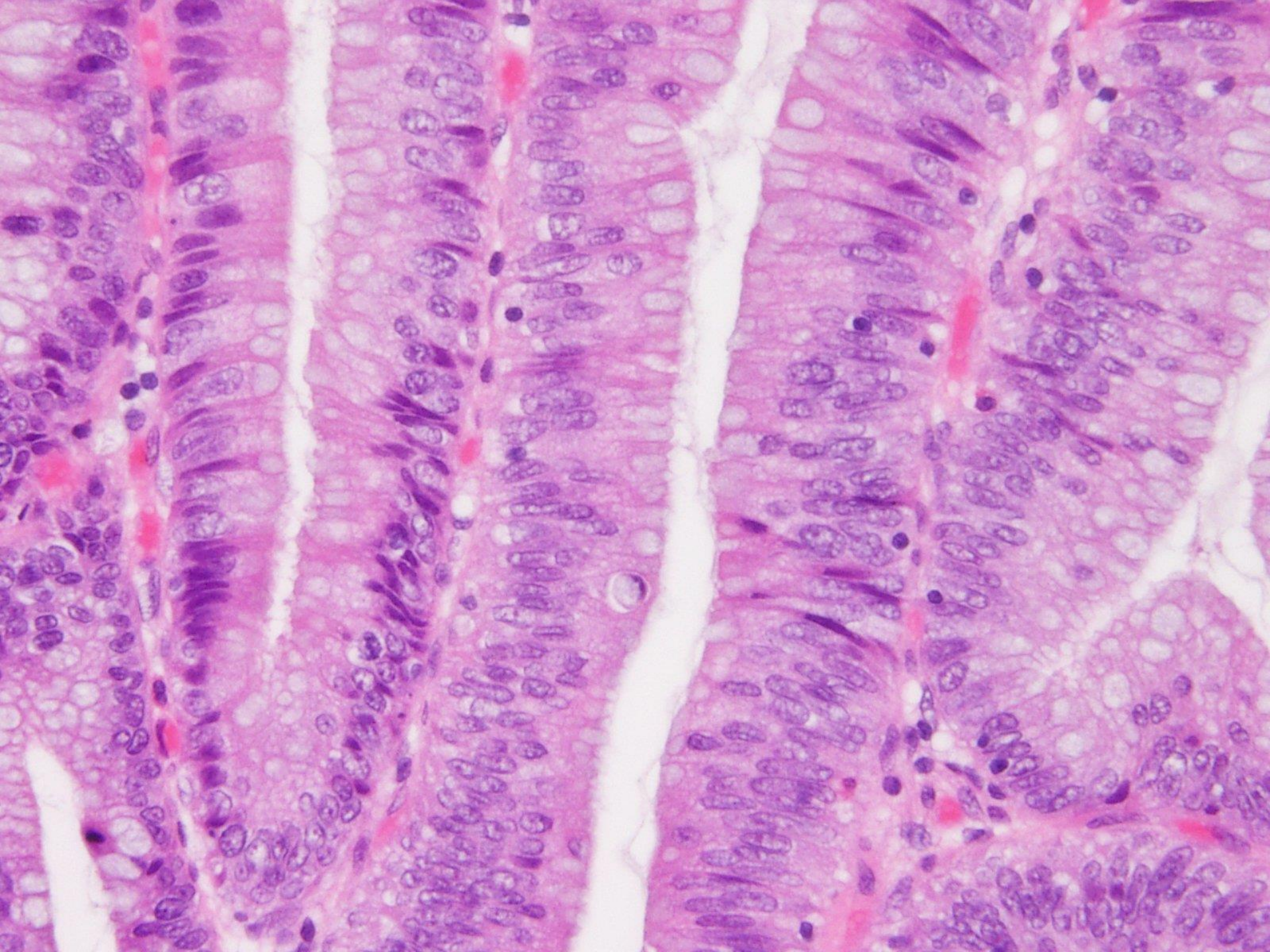
Am J Surg Pathol 27(1): 65-81, 2003

So-called Snover classification

- HP, microvesicular type (MVHP)
- HP, goblet cell type (GCHP)
- HP, mucin poor type (MPHP)







Sessile serrated adenoma/polyp

大腸癌取扱い規約第9版 (2018)

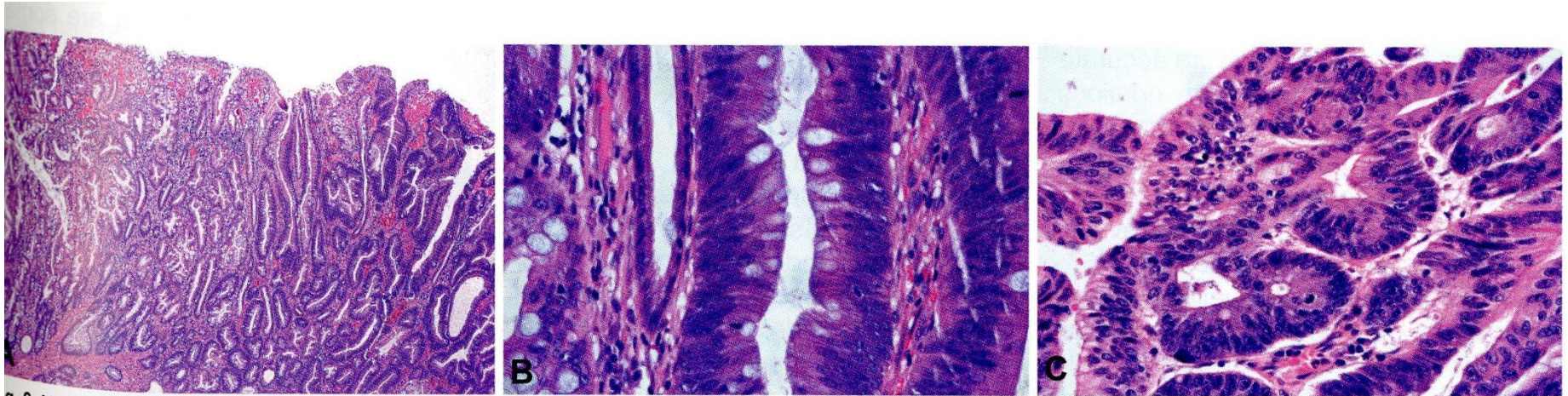
明らかな腫瘍とは判定できない鋸歯状病変で、

- ① 陰窩の拡張
- ② 陰窩の不規則分岐
- ③ 陰窩底部の水平方向への変形
(逆T字、L字型陰窩の出現)

2項目以上を、
病変の10%以上の領域に認める

SSA/P with cytological dysplasia

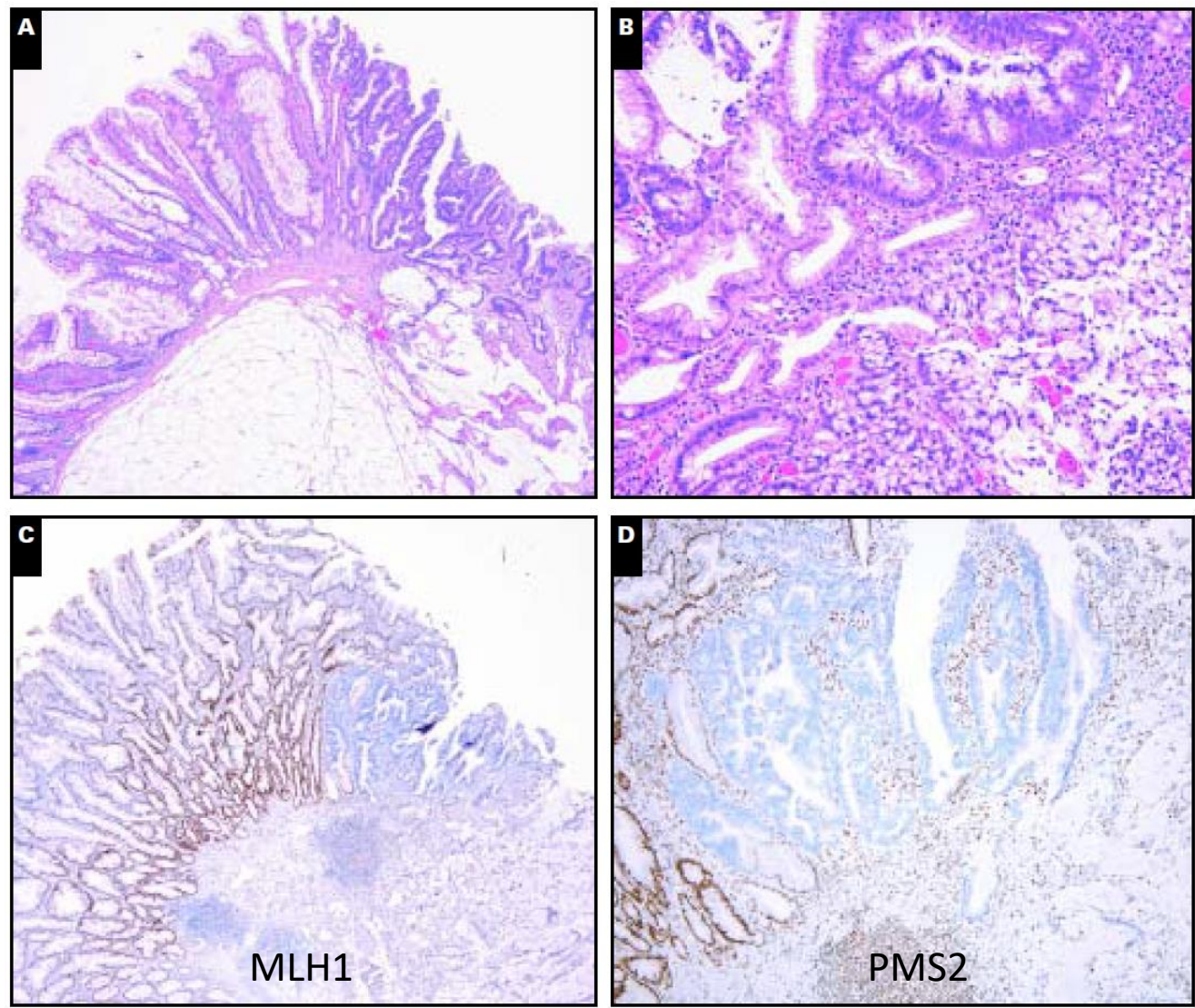
As for SSA/P but with more proliferation in cytologically dysplastic areas



