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CD 10 Expression In Colorectal Carcinoma And Premalignant Lesions In A Tertiary Care Hospital

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Abstract: *The aim of this work is to study the tumour and stromal expression of CD10 in colorectal adenoma and carcinoma and to study the relationship of CD10 expression in Tumour prognostic factors such as Depth of invasion andTumour staging. Materials and methods:CD10 expression was studied in tumour cells and stromal cells in 30 colorectal adenomas and 30 colorectal carcinomas using monoclonal antibody to CD10 by immunohistochemistry. Results: Significant progression of CD 10 immunohistochemical expression in tumour cells from adenomas to carcinomas was reported in this study ($p<0.05$).Inverse significant correlation was detected between CD10 expression in tumour cells and depth of tumour invasion as 100% and 80% of T2 and T3 cases respectively showed positive CD10 expression and 100% of T4 cases showed negative Tumour CD10 expression with strong stromal staining.*

Keywords: *CD 10 EXPRESSION,ADENOMAS,ADENOCARCINOMAS,TUMOURDEPTH OF INVASION,NODAL STATUS*

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I. Introduction:

Colorectal carcinomas account for approximately 9% of all cancers. It is the fourth most common cause of cancer mortality in the world[1]Colorectal cancer is the 4th most common cause of cancer mortality worldwide and third most commonly diagnosed malignancy among men.It accounts for 9% of newly diagnosed cancer and mainly a disease of developed countries.In India, the annual incidence rates of colon and rectal carcinomas are 4.4 and 4.1 per 100000 respectively. The annual incidence rate for colon cancer in women is 3.9 per 100000. However the incidence of rectal cancer is higher in rural india[2]

CD 10 is a single pass type II trans membrane matrixmetallopeptidase and zinc dependent enzyme involved in carcinogenesis weighing 90-110kDa.It acts through the release of bioactive molecule that stimulate invasion,extracellular matrix degradation,inhibition of apoptosis and stimulating angiogenesis and immune response modulation.Earlier it was used as cellsurface marker to identify and differentiate between haematological malignancies.Later CD 10 plays an important role in cancer development and progression in various malignancies[3]

In colorectal cancer CD 10 has been expressed in tumour cells, tumour associated fibroblast and infiltrating inflammatory cells[4].Studies have associated this marker with the liver metastasis, venous invasion and progression of tumours to more advanced stages in patients with colorectal neoplasm[5].Some studies have postulated that CD10 expression may be a useful marker for estimating the biological properties of early colorectal carcinomas[6]

II. Materials And Methods:

The study was conducted during the period of January 2017 to January 2018. It was carried out in specimens obtained from patients with confirmed histopathological diagnosis of colorectal adenomas and adenocarcinomas. The study was approved by the Ethical committee of Government Stanley Medical College and hospital. It is a Retrospective and comparative study.

STUDY GROUP:

The study sample comprised of 60 cases, 30of colorectal adenoma and 30 of adenocarcinoma patients. Cases were chosen from the Department of Surgical Gastroenterology, Government Stanley Medical College and hospital. Age, sex, tumour site, histological grade and tumour stage were obtained for all cases. All the 60 cases were screened for CD 10 expression through immunohistochemical assay. Cancer types other than adenocarcinomas, Recurrent and metastatic adenocarcinomasChemotherapy and/or radiotherapy prior to sampling were all excluded from the study.

HISTOPATHOLOGICAL EXAMINATION:

The tissues so obtained were processed and sectionswerecutat5microns.Hematoxylinandeosinstainingofthe sections were done and analysed. Adenomas were classified in to low grade and high grade based on dysplasia.In low grade dysplasia stratified nuclei tend to remain in the basal epithelium with minimal nuclear hyperchromasia.In High grade dysplasia the nuclei consistently come to the surface of epithelium, loss of columnar shape with nuclear irregularity and loss of polarity.In Adenocarcinoma there will be loss of architecture, nuclearpleomorphism and invasion.

The clinico-pathological characteristics including age, sex, tumour site, histological diagnosis (normal/adenoma/adenocarcinoma), histological grade (adenomas- low grade/high grade dysplasia ; adenocarcinoma – low/high) and adenocarcinoma stage were obtained for all the cases.

