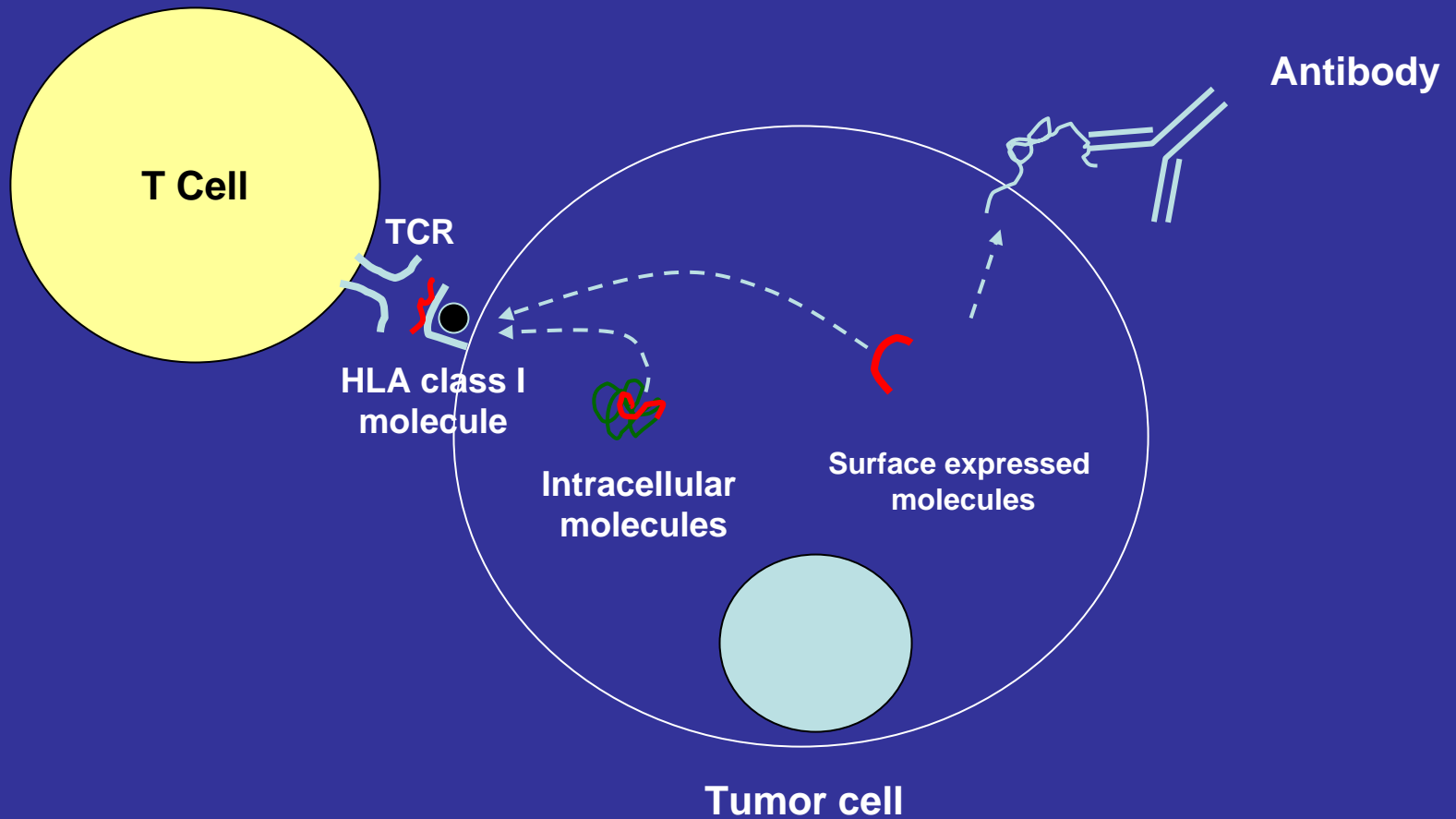


The human high molecular weight-melanoma associated antigen (CSPG4) as a target of antibody-based immunotherapy

