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Coxsackievirus type B3 is a potent oncolytic virus against KRAS-mutant non-small-cell lung cancer

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Background: Lung cancer is one of the most leading causes of cancer-related death worldwide. Over 85% of lung cancers are non-small-cell lung cancer (NSCLC), for which the 5-year survival rate is extremely low (~15.9%). Most NSCLCs are caused by the accumulation of genomic alterations, among which epidermal growth factor receptor (EGFR) mutation and KRAS mutation are two of the most predominant types. Although patients with EGFR-mutant NSCLCs have manifested a good response to EGFR inhibitors, there is a paucity of effective treatments for the KRAS-mutant NSCLCs and new strategies are urgently needed. Coxsackievirus type B3 (CV-B3) is a non-enveloped, human pathogenic enterovirus that causes mild flu-like symptoms in adults. Due to its highly lytic nature, CV-B3 has yielded an increased efficacy of viral-mediated oncolysis as compared to other viruses, which makes it as a good candidate for cancer treatment.

Methods: Seven NSCLC cell lines (A549, H2030, H23, H1975, PC-9, H3255 and HCC4006) and three normal lung epithelial cells (HPL1D, HAE and BEAS2B) were selected for this study. Cells were infected with CV-B3 (MOI 0.01) for 48 hrs. Cytopathic effects caused by virus infection were observed by light microscope, followed by crystal violet staining. MTS assay were conducted to examine the resistance of normal lung epithelial cells upon CVB3 infection. The supernatants were collected

to determine the virus titres by plaque assay. Coxsackievirus and adenovirus receptor (CAR) expression was examined via western blot.


Results: Our studies found that CV-B3 treatment led to a significant reduction of cell survival in KRAS-mutant NSCLCs but not EGFR-mutant NSCLCs nor normal lung epithelial cells. MTS assay results demonstrated CV-B3 infection didn't lead to a significant enhancement of cell death in normal lung epithelial cells. Furthermore, we showed that virus titres within the supernatants of KRAS-mutant NSCLCs are significantly higher than both EGFR-mutant NSCLCs and normal lung epithelial cells. Finally, we demonstrated that CAR expression levels were significantly increased in KRAS-mutant NSCLCs.

Conclusions: Our study found that CV-B3 is an effective and safe oncolytic virus against KRAS-mutant NSCLCs.

Speaker Biography

Haoyu Deng is a PhD student from St. Paul's Hospital, Canada. His supervisor is Dr. Honglin Luo and his former major was surgery. The medical science of UBC has become one of its priority fields which are making great contributions to the medical development. His current project is about the functional role of Gab1 in heart disease, especially looking at the mechanisms involved in the role of Gab1 in molecular signaling pathways when cardiomyocytes are infected by CVB3.

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