MODULATION OF MIR-663A EXPRESSION BY EBV-ENCODED G PROTEIN–COUPLED RECEPTOR (GPCR), BILF1, IN BURKITT LYMPHOMA

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The Epstein–Barr virus (EBV) is a γ-herpesvirus infecting over 90% of adults worldwide [1]. Similar to other herpesviruses, EBV encodes for a G protein–coupled receptor (GPCR), BILF1, affecting a multitude of cellular signaling pathways. BILF1 has been identified to promote immune evasion and tumorigenesis, ensuring a life-long persistence of EBV [2]. The structure of BILF1 have been well studied, but its role is not fully understood. Given the important role of miRNAs in regulating nearly every aspect of biology, here, we have studied the impact of BILF1 on genes encoding miRNAs in B-cells and BL primary tumours [3]. We transfected isolated primary human germinal centre (GC) B cells, the presumed progenitors of BL, with BILF1 plasmid and performed RNAseq assay. In parallel, we re-analyzed BL cases by Abate et al [4] with the aim to identify the transcriptional targets of BILF1 in primary tumours. We found that when expressed in B cells, BILF1 was able to regulate the expression of several genes encoding miRNAs. In particular, BILF1 expression was significantly associated with an upregulation of miR-663a host gene (HG). This gene encodes for miR663a which has been described as oncomiR in other diseases; however, its role in BL has never been studied. The dynamic changes in miR663aHG expression observed in B cells after BILF1 transfection were validated in BL primary tumorus where miR663aHG was similarly up-regulated in primary eBL showing a marked expression of BILF1. Moreover, we observed that the expression levels of miR-663aHG significantly correlated with miR-663a, suggesting that miR-663a was co-expressed with its host gene miR663aHG under the regulation of the host gene promoter. ddPCR showed a positive correlation between BILF1 and miR663a in both B-cells and primary tumours. By using a bioinformatic approach, we identified the validated and predicted target genes of miR-663a. We found that miR663a-targets were enriched for genes involved in B-cell proliferation and differentiation, MYC translocation, immune response to viruses and fatty acid metabolism. **Conclusions:** This study defined a new role of BILF1, highlighting a positive correlation with miR663a which may play a substantial role in the aetiology of BL by regulating networks involved in B-cell proliferation.

References.

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