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In silico evidence of de novo interactions between ribosomal and Epstein - Barr virus proteins

Edmund Ui-Hang Sim* and Shruti Prashant Talwar

Abstract

Background: Association of Epstein-Barr virus (EBV) encoded latent gene products with host ribosomal proteins (RPs) has not been fully explored, despite their involvement in the aetiology of several human cancers. To gain an insight into their plausible interactions, we employed a computational approach that encompasses structural alignment, gene ontology analysis, pathway analysis, and molecular docking.

Results: In this study, the alignment analysis based on structural similarity allows the prediction of 48 potential interactions between 27 human RPs and the EBV proteins EBNA1, LMP1, LMP2A, and LMP2B. Gene ontology analysis of the putative protein-protein interactions (PPIs) reveals their probable involvement in RNA binding, ribosome biogenesis, metabolic and biosynthetic processes, and gene regulation. Pathway analysis shows their possible participation in viral infection strategies (viral translation), as well as oncogenesis (Wnt and EGFR signalling pathways). Finally, our molecular docking assay predicts the functional interactions of EBNA1 with four RPs individually: EBNA1-eS10, EBNA1-eS25, EBNA1-uL10 and EBNA1-uL11.

Conclusion: These interactions have never been revealed previously via either experimental or in silico approach. We envisage that the calculated interactions between the ribosomal and EBV proteins herein would provide a hypothetical model for future experimental studies on the functional relationship between ribosomal proteins and EBV infection.

Keywords: Epstein-Barr virus, Ribosomal proteins, EBNA1, Protein-protein interactions, Computational prediction

Background

Epstein-Barr virus (EBV), a type of herpesvirus that is common in human, has been known to be associated with cancers such as Hodgkin's lymphoma, Burkitt's lymphoma, gastric cancer, and nasopharyngeal carcinoma [1]. At the same time, the roles of ribosomal protein (RP) genes in tumourigenesis of various cancers, mainly via their extraribosomal functions, have been widely revealed [2, 3]. Despite this, there is limited understanding of the interactions between EBV and human ribosomal proteins in condition of carcinogenesis, although such interactions do exist. The EBV Nuclear Antigen 1 (EBNA1) protein has been found to bind Ribosome Protein L4 (uL4) in a complex that includes Nucleolin (NCL), and has the functional relevance of an EBV-mediated tumourigenesis [4]. Ribosomal protein s27a (eS31), on the other hand, interacts with and regulates the stability of EBV-encoded latent membrane protein 1 (LMP1) by inhibiting proteasome-mediated ubiquitination [5]. These findings represent a scant insight of the complete repertoire of functional interactions between the proteins of EBV and ribosome, of which is yet to be fully explored. Protein-protein binding assays and associated functional studies of the 80 known human RPs and 9 EBV proteins will undoubtedly be a resource-intensive and time-consuming endeavour if experimental approach is the only means of study.

As such, computational approaches for predicting host-virus protein interactions can provide viable hypothetical model for identifying potential protein-protein interaction scenarios to benefit future experimental design on the study of EBV-RP interactions. A valid in

* Correspondence: uhsim@unimas.my
Faculty of Resource Science and Technology, Universiti Malaysia Sarawak, 94300 Kota Samarahan, Sarawak, Malaysia