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EFFECTS OF ANTIBODY TARGETING OF CD24 AN L1 CELL ADHESION MOLECULE ON TUMOR MICROENVIRONMENT

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CD24 is over-expressed in a variety of human carcinomas and is correlated with poor prognosis in ovarian and lung cancer amongst others. *In vitro* studies showed that CD24 stimulates proliferation and invasion of tumor cells and in *in vivo* tumor models its over-expression promoted tumorigenicity. Treatment with the monoclonal antibody (mAb) SWA11 in xenograft experiments lead to promising results as it efficiently reduced tumor load in immunodeficient mice.

The purpose of this study was to investigate SWA11 targeting of CD24 and its effects on tumor growth as well as on the tumor microenvironment. Therefore, three independent xenograft experimental models were set up, in which mice were injected with human ovarian and lung cancer cells and treated with the mAb SWA11.
In the ovarian cancer xenograft model mice were injected with the L1-9.3 mAb, which targets the L1-cellular adhesion molecule (L1-CAM), to compare the L1-9.3 and SWA11 mAb with respect to therapeutic efficacy and effects on the cytokine milieu. In a lung cancer xenograft experiment mAb treatment with SWA11 was combined with injections of gemcitabin to evaluate potential additive therapeutic effects.

SWA11 mAb was able to efficiently retard tumor growth in all three xenograft experiments. Analysis of immunohistochemical stainings revealed that after treatment with SWA11 the tumor cell proliferation was decreased and tumor cell apoptosis was increased. The decrease in proliferation was most likely to be responsible for the therapeutic success. The mAb SWA11 had some effects on the recruitment of macrophages and neutrophils into the tumors and lead to major changes in the cytokine milieu of the tumors.
Therapy with SWA11 was more efficient in inhibiting tumor growth of ovarian carcinomas than treatment with the L1-9.3 mAb. Like SWA11, L1-9.3 mAb was able to alter the cytokine milieu, but differently, thus indicating that changes in the cytokine profile are specific to the molecule targeted and the antibody used.
Combined therapy with SWA11 mAb and gemcitabin achieved the highest therapeutic efficacy in a lung carcinoma model. Unlike SWA11, the chemotherapeutic drug gemcitabin had no effects on the cytokine milieu demonstrating that alterations in the cytokine expression levels are specific for treatment with mAbs.

These results show that SWA11 mAb presents a promising tool in the treatment of CD24-positive tumors. Furthermore, they provide novel insights into the effects of SWA11 antibody therapy on the tumor microenvironment.