

# Anti-PSMA Antibodies

## Novel Agents for Diagnosis and Therapy of Prostate Cancer

Albert-Ludwigs-Universität Freiburg



UNI  
FREIBURG

## 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.

### Responsible Scientist

Prof. U. Elsässer-Beile

Dept. of Experimental Urology

### Branch

Pharma, Oncology

### Patent Status

WO 2006125481 A1

Filed (PRD) May 27th 2005

EP 1 883 698 B1

AUS 2006251445 B2

EP 11151622 (DA)

Intern. Patent Appl. pending in US, CA, IN, RU, JP, CN

### Reference Number

ZEE20050222c

Status: Jun-11

### Contact

Campus Technologies Freiburg GmbH | Stefan-Meier-Str. 8 | D-79104 Freiburg  
Email: [Claudia.Skamel@campus-technologies.de](mailto:Claudia.Skamel@campus-technologies.de)  
Tel: +49 (0)761 203-4987  
Fax: +49 (0)761 203-5021



# Anti-PSMA Antibodies - Novel Agents for Diagnosis and Therapy of Prostate Cancer

U. Elsässer-Beile, P. Bühler, P. Wolf, D. Gierschner, U. Wetterauer

Department of Urology, Experimental Urology, University Hospital Freiburg, Breisacher Strasse 117, D-79106 Freiburg, Germany

## Background

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.

## Materials & Methods

### Binding to PSMA

Specific binding of the three mAbs to the extracellular domain of PSMA was investigated by flow cytometric analyses with PSMA expressing LNCaP and C4-2 prostate cancer cells. Different PSMA-negative cell lines served as controls.

To test the binding of the mAbs to distinct extracellular PSMA epitopes, competitive binding studies were performed with each of the biotinylated mAbs and the three non-biotinylated mAbs