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Orthotopic tumor models

Implantation of tumor cells into the organ of origin allows organotypical interaction between tumor cells and surrounding stroma affecting growth, differentiation, and drug sensitivity of tumor cells. Moreover, tumor cells can spread to metastatic sites in other organs, with specificities comparable to the human situation.

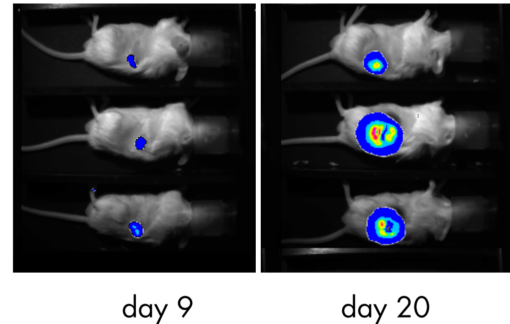
B16-F10 Luc cells (CPQ-504)

Origin: skin / mouse C57BL/6
Description: melanoma
Modification: stable expression of the firefly luciferase

Study outline

- intradermal implantation of B16-F10 cells
- randomization into treatment groups according to tumor sizes
- tumor sizes are measured either via bio-luminescence of luciferase-expressing B16-F10 once weekly or via calipering twice weekly
- animal behavior is monitored daily
- animal weights are measured three times weekly

- Accessory services: tumor wet weight and volume measurement at necropsy, blood sampling, immune cell frequency determination in the tumor and lymphatic tissues by flow cytometry, paraffin embedding of tumor tissue, histological & pathological analysis, cytokine determination, provision of tumor tissue for target validation



day 9 day 20

***Figure 1:** Mice with intradermally implanted B16-F10 cells were measured 9 days (left panel) and 20 days (right panel) after implantation.*

Study example – Gemcitabine treatment

Mice bearing orthotopically implanted B16-F10 tumors were treated with Gemcitabine.

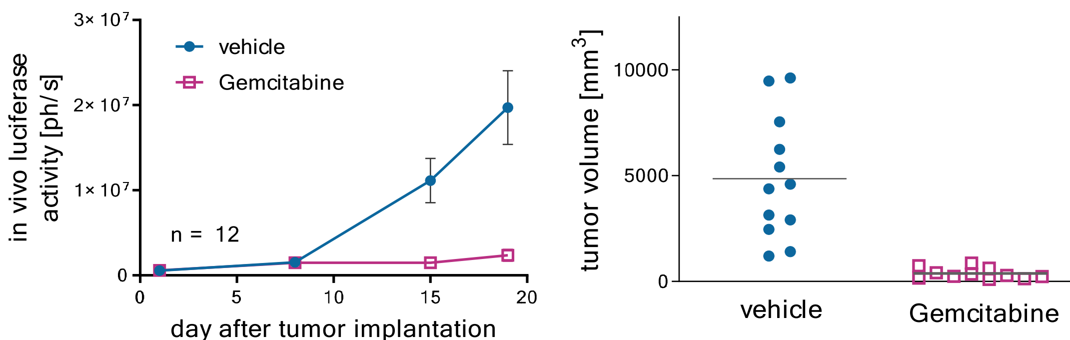


***Figure 2:** Tumor growth was monitored using BLI (left panel) and calipering (right panel) in comparison. Dot blot shows data of day 20.*

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➢ Study example – immune checkpoint inhibition

Treatment of B16-F10 tumor-bearing mice with checkpoint inhibitors anti-PD-L1, anti-PD-1 and anti-CTLA-4 antibody does not result in significant tumor growth inhibition.

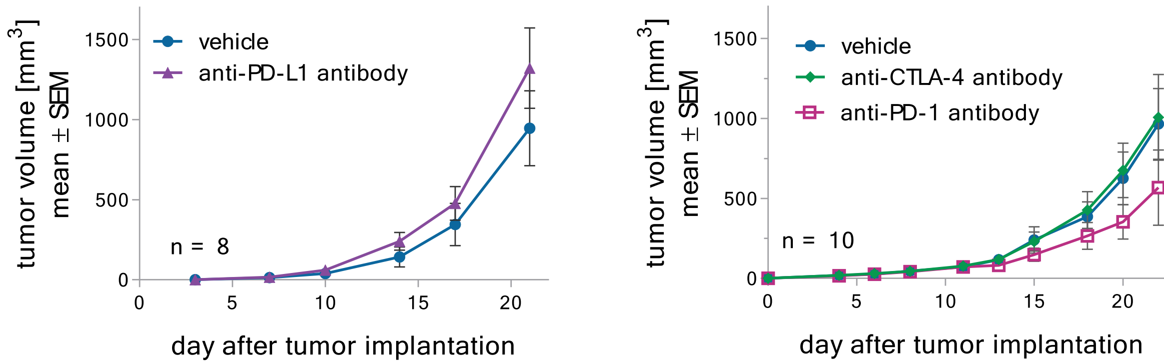

Figure 3: *Orthotopically implanted B16-F10 tumors were treated with anti-PD-1 and anti-CTLA-4 antibodies starting at day 11 and anti-PD-L1 treatment starting at day 8. Tumor sizes were measured via calipering twice weekly.*

➢ Study example – Flow cytometry analysis

The mode of action of immuno-modulating therapies can be investigated via detection of changes in the frequency of tumor-infiltrating immune cells.
The frequencies of a variety of immune cell populations in subcutaneous B16-F10 tumors is shown on the right.

For flow cytometry analysis we offer a 17-marker staining panel including

Live/dead dye, CD3, CD4, CD8a, CD45, CD25, CD11b, Ly6C, Ly6G, F4/80, CD11c, MHC class II, CD206, CD335, CD49b, B220 and FoxP3

for investigation of
T cells (CD8+, CD4+, Treg), B cells, NK cells,
Macrophages (M1, M2), dendritic cells,
Neutrophils/Granulocytes, M-MDSCs

Please find more information on the flow cytometry info sheet.

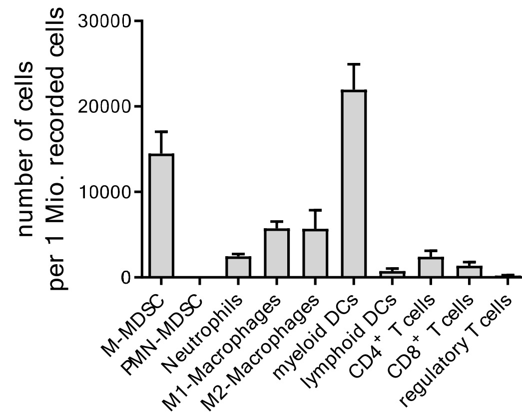

Figure 4: *Distribution of immune cells infiltrating B16-F10 tumors per 1 Million tumor suspension cells.*

➢ The B16-F10 melanoma model is also established as

- subcutaneous model
- subQperior model
- metastasis model with intravenous implantation

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