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Particulate antigenic structures: highly immunogenic carriers for T cell epitopes derived from tumour antigens

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Polyomavirus-like-particles (PLPs) are empty, non-replicative, non-infectious particles that represent a potent antigen-delivery system [1]. Due to the high immunogenicity of heterologous PLPs consisting of the major polyomavirus coat protein VP1 and a foreign CD8 T cell epitope at its C-terminus it is possible to protect mice against B16-OVA melanoma [2]. Here we show that in mice protective anti-tumour immunity can be already induced by means of subcutaneous vaccination with particulate antigens, heterologous VP1-pentamers (8–9 nm in size). These VP1-pentamers carrying an immunodominant H-2K^b ovalbumin $(OVA)_{257-264}$ epitope evoked full protection in C57BL/6 mice against lethal B16-OVA melanoma challenge upon twice subcutaneous immunisations in a weekly interval. Furthermore, 60 % of mice vaccinated with VP1-pentamers carrying an immunodominant H-2K^b-restricted self-epitope of tyrosinase-related protein 2 $(TRP2)_{180-188}$ survived to lethal B16-OVA challenge. This experiment additionally underlines the capacity of PLPs to break T cell tolerance against a differentially expressed self-antigen. More importantly, heterologous capsoids of VP1- $OVA_{252-270}$ (~45 nm in size) cured mice from B16-OVA melanoma cells that had been administered 5 days prior to the first therapeutic treatment. As correlate for protection the number of $OVA_{257-264}$-specific CD8 T cells were significantly increased within the splenocyte population of treated mice even in the absence of an adjuvant (QuilA) as measured by H-2K^b-$OVA_{257-264}$-PE tetramers. The weekly treatment intervals appeared to be crucial for vaccine efficacy due to VP1-specific antibody interference. These results reveal that heterologous PLPs and even chimerical polyomavirus-specific pentamers represent highly efficient antigen carriers for inducing cell-mediated immunity against malignant diseases underlining their potency in the fight against cancer.

References

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