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Anti-PSMA antibodies and fragments for diagnosis and therapy of prostate cancer

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The Prostate Specific Membrane Antigen (PSMA) represents an excellent target for diagnosis and therapy of prostate cancer. PSMA is specifically expressed in high density as a homodimer on the surface of prostate epithelial cells. It is upregulated in all stages of prostate cancer, not secreted into the circulation and internalized after antibody binding.

Recently, we have generated three monoclonal antibodies (mAbs) and single chain antibody fragments (scFv) that react with cell-adherent PSMA and bind with a high affinity to PSMA-expressing prostate cancer cells. From these mAbs two single chain antibody fragments were developed by phage display. Their binding pattern was comparable to the parental antibodies.

As diagnostic tools, we used the ^{64}Cu-DOTA-labelled mAbs for imaging of prostate cancer xenografts in SCID mice. Static small-animal PET images of mice with PSMA-positive tumors revealed a high tumor-to-background ratio. In contrast, no significant tracer uptake was observed in the PSMA-negative DU 145 tumors.

As therapeutic tools, we have generated recombinant immunotoxins with a truncated form of pseudomonas Exotoxin A as toxic domain attached to the scFv as binding domain. These immunotoxins showed a high and specific cytotoxicity against PSMA-expressing C4-2 prostate cancer cells *in vitro* and a growth inhibition of human C4-2 Xenografts in SCID mice *in vivo*.

Due to the specific binding to prostate cancer cells and their high uptake in PSMA-positive tumors our mAbs and scFv bear a high potential for diagnosis and therapy.

Biography

Ursula Elsässer has a university background as MD and PhD. She is scientific director of the Experimental Urology Unit at the Department of Urology, University of Freiburg. Her main expertise is in new diagnostic and therapeutic approaches for prostate cancer.