Determination of oncolytic activity of Pteropine orthoreovirus in killing acute myeloid leukaemia

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ABSTRACT

Introduction: The study of Pteropine orthoreovirus (PRV) as a promising candidate for oncolytic virotherapy has gained attention since the discovery of its cytotoxic effects on solid tumours. This research experiment focuses on evaluating the anti-tumour effect of the Sikamat virus (PRV7S) against acute myeloid leukaemia (AML) using THP-1 cell line and AML-M5-specific induced pluripotent stem cells (iPSCs). **Materials and Methods:** The percentage of apoptotic cells amongst PRV7S-infected THP-1 cells is measured indirectly by MTT assay and directly by flow cytometry analysis. MTT assay was performed to measure cell viability, whereas flow cytometry analysis assessed apoptotic cells. Viral replication in both cells was confirmed by TCID50 assay and real-time qPCR. Transcriptomic profiling is performed to determine the genes that are involved in the apoptotic mechanisms of PRV7S. **Results:** After 5 dpi, MTT assay indicates PRV7S significantly induces cytopathic effect (CPE) on THP-1 cells and iPSCs, which tally with the increased percentage of apoptotic THP-1 cells assessed by flow cytometry analysis. TCID50 assay and qPCR demonstrated that both cells support the viral cycle of PRV7S, with no persistent infection observed. mRNA-sequencing reveals involvement of Fas, caspase-3, caspase-7, Bax, Bak pro-apoptotic genes in the PRV7S-activated cell death pathway. **Conclusion:** The current study highlights that PRV7S could be a revolutionising treatment option for treating non-solid tumours in the future. However, these findings do not necessarily apply to other types of leukaemia. This warrants future research to explore the complex signalling pathways of oncolytic PRV and develop measures to circumvent the host antiviral response.