IMMUNOHISTOCHEMICAL STAINING:

IHC was performed on the selected blocksforCD10.For immunohistochemistry sections were cut at 5 micrometre thiknesss.Slides coated with home alum were used.Sections weresubjectedtoantigenretrieval using pressure cooker techniques TRISEDTA(pH9.2)buffersolutionandthentreatedbyHRP(horseradishperoxidase)polymertechnique.Finally DAB was used as a chromogen and hematoxylin as a counterstain.Positive control was obtained from renal cell carcinoma which exhibited strong intensity of CD 10 immunostaining.

EVALUATION OF IMMUNOHISTOCHEMICAL EXPRESSION OF CD10:

Tumour CD10 was considered positive if more than 10% of tumour cells express fine to coarse cytoplasmic granules.Stromal CD10 was graded according to a 4 point scale based on percentage of positively stained area[7]

0- <10%positive tumour cells
+1 -10-25%positive tumour cells
+2 -25%-50%positive tumour cells
+3 ->50%positive tumour cells

III. Observation And Results:

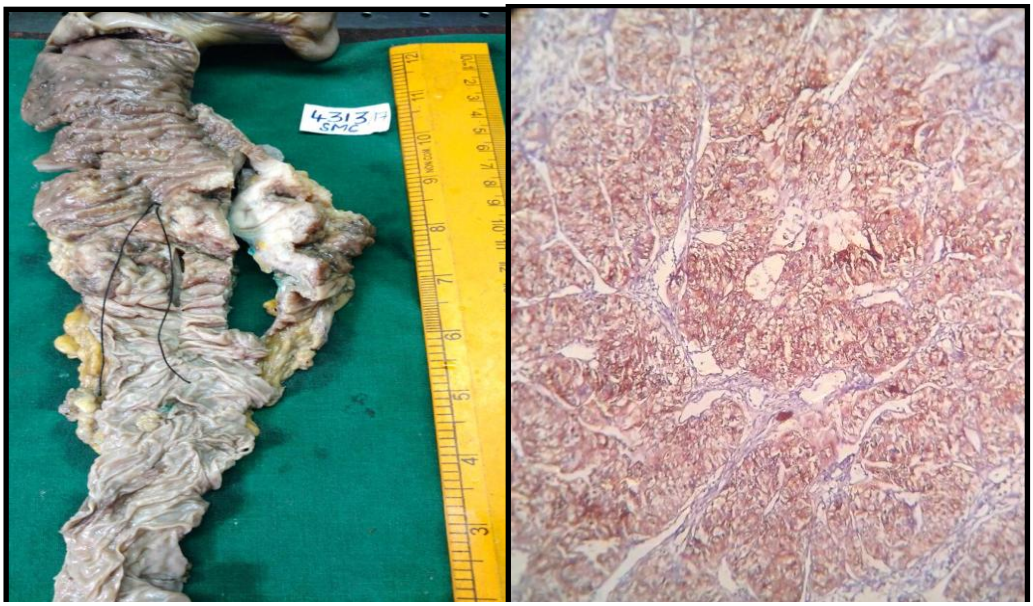

Fig1:Gross picture of infiltrative growth

Fig1: Gross picture of infiltrative growth in left side colon.

