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Role of different regions of Newcastle disease virus fusion protein for its pathogenicity

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Newcastle disease virus (NDV), the causative agent of a notifiable disease of poultry, exhibits different levels of pathogenicity, dependent on the virus strain. However, the molecular determinants of NDV virulence are not fully understood.

The efficiency of proteolytic cleavage of the fusion protein (F) which is determined by presence or absence of a polybasic cleavage site, has long been considered a major determinant of NDV virulence. However, especially pigeon type paramyxovirus-1 (PPMV-1) isolates can exhibit low pathogenicity despite presence of a polybasic F cleavage site. Substitution of the genes encoding surface glycoproteins F and hemagglutinin-neuraminidase (HN) of a lentogenic (low virulence) NDV Clone 30 by those of a mesogenic (intermediate virulence) PPMV-1 (isolate R75/98) resulted in a recombinant NDV which possesses a polybasic F cleavage site (^{112}RRKKR*F^{117}), but low pathogenicity, demonstrated by an intracerebral pathogenicity index (ICPI) of 0.1. Substitution of only the Clone 30 F gene by that of PPMV-1 resulted also in a lentogenic recombinant NDV with an ICPI of 0.6, whereas the substitution of only the NDV Clone 30 sequence motif at the F cleavage site ^{112}GRQGR*L^{117} by that of PPMV-1 R75/98 ^{112}RRKKR*F^{117} resulted in a recombinant NDV with an ICPI of 1.36, indicating a mesogenic virus. The stepwise substitution of selected sequence regions of the F gene of NDV Clone 30 by those of PPMV-1 R75/98 and the characterization of the respective recombinant viruses demonstrated that the cytoplasmic tail of the F protein plays an important role in NDV pathogenicity in this context.

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