

P2X₇: Improved detection of bowel cancers and dysplastic bowel conditions by quantifying a novel cell membrane receptor

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Background

- P2X₇ is an apoptotic calcium channel receptor that is non-functional on cancer cells and has been shown to be a reliable marker for identification of malignancy in epithelial cell cancers including prostate, breast, skin, cervix and ovary.
- The receptor locates strongly to the apical membrane of malignant and adjacent “normal” prostate glands (field effect) making it useful in treatment decisions after PSA screening.

Aim

- To evaluate this biomarker for its sensitivity and specificity for neoplasia/dysplasia in the bowel

Materials & Methods

- 332 biopsies and surgical pathology specimens were ascertained from 178 consecutive patients as per the table.
- Staining pattern and intensity towards P2X₇ was read by a pathologist, blinded to the primary pathologist's diagnosis and Dukes' cancer staging

Staining Methods

- Paraffin embedded blocks freshly sectioned
- Sections required heat-induced epitope retrieval prior to staining
- Standard IHC protocol for staining sections

Results

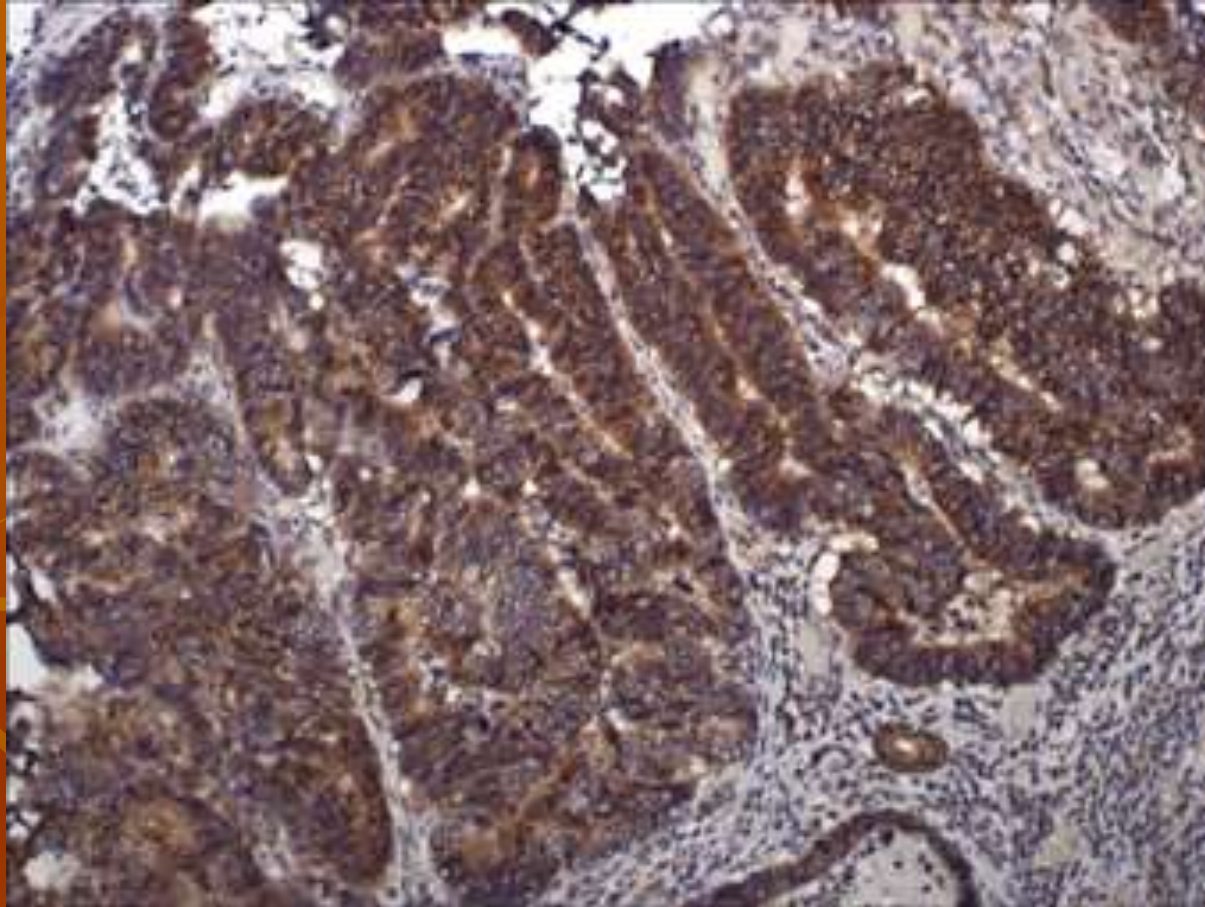
- Staining in colonic neoplastic tissue was dominantly in the cytoplasm
- Absent staining in normal bowel tissue
- Cytoplasmic staining judged simply as positive or negative gave best sensitivity and specificity

