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Molecular Targeting of EBERs, EBV- LMP-1 and Cyclin-Dependent Kinases Products in Colorectal Carcinoma Tissues of Iraqi Patients

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Abstract: Colorectal cancers (CRC) have a major toll to healthcare systems worldwide, often fatal cancers with a rapidly increasing incidence. Epstein-Barr virus (EBV) is ubiquitous virus and its role in tumor development and maintenance remains unclear. However, latent membrane protein 1 (LMP-1) of EBV is essential for cellular transformation. Cyclin-dependent kinases (CDK) comprised a family of heterodimeric kinases, playing a central role in the regulation of cell cycle progression, transcription, differentiation and metabolism. To examine the impact of cellular dysregulation mediated by the concordant protein expressions of CDK and EBV- latent genes in implicated in colorectal carcinogenesis. Seventy-five formalin-fixed, paraffin embedded colorectal tissues were enrolled, among them, 60 biopsies obtained from patients with colorectal carcinomas (30 biopsies from the cancer mass and another 30 biopsies from themarginal tissues of these colorectal cancers) and 15 tissues as control group, which were proved by colonoscopic and histopathological examinations as an apparently normal colorectal tissues. Detection of EBERs was done by an ultra sensitive version of in situ hybridization method where asimmunohistochemistry detection system was used to demonstrate the expression of LMP-1& CDK genes. Detection of EBERs-ISH reactions in mass tissues with CRC was documented in 56.7% (17 out of 30 cases), in the colorectal cancermarginal tissues was 26.7% (8 out of 30 cases), and in the control colorectal tissues constituted 20% (3 out 15). Expression of LMP1 was detected by IHC in 43.4% (13 out of 30) of the mass - colorectal cancer group, in 23% (7 out of 30) marginal tissues with colorectal cancer, and in 13.3% of the control tissues. Expression of total CDK-protein was detected by IHC in 17 cases (56.7%) of the CRC- mass group, 11 cases (36.7%) of CRC-marginal group, and 3 cases (20%) in control colorectal tissues group. The differences between the percentages of EBERs-EBV -ISH, LMP-1 and CDK in CRC and control tissues groups are statistically highly significant (P value = < 0.0001). Our results indicate that the significance prevalence of CDK as well as EBV-latent genes - expression in colorectal carcinoma could point to an important contributing role of these molecular and viral factors in the development and carcinogenesis of a subset of colorectal cancers.

Key word: EBERs, LMP-1, EBV,CDK, ISH, IHC.