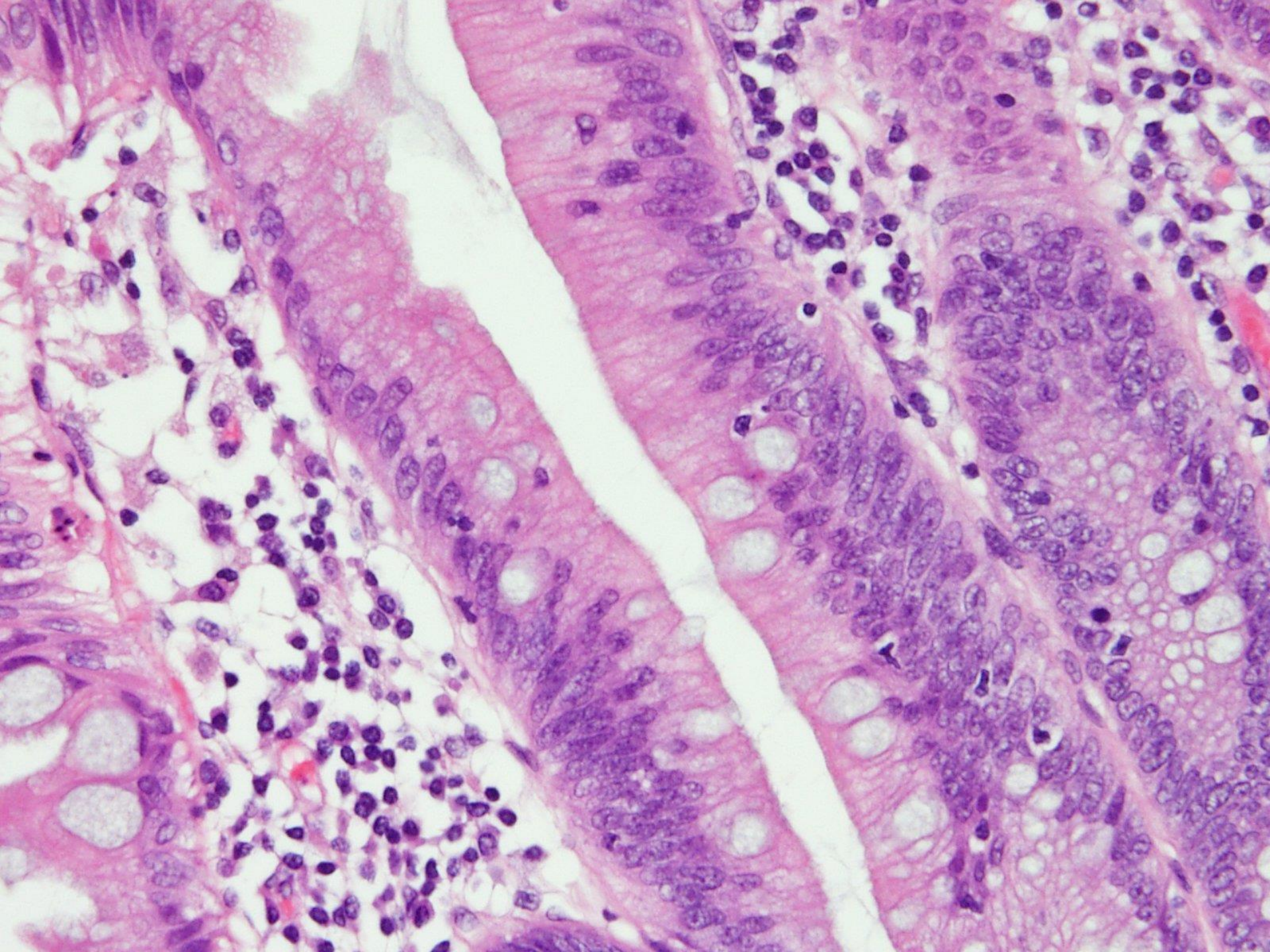
Sessile Serrated Adenomas With Low- and High-Grade Dysplasia and Early Carcinomas

Am J Clin Pathol 2006;126:564-571
DOI: 10.1309/C7JE8BVL8420V5VT

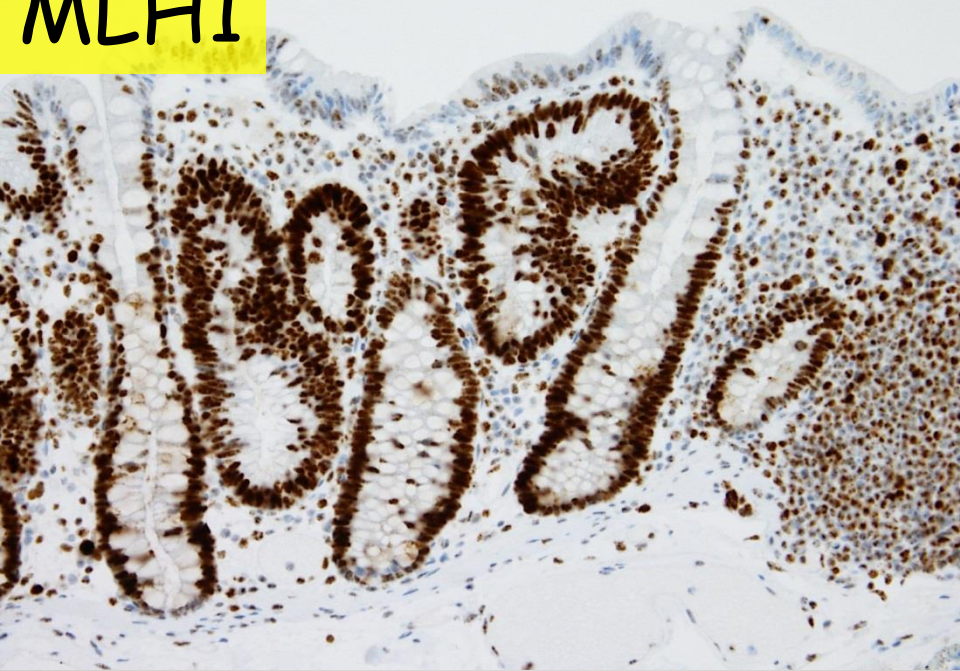
An Immunohistochemical Study of Serrated Lesions "Caught in the Act"



