# Carcinogen-induced Mouse-Derived Isograft (cMDI) – JA-2042

REACTION BIOLOGY

IN VIVO TESTING SERVICES

## ➢ Establishment of new carcinogen-induced mouse tumor models

CBA/J mice were subcutaneously treated with Methylcholanthrene (MCA). Mice were monitored until tumorous growth appeared. Pieces of altered tissue was further engrafted in syngeneic animals to investigate tumor growth and to expand malignant tumor tissue.

These tumor graft models from carcinogen-induced malignant tissues (**C**arcinogen-induced **M**ouse-**D**erived **I**sografts, cMDI) at low passage number conserve original tumor characteristics similar to PDX models and in particular reflect original intratumoral immune cell populations.

**Characteristics**

- **Derived from carcinogen-induced tumors in mice**
- **Low passage number**
- **Propagation in mice only, no cell culture**

**Special Features**

**→ Conservation of original tumor characteristics**

**→ Original intratumoral immune cell populations**

## ➢ Sarcoma JA-2042 model

JA-2042 was isolated from a skin of a male CBA/J mouse (Fig. 1).
A syngeneic tumor model was developed with subcutaneously implanted JA-2042 tumor pieces in male CBA/J mice.
The tumor is classified as a sarcoma, containing cell from well differentiated with clear cytoplasm to anaplastic, but no giant cells.

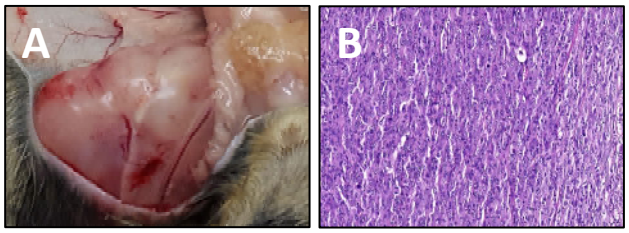


***Figure 1:*** *(A) Enlarged tumorous tissue, origin of JA-2042. (B) Subcutaneous JA-2042 tumor paraffin HE-section. Histopathological service by TPL , Freiburg, Germany*

## ➢ Study examples – Immune checkpoint inhibition

JA-2042 tumor pieces were subcutaneously implanted in CBA/J mice. Animals were treated after randomization with immune checkpoint inhibitors. Immune checkpoint inhibitor treatment was marginally anti-tumoral as single therapy, but reduced tumor growth significantly when treated in combination (anti-CTLA-4/anti-PD-1), making it an ideal tool for combination experiments (Fig.2).

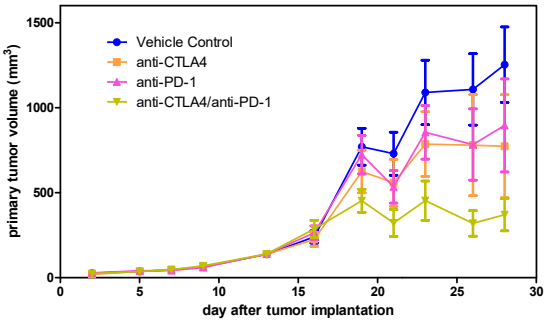


***Figure 2:*** *JA-2042 tumors were treated with vehicle, anti-CTLA-4, anti-PD-1 or anti-CTLA-4/ anti-PD-1 as indicated. Tumor volume, mean values +/- SEM*

## ➢ Target Validation

To verify the presence of your target protein in the tumor tissue, we can provide the following tumor materials: Formalin-fixed or cryo-conserved tumor tissue.

➢ *please turn over* ➢

## ➢ Study example – Flow cytometry analysis

The mode of action of immuno-modulating therapies can be investigated via flow cytometry analysis. Immune cells in the tumor, lymphatic tissues or other organs will be isolated and their distribution examined via staining with various antibody panels. Examples for JA-2042 tumors are presented (Fig. 3).