Fig2: Strong cytoplasmic staining of CD10 in Renal cell carcinoma-control

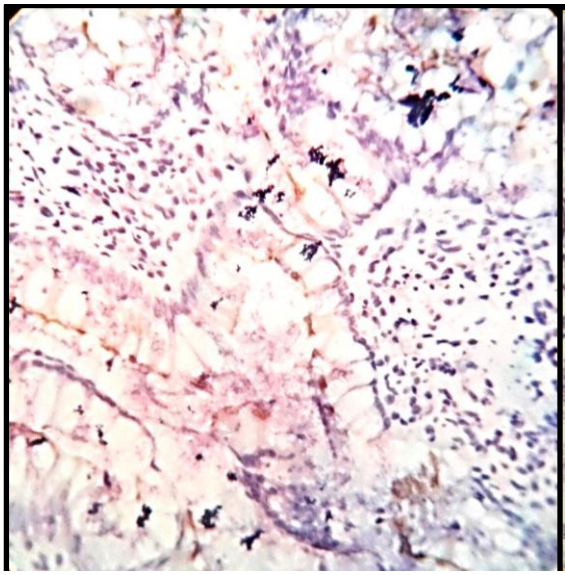

Fig3: Faint cytoplasmic CD10 Expression in low grade adenoma

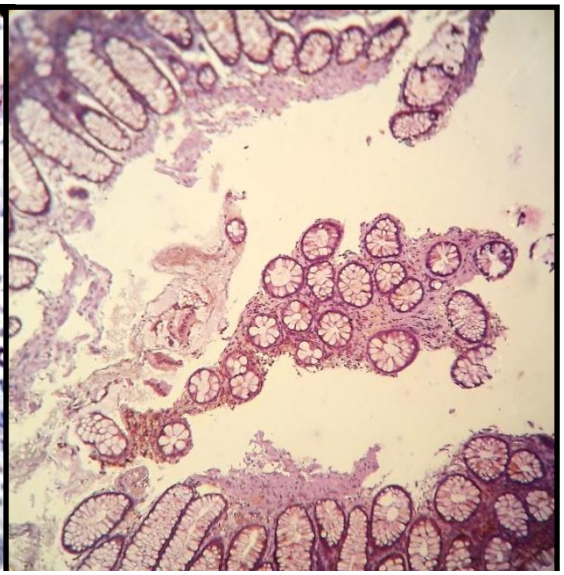

Fig 4: Moderate cytoplasmic and membrane CD10 staining in high grade adenoma

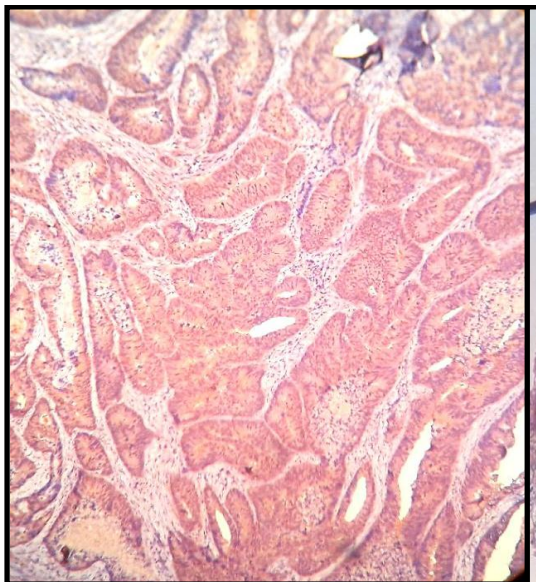

Fig 5: Strong cytoplasmic and membrane staining in T2 Depth of invasion with minimal stromal staining.

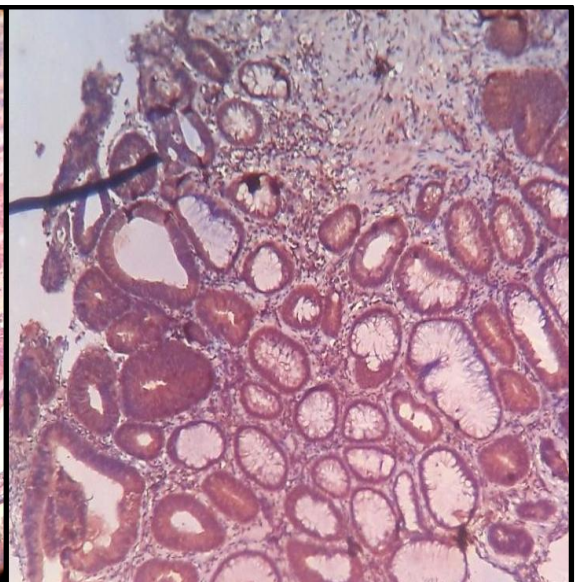

Fig 6: Moderate cytoplasmic and membrane CD10 Staining in T3 Depth of invasion with moderate stromal cell staining

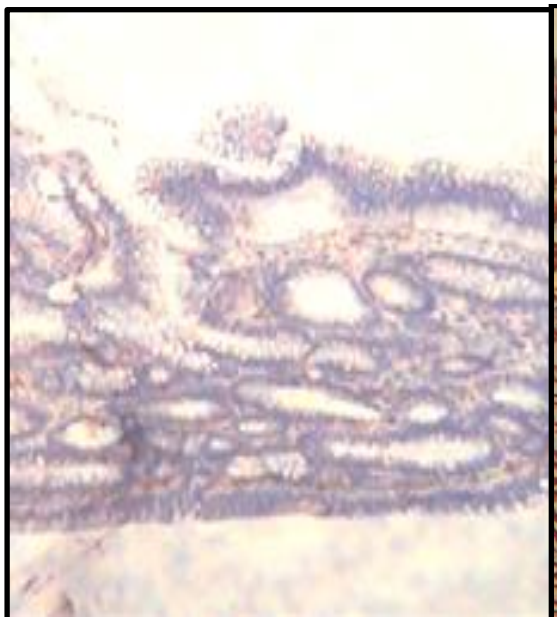

Fig 7: Weak cytoplasmic CD10 Tumour staining in T4 depth of invasion with strong stromal cells staining.

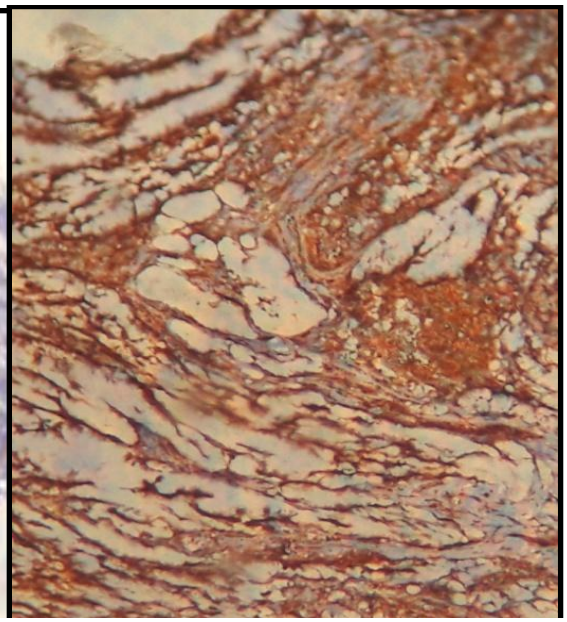

Fig 8: Strong CD10 stromal cell staining in T4 depth of invasion

IV. Results

Gross, Depth of Tumour invasion, Node ,Tumour CD10 , Stromal CD10 are Primary explanatory variable. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(1)

Table 1: Comparison of mean TUMOURCD10 across study groups (N=60)

Group	TUMOURCD10 Mean±STD	Mean difference	95% CI		P value
			Lower	Upper	
Carcinoma	59.79 ± 39.55	41.41	26.48508	56.33492	0.001
Adenoma	18.38 ± 10.16				

The mean TUMOURCD10was 59.79±39.55 in subjects with Carcinoma and meanTUMOURCD10 was18.38 ± 10.16 in subjects with Adenoma. The mean difference across the group is (41.41). It is statistically significant (P Value 0.001) (Table 1).

Table2: Comparison of mean STROMALCD10 across study groups (N=60)

Group	STROMALCD10 Mean±STD	Mean difference	95% CI		P value
			Lower	Upper	
Carcinoma	61.07 ± 19.88	43.80	35.90196	51.68937	<0.001
Adenoma	17.28 ± 8.442				

The mean STROMALCD10 was 61.07±19.88 in subjects with Carcinoma and meanSTROMALCD10was 17.28 ± 8.442 in subjects with Adenoma. The mean difference across the group is (43.80). It is statistically significant (P Value 0.001)

Table 3: Comparisonof in Depth of Tumor and Tumourcd10 among study group (N=30)

Depth of Tumor	Tumour CD10 Median (IQR)	P value (Kruskal Wallis Test)
T2	98 (98 to 99)	<0.001
T3	70 (65 to 75)	
T4	2 (0 to 5)	

Among the study participants, Tumour CD10 Median was 98 (IQR 98 to 99) of T2 , Tumour CD10 Median was 70 (IQR 65 to 75) of T3 and Tumour CD10 Median was 2 (IQR 0 to 5) of T4.

The difference in between TumourCD10 Median and Depth of Tumouris statistically significant (P Value 0.001) (Table 3).

Table 4: Comparison of improvement in Depth of Tumor and StromalCD10 among study group (N=30)

Death of Tumor	StromalCD10 Median (IQR)	P value (Kruskal Wallis Test)
T2	53 (50 to 55)	0.001
T3	64 (62 to 65)	
T4	82 (78 to 83)	

Among the study participants, StromalCD10 Median was 53 (IQR 50 to 55) of T2 , Tumour CD10 Median was 64 (IQR 62 to 65) of T3 and Tumour CD10 Median was 82 (IQR 78 to 83) of T4. The difference in between stromal CD10 Median and Depth of Tumouris statistically significant (P Value 0.001) (Table 4).

Table 5: Comparison of mean STROMALCD10 across study groups (N=30)

GROSS	STROMALCD10 Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Ulcer proliferative	70.54 ± 20.17	18.69	0.25	37.14	0.047
Infiltrating	51.85 ± 28.67				

The mean STROMALCD10 was 70.54 ± 20.17 in subjects with Ulcer proliferative type of growth and meanSTROMALCD10was 51.85 ± 28.67 in subjects withInfiltrating type of growth. The mean difference across the group is (18.69). It is statistically significant (P Value 0.047) (Table 5).

Table 6: Comparison of mean TUMOURCD10 across study groups (N=30)

NODE	TUMOURCD10 Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Present	73.49 ± 32.04	26.25	0.12	52.37	0.049
Absent	47.24 ± 37.12				

The mean TUMOURCD10was73.49 ± 32.04 in subjects with nodal positivity and meanTUMOURCD10was 47.24 ± 37.12in subjects with negative node. The mean difference across the group is (26.25). It is statistically significant (P Value 0.049)

Table 7: Comparison of mean STROMALCD10 across study groups (N=30)

NODE	STROMALCD10 Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Present	80.51 ± 11.78	30.38	15.81	44.94	<0.001
Absent	50.14 ± 24.17				

The mean STROMALCD10 was 80.51 ± 11.78in subjects with nodal positivity and meanSTROMALCD10was 50.14 ± 24.17 in subjects with negative node. The mean difference across the group is (30.38). It is statistically significant (P Value <0.001) (Table 7).

V. Discussion:

CD 10 is an important molecule involved in integrating signals from either the cell environment or the intracellular compartment by cleaving peptides through enzymatic activity and through intracellular signalling pathways that interfere with other major signalling pathways. It is significant that CD10 expression derangement is associated with development of different tumourtypes. Among the study participants,30(50.00%) were adenocarcinomas and 30(50.00%)were adenomas. Out of the 30 adenocarcinomas that were studied, 10 were well differentiated, 10 were moderately differentiated and 10were poorly differentiated. TNM staging was used. 2(6.67%) were stage I, 12(40.00%) were stage II , 12(40.00%)belonged to stage III and4(13.33%) were stage IV.

In the present study, CD10 expression gradually increased in adenomas from low grade dysplasia to high grade dysplasia and was maximally expressed in adenocarcinomas. The difference in mean CD 10 expression between adenomas and adenocarcinomas was statistically significant (P value less than 0.001).

This observation of gradually increased expression of CD10 in adenomas and significantly increased expression in adenocarcinomas makes CD10 a potentially exploitable target of anti-cancer therapy with maximal targeting of the tumour and minimal damage to the normal epithelium. Also the significant increase is observed in CD10expression from adenoma to adenocarcinoma suggests that CD 10 has an important role in colorectal tumorigenesis and malignant transformation of adenomas(the adenoma-carcinoma sequence).

The mean difference of Tumour CD10 and stromal CD10 expression in subjects with carcinoma and adenoma was 41.41.It is statistically significant(p value 0.001) .This result of the present study correlates with that of Jang et al[5] in 2013 stated that tumour CD 10 Expression significantly increased from 14% in low grade adenoma(3 cases out of 22 cases),to 22% in high grade adenomas(6 cases out of 27 cases) and 44% in invasive colorectal carcinoma(14 cases out of 32 cases) and this support the involvement of CD10 in progression and carcinogenesis of colorectal carcinoma.

Wang et al[8] in 2013 reported there was progression in tumour CD10 Expression from 0.8%in low grade adenoma to 9.1% in high grade adenomas and 40% in invasive colorectal carcinoma.

Hirano et al[7] in 2012,Koga et al[7] in 2008,Iwase et al[10] in 2005 also supported that CD 10 Expression were reported more frequently in invasive phenotype rather than adenomas.

The present study includes 30 cases of colorectal adenocarcinomas of which , 10 were seen in T2 depth of tumour(Tumour invades muscularis propria), 11 were seen in T3 depth of tumour(Tumour invades through the muscularis propria in to the pericolorectal tissue) and 9 were seen in T4 depth of tumour(Tumour penetrates the visceral peritoneum)The difference in between Tumour CD 10median and depth of invasion is statistically significant (P value less than 0.001). A significant correlation is observed between Tumour and Stromal CD10 expression and depth of invasion.

Hirano et al reached similar conclusions in their study on colorectal carcinomas which showed that CD 10 expression correlated significantly with depth of tumour invasion.

The results of the present study are in agreement with koga et al who in their study conducted in 2008 comprising 48 cases of colorectal adenocarcinomas concluded that CD10expression correlated with the depth of tumour invasion.

Ogawa et alanalysed the expression of CD10 in the cell stroma and showed significantly more positivity in protruding lesion.Waisberg et al also reported positivity for CD10 more in exophytic appearance of tumour.Yao et al[9] in 2002 also supported the findings of significant CD 10 positivity high in proliferative lesion than in infiltrating lesion

On comparing the CD10 expression between stage I and II adenocarcinomas and stage III adenocarcinomas it was found that the difference in mean cd10 expression between the two groups was not statistically significant showing that CD10 expression does not correlates with the stage of colorectal adenocarcinomas.

Fujita et al in 2007 also showed expression of CD 10 did not show any statistical significance with the clinical staging of colorectal adenocarcinoma.Waisberg et al in 2012 analysed the expression of CD 10 in various stage of colorectal carcinoma and found no positive correlation.

VI. Conclusion:

The aim of the present study was to examine the expression of CD10cell membrane metallopeptidase in colorectal neoplasia, its role in the transition sequence from adenoma to adenocarcinoma and its association with various clinicopathological characters of adenocarcinomas. The following are the conclusions of the present study

- CD 10 expression showed a significant increase from adenoma to adenocarcinoma. This signifies that CD10 plays an important role in all stages of the adenoma-carcinoma sequence, which includes the early event of adenoma formation from normal epithelium and its malignant transformation.
- The expression of CD10 showed significant correlation with Depth of tumour invasion and nodal metastasis
- These results highlight the association of CD 10expression with malignant behaviour of colorectal adenocarcinomas and CD10 could prove to be a new biomarker for aggressiveness and prognostic information in these tumours.
- There was however no correlation between CD 10expression and the age , gender of the patient and stage of the tumour.
- The finding of gradually increasing CD 10 expression in adenoma to significantly higher expression in adenocarcinomas makes CD 10 an attractive and potential therapeutic target, which when implemented will result in maximal targeting of cancerous and also pre-cancerous tissues with minimal damage to the surrounding normal mucosa.

References:

[1]. World Cancer Report 2014. International Agency for Research on Cancer, World Health Organization.2014. ISBN 978-92-832-0432-9.
[2]. National cancer registry programme. Accessed at http://www.icmr.nic.in/ncrp/cancer_reg.htm
[3]. DeepikaMishra,SunitaSingh,Role of B cell development marker CD10 in cancer progression and prognosis. Molecular Biology International vol 2016, Article ID 4328697

[4]. Tae Jung Jang, Jeong Bae Park and Jong Im Lee, The Expression of CD10 and CD15 is progressively increased during Colorectal carcinoma development, Korea Journal of Pathology,47(4):340-347.
[5]. Levindo Alves de oliveria et al, Tissue expression of CD 10 Protein in colorectal carcinoma: Correlation with anatomopathological features of tumour with lymph node and liver metastases.JColoproctol 2012; 32(1)34-9
[6]. Kimikazu Hirano et al, Early Colorectal carcinoma: CD10 expression, mucin phenotype and submucosal invasion.PathologyInternation Aug 2012,10.1111/j.1440-1827.2012.02550.
[7]. Koga.Y., T.Yao and M.Hirahashi, 2008.Flat adenoma-carcinoma sequence with high-malignancy potential as demonstrated by CD10 and Beta Catenin expression: a different pathway from the polypoid adenoma-carcinoma sequence.Histopathology, 52(5):569-577.
[8]. Wangj.,N.El-Masry,L.Talbot,L.Tomlinson,M.Alisonand M.ElBahrawy,2013.Expression profiling of Proliferation and apoptotic markers along the adenoma -Carcinoma sequence in Familial Adenomatous Polyposis patients.Gastroenterol Respract.,pp:107534.
[9]. YaoT,TakataM,TustsumiS,NishiyamaK,Taguchik,etal.Phenotypic expression of gastrointestinal differentiation makers in colorectal adenocarcinomas with liver metastasis.pathology 2002; 34(6):556-560 10. Iwase,T.,R.Kushima,K.Mukaisho,S.Mitsufuji et al 2005.Overexpression of CD10 and reduced MUC2 expression correlate with the development and progression of colorectal neoplasms.Pathol Res Pract;201(2):83-91

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