Spontaneous Mouse-Derived Isografts (sMDI) – JA-0009

REACTION BIOLOGY

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➢ Establishment of new spontaneously arisen mouse tumor models

Different mouse strains are monitored during aging until when signs of illness occur a necropsy is performed. Pieces of any altered tissue are further engrafted in syngeneic animals to investigate tumorous growth and to expand malignant tumor tissue.

These tumor graft models from spontaneously occurring malignant tissues (**s**pontaneous **M**ouse-**D**erived **I**sografts, sMDI) at low passage number conserve original tumor characteristics similar to PDX models and in particular reflect original intratumoral immune cell populations.

Characteristics

- **Derived from spontaneous 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

➢ Adenocarcinoma JA-0009 model

JA-0009 was isolated from a lymph node of a two years old DBA/2N mouse (Fig. 1A). A syngeneic tumor model was developed with subcutaneously implanted JA-0009 tumor pieces in female DBA/2N mice.
The tumor is of epithelial origin, possibly exocrine such as mammary gland, pancreas, salivary etc. (under investigation). There are areas of neoplasia suggesting epithelium to mesenchymal transition (Fig. 1B).

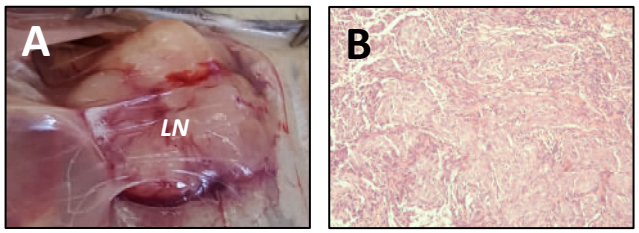

Figure 1: *(A) Enlarged axillar lymph node (LN), origin of JA-0009. (B) Subcutaneous JA-0009 tumor paraffin HE-section. Histopathological service by TPL , Freiburg, Germany*

➢ Study examples – Immune checkpoint and chemotherapeutic inhibition

JA-0009 tumor pieces were subcutaneously implanted in DBA/2N mice. Animals were treated after randomization with immune checkpoint inhibitors or Gemcitabine. Whereas Gemcitabine abolished tumor growth, immune checkpoint inhibitor treatment was, if at all, only partially effective (Fig. 2).

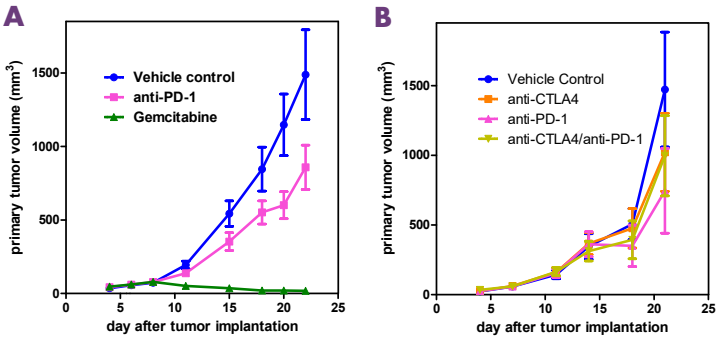

Figure 2: *JA-0009 tumors were treated with (A) vehicle, anti-PD-1 antibody or Gemcitabine or (B) vehicle, anti-CTLA-4, anti-PD-1 or anti-CTLA-4/anti-PD-1 as indicated. Tumor volume, mean values +/- SEM*

➢ 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* ➢

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➢ 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-0009 tumors are presented (Fig. 3).

