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The regulation of the pro-inflammatory cytokine interleukin 6 (IL6) by Epstein-Barr virus (EBV)

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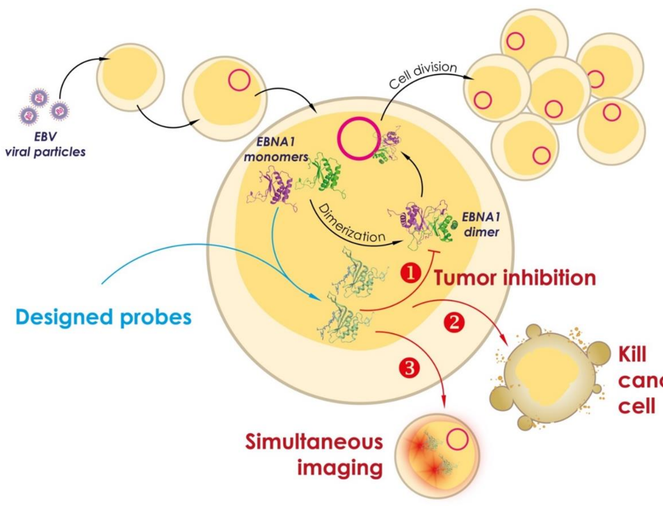
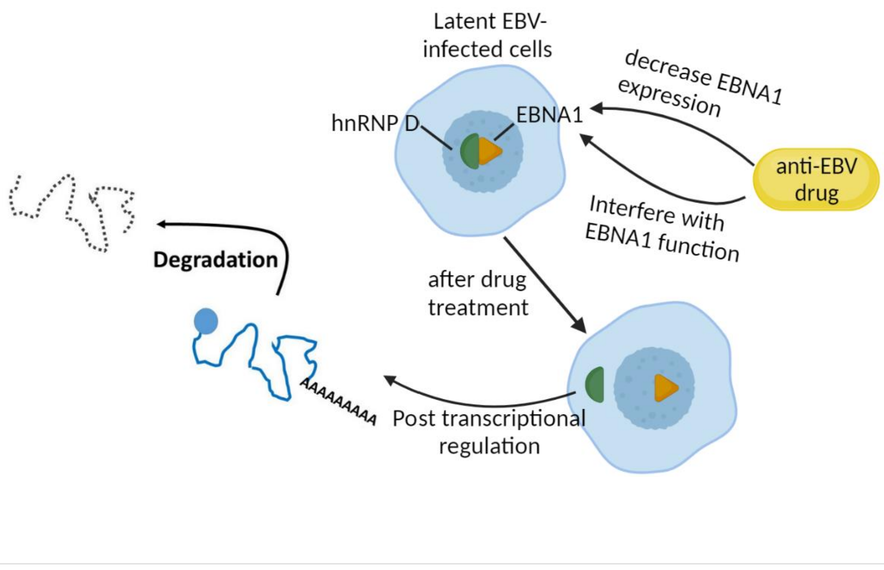
Introduction

The Epstein–Barr virus (EBV) is a human herpesvirus closely related to many malignancies of lymphocyte and epithelial origins, such as gastric cancer, Burkitt's lymphoma, and nasopharyngeal carcinoma (NPC). NPC is a malignant epithelial tumor which is 100% associated with EBV latent infection. Most of the NPC cases are concentrated in southern China, especially in Guangdong and Hong Kong. To our knowledge, overexpression of pro-inflammatory cytokines may result in a loss of balance of the immune system and cause damage to human bodies. Interleukin 6 (IL6) is a pro-inflammatory cytokine which is important in tumor progression. In addition, gene expression is regulated by both transcriptional and post-transcriptional pathways, post-transcriptional regulation is an important mechanism to modulate the mature mRNA level in mammalian cells. AU-rich element binding factor 1 (AUF1)/heterogeneous nuclear RNP D (hnRNP D) is known for its function in destabilizing mRNAs, including cytokines and cell cycle regulators. In this project, our aim is to determine the role of hnRNP D played in EBV-infected cells and how our anti-EBV agents will affect the function of hnRNP D. The results of this study will provide a new insight of how the pro-inflammatory cytokine expression can be regulated by EBV.

