University of Baghdad				
College Name	**MEADICIAL**			
Department	***Medical Microbiology***			
Full name as written in passport	**Ibrahim Fadhil Ibrahim Aldrubi**			
e-mail				
Career	◌ **Assistant Lecturer**	◌ **Lecturer**	◌ **Assistant Professor**	◌ **Professor**
	◌ **Master**		**PhD** ◌	● **diploma**
Thesis Title	**MOLECULAR DETECTION OF JC VIRUS, P53, RETINOBLASTOMA GENES AND β-CATENIN IN PATIENT WITH COLORECTAL ADENOCARCINOMA**			
Year	**2015**			
Abstract	**John Cunningham Virus (JCV) a member Polyomaviridae family is a type of human polyomavirus. It's widespread virus detected in different populations throughout the world. JCV encodes for T-Ag which have oncogenic capability through interaction with different regulatory pathways and can interfere with cell cycle control and genomic instability mechanisms. The association between JCV and colorectal carcinoma still awaits the final conformation.** **Aims of study:** **1. Determine the possible role of JCV in colorectal carcinoma by detection, quantification of T-Ag gene and agnoprotein gene load and demonstrating JCV DNA in both colorectal carcinoma and normal colonic tissue biopsies.** **2. Detect the seropositivity of JCV antibodies among the study groups.** **3. Estimate the possible interaction of T-Ag with *B*-catenin and P53 and retinoblastoma tumor suppressor genes.** **Methods:** **This study was designed as prospective case-control study that involved fresh colonic tissue biopsies taken through colonoscopy from 28 patients with colorectal cancer and from 33 patients who did not have colorectal carcinoma attending to GIT endoscopic unit of Oncology Hospital, Baghdad Teaching Hospital, and Al-Yarmouk Teaching Hospital during the period from June 2013 to march 2014. JCV DNA was detected and quantified by real time PCR for T- Ag gene and agnoprotein genes. Using JCV bioprobe, chromogenic in situ hybridization (CISH) technique was used to detect JCV in tissue biopsies. Serological detection of JCV IgG antibodies was detected by ELISA. *B*-catenin II** **and retinoblastoma protein products were detected by immunohistochemistry. Tumor suppressor gene P53 was detected by fluorescent in situ hybridization technique.**			

	Results: **□ Among the total 28 colorectal carcinoma cases, the highest frequency 10/28(35.7%) were detected in age group 50-59 years and its more frequent in male than female with ratio 1.8:1.** **□ Histopathological finding revealed that 24(85.72%) cases were non mucinous adenocarcinoma and moderately differentiated adenocarcinoma was more frequent 21/28 (75%) among grades of CRC.** **□ JCV T-Ag was detected in 16 (57.1%) of CRC group and 9/33(27.3%) of control group, with viral load VL mean 416.93 ± 217.77 copy/µg for CRC group and 229.866 ± 111.49 copy/µg for the control group which in turn showed significant difference between the study groups** **□ Agnoprotein gene was detected in 12/28 (42.9%) of CRC group with VL mean (317 ± 129.12) compared to 5/33 (15.2%) with VL mean (152.94 ± 105.14) in non CRC patient (p=0.016).** **□ Substantial agreement was found between T Ag gene and agnoprotein gene by real time PCR for both CRC group K=0.72 and control group K=0.784.** **□ Using chromogenic in situ hybridization technique JCV DNA was detected in 15/28(53.6%) of CRC compared to 10/33(30.3%) in control group (p=0.065). Significant differences were detected comparing the percentage of JCV DNA in study groups according to intensity, score and signal pattern of involvement (p<0.05).** **□ Substantial agreement was found between T Ag by qPCR and JCV DNA by CISH among the study groups. Moderate agreement was found between JCV agnoprotein gene by qPCR and JCV DNA by CISH among the study groups.** **□ Serological detection of JCV antibodies by ELISA revealed 14/22 (63.6%), 15/28 (53.6%) of CRC group and control group showed positive results respectively. (p=0.474). Poor agreement was found between (T Ag by real time PCR and by CISH) and JCV antibodies by ELISA in the study groups.** **□ Nuclear localization of *B*-catenin was detected by immunohistochemistry in 12/28(42.86%) of CRC groups, while none of the control group revealed positive nuclear staining (p<0.05). No significant associations found neither to grades nor to the site of tumor.** **□ Retinoblastoma protein was detected by IHC. Only ten out of 28 (35.7%) showed positive nuclear staining, 18/28 (64.3%) of CRC revealed negative nuclear staining. All control group showed positive nuclear staining (p=0.000). No agreement was found between Rb protein and JCV T Ag, agnoprotein gene and JCV DNA by CISH among study groups.** **□ P53 deletion was detected using FISH technique. Five cases out of 25 were with deleted p53 region, 3/25 were with deleted whole**

chromosome 17, and 1/25 revealed combination signals of deleted p53 region and deleted whole chromosome 17. The results were invalid for statistical analysis.

Conclusion:

This study highlighted the possible role of JCV which might participate in different ways in the pathogenesis of colorectal carcinoma, which in agreement with other studies. Despite these evidences the role of JCV in colorectal malignancies and its oncoproteins in promoting transformation is still far from clear.