

**Role of the calcium binding GPRC6a
receptor in chemotherapy
mediated immunogenic cell death
induced tumor control**

Dagmar Quandt

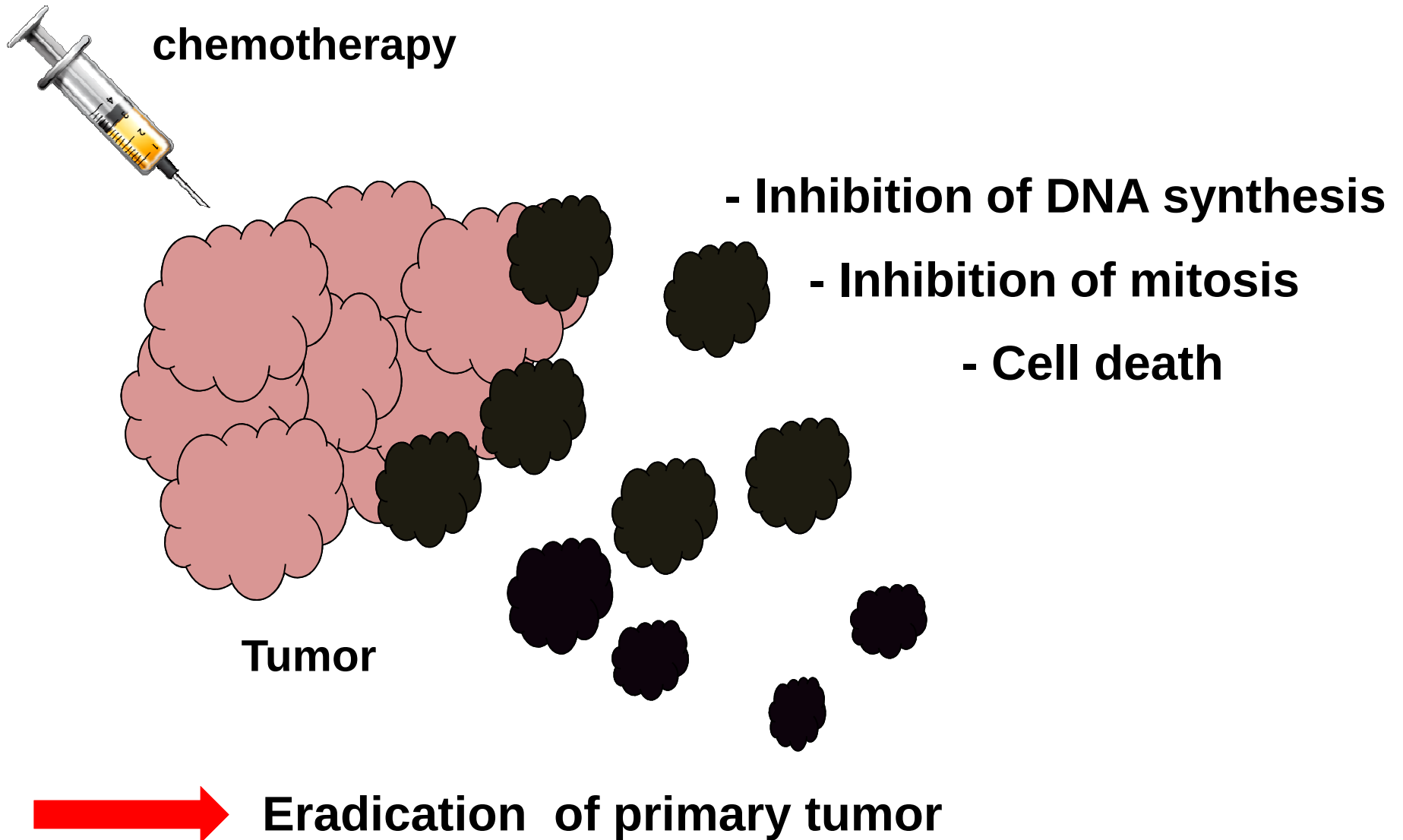
Institute for Medical Immunology

Presenter Disclosure

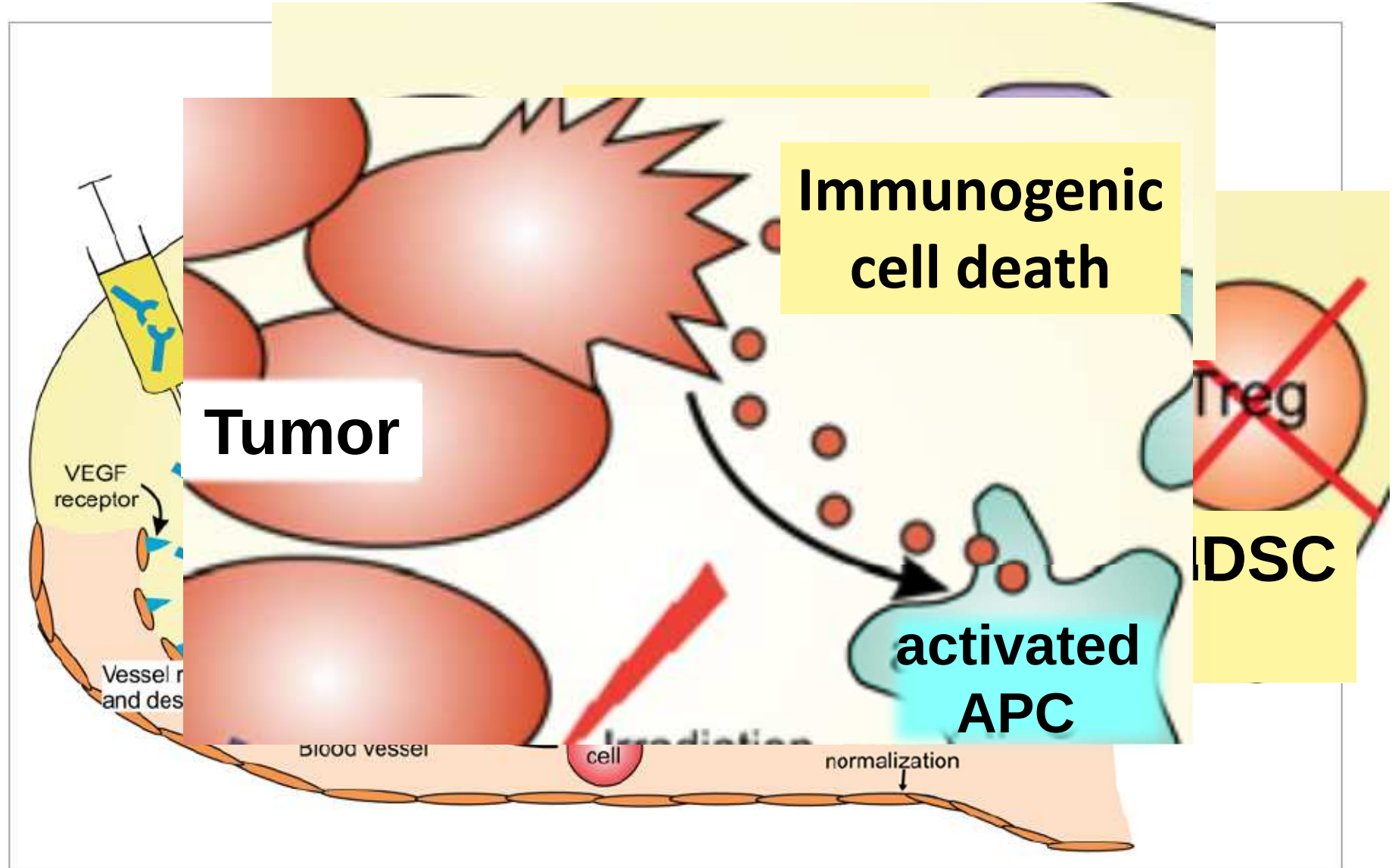
Dagmar Quandt

No Relationships to Disclose

Chemotherapy induces cytotoxicity and tumor growth arrest



Chemotherapy modulates tumor microenvironment



verändert aus Kershaw et al. OncoImmunology, 2013; Tel et al. Cancer Immunol Immunother. 2012