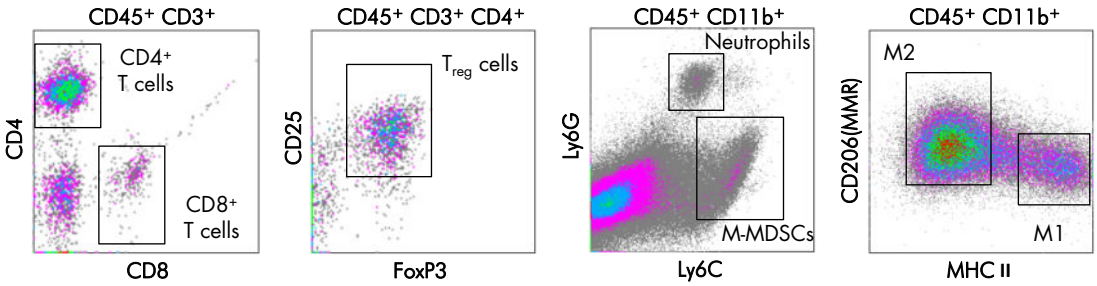

Figure 3: *Representative flow cytometry blots of tumor-infiltrating immune cell subsets in JA-0009 tumors. MDSC = myeloid-derived suppressor cells, M = monocytic, MMR = Macrophage mannose receptor*

➢ 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-0009 tumors is the high number of M2 macrophages and the low number of T cells, especially CD8+ T cells are found to be almost absent.

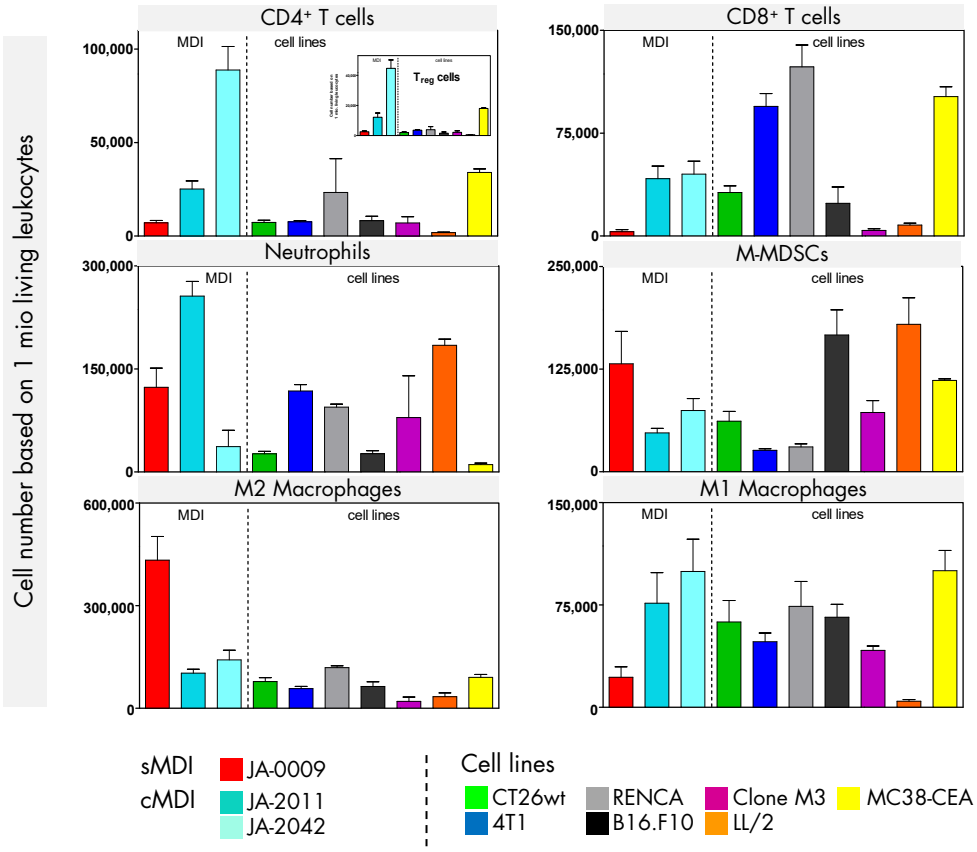

Figure 4: *Proportion of immune cells infiltrating tumors per 1 million living leukocytes.*