O-37

Engineering MVM Capsid Loci with VEGF-R Binding Peptides: Structural, Immune, and Re-Targeting Implications

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The *Protoparvovirus* Minute Virus of Mice (MVM) showed lytic capacity against human cancer cells, but its wide tropism toward non-transformed proliferative cells, and the powerful immunogenicity of the capsid, may hamper its therapeutic oncolytic aplications. Attempting to overcome these restrictions, thereby enhancing MVM oncolysis, we have explored whether distinct loci of the MVM capsid may be engineered with heterologous Vascular Epidermal Growth Factor Receptor binding peptides (VEGFR-bp), a factor playing major role in the neovascularization of solid tumours. Our study was focused in determining the: (i) structural tolerance of MVM capsid loci to the heterologous VEGFR-bp; (ii) the capacity of infectious chimeric MVM/VEGFR-bp viruses to evade neutralizing antibodies; and (iii) the possibility to re-target MVM tropism toward VEGF-R expressing cells. The results suggest a markedly different tolerance of the MVM capsid loci to genetic manipulations, also influenced by the VEGFR-bp configurations. The possibility to endow MVM with novel VEGFR-based oncolytic properties will be critically discussed along these lines.

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