Immunogenic cell death (ICD) inducing and non-inducing chemotherapy

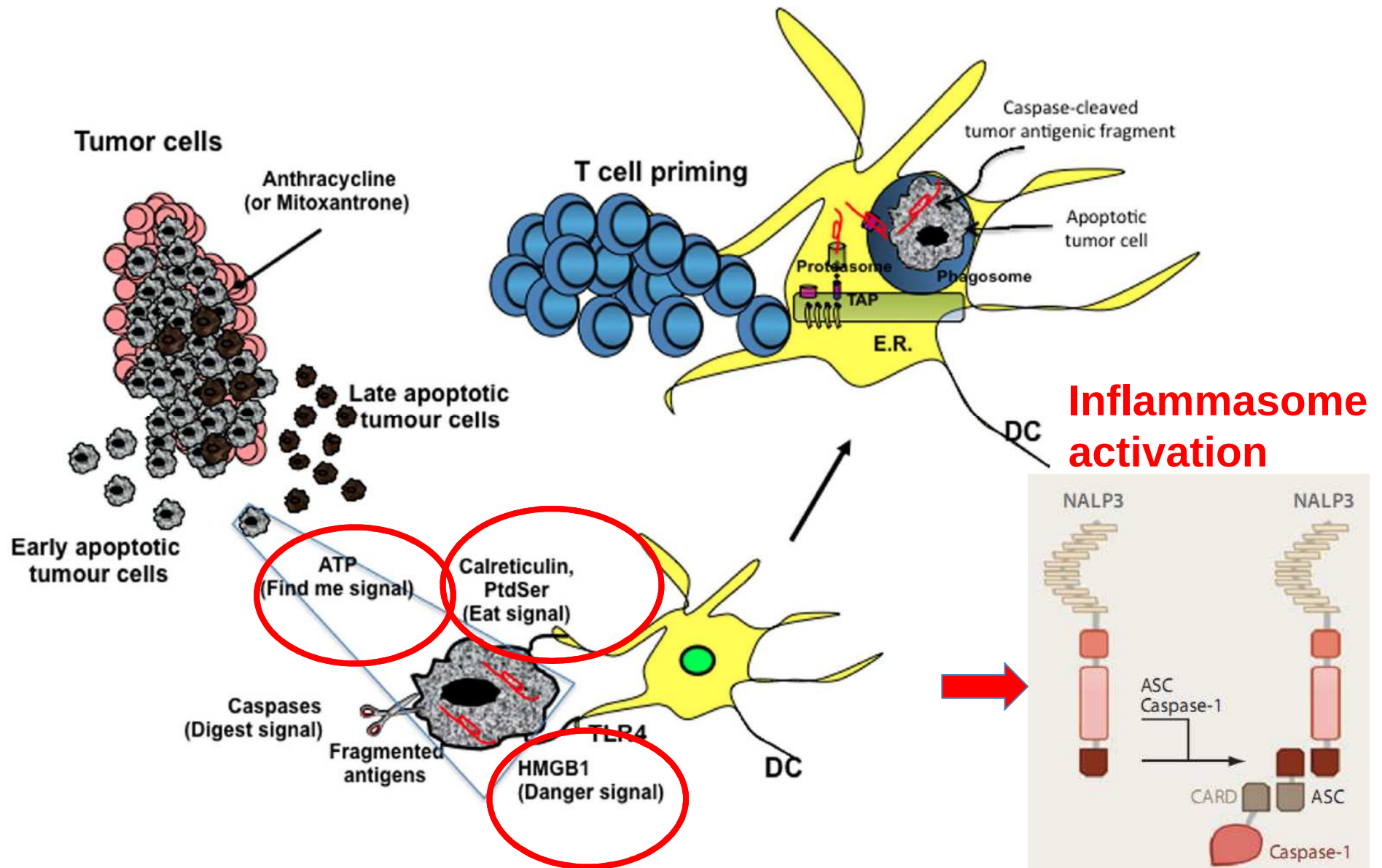
inducing

- **Oxaliplatin**
- **Doxorubicin**

non - inducing

- **Mitomycin C (MMC)**
- **Cisplatin (CDDP)**

Mediators of the immunogenic cell death



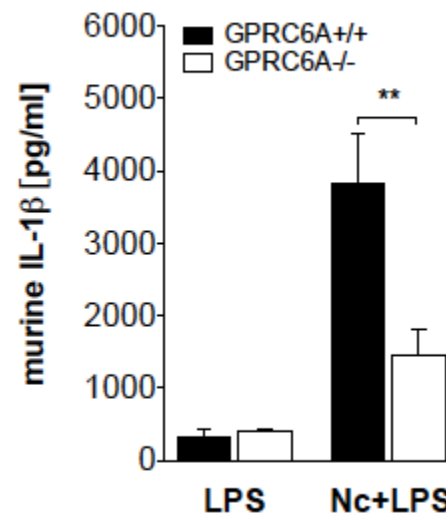
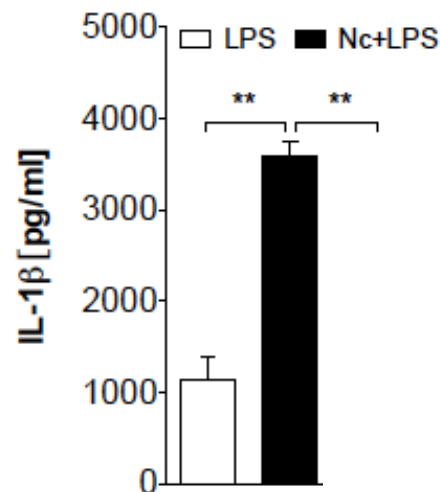
exCa²⁺ as new DAMP acting via GPRC6a

GPRC6a: G-protein coupled receptor, family C, typ 6a

CaSR: Calcium sensing receptor

→ expressed on myeloid cells and in different tissues cells

→ binds ex-calcium, antibiotics and gets activated when cells dye



Hypothesis

**exCa²⁺ as a new DAMP mediates ICD via
calcium receptors**

experimental design – I

MCA205, fibrosarcoma

(intermediate immunogenicity)

