Anti-PSMA Antibodies

Novel Agents for Diagnosis and Therapy of Prostate Cancer

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Technology

The Prostate Specific Membrane antigen (PSMA) is highly expressed by virtually all prostate cancers and is currently the focus of several diagnostic and therapeutic strategies for this most common cancer among men. We have generated three monoclonal antibodies (mAbs), called 3/A12, 3/E7 and 3/F11 against the extracellular domain of PSMA. Their binding to PSMA-expressing cells and tissue is highly specific. After conjugation with DOTA and radiolabelling with [64Cu] the three mAbs were used for microPET imaging of prostate cancer xenografts. In the scans a high tumor to background ratio of about 8:1 was measured in PSMA expressing tumors, whereas no significant targeting of PSMA-negative tumors was seen. These results were confirmed by direct gamma-counting of tissues after the final imaging. Therefore, these mAbs represent excellent candidates for prostate cancer imaging and may also be suitable for radioimmunotherapy.

Innovation

- The monoclonal anti-PSMA antibodies 3/A12, 3/E7 and 3/F11 specifically target PSMA-expressing prostate epithelial cells
- The mAbs are excellent tools for the imaging of prostate cancer
- The antibodies bear a high potential for the use in radioimmunotherapy of prostate cancer
- Due to PSMA expression in the neovasculature of virtually all solid tumors, the antibodies may generally be applied as anti-tumor vasculature-targeting agents

Application

- mAbs for specific targeting of PSMA-expressing cells
- mAbs for imaging of prostate cancer
- mAbs for radioimmunotherapy of prostate cancer

Market Potential

Prostate cancer is the most frequent malignant disease among men in the Western world. The mAbs 3/A12, 3/E7 and 3/F11 improve prostate cancer imaging and radioimmunotherapy.

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Prostate cancer is the most common cancer and second leading cancer-related cause of death among men in the Western civilization. There is as yet no curative therapy after progression beyond resectable boundaries. Therefore this tumor is currently the focus of new diagnostic and therapeutic strategies.

PSMA represents an excellent target for prostate cancer. It is abundantly expressed on the surface of prostate epithelial cells, is upregulated in prostate cancers according to tumor progression, and is not shed into the circulation. Therefore we have chosen this antigen for the generation of mAbs for specific diagnostic and therapeutic purposes.

We have generated three different mAbs, called 3/A12 (IgG1), 3/E7 (IgG2b) and 3/F11 (IgG2a) with a high and specific binding to PSMA expressing prostate cancer cells. Competitive binding studies showed that the three mAbs bind to different extracellular epitopes of PSMA.

Specificity of the mAbs for prostate epithelial cells was shown by immunohistochemistry on frozen sections of prostate cancer tissue and by immunofluorescence on PSMA-positive LNCaP cells. PSMA-negative tissues and cell lines were not stained.

Small animal PET Imaging with the [64Cu]-DOTA-3/A12 revealed a high uptake in PSMA positive tumors with a tumor to background ratio of about 8:1. Similar results were obtained with mAbs 3/E7 and 3/F11.

Due to the high and specific binding to prostate cancer cells and their high uptake in PSMA-positive tumors the mAbs 3/A12, 3/E7 and 3/F11 represent excellent candidates for prostate cancer imaging and radioimmunotherapy.

References