Results

- Positive in all adenocarcinomas in cytoplasm
- Positive in moderately dysplastic adenomas
- Negative in adenomas with mild or no dysplasia
- Absent staining in normal bowel tissue

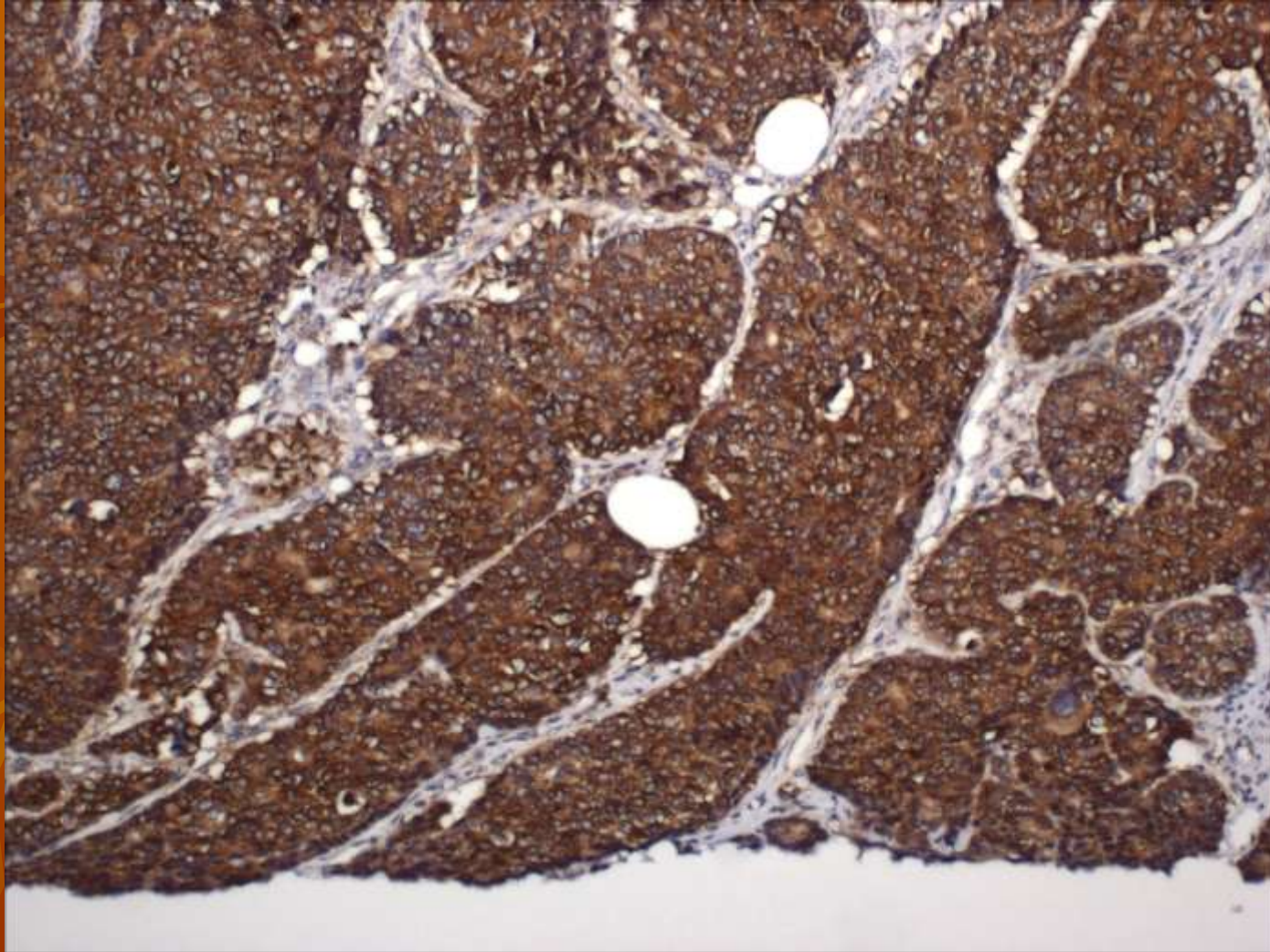
Cell type (patients)	P2X ₇ stained sections		
	Negative	Positive	Total
Adenocarcinoma (n=96)	0 (0%)	109 (100%)	109
Adenoma (n=30)	13 (25.5%)	38 (74.5%)	51
Hyperplastic polyp (n=13)	15 (46.9%)	17 (53.1%)	32
Barrett's, no dysplasia (n=12)	10 (47.6%)	11 (52.4%)	21
Barrett's with dysplasia (n=4)	0 (0.0%)	6 (100.0%)	6
Ulcerative colitis (n=3)	24 (100%)	0 (0.0%)	24
Normal (n=20)	89 (100%)	0 (0%)	89
Total patients (n=178)	151 (45.5%)	181 (54.5%)	332