C57/BL6



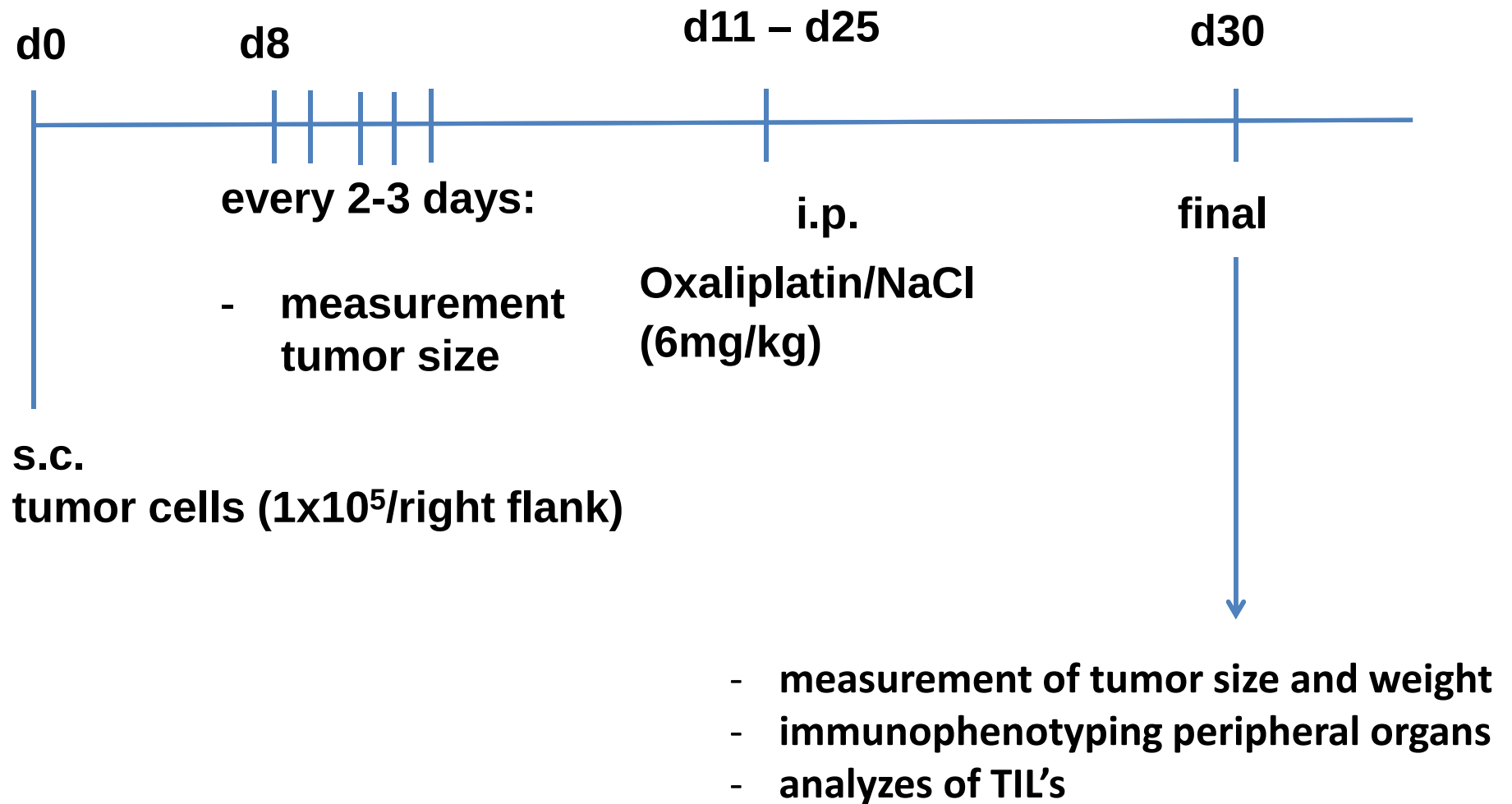
GPRC6a ko



Asc ko

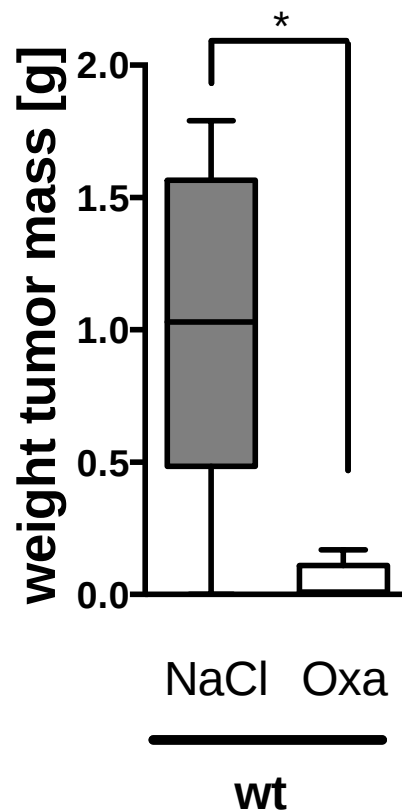


experimental design – II

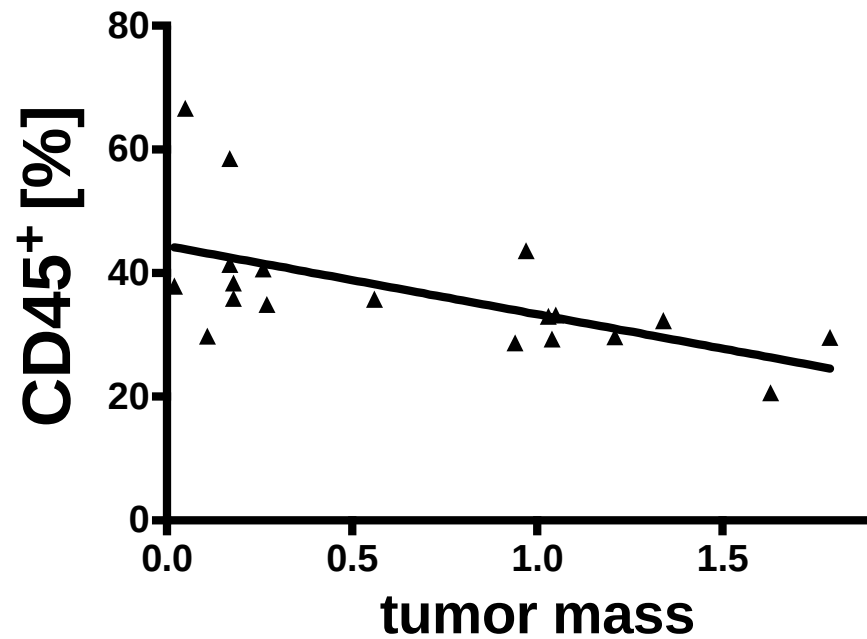


Reduced growth and no oxaliplatin