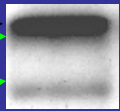
Soldano Ferrone

Recognition of tumor antigens by T cells and antibodies



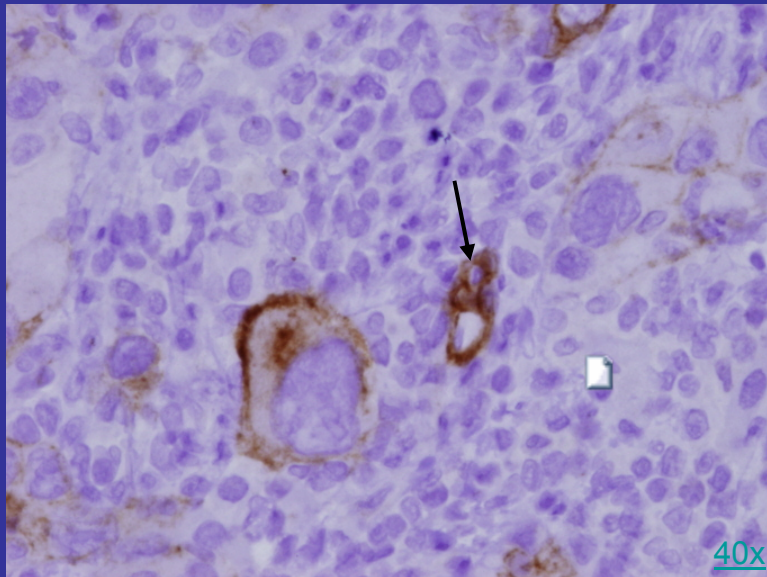
Human HMW-MAA characteristics

450 kDa →
280 kDa →

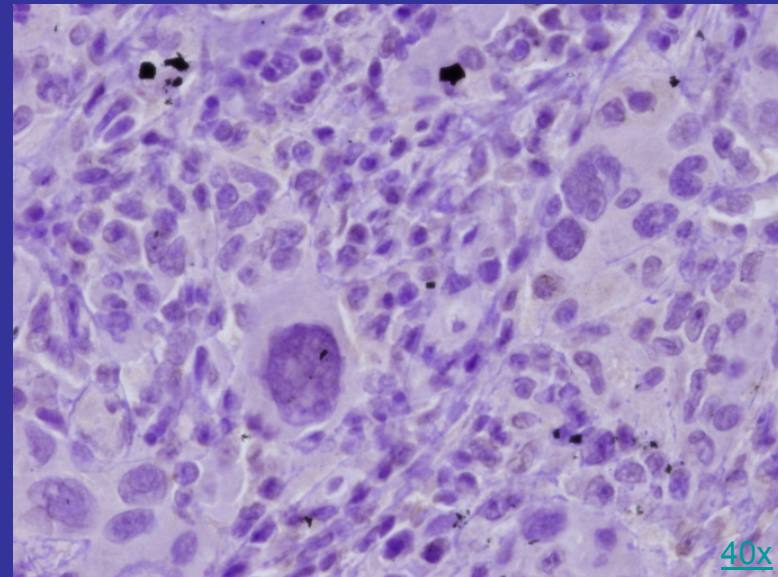


- Expressed with high density on cell membrane.
- Expressed in melanoma (85%), glioma (70%), chondroma and chondrosarcoma (50%) lesions and on acute lymphoblastic leukemic (55%) cells.
- Expressed on tumor activated pericytes.
- Expressed on breast carcinoma stem cells.
- Restricted distribution in normal tissues.
- Targeted by CTL.
- Highly conserved through phylogenetic evolution.

HMW-MAA expression in pericytes and endothelial cells in a non-small cell lung carcinoma lesion



