Braf cells

Mouse Braf cells were isolated from a $BRAF^{V600E}$ mutated melanoma. BRAF is mutated in 50%–70% of human melanomas, and we have developed a mouse model of melanoma that is driven by $Braf^{V600E}$, the most common BRAF mutant found in the human disease. This model is relevant because it is driven by the most important human oncogene expressed at physiological levels.

Tumour growth *in vivo*

The cells were collected from a tissue culture flask and injected subcutaneously in the right flank of C57/Bl6 mice. The resulting tumours were monitored by measuring two diameters with calipers, and extrapolating the volume to a sphere.
The mice bearing Braf tumours can be treated by intra-peritoneal, intra-venous, intra-tumoral or subcutaneous injection of the compounds. Per os administration is also possible.

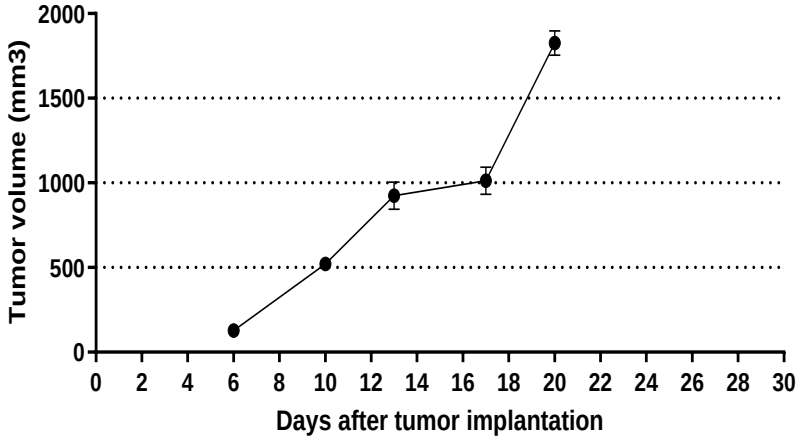

Figure 1: Tumour growth curve of the Braf WT cells as subcutaneous tumors, Mean ± SEM (n=6)

Development of the anti-PD1 & anti-PD-L1 resistant models

The resistant Braf model was developed *in vivo* from the parental Braf WT model, without genetic modifications. Braf cells have been treated intraperitoneally once a week with 12,5 mg/kg of anti-PD1 or anti-PD-L1.

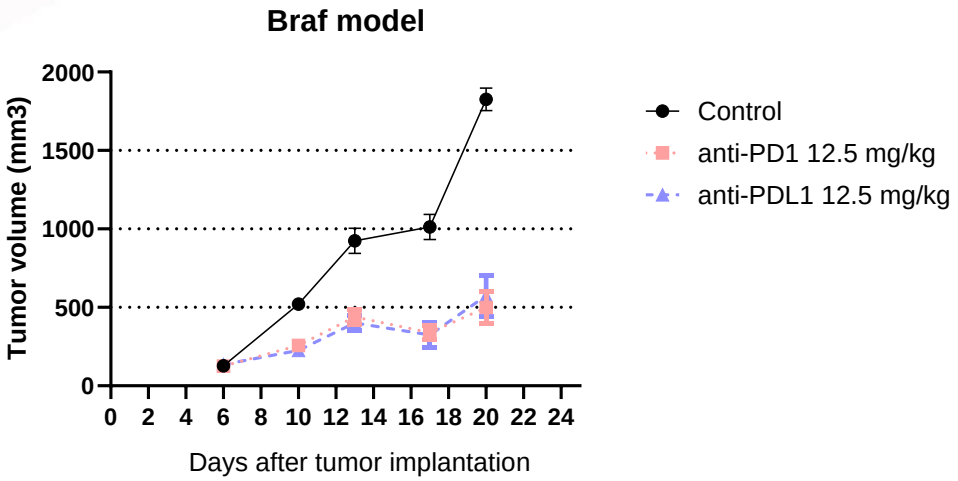

Figure 2: Effect of anti-PD1 and anti-PD-L1 treatment at 12.5mg/kg on Braf WT tumour growth, Mean ± SEM (n=6)

From D10 tumor volume was significantly reduced (at D10 pvalue= 0.0022, at D13 pvalue=0.0043, at D17 pvalue =0.0022 and at D20 pvalue = 0.0022) for the anti-PD1 and for the anti-PD-L1 treated groups compared to control group.