induced fibrosarcoma control in GPRC6a ko mice

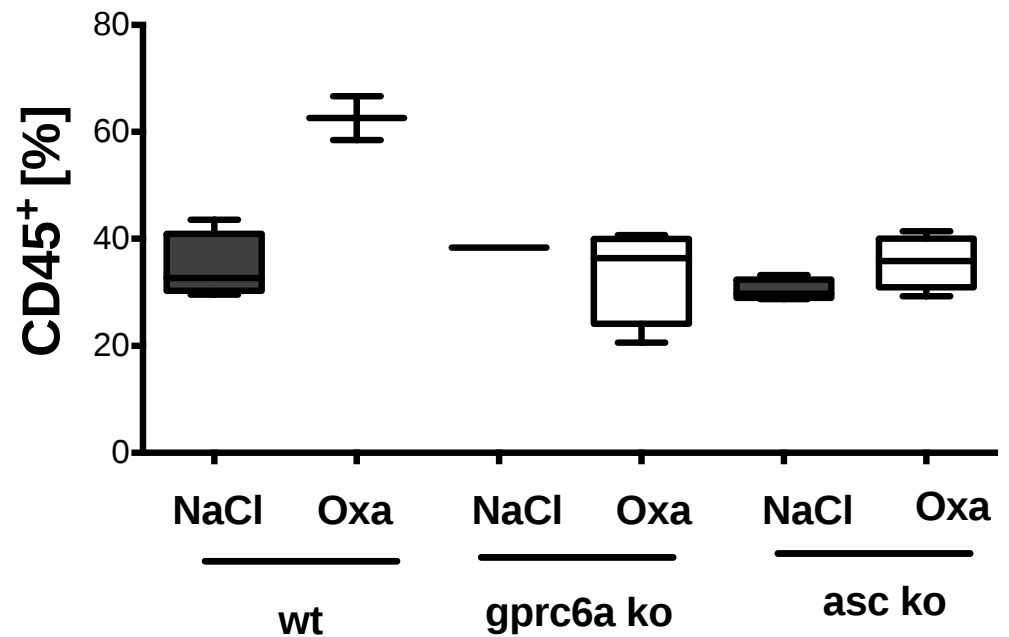
s.c. MCA 205



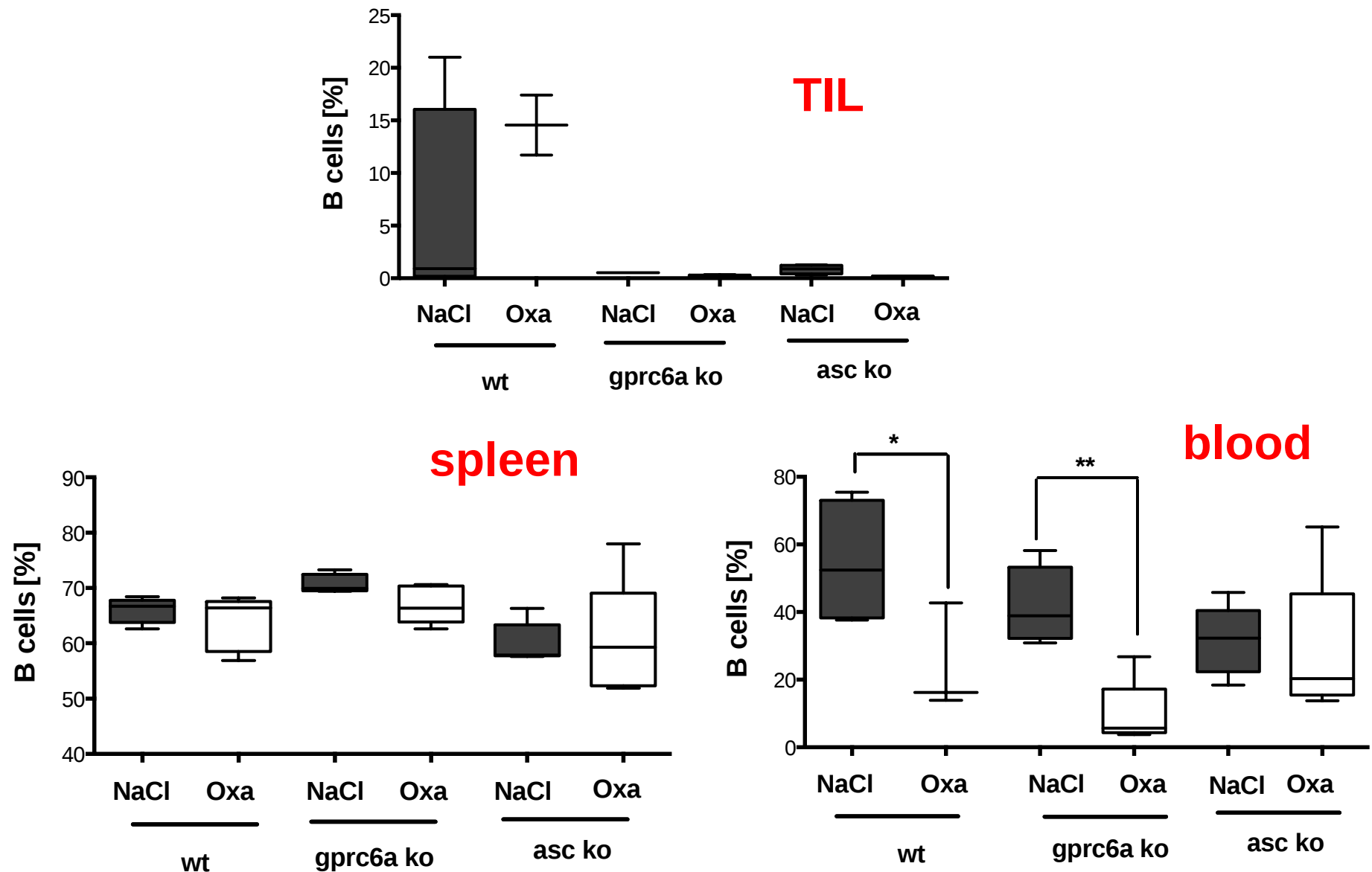
Frequency of CD45 immune cell infiltration correlates with tumor size



