Novel vaccination strategies using tumour-independent antigens to induce anti-tumour immunity in solid tumours

Vinod Sommandas[1], Satwinder Kaur Singh[1], Erik H Manting[1]
[1]DCprime, Leiden, The Netherlands

Introduction

Induction of optimal anti-tumour immune response is challenging as tumour antigens are self-antigens that induce central and peripheral tolerance and antigen-specific receptors against self-antigens are negatively selected in the body. Therefore, anti-tumour responses harbour low-affinity antigen-specific receptors, that will not optimally eradicate tumours.

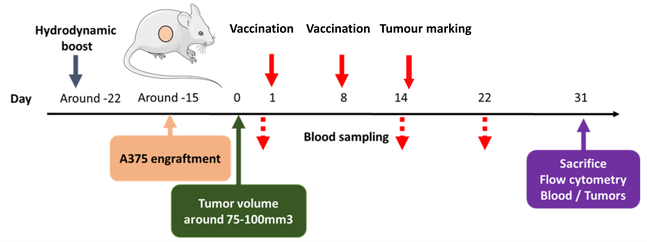
Novel insights in tumour-specific antigens, which are only present on tumour cells, has led to personalised vaccines. However, not every tumour type has a high mutation burden resulting in TSA and thus these tumour types cannot rely on these strategies. TSA are patient-specific and therefore limited for broad application in cancer patients.

In this study we present a novel vaccination strategy using foreign (non-self) antigens to mount robust immune responses which enable eradication of solid tumours. This novel strategy is based on two pillars: induction of immunity against a foreign antigen and marking the tumour as target for the induced immune response with the same foreign antigen. To proof the novel concept, we selected keyhole limpet hemocyanin (KLH) as a foreign immunogenic neo-antigen, which will serve both as vaccine composition and tumour marker to elicit effective anti-tumour immune responses.

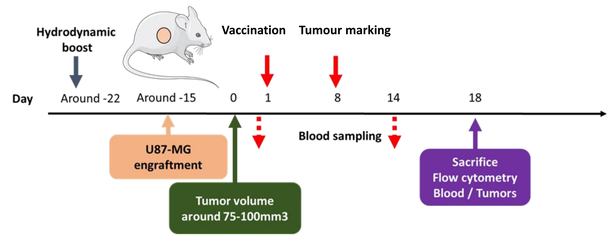
Methods

As solid tumour models, A375 melanoma or U87-MG glioblastoma cells were subcutaneously engrafted in CD34 humanised NCG mice. Mice received intraperitoneal (i.p.) vaccination with KLH. Tumour marking was performed intratumourally (i.t.) using KLH protein or DCOne® mDC loaded with KLH protein. Tumour reduction and induced immune responses were evaluated.

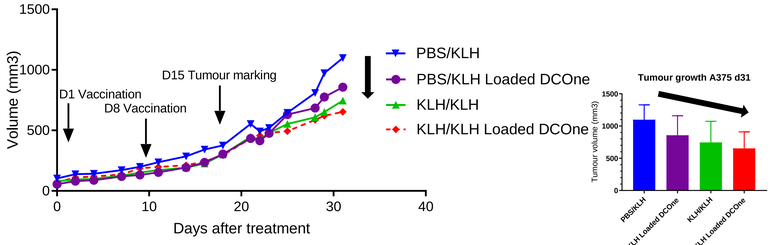
Experimental schedule A375 melanoma model



Experimental schedule U87-MG glioblastoma model



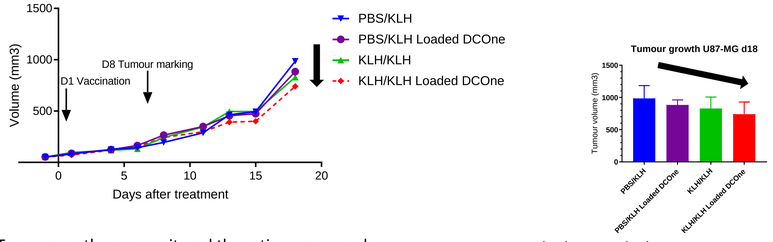
Tumour growth in humanised A375 melanoma model



Tumor growth was monitored three times per week. Top graphs represent the average of tumor growth.

The bar graph shows mean + SEM.

Tumour growth in humanised U87-MG glioblastoma model

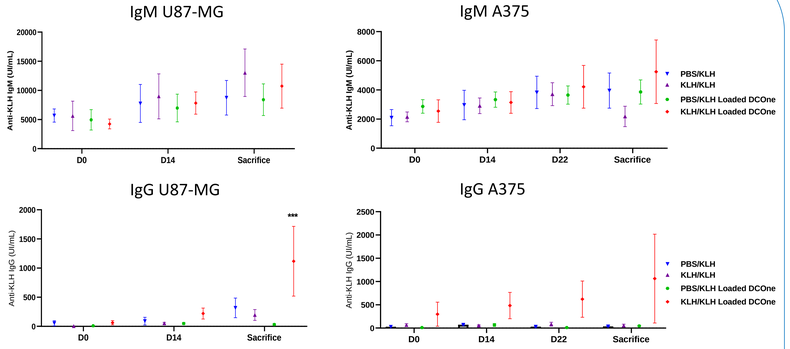


Tumor growth was monitored three times per week. Top graphs represent the average of tumor growth.

The bar graph shows mean + SEM.

IgM/IgG U87-MG glioblastoma

IgM/IgG A375 melanoma



KLH antibody response was measured in the serum. Anti-KLH IgG and IgM concentration (UI/mL) was measured with an ELISA test on the serum of mice taken at D0, D14 and at sacrifice. Graphs show the mean + standard error of the mean. Two-way ANOVA with Dunnet's multiple comparison test was used.

Conclusion

The findings in the solid tumour models support the concept that tumour-independent antigens can be used to develop vaccines against solid tumours. Importantly, DCOne® cells can be used as a carrier for intratumoural delivery of foreign proteins.