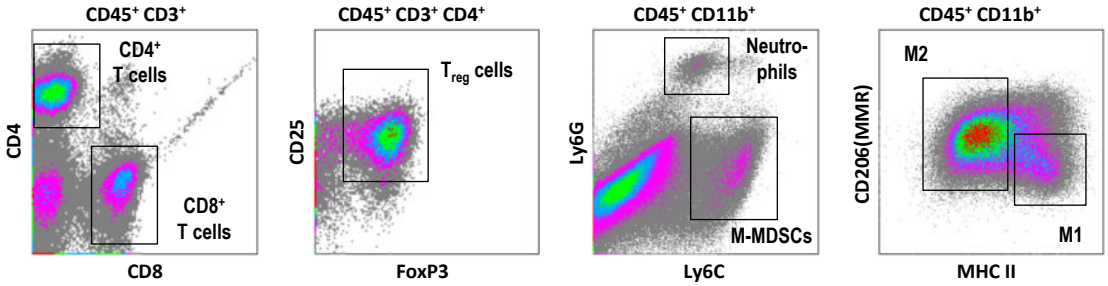


***Figure 3:*** *Representative flow cytometry blots of tumor-infiltrating immune cell subsets in JA-2042 tumors. MDSC = myeloid-derived suppressor cells, M = monocytic, MMR = Macrophage mannose receptor*

## ➢ Comparison of immune cell populations from newly developed MDI tumors to cell-derived syngeneic tumor models

The proportion of immune cell populations differs between syngeneic models. Striking in the newly established primary JA-2042 tumors is the high number of T cells, especially $T_{reg}$ cells.

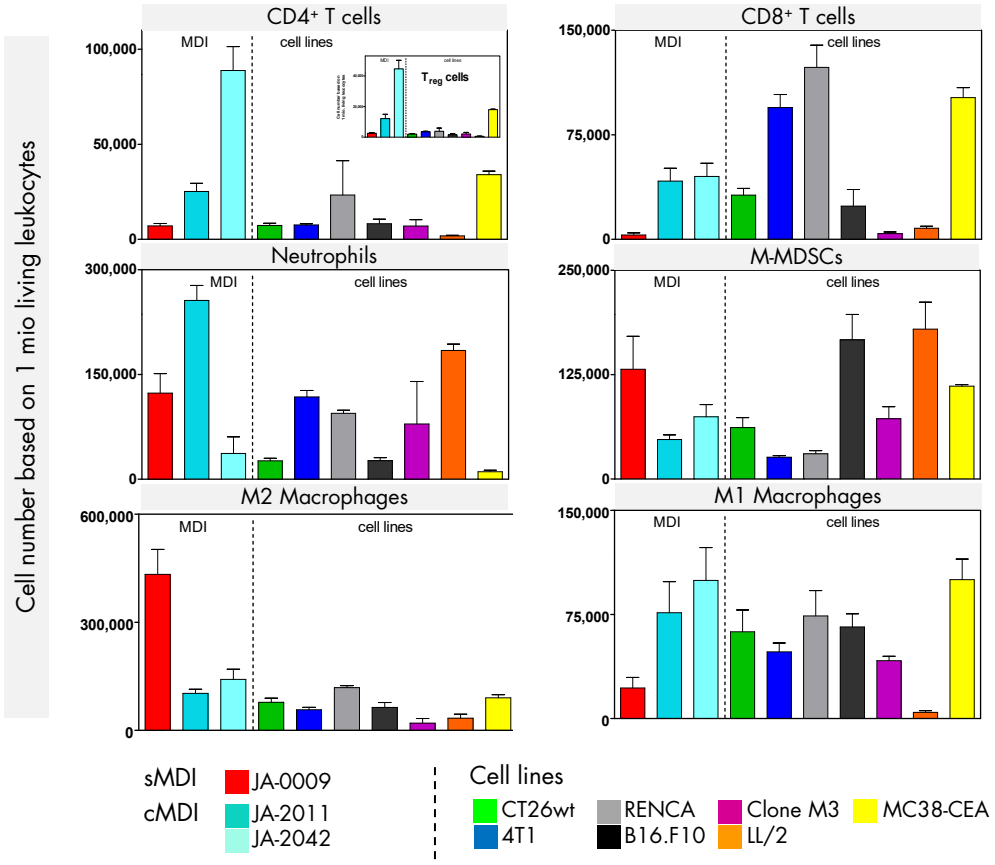


***Figure 4:*** *Proportion of immune cells infiltrating tumors per 1 million living leukocytes.*