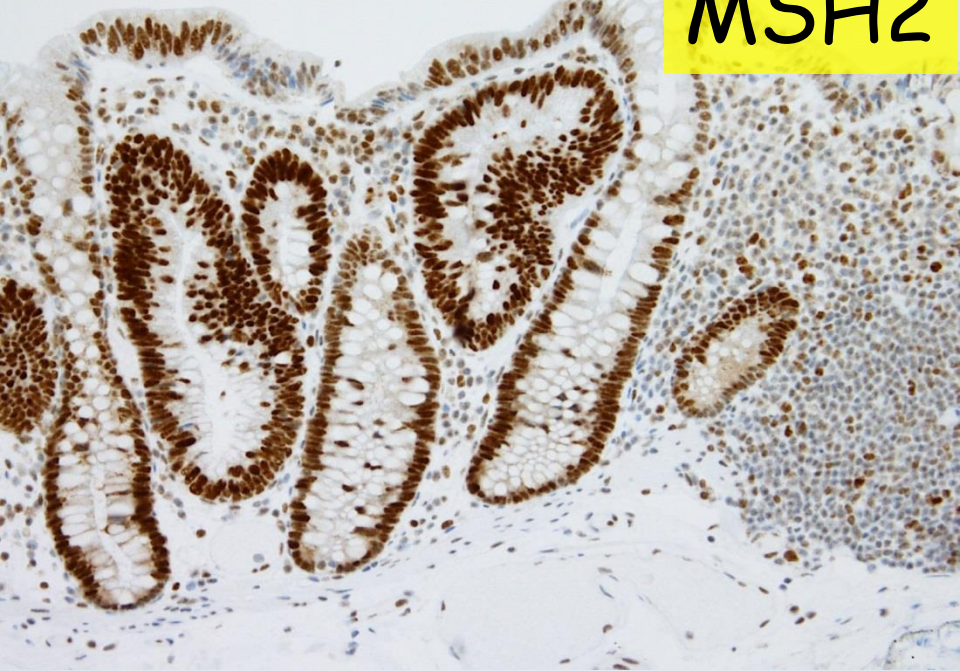




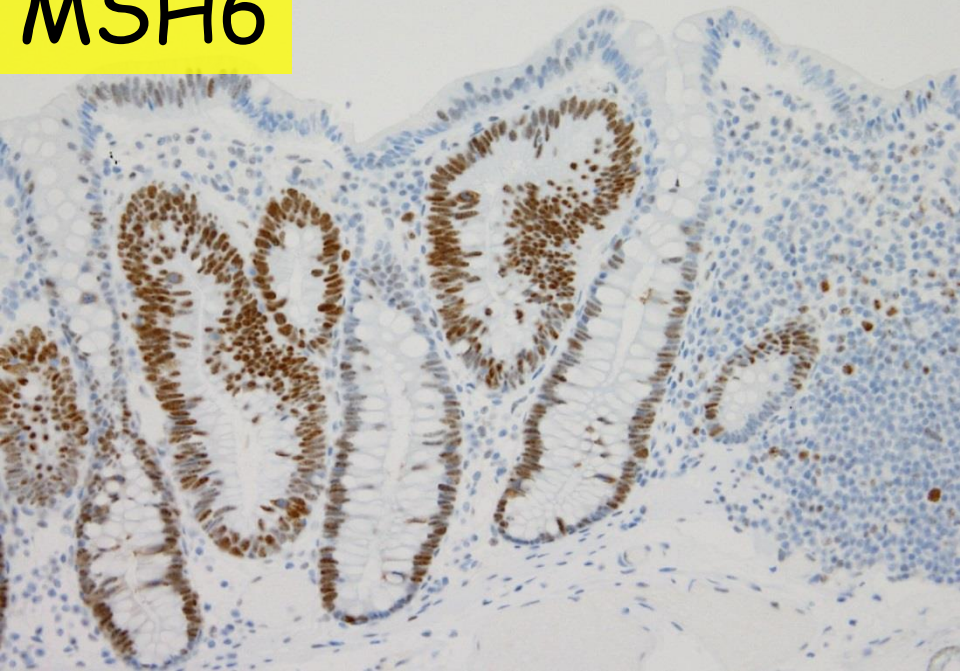
MLH1



MSH2



MSH6

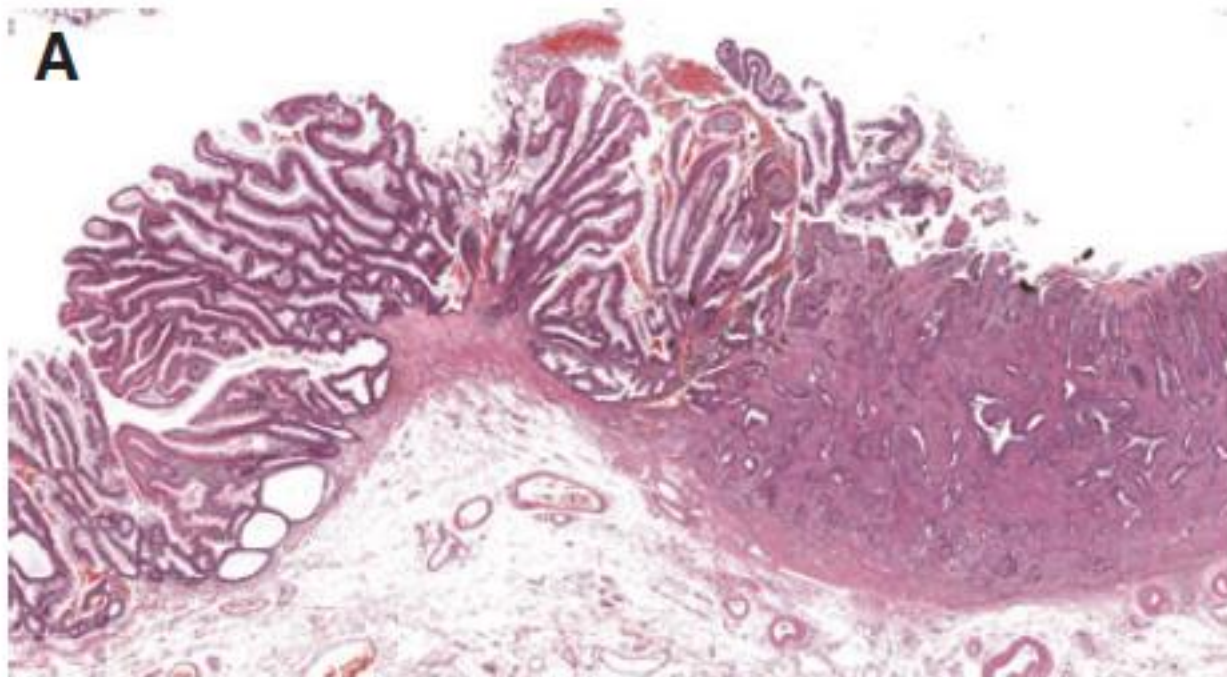


PMS2



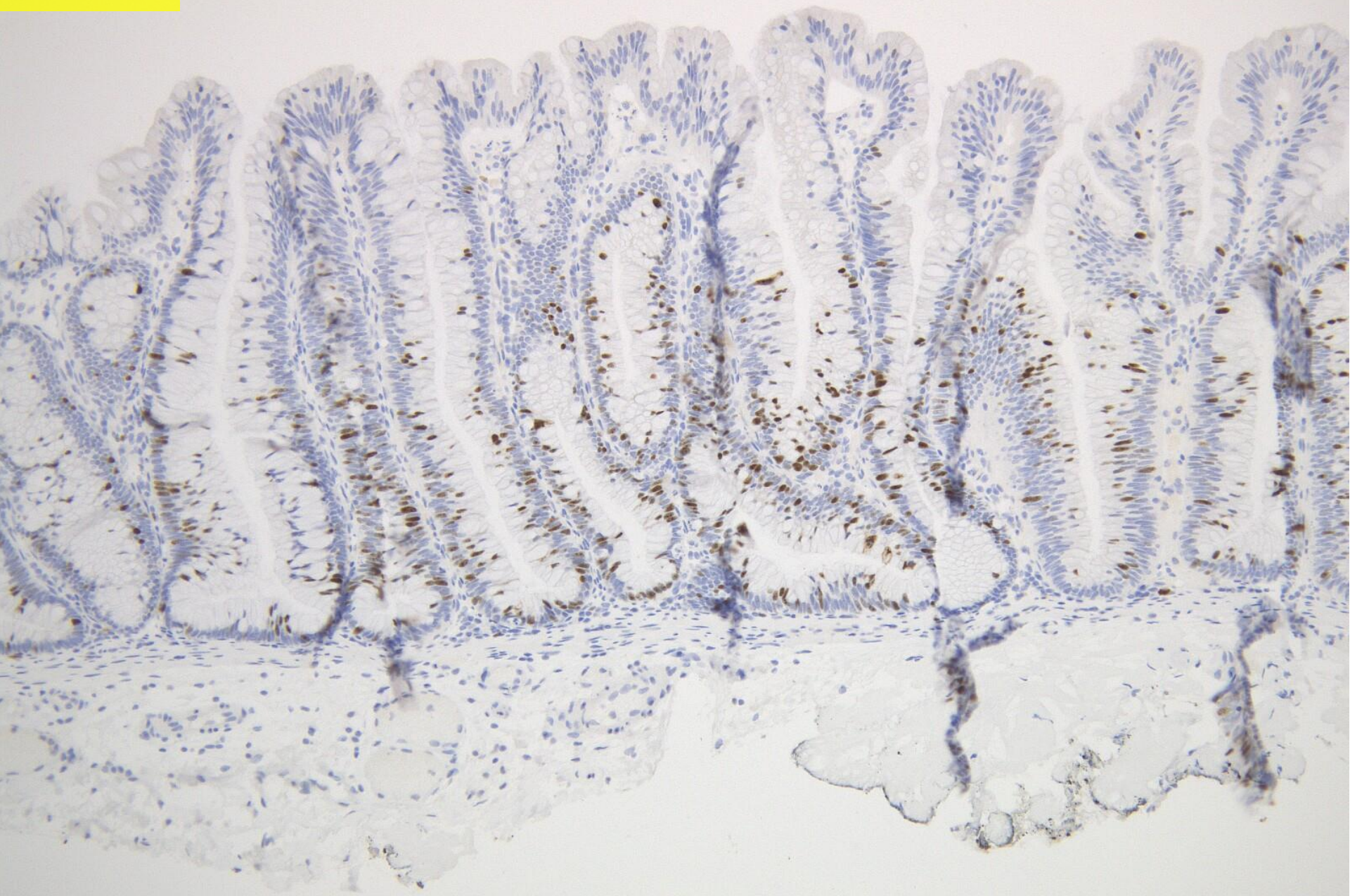
Serrated tubulovillous adenoma of the large intestine

Mark Bettington,^{1,2,3} Neal Walker,^{2,3} Christophe Rosty,^{2,3,4} Ian Brown,^{3,5}
Andrew Clouston,^{2,3,5} Diane McKeone,¹ Sally-Ann Pearson,¹ Kerenaftali Klein,⁶
Barbara Leggett^{1,2,7} & Vicki Whitehall^{1,2,8}



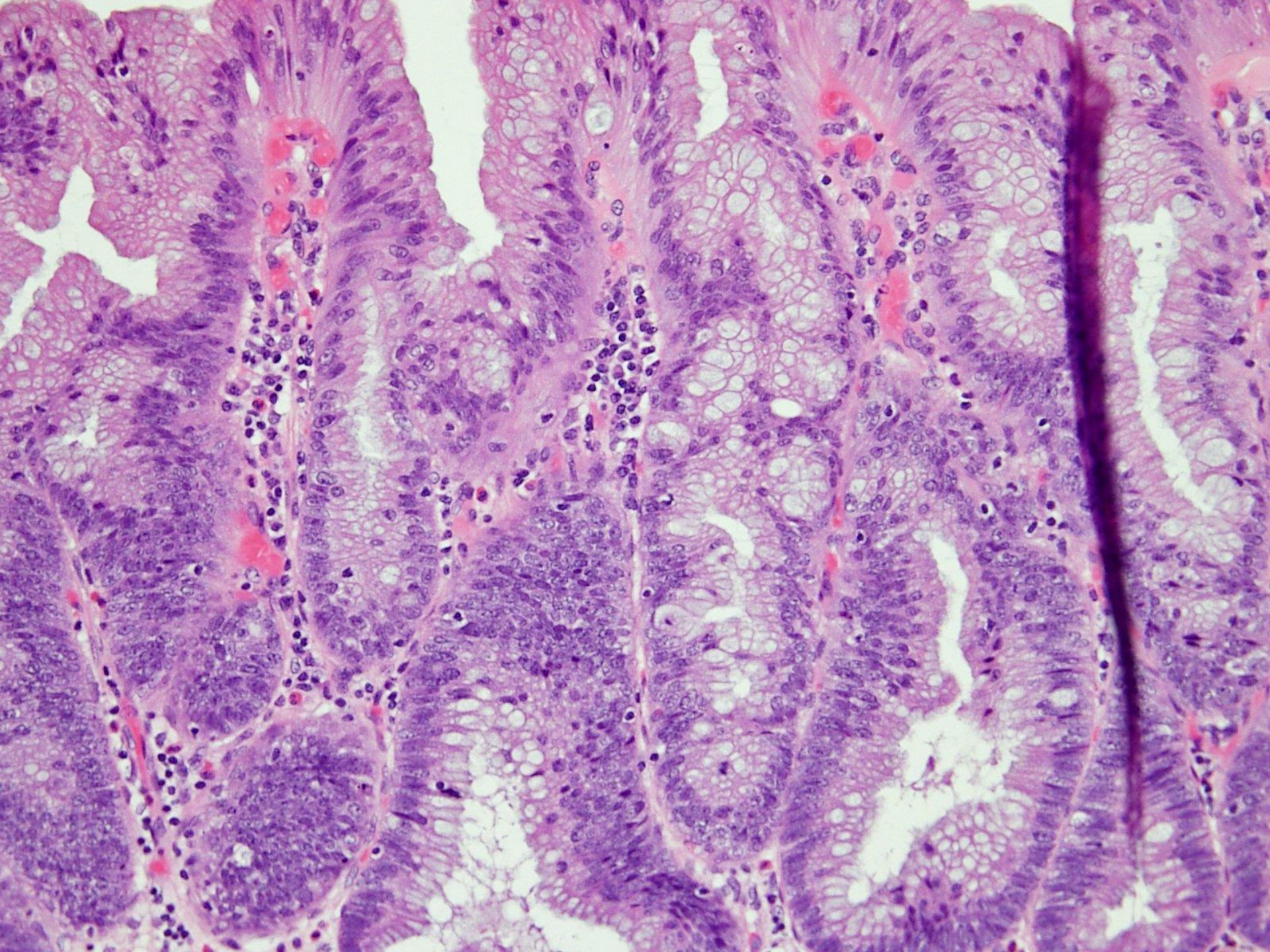


Ki-67



Traditional serrated adenoma

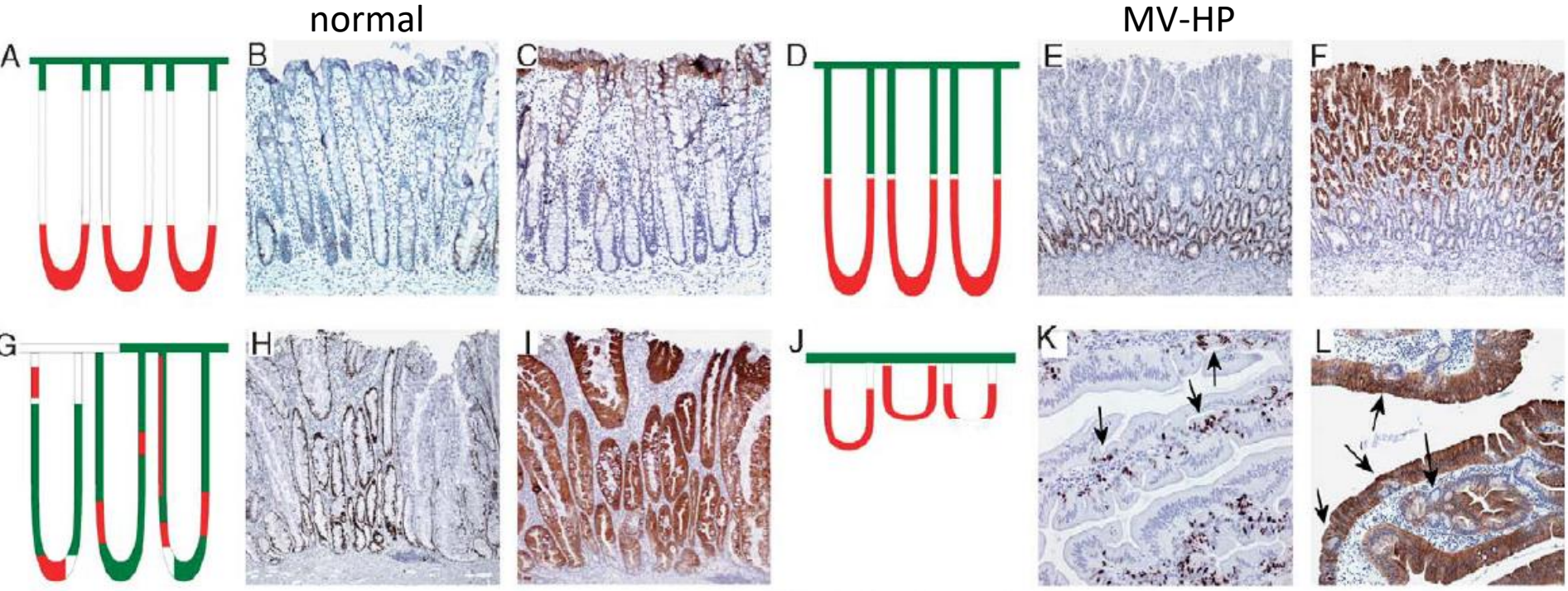
- 腺管の上半部で上皮が鋸歯状形態を示す点で過形成性ポリープに類似するが、それとは異なり、核の腫大や偽重層化、核分裂像が表層部にも出現し、杯細胞の減少、細胞質の好酸性化などを示す。SSA/PやHPと区別する特徴的な所見として、芽出像あるいは異所性陰窩(ectopic crypt formation, ECF)と呼ばれる組織像がある。(大腸癌取扱い規約第9版)
 - conventional TSA (BRAF > KRAS)
 - filiform TSA (突出する絨毛状構造が細長い形状を示す)
 - flat TSA (隆起の高さが周囲正常粘膜の2倍以下)
 - mucin-rich TSA (杯細胞が全体の50%以上)



Sessile Serrated Adenoma (SSA) vs. Traditional Serrated Adenoma (TSA)

(*Am J Surg Pathol* 2008;32:21–29)

Emina Emilia Torlakovic, MD, PhD, Jose D. Gomez, MD,†
 David K. Driman, MBChB, FRCPC,‡ Jeremy R. Parfitt, MD,‡ Chang Wang, MD,*
 Tama Benerjee, MD,* and Dale C. Snover, MD§*