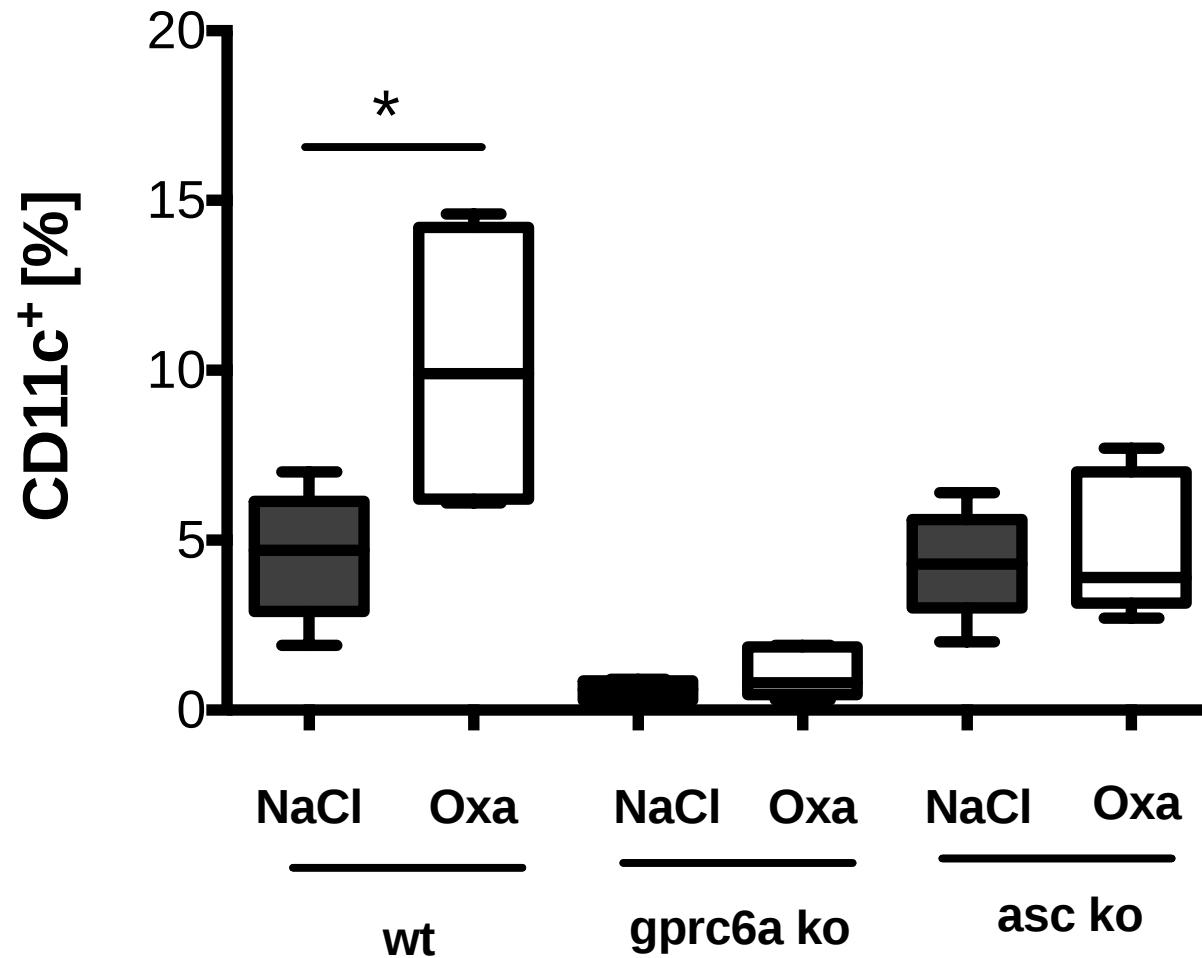
$r = 0.36$
 $p = 0.0067$



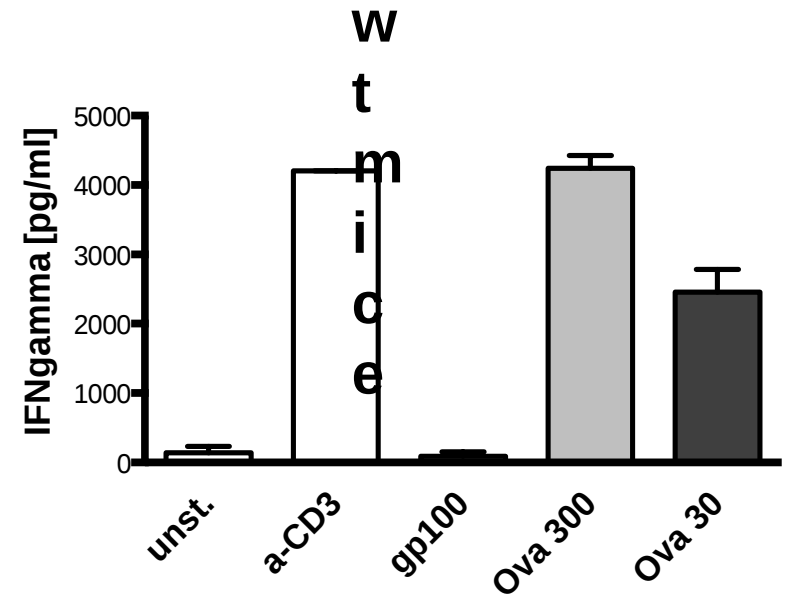
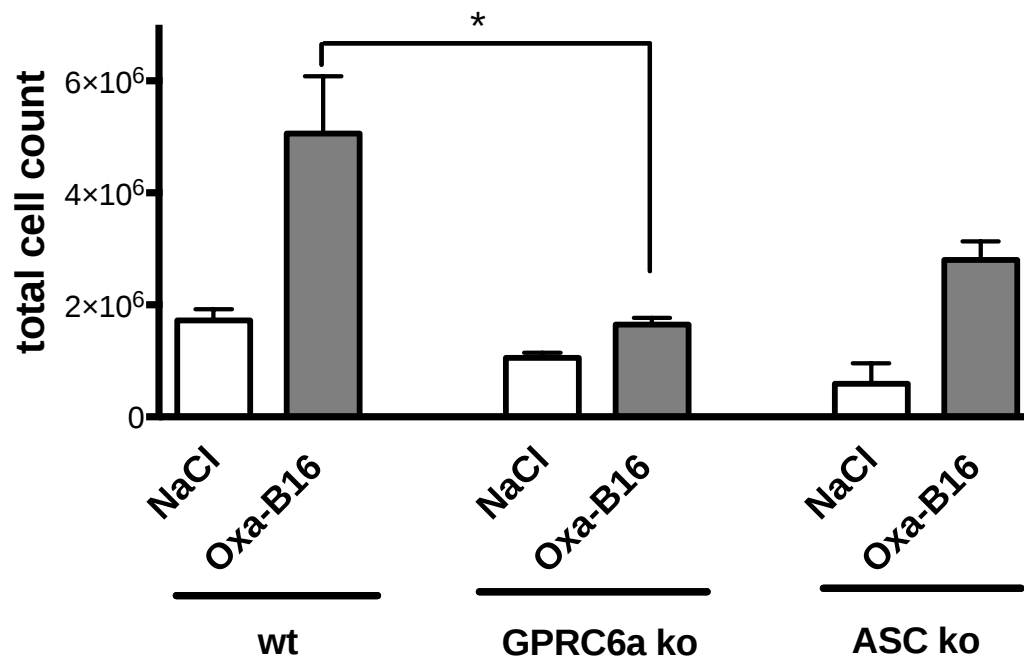
