FUNCTIONAL CHARACTERIZATION OF EBER2 VARIANTS OF EPSTEIN-BARR VIRUS IN THE PATHOGENESIS OF NASOPHARYNGEAL CARCINOMA

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Genome-wide association studies of Epstein-Barr virus (EBV) genomic sequences harbored in primary tumour biopsies of nasopharyngeal carcinoma (NPC) and saliva of healthy adult donors in Hong Kong demonstrated that EBV variants containing 4-bp deletion 3' of EBER2 gene and eight single nucleotide polymorphisms (SNPs) in the EBER2 region (designated NPC-EBV), as compared to the wild type EBV (wt-EBV), are highly associated with NPC [1]. In this project, we investigate whether the EBER2 variants have different structures and functions in NPC.

The structures of in-vitro transcribed EBER2 variants are determined by selective 2′-hydroxylacylation analyzed by primer extension and mutational profiling (SHAPE-MaP). The EBER2 variants of NPC-EBV and wt-EBV, represented by M81 and B95-8, respectively, share similar structures but differ in the arms of the secondary loop structure near the 5' end (5' arm) which contains most of the SNPs, in accordance with the predicted secondary structure by RNAfold WebServer. Interestingly, the 5' arm of EBER2 was found to contain the binding sites of the terminal repeats of EBV and a B cell-specific transcription factor known as PAX5 [2]. We postulate that the EBER2 variants can have different functions in NPC. Overexpression of either M81 or B95-8 EBER2 promotes the proliferation of C17 cell line whilst silencing of EBER2 in C666-1 cell line decreases the proliferation rate significantly. We conclude that M81 and B95-8 EBER2 have different secondary structures and both of these variants have proliferative function in NPC. Further work to delineate the function of the EBER2 variants will be performed.

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