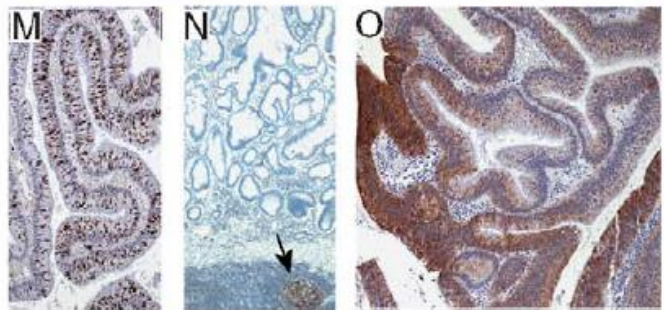


SSA/P

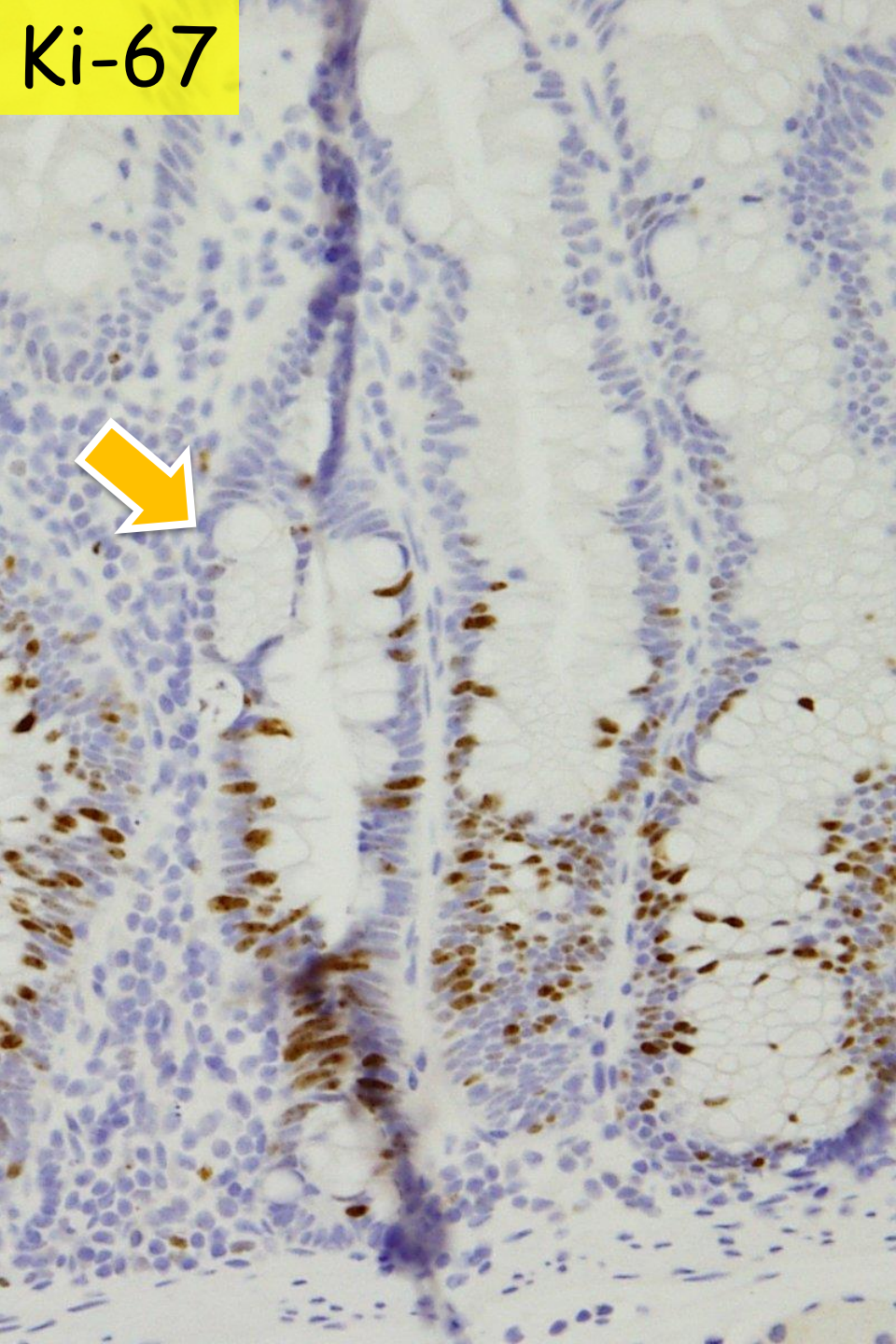
TSA

緑: CK20
 赤: Ki-67

NO PATTERN
 TA



Ki-67

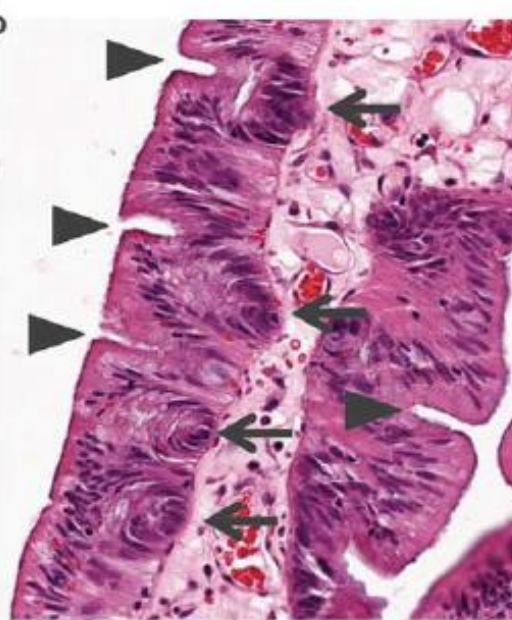
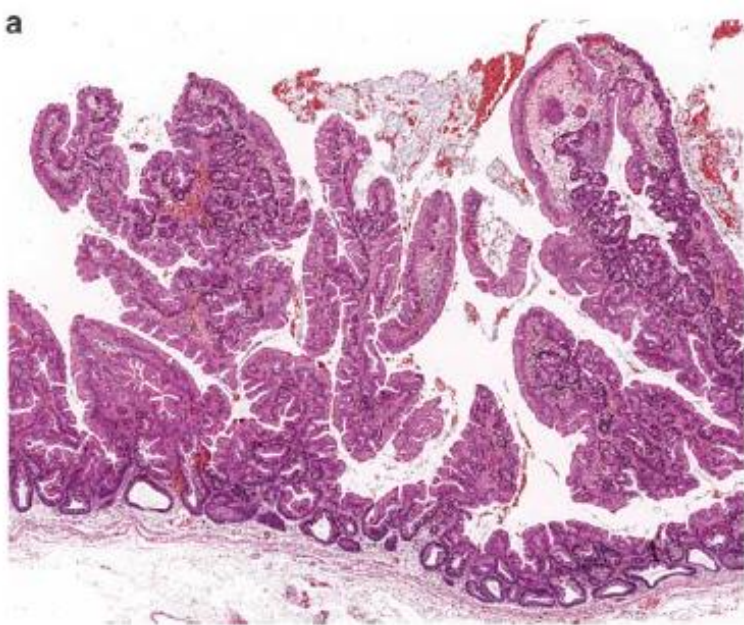


CK20

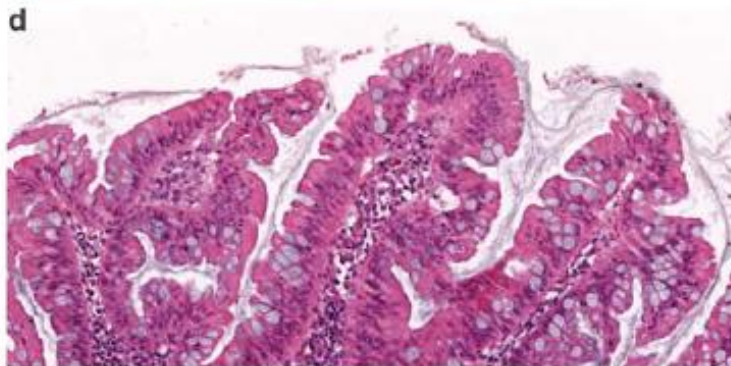
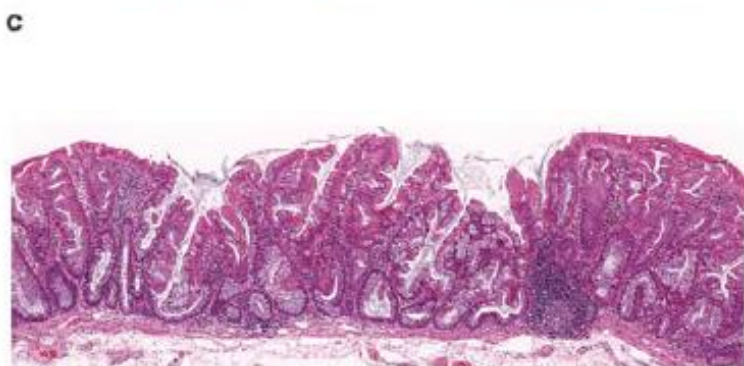


A clinicopathological and molecular analysis of 200 traditional serrated adenomas

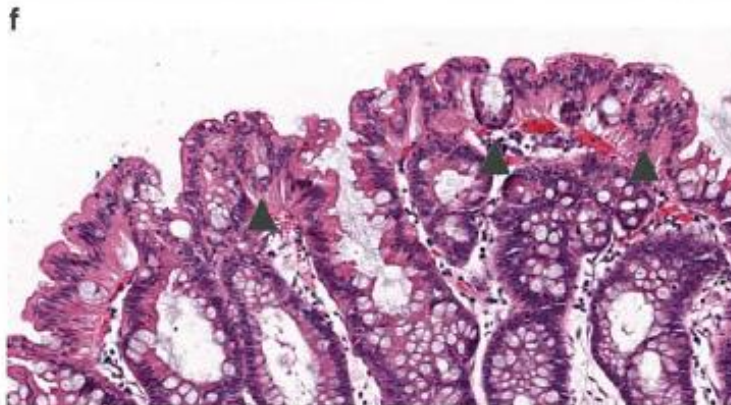
Mark L Bettington^{1,2,3}, Neal I Walker^{2,3}, Christophe Rosty^{2,3,4}, Ian S Brown^{3,5}, Andrew D Clouston^{2,3,5}, Diane M McKeone¹, Sally-Ann Pearson¹, Kerenaftali Klein⁶, Barbara A Leggett^{1,2,7} and Vicki LJ Whitehall^{1,2,8}



Filiform TSA (*BRAF*)

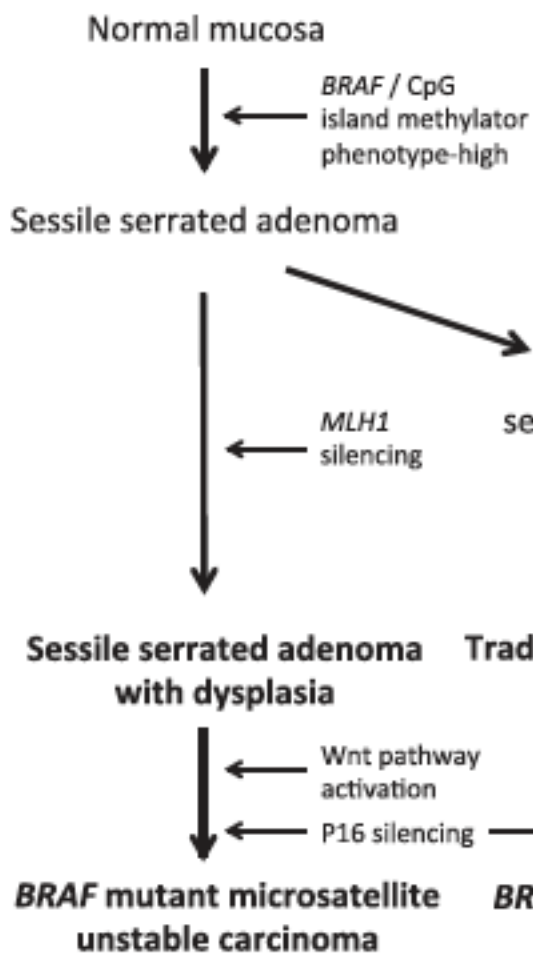


Flat TSA (*BRAF*)



Flat TSA (*KRAS*)