▪ Usage of the anti-PD1 resistant model

Due to its peculiar nature of resistant model developed *in vivo*, the PD1R model can only be implanted surgically as tumour fragments, and cannot be used for *in vitro* experiment. Braf PD1R model has been treated intraperitoneally once a week with anti-PD1.

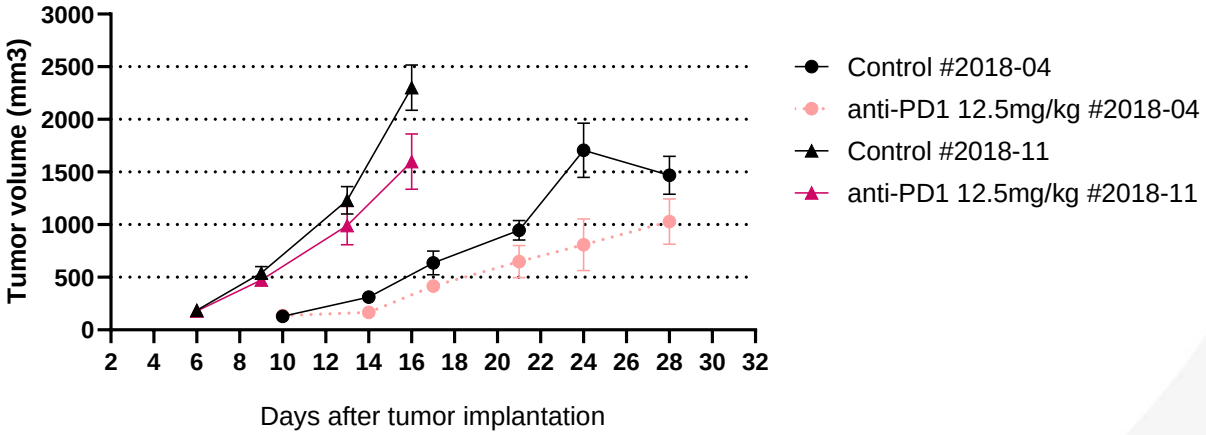

Figure 3: Effect of anti-PD1 treatment at 12.5mg/kg on Braf PD1R tumour growth, Mean ± SEM (n=6)

Both studies showed that the group treated with anti-PD1 a weak response to the ICI compared to the non-resistant model.

Usage of the anti-PD-L1 resistant model

Due to its peculiar nature of resistant model developed *in vivo*, the PD-L1R model can only be implanted surgically as tumour fragments, and cannot be used for *in vitro* experiment. Braf PD-L1R model has been treated intraperitoneally once a week with anti-PD-L1.

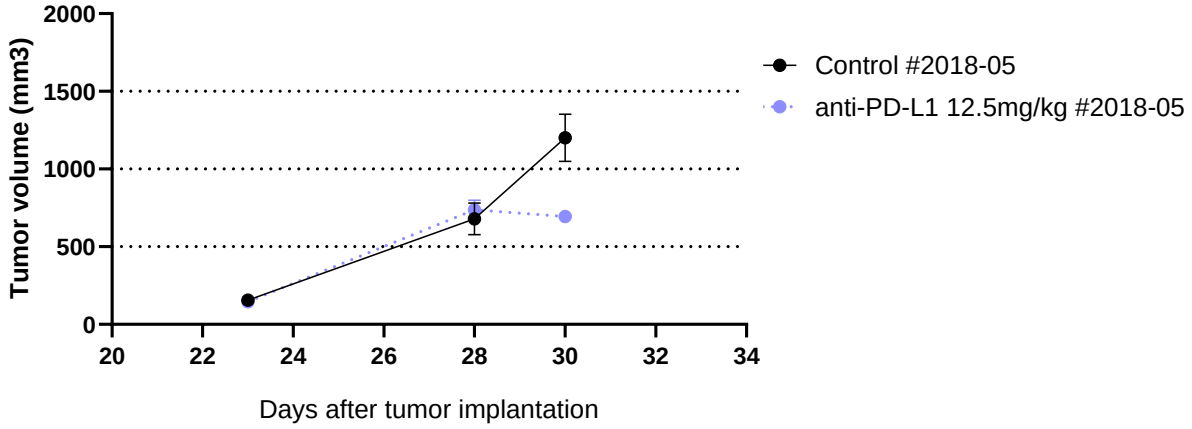

Figure 4: Effect of anti-PD-L1 treatment at 12.5mg/kg on Braf PD-L1R tumour growth, Mean ± SEM (n=6)