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主論文の題名

Human Parainfluenza Virus Type 2 Vector Induces Dendritic Cell Maturation Without Viral RNA Replication/Transcription

主論文の要旨

Introduction

Viral vector-based vaccine therapies against various human diseases are being developed around the world. Although those candidates have been reported in laboratory animal models and also in clinical trials, few have been licensed because of their unpredictable adverse effects, low efficiencies of the antigen expression, and poor immunogenicity. Thus, it is required to develop novel types of the viral vector to overcome these problems.

Background

Human parainfluenza virus type 2 (hPIV2) vector lacking the *F* gene (hPIV2ΔF) is a newly developed paramyxoviral vector that limits the infectivity to a single round, and is capable of transducing the exogenous antigen into various types of the cell. However, the immunogenicities of hPIV2ΔF itself, such as effects on dendritic cell (DC) maturation, are still elusive.

Objectives

To clarify the transduction efficiencies and DC-stimulatory activities of hPIV2ΔF in human and murine DCs.

Methods

Using reverse genetics technology, hPIV2ΔF viruses carrying the jellyfish gene encoding enhanced green fluorescent protein (hPIV2ΔF/EGFP) were generated in the packaging cell line for hPIV2ΔF. hPIV2ΔF/EGFP was infected to human or murine DCs at various multiplicities of infection (MOIs). In some experiments, retroviral vector (ReV/EGFP) was used as a control vector, and hPIV2/EGFP viruses were genomically inactivated with β-propiolactone (BPL-hPIV2ΔF) to prevent viral replication/transcription.

Results and Discussion

The transduction efficiencies were much higher in human DCs infected with hPIV2ΔF/EGFP than those with ReV/EGFP. Nearly 60% of the hPIV2ΔF/EGFP-infected human DCs expressed abundant levels of exogenous protein even at a low MOI, suggesting that hPIV2ΔF is a promising transient gene-delivering vehicle compared with other vectors. Although replication/transcription of hPIV2ΔF/EGFP were relatively suppressive in murine DCs, hPIV2ΔF/EGFP significantly matured murine DCs to comparable levels of those with lipopolysaccharide (1 μg/ml) stimulation. Furthermore, hPIV2ΔF/EGFP-induced maturation of murine DCs was mostly independent of the viral genomic replication/transcription. These results indicate that hPIV2ΔF itself has the adjuvanticity without viral replication/transcription. hPIV2ΔF carrying the exogenous gene and BPL-hPIV2ΔF carrying the exogenous protein on the viral surface may be new options for viral vector-based vaccine therapy.

Conclusions

A single round infectious hPIV2ΔF is a useful gene delivery vector. Moreover, genomically inactivated form of hPIV2ΔF still maintains its DC-stimulatory activities. Further study is required for clinical application of this vector system against human diseases.