***BRAF* mutation pathway**



***KRAS* mutation pathway**

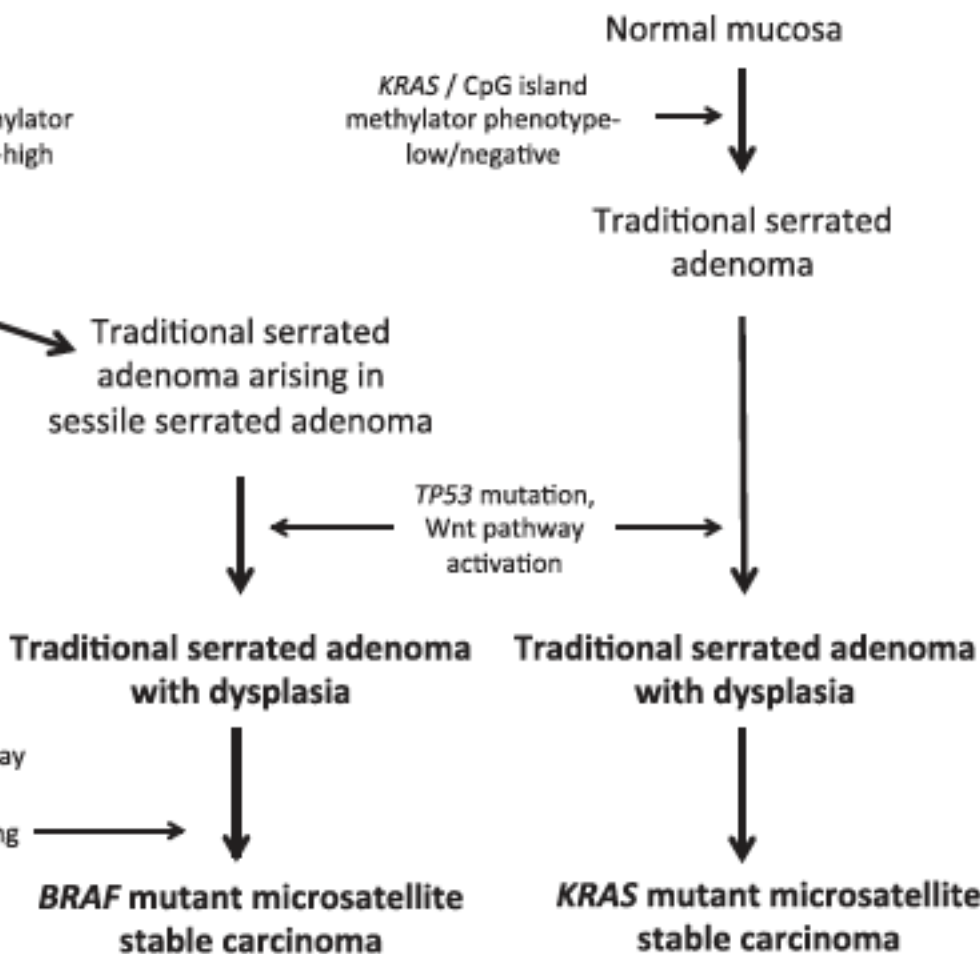



Figure 4 Proposed molecular pathways of malignant progression in *BRAF* and *KRAS* mutant traditional serrated adenoma.

Mucin-rich variant of traditional serrated adenoma: a distinct morphological variant

Sangeetha N Kalimuthu,¹ Stefano Serra,¹ Sara Hafezi-Bakhtiari,¹ Richard Colling,²
Lai Mun Wang² & Runjan Chetty¹ 

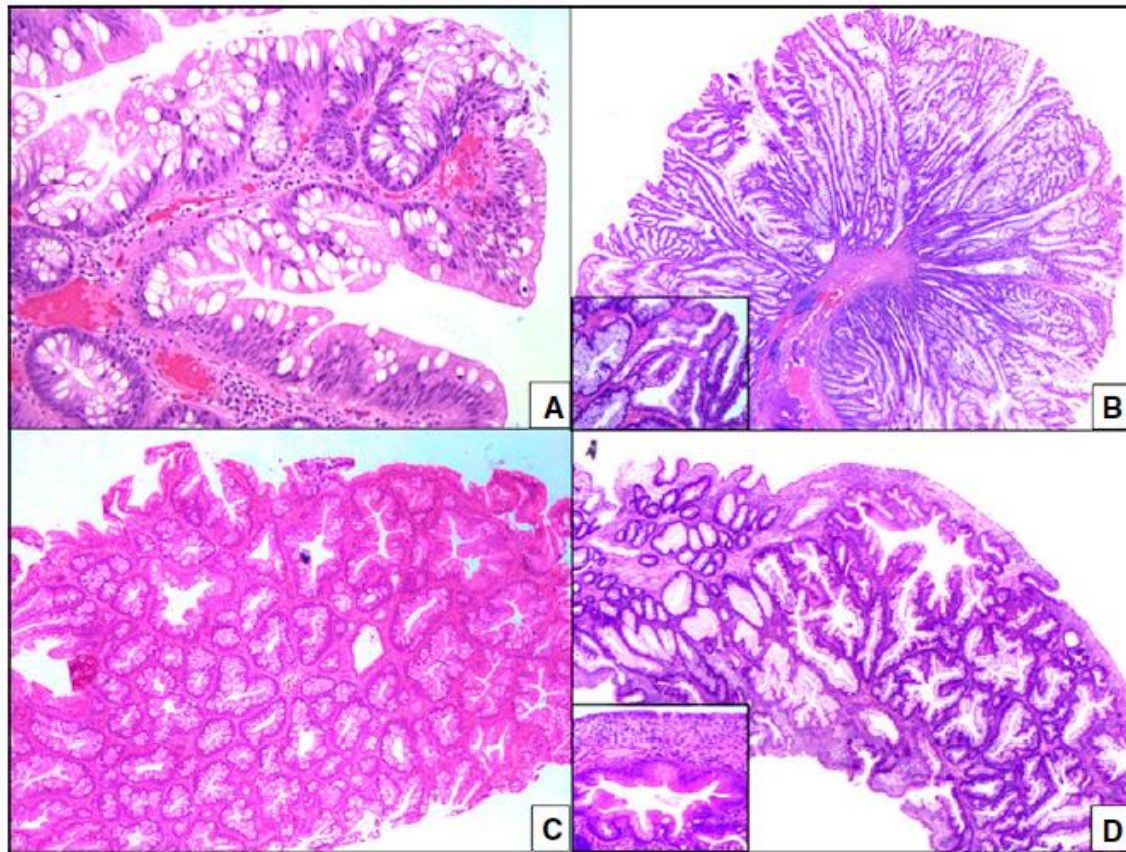


Figure 2. A, Mucin-rich traditional serrated adenoma (MrTSA) with $\geq 50\%$ goblet/mucin-rich cells with a goblet cell (GC)/eosinophilic absorptive cell ratio of at least 1:1 [haematoxylin and eosin H&E]. B, MrTSA with an arborizing growth pattern and branching central core, almost entirely composed of GCs ($>95\%$), resembling gastric foveolar epithelium (inset), overall reminiscent of a hamartomatous polyp (H&E). C, MrTSA with a mixed exophytic and endophytic growth pattern (H&E). D, An inflamed and focally ulcerated MrTSA with an entirely endophytic growth pattern, mimicking an inflammatory polyp, but, at least focally, retaining the characteristic serrations (inset) (H&E).

Superficially serrated adenoma


Modern Pathology (2018) 31:1588–1598
<https://doi.org/10.1038/s41379-018-0069-8>



ARTICLE



Superficially serrated adenoma: a proposal for a novel subtype of colorectal serrated lesion

Taiki Hashimoto¹ · Yusaku Tanaka² · Reiko Ogawa³ · Taisuke Mori^{1,3} · Hiroshi Yoshida¹ · Hirokazu Taniguchi¹ · Nobuyoshi Hiraoka ^{1,3} · Motohiro Kojima⁴ · Yasuhiro Oono⁵ · Yutaka Saito² · Shigeki Sekine^{1,3}

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- S状結腸、直腸がほとんど(90%)

Fig. 1 Endoscopic findings of superficially serrated adenomas. **a** Small sessile polyp with mildly lobulated surface in the rectum (SuSA01). **b, c** Small sessile polyps in the rectum (**b**, SuSA07; **c**, SuSA19). **d** Large slightly elevated lesion in the sigmoid colon highlighted by chromoendoscopy (SuSA03)

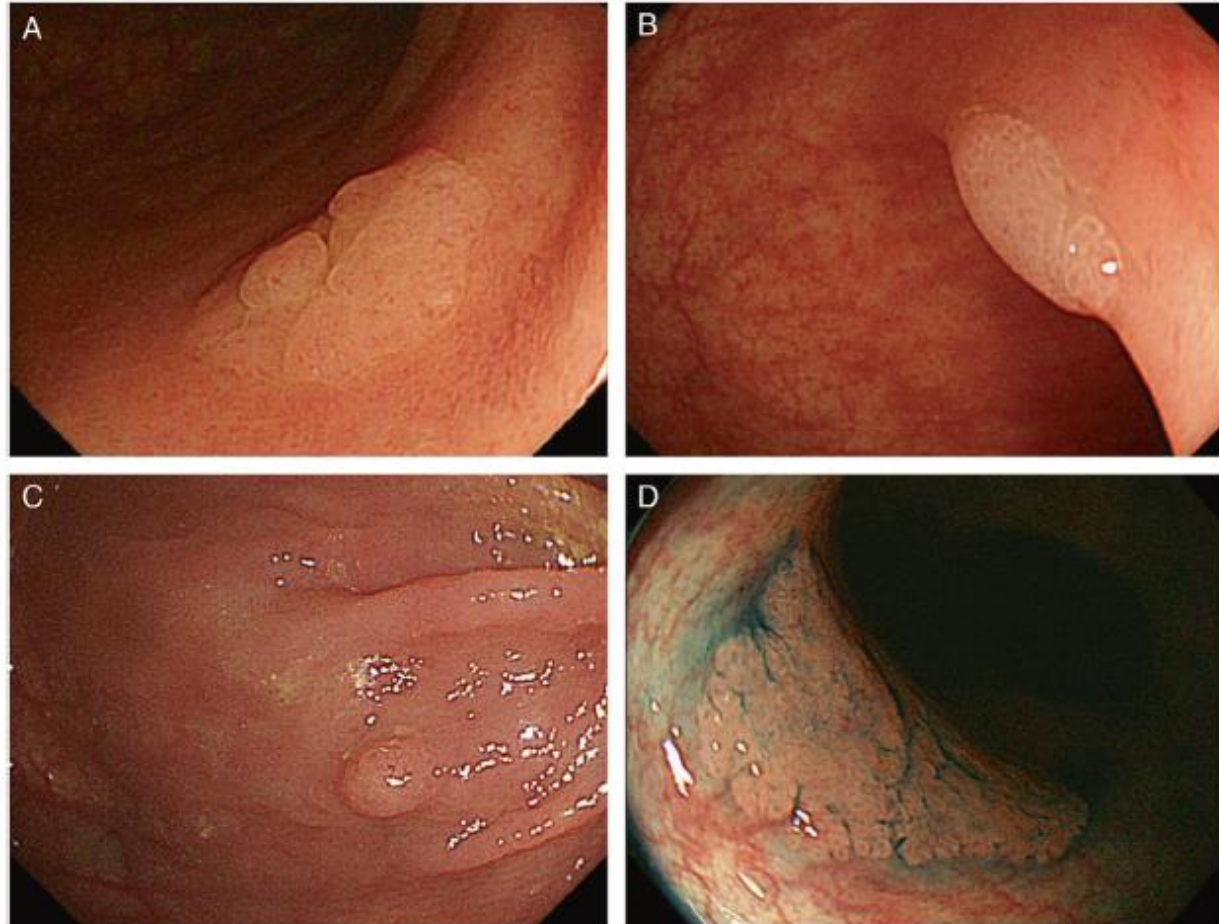
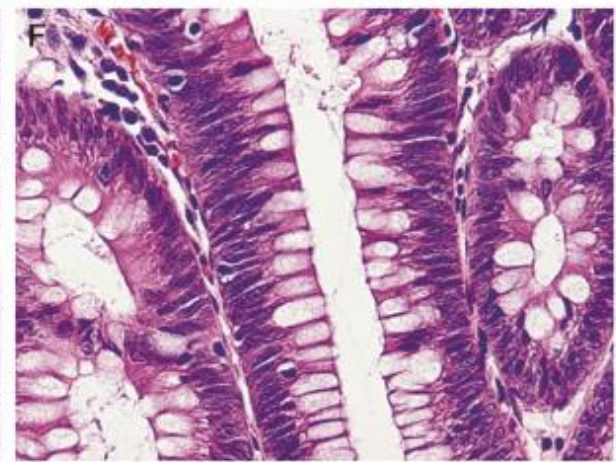
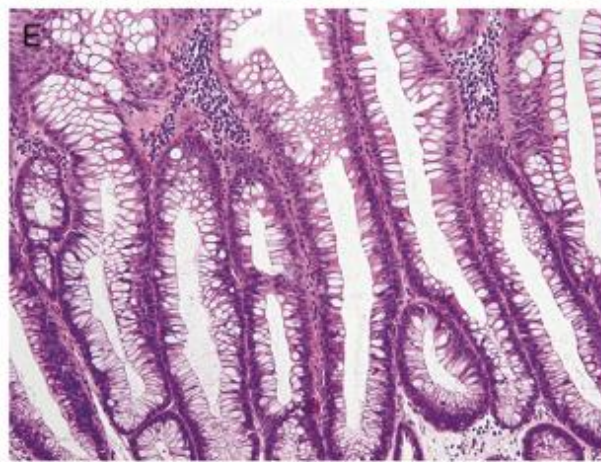
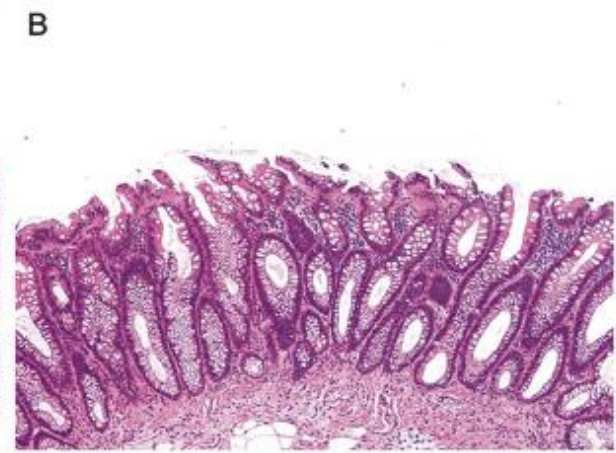