Moderately differentiated adenocarcinoma



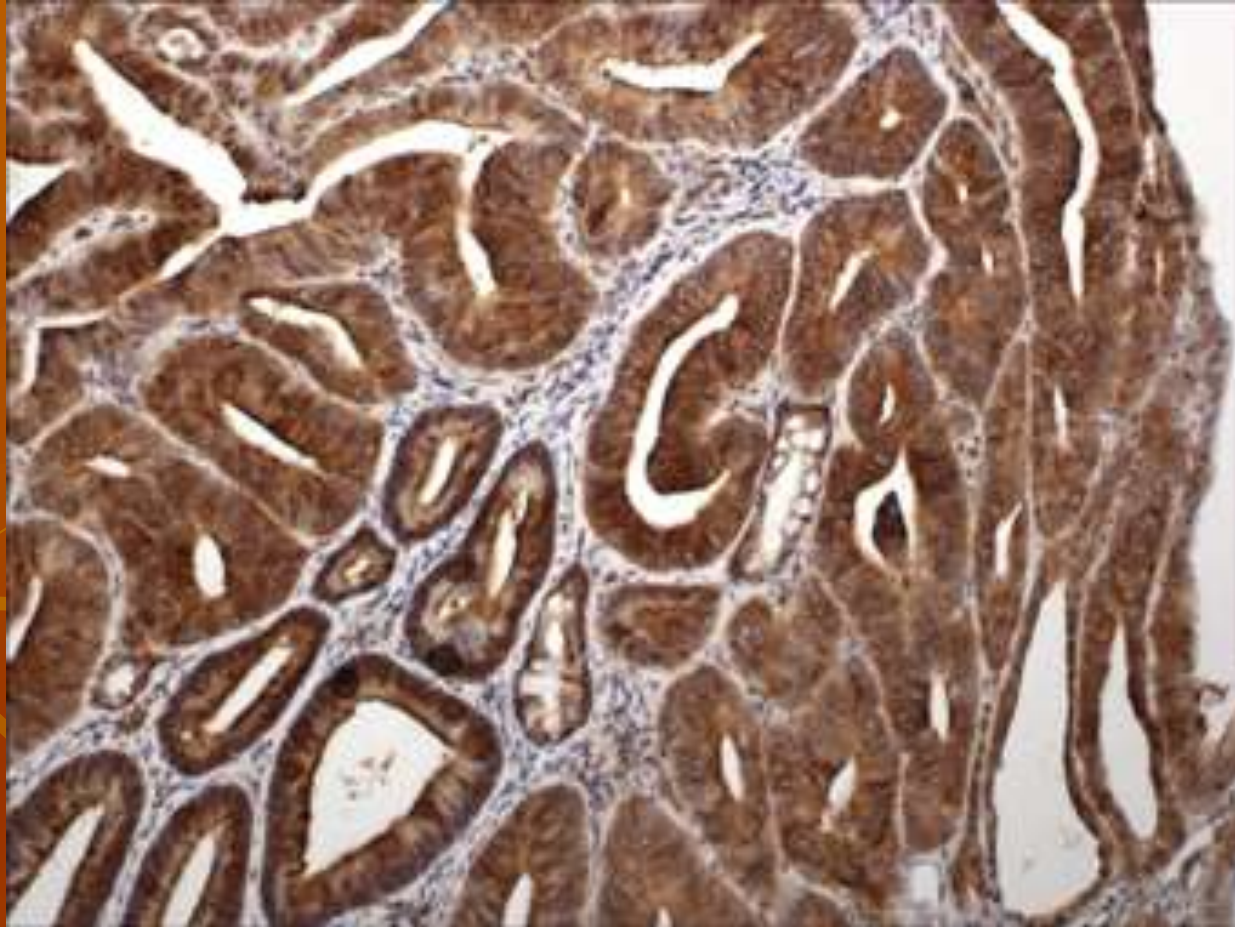
Positive cytoplasm stain

Poorly differentiated adenocarcinoma



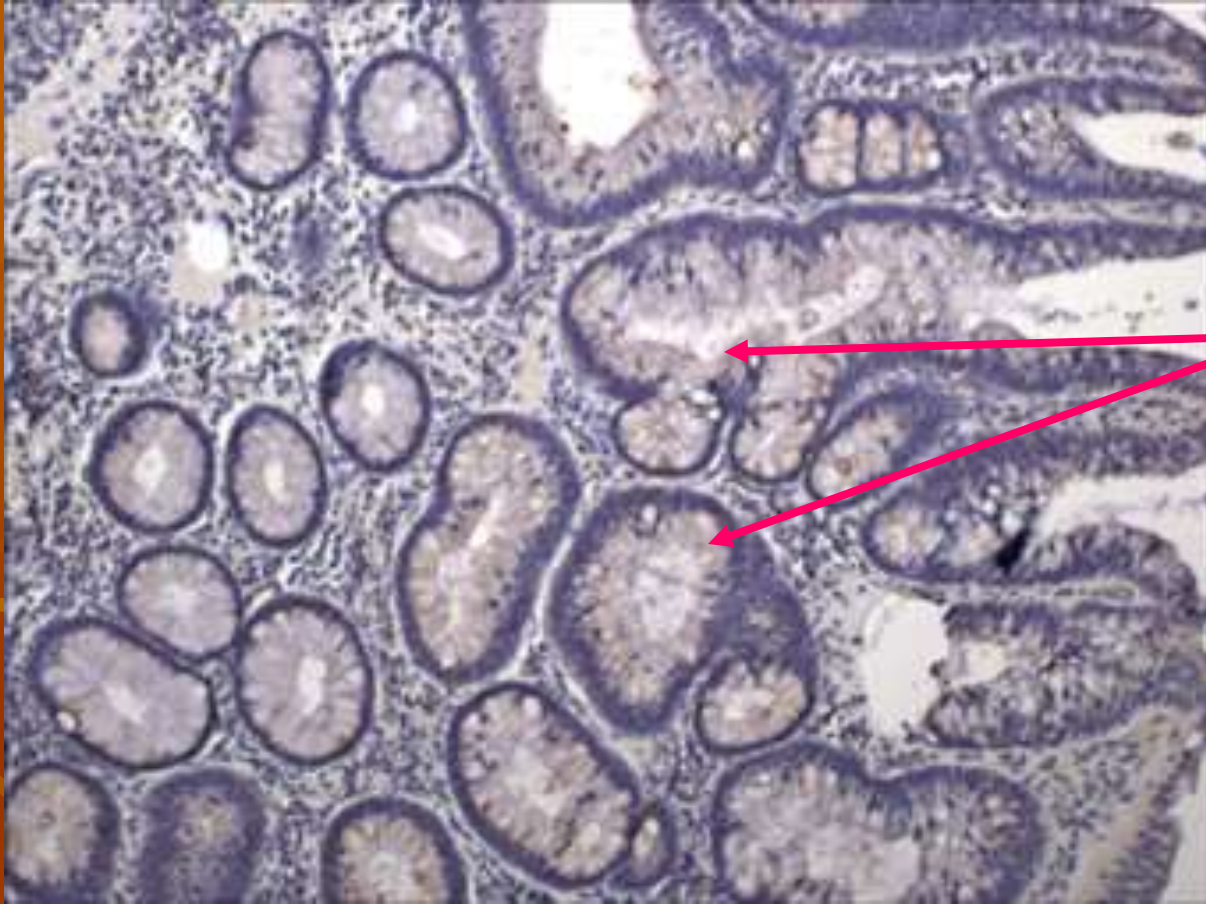
Positive cytoplasm stain

TVA with moderate dysplasia



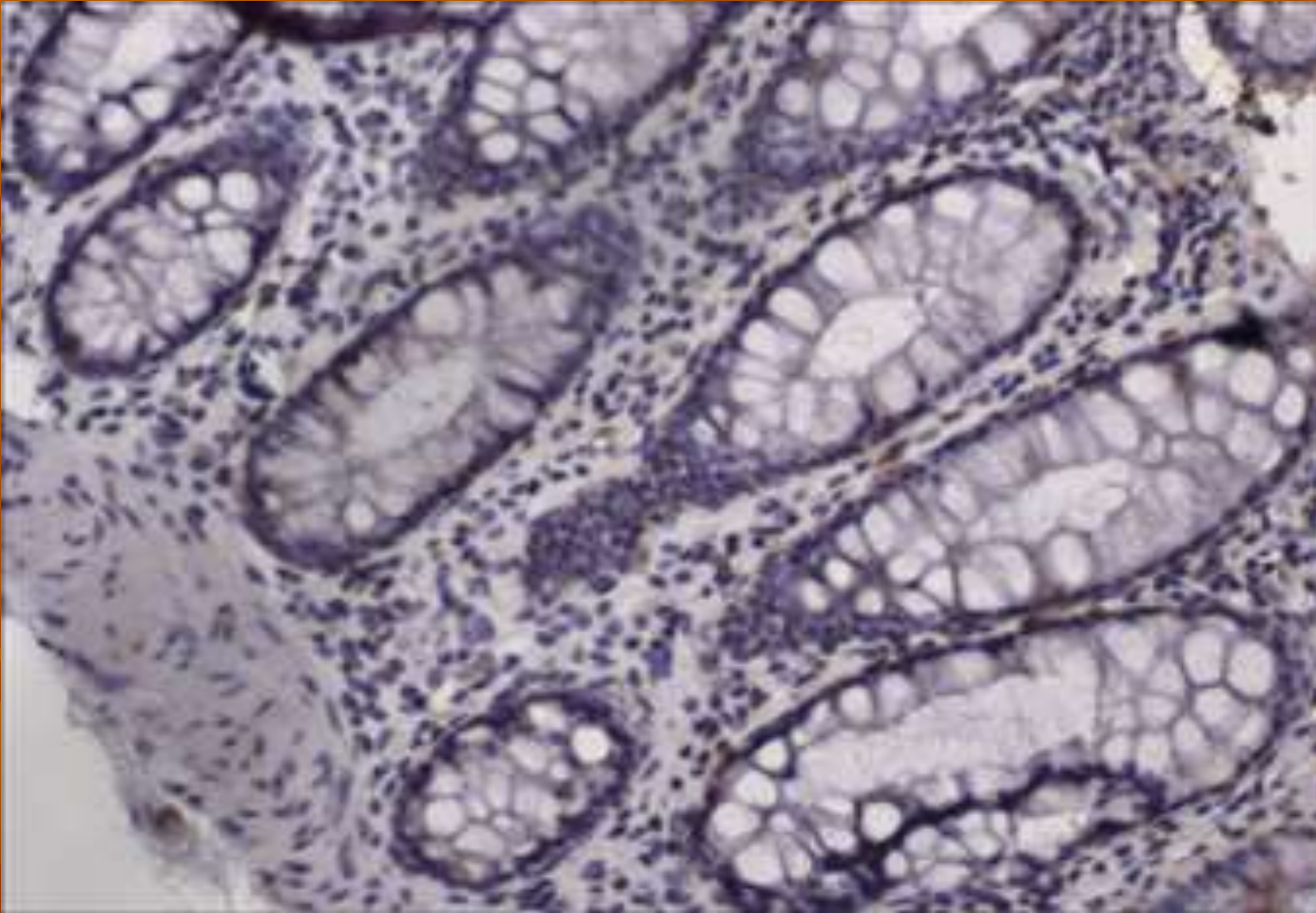
Positive cytoplasm stain

Tubular adenoma mild dysplasia



Negative stain

Normal colon



Negative stain

- There was no correlation of staining with Dukes' staging
- Sensitivity for cancer was 100% and for adenomas 74.5%
- Specificity was 100% (negative in normal biopsies)
- The rate of positive staining on adenocarcinoma sections was significantly greater (Fisher Exact Test $p < 0.000$) than the other groups except for Barrett's oesophagus with dysplasia. ($p=1.00$)

Conclusion

- Differentiation of adenocarcinoma from normal biopsies was high
- Larger series being conducted for evaluation of P2X₇ sensitivity and specificity in Barrett's oesophagus (with and without dysplasia) and ulcerative colitis

Terima kasih