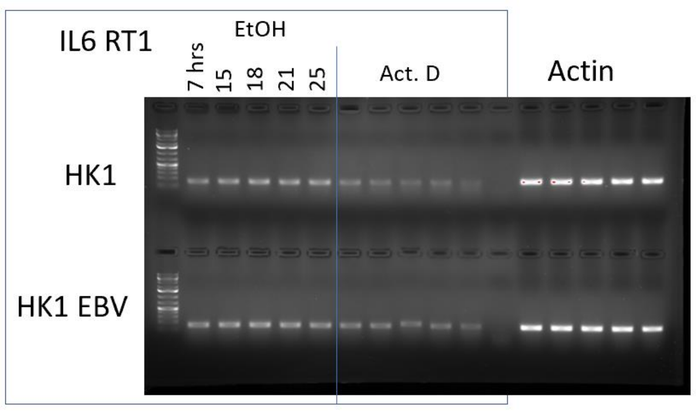
Methods





Results

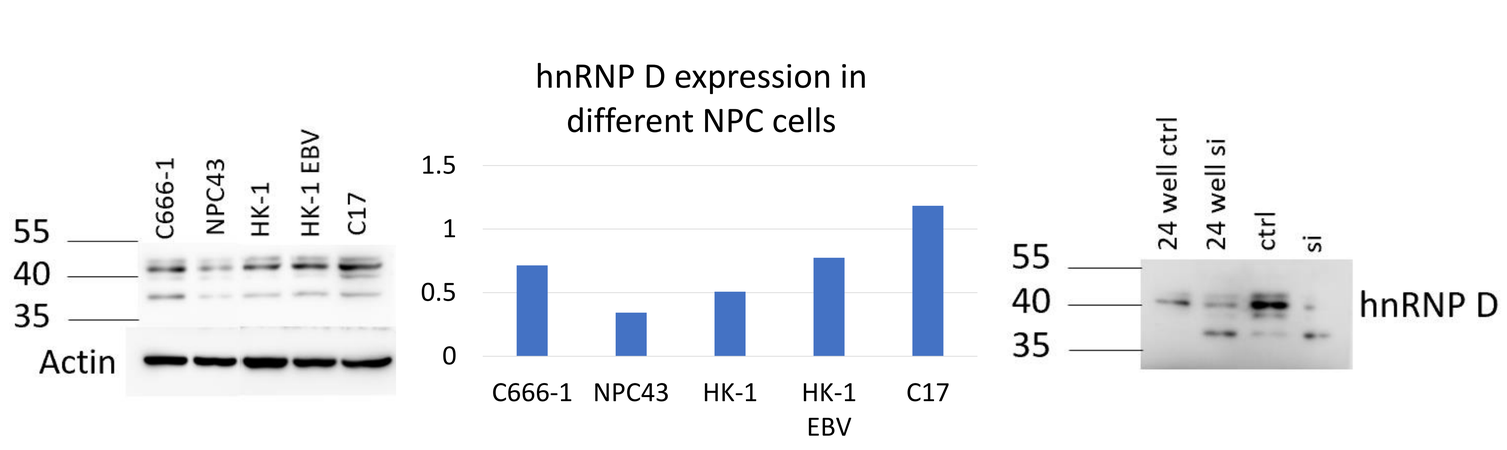
The IL6 mRNA degraded significantly faster in the HK1 cells when compared with the matched HK1-EBV cells, suggesting that the higher IL6 production could be due to the higher mRNA stability maintained by the presence of EBV.



Results

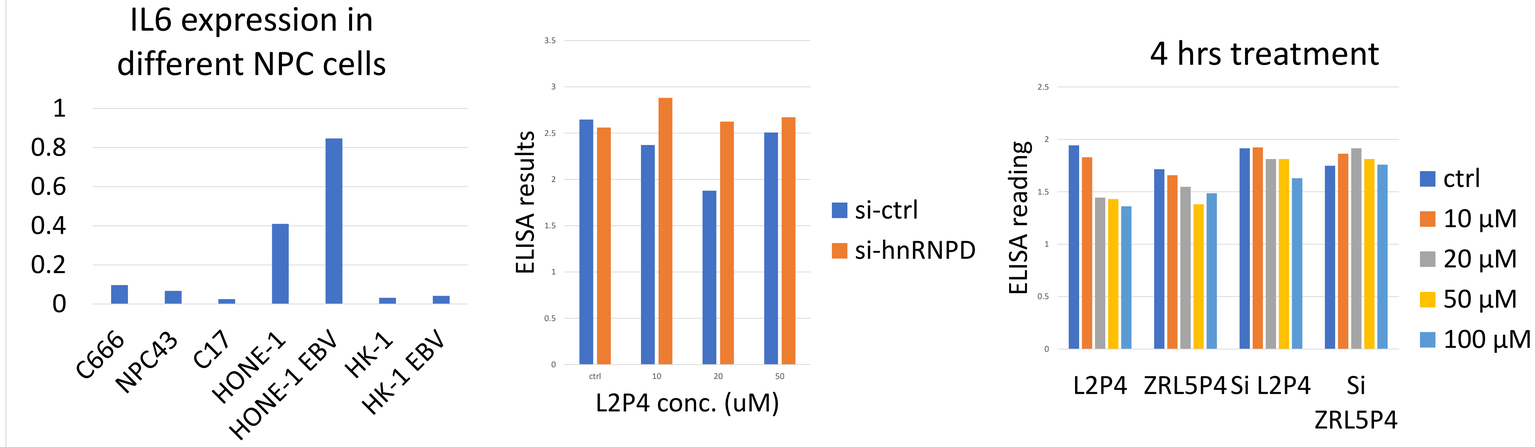
We aim to investigate the role of hnRNP-D played in EBV-infected cells. Western blot was performed to study the hnRNP D expression levels in several EBV-positive/negative NPC cell lines

The right figure showed hnRNP D knock down in EBV-positive HONE-1 EBV cell



Results

ELISA was performed to detect the secreted IL6 expression in HONE-1 EBV cells with various concentrations of L2P4 or ZRL5P4. In the hnRNP-D depleted cells, the reduction of IL6 levels by both L2P4 and ZRL5P4 were disrupted, which illustrated that hnRNP-D is essential for L2P4 and ZRL5P4 to decrease the IL6 expression levels in EBV-positive NPC cell lines.



Conclusions

As a summary, we successfully reduced hnRNP D protein expression in EBV-positive NPC cells, as to investigate the role of hnRNP-D in regulating the gene expression of the pro-inflammatory cytokines IL6. Also, The presence of EBV can play an important role of the IL6 mRNA stability to regulate the secreted IL6 production in EBV-positive NPC cells.

Acknowledgements

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