Fig. 2 Histological features of superficially serrated adenomas. **a, b** Low-power images of polyps showing proliferation of adenomatous glands and superficial serration. **c** Abrupt transition of the neoplastic glands and normal mucosa at the periphery of the lesion. **d** Tufting of the overlying epithelium. **e** Straight tumor glands lacking serration in the middle to bottom layer. **f** Glands lined by columnar epithelium with uniform elongated basal nuclei



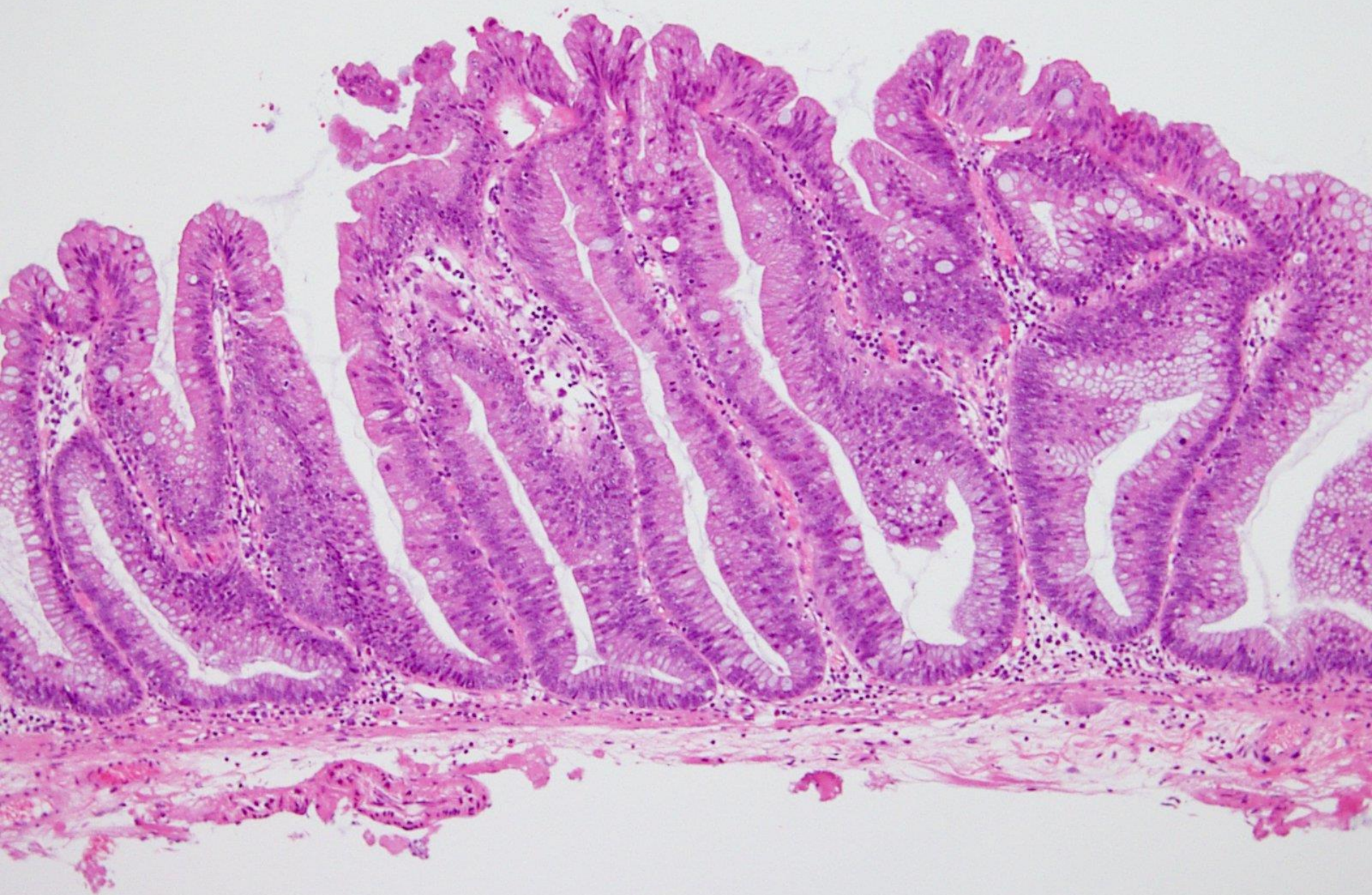
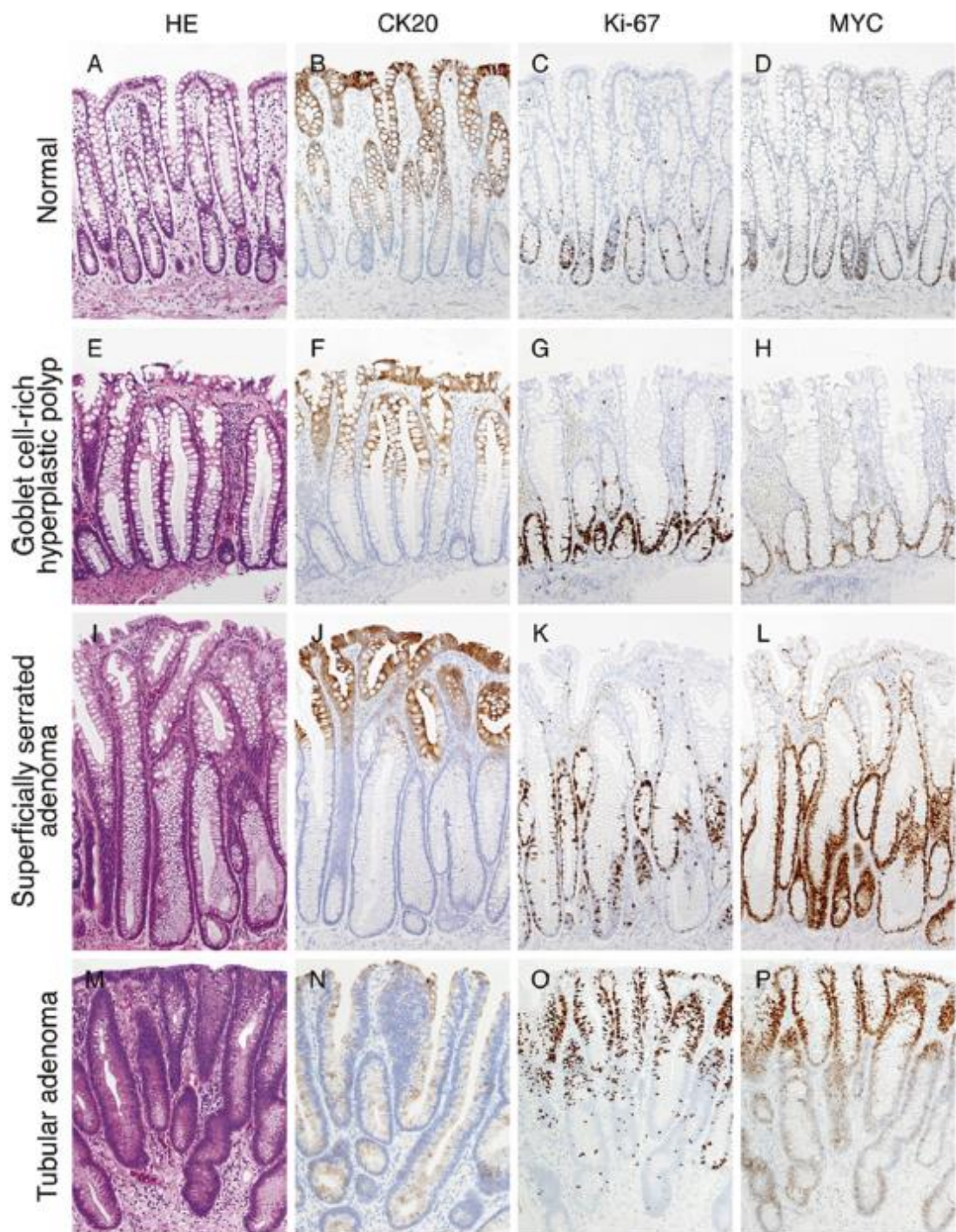
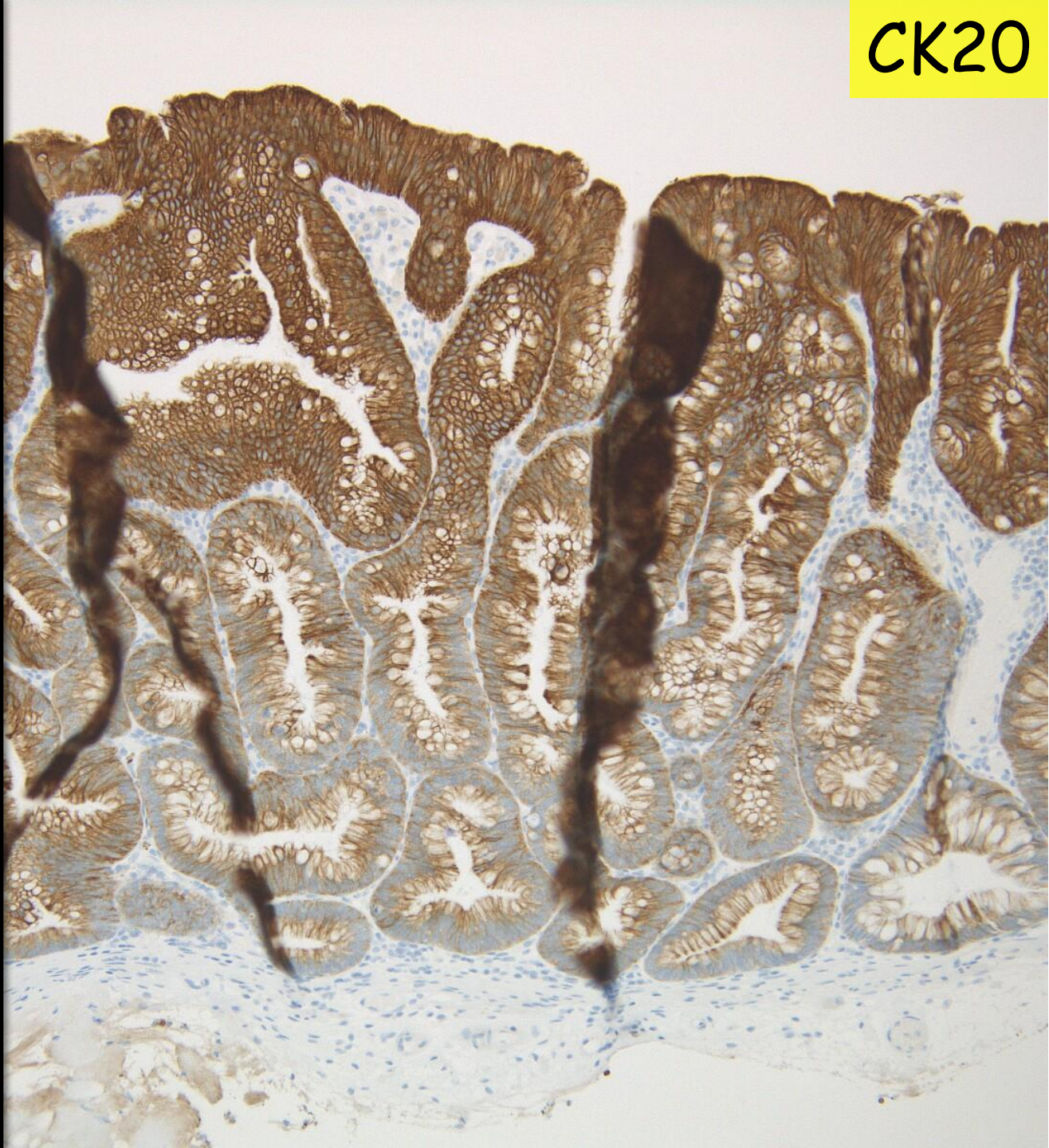


