Differential attenuation of Marek's disease virus-induced tumours and late-Marek's disease virus-induced immunosuppression

ABSTRACT

Marek's disease virus (MDV) is a herpesvirus that induces lymphoma and a variety of non-neoplastic syndromes in chickens. Furthermore, very virulent plus (vv+) MDVs induce a form of immunosuppression (late-MDV-IS) that might involve both neoplastic and non-neoplastic mechanisms. The objective of this study was to evaluate whether the attenuation of MDV-induced tumours and late-MDV-IS occurs simultaneously or can be dissociated. The immunosuppressive ability of three viruses derived from vv+ MDV strain 686 (wild-type 686, the somewhat attenuated molecular clone 686-BAC, and the nononcogenic molecular clone lacking the two copies of the oncogene meq 686-BACΔMEQ) was evaluated. Late-MDV-IS was evaluated indirectly by assessing the negative effect of MDV strains on the protection conferred by infectious laryngotracheitis (ILT) vaccines. Our results showed that the ability to induce late-MDV-IS was attenuated before the ability to induce tumours. Strain 686 induced both tumours and late-MDV-IS, 686-BAC induced tumours but did not induce late-MDV-IS and 686-BACΔMEQ did not induce either tumours or late-MDV-IS. Further comparison of strains 686 and 686-BAC revealed that strain 686 reduced the humoral immune responses to ILTV (1132 vs 2167) more severely, showed higher levels of meq transcripts (2.1E+09 vs 4.98E+8) and higher expression of MDV microRNAs (mdv1-miR-M4-5p and mdv1-miR-M2-3p) in the spleen, and further reduced the percentage of $CD45^{+}$-$MHC\text{-}I^{+}$splenocytes (13 vs32%) compared to molecular clone 686-BAC. This study suggests that the immunosuppressive ability of MDV might follow a continuous spectrum and only the most virulent MDVs can overcome a certain threshold level and induce clinical MDV-IS in the ILT model.

Keyword: MHC-I; Marek's disease virus; Immunosuppression; Meq; Virulence