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Abstract

Expression of Two Foreign Genes from the Optimal Insertion Sites of Newcastle Disease Virus Vector for Use as a Multivalent Vaccine and Gene Therapy Vector †

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Abstract: Many Newcastle disease virus (NDV) strains have been developed as vectors to express a foreign gene (FG) for vaccine and gene therapy purposes. A majority of these NDV vectors express only a single FG or two FGs from suboptimal insertion sites in the NDV genome, obtaining various levels of FG expression. To improve the FG expression, we generated NDV LaSota vaccine strain-based recombinant viruses to express two FGs, green fluorescent protein (GFP) and red fluorescent protein (RFP) genes, from the identified optimal insertion sites, through a combination of the independent transcription unit (ITU) and the internal ribosomal entry site (IRES) dependent expression approaches. Biological assessments showed that these recombinants expressing two FGs were slightly attenuated with approximately one order of magnitude lower in virus titers than those containing a single FG. The FG expression efficiencies from two-FG viruses were also lower than those from the single-FG viruses. However, the expression of two FGs from the optimal insertion sites was significantly ($p < 0.05$) higher than those from the suboptimal insertion sites. The expression of FGs through the ITU approach was approximately 4-fold more efficient than that through the IRES-dependent approach. These results suggest that the NDV LaSota vector could efficiently express two FGs from the identified optimal insertions sites. The ITU strategy could be used for the expression of a higher amount of FG products, whereas the IRES tactic might be useful when a lower amount of FG products are needed.

Keywords: NDV; foreign genes; GFP and RFP; optimal insertion sites; co-expression; multivalent vector