Fig. 3 Comparative immunohistochemical analysis. **a–d** Normal mucosa. **e–h** Goblet cell-rich hyperplastic polyp. **i–l** Superficially serrated adenoma. **m–p** Tubular adenoma. CK20 is expressed in the upper layer of normal mucosa, goblet cell-rich hyperplastic polyp, and superficially serrated adenoma (b, f, j). Tubular adenoma showing diffuse weak CK20 expression (n). Ki-67 and MYC expression is localized to the bottom layer in normal mucosa and goblet cell-rich hyperplastic polyp (c, d, g, h), whereas distributed in the middle to lower layers in superficially serrated adenoma (k, l) and in the upper layer in tubular adenoma (o, p)

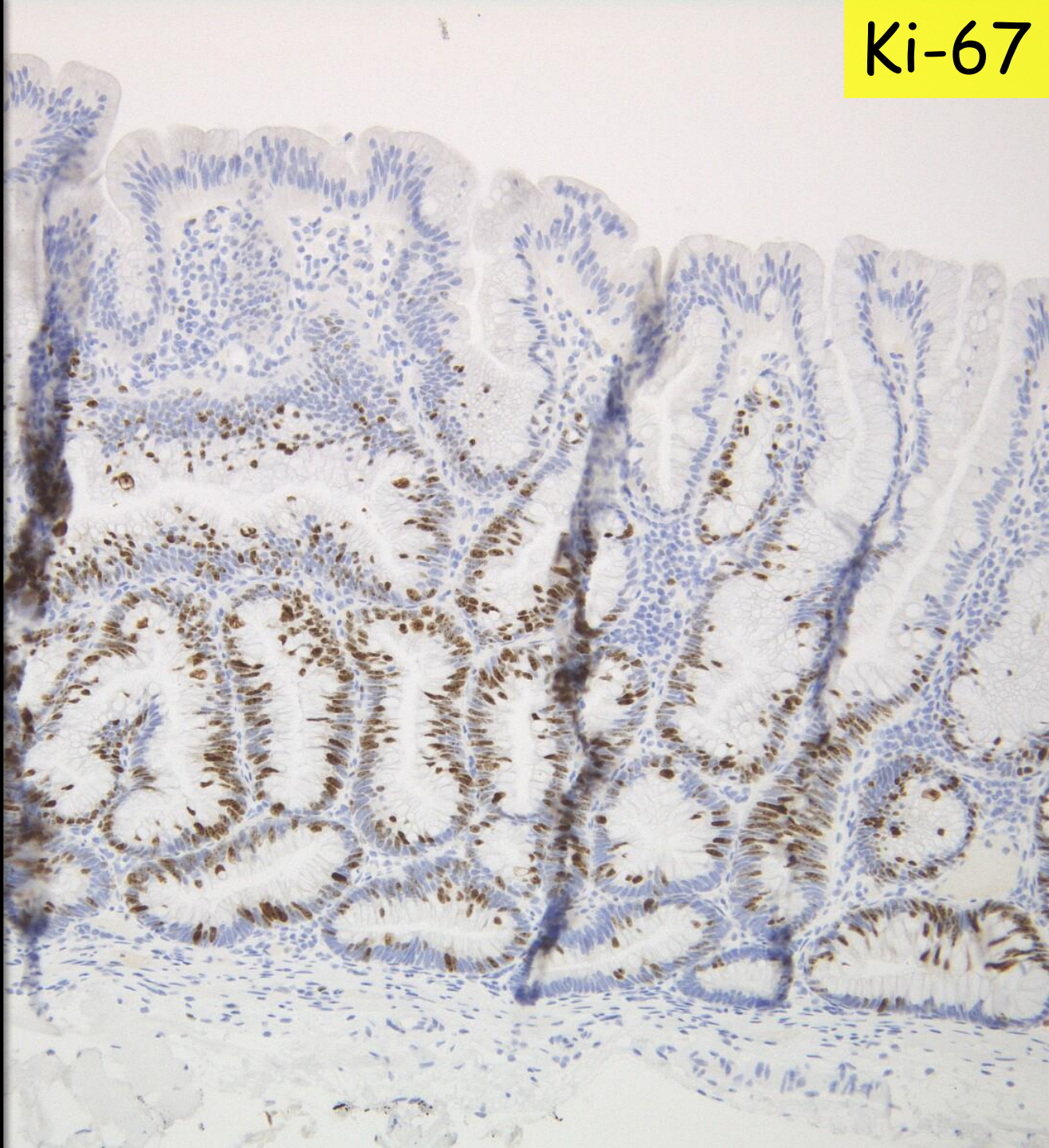
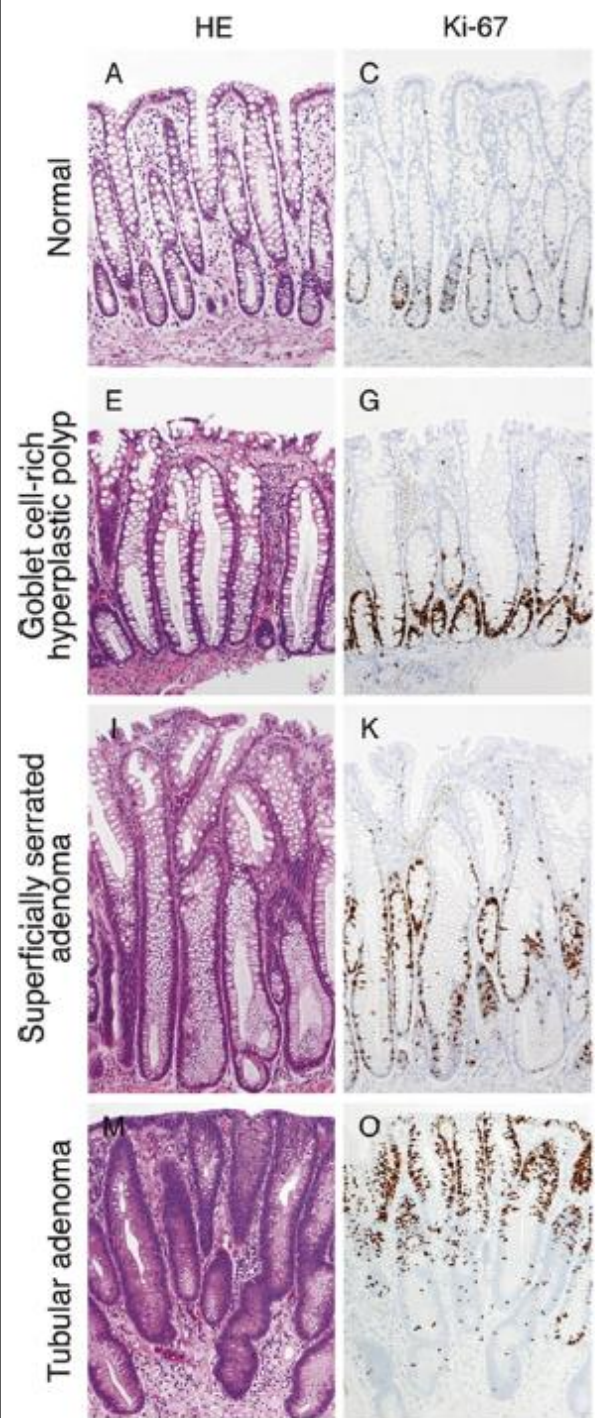