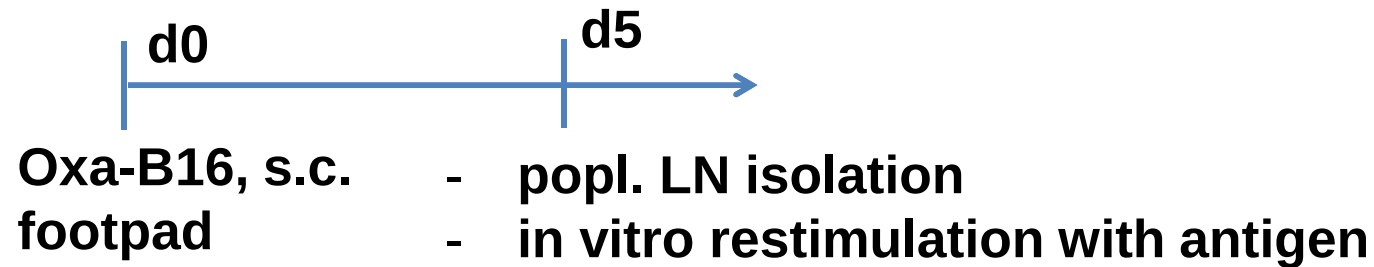
No B cells among immune infiltrates in tumors of GPRC6a and ASC ko mice



splenic CD11c correlate with oxaliplatin induced tumor control in wt mice



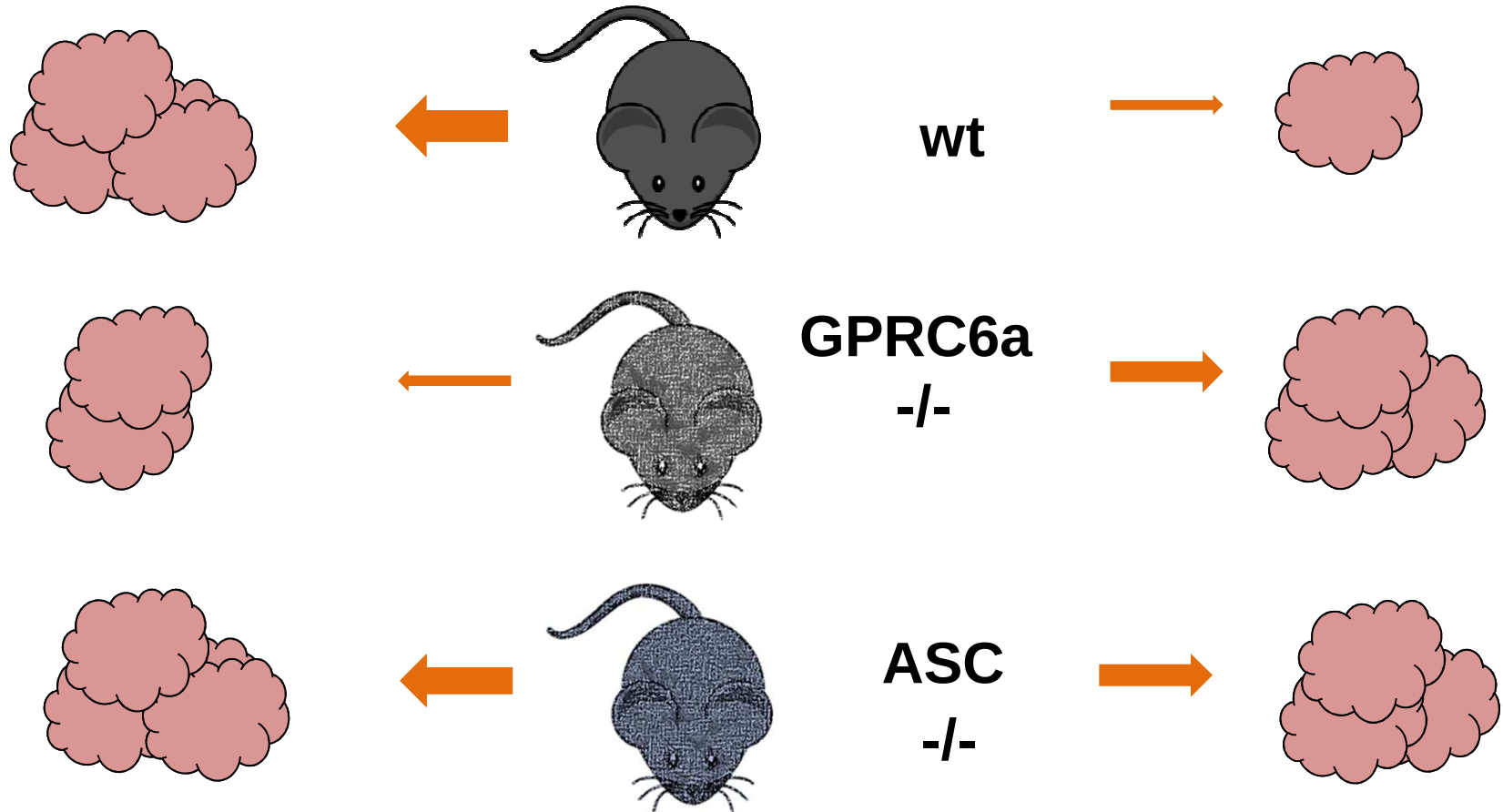
GPRC6a is mandatory for the chemotherapy induced immune activation



Lessons and Take Home Messages

untreated tumor growth

chemotherapeutic tumor growth



Thanks

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