HMW-MAA-specific mAb

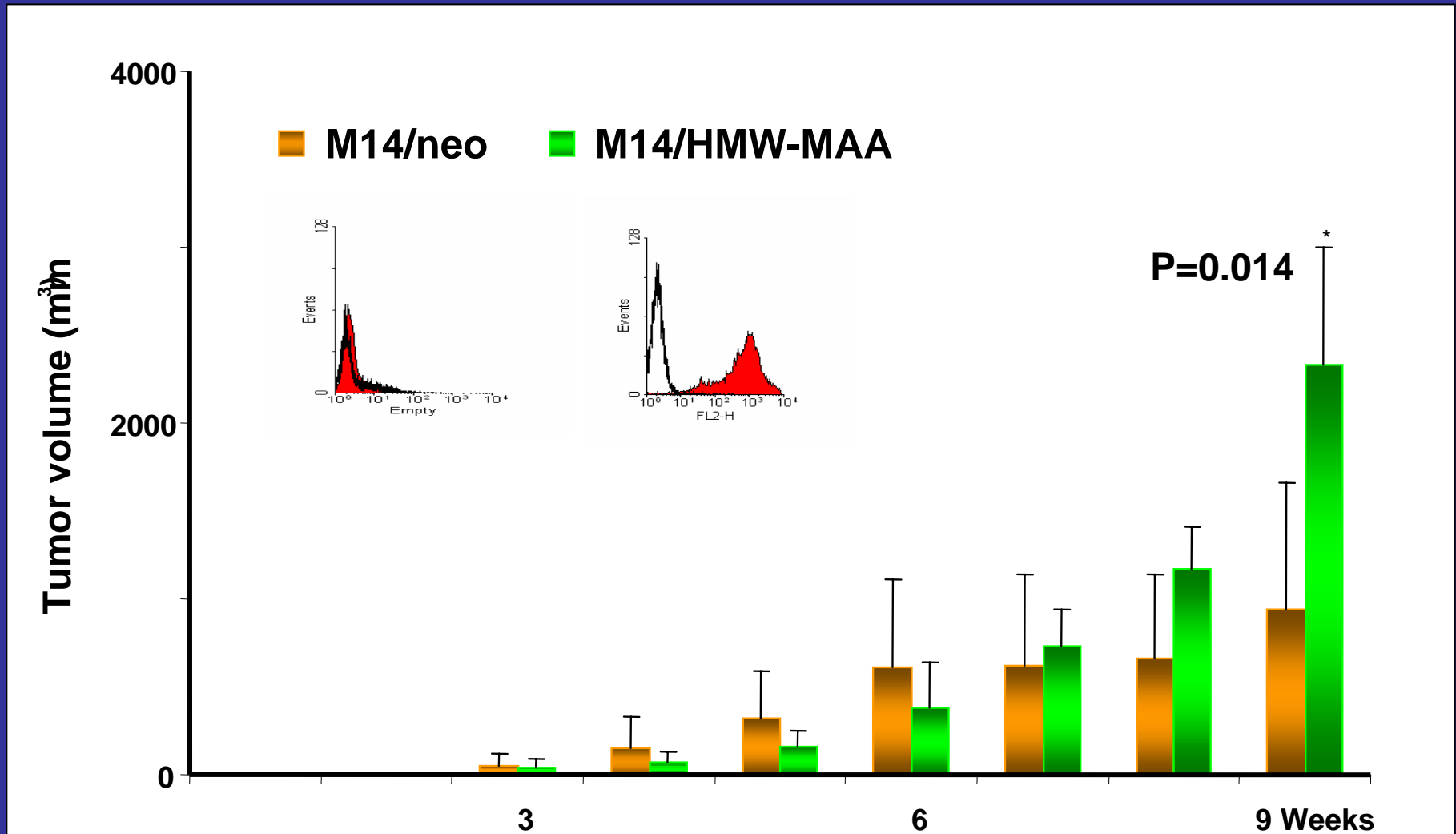


Isotype control

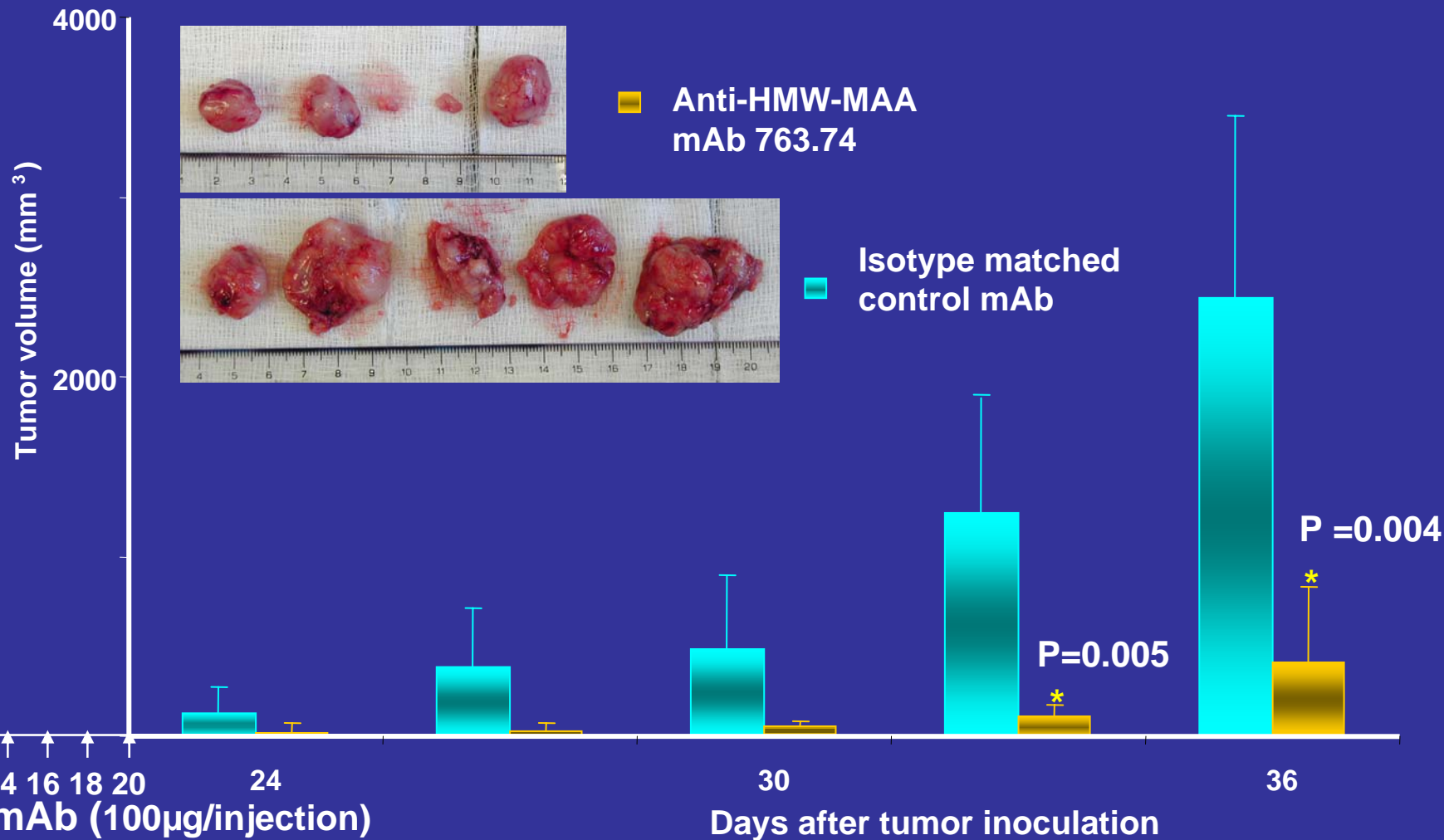
Role of HMW-MAA in melanoma progression

- **Adhesion**
- **Migration**
- **Invasion**
- **Metastasis**

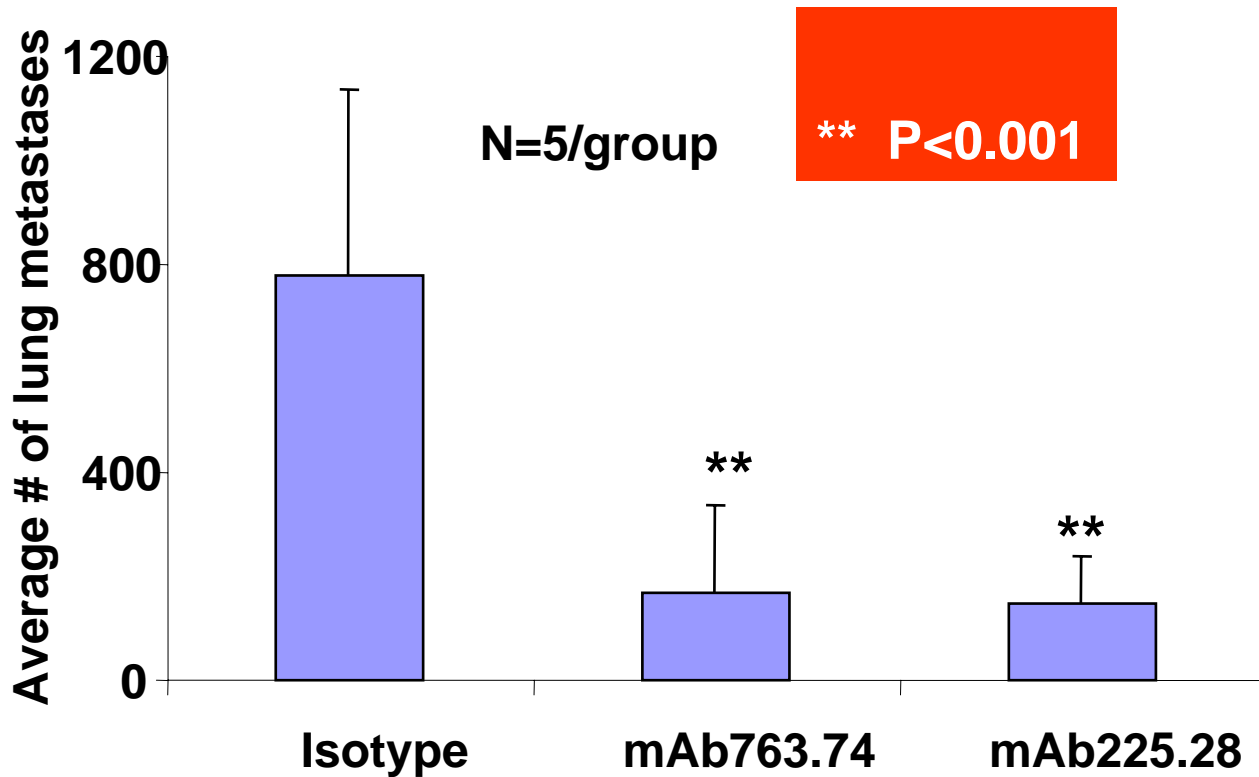
Potential role of HMW-MAA in human melanoma cell growth in SCID mice



Inhibition by anti-HMW-MAA mAb 763.74 of human MV3 melanoma cell growth in SCID mice



Inhibition by HMW-MAA-specific mAb of experimental lung metastases in SCID mice transplanted with MDA-MB-435s cells



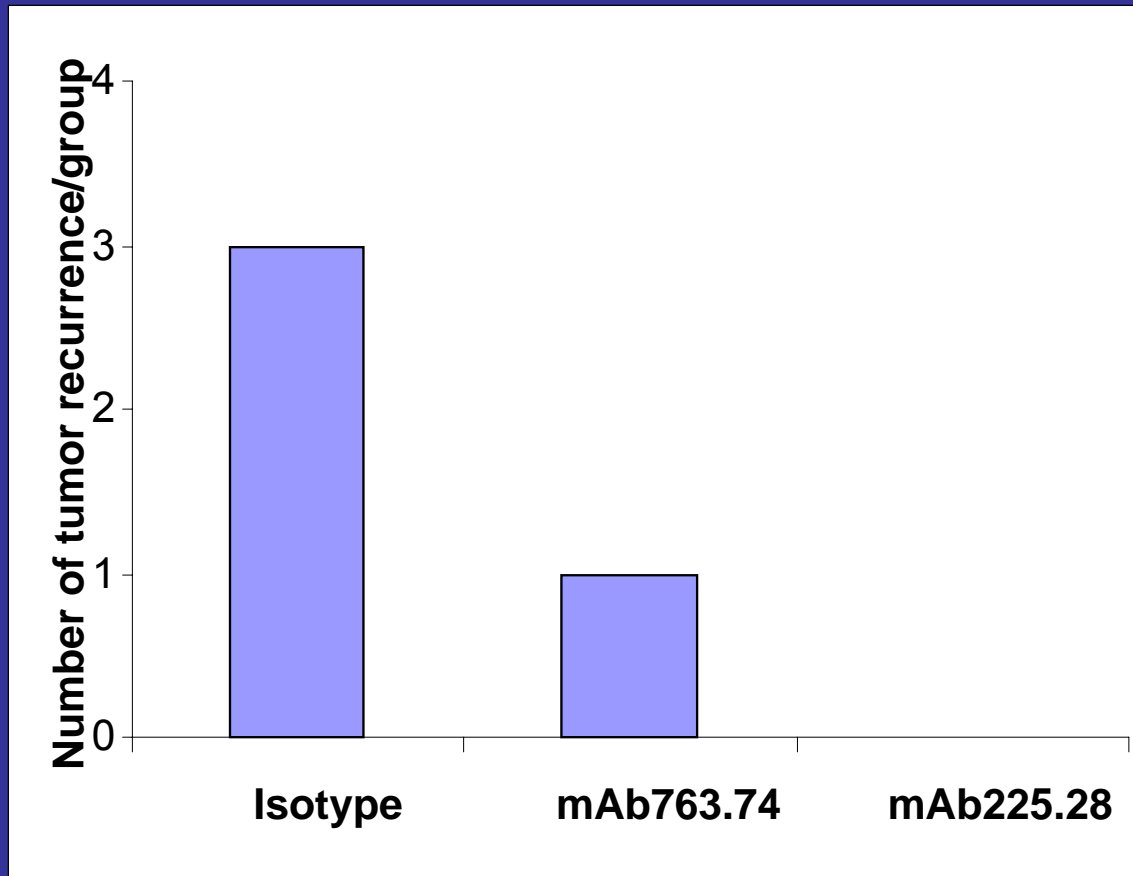
Timeline:

Day 0: i.v. injection of tumor cells

Day 3: i.p. mAb (100µg) injection, 2 x weekly for 4 and ½ weeks

Day 34: Sacrifice of mice and enumeration of lung metastases

Inhibition by HMW-MAA-specific mAb of post-surgery recurrences in SCID mice transplanted with human MDA-MB-435s breast cancer cells



Timeline:

Day 0: intramammary fat inoculation of tumor cells

Day 7: i.p. mAb (200 μ g) administration, 2x weekly, for 9 weeks

Day 71: surgical removal of tumor

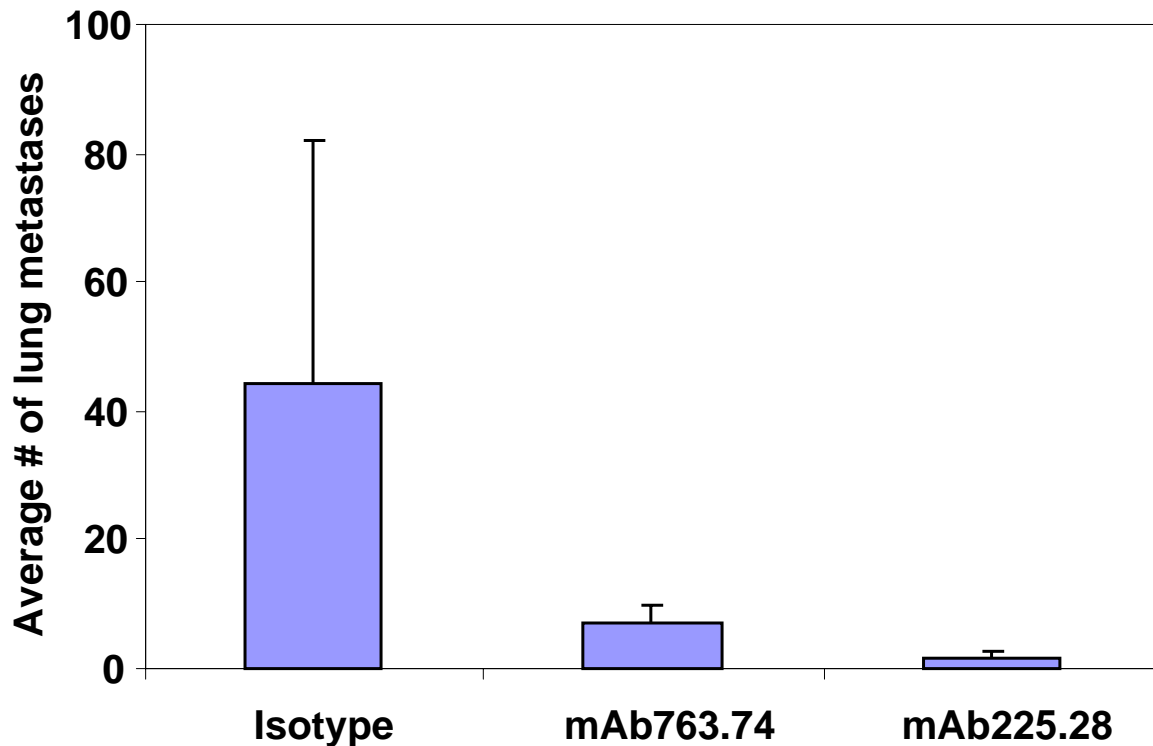
Day 71: i.p. mAb (200 μ g) administration, 2x weekly, for 4 weeks

Day 134: sacrifice of mice and detection of tumor recurrences

Inhibition by HMW-MAA-specific mAb of post-surgery lung metastases in SCID mice transplanted with human MDA-MB-435s breast cancer cells

N=5/group

* P=0.03



Timeline:

Day 0: intramammary fat inoculation of tumor cells

Day 7: i.p. mAb (200 μ g) administration, 2x weekly, for 9 weeks

Day 71: surgical removal of tumor

Day 71: i.p. mAb (200 μ g) administration, 2x weekly, for 4 weeks

Day 134: sacrifice of mice and enumeration of lung metastases.

Association between survival and development of humoral anti-HMW-MAA immunity in patients immunized with mouse anti-idiotypic mAb MK2-23