CK20

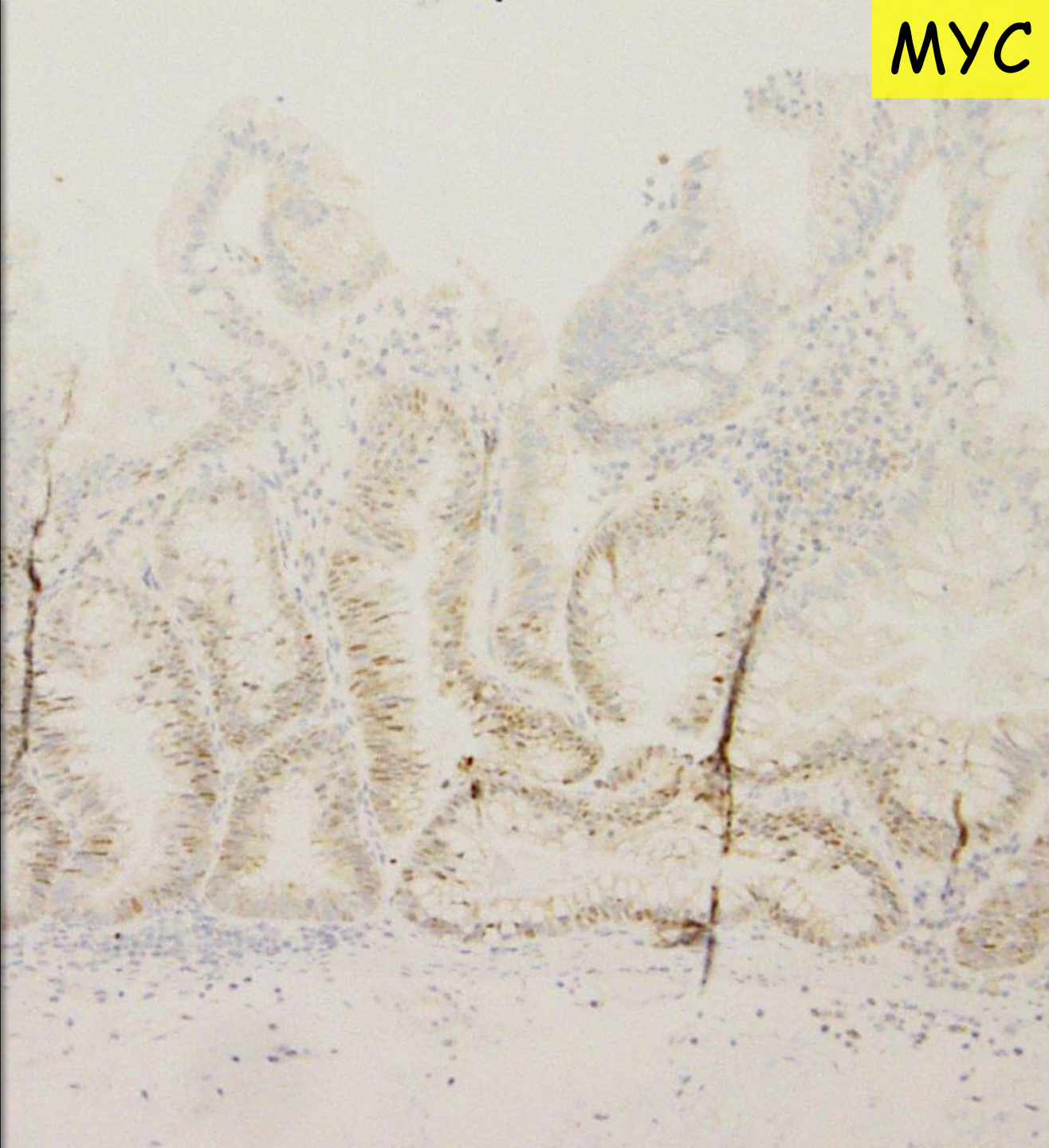
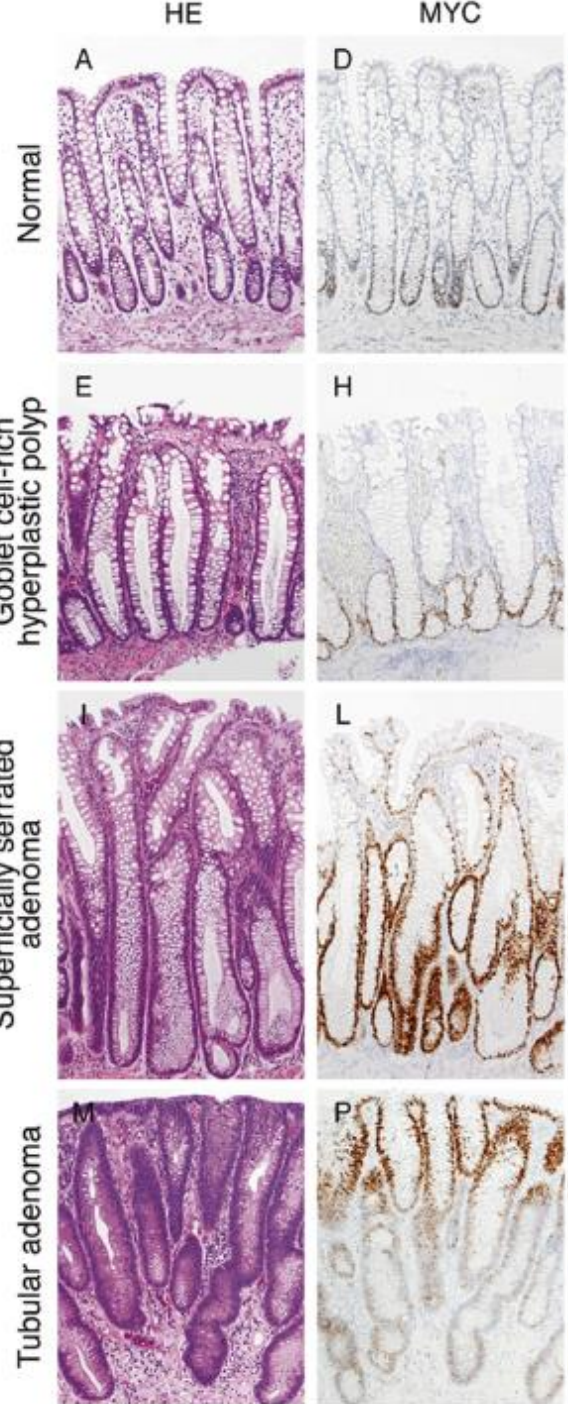
	HE	CK20
Normal		
Goblet cell-rich hyperplastic polyp		
Superficially serrated adenoma		
Tubular adenoma		



Ki-67



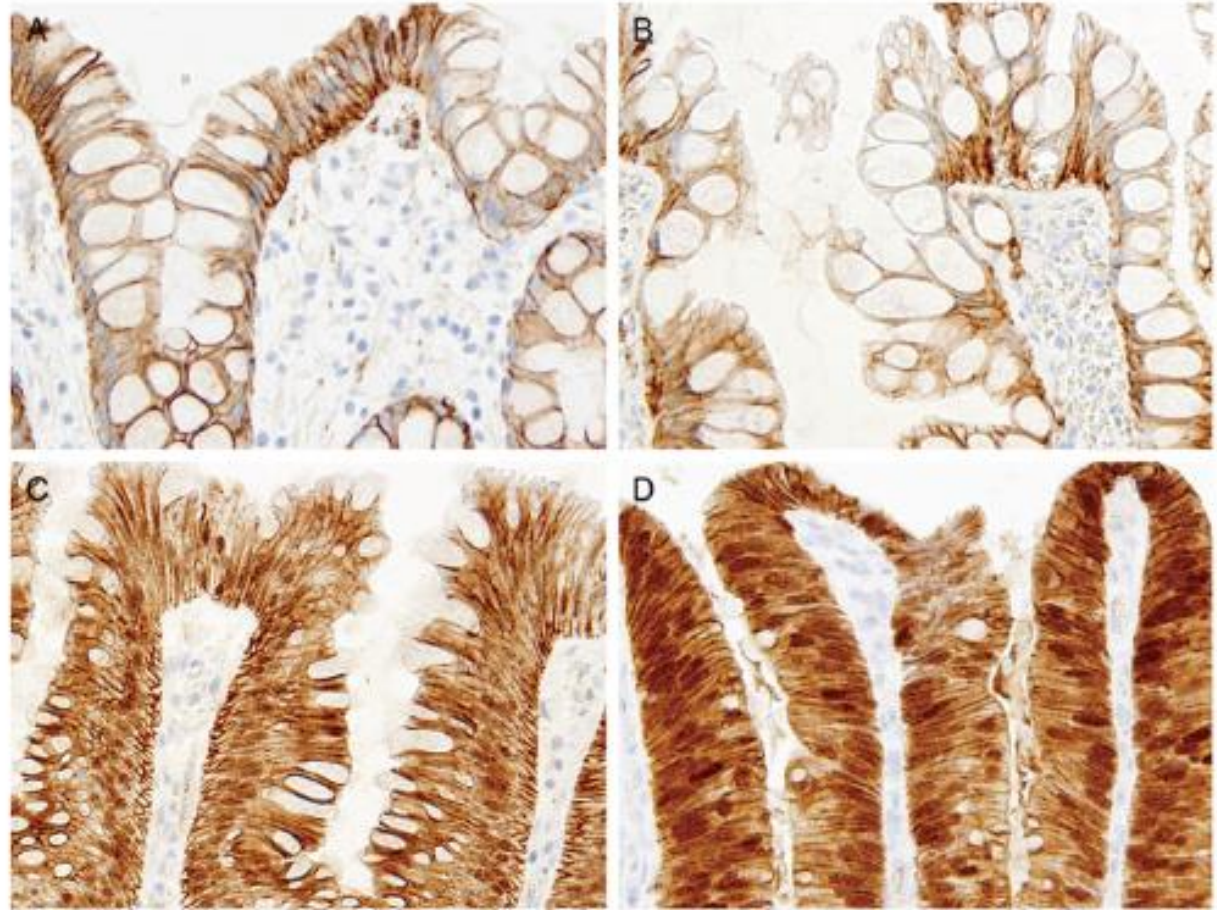
MYC



normal

Goblet HP

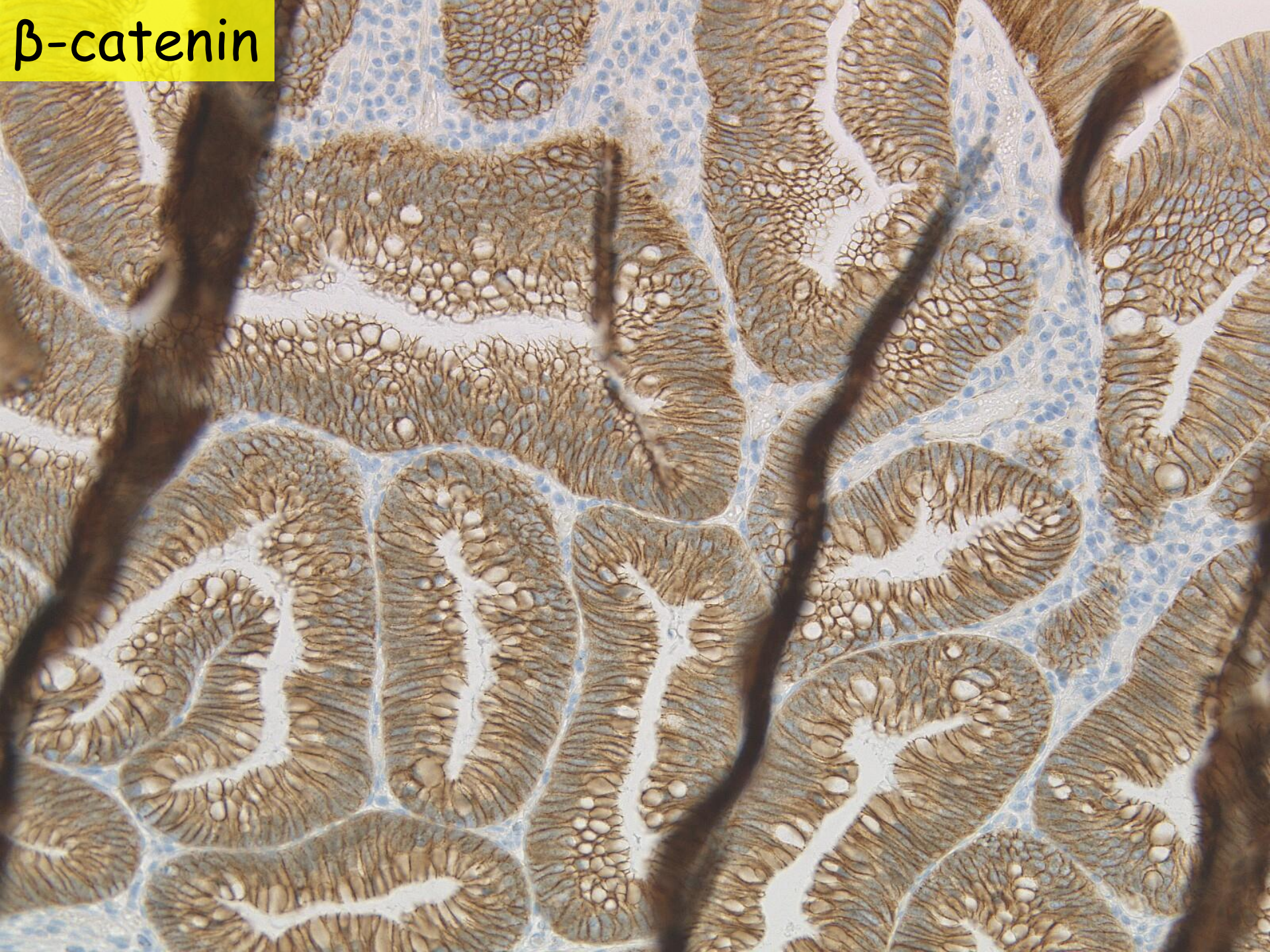
Fig. 4 β -Catenin expression in normal mucosa, a goblet cell-rich hyperplastic polyp, a superficially serrated adenoma, and a tubular adenoma. a, b Epithelial cells of normal mucosa (a) and a goblet cell-rich hyperplastic polyp (b) show exclusively membranous β -catenin expression. c A superficially serrated adenoma shows moderate nuclear β -catenin staining in addition to membranous staining. d A tubular adenoma shows diffuse strong nuclear β -catenin accumulation



Superficially serrated adenoma

Tubular adenoma

β -catenin





ちなみに・・・

D133N
397G>A

KRAS mutation +
BRAF mutation -

Speaker's Diagnosis;

ご意見をください！

Serrated lesion, KRAS

- Hyperplastic polyp
 - microvesicular type
 - goblet cell type
 - mucin poor type
- Sessile serrate adenoma/polyp BRAF
- Sessile serrated adenoma with cytological dysplasia BRAF
- Serrated tubulovillous adenoma KRAS
- Traditional serrated adenoma BRAF > KRAS
 - Filiform TSA BRAF > KRAS
 - Flat TSA
 - Mucin-rich variant of TSA BRAF
- Superficially serrated adenoma KRAS