Summary and Conclusions

Colorectal cancer is the fourth common tumor in Egypt after lymphoid ,breast and urinary tumors .

Cancer is a stem cell disease because only stem cells have the ability to self-renewal and neoplasia is essentially dysregulated self-renewal**.**

Cancer stem cells hypothesis suggest that CSCs can initiate and sustain tumor growth.

Lgr5 is a marker of intestinal stem cells that has been proposed to be implicated in carcinogenesis of intestinal tumors.

The aim of this study was to evaluate the expression of lgr5 in normal colonic mucosa , colonic adenoma and CRC and to compare these results with the clinicopathological data such as tumor type, grade and tumor stage .Statistical analysis was made for all variants.

This retrospective study was carried on 40 cases of colorectal neoplastic lesions including 6 cases of colonic adenoma and 34 cases of CRC , in which 20 cases were cribriform adenocarcinoma ,8 cases were mucoid carcinoma and 6 cases were signet ring carcinoma . Six cases of normal colonic mucosa were taken as control.

Malignant lesions were graded into 21cases of moderatly differentiated carcinoma and 13 cases were poorly differentiated . TNM staging system was applied for every case where 9 cases were stage II ,6 cases were stage III and 19 cases were stage IV.

Lgr5 immunostaining was performed for each case and was correlated with clinicopathological parameters.Lgr5 expression was detected as cytoplasmic brown granules and was scored as score group (1),(2) and (3). All cases of adenoma showed score group (1) .Out of 34 cases of CRC (23.5%) cases were score group (1), (23.5%) were score group (2) and (53%) were score group (3).

A significant correlation was found between lgr5 expression and the type of colorectal lesions as score of lgr5 expression increased with progression of lesions from adenoma to carcinoma (p value <0.01) this means that lgr5 expression might be involoved in colorectal carcinogenesis .

A significant correlation was found between lgr5 expression and the stage of CRC (p value <0.05) where out of 9 cases of stage II, (66.7%) showed score of lgr5 (1) , (22.2%) showed score of lgr5(2) and (11.1%) showed score of lgr5 (3) , out of 6 cases of stage III (16.7%) showed score of lgr5 (1), (33.3%) showed score of lgr5 (2) and (50%) showed score of lgr5 (3) ,out of 19 cases of stage IV , (5.3%) showed score of lgr5 (1) , (21%) showed score of lgr5 (2) and (73.7%) showed score of lgr5 (3). This suggest that lgr5 expression may play a role not only in tumor initiation but also in the progression of the tumor.

No correlation was found between lgr5 expression and the histopathological type of CRC and the grade of CRC (p value >0.05) .As for histopathological type of CRC, in cribriform adenocarcinoma**,** (20%) showed score group (1), (10%) showed score group (2) and (70%) showed score group (3).In mucoid carcinoma , (12.5%) showed score group (1) , (62.5%) showed score group (2) and (25%) showed score group(3).In signet ring carcinoma ,(50%) showed score group(1), (16.7%) showed score group (2) and (33.3%) showed score group (3) .As regard the grade of CRC out of 21 cases of grade II,(19%) showed score group (1) , (19%) showed score group (2) and 62% showed score group (3). Out of 13 cases of

grade III, (30.8%) showed score group (1), (30.8%) showed score group (2) and (38.4%) showed score group (3).

In conclusion the present study showed that lgr5 as stem cell marker of cells with intestinal differentiation was expressed and presented with different expression in normal colonic mucosa ,adenoma and CRC.The study also showed increased lgr5 expression in advanced stage of CRC. This may suggest its possible involvement in colorectal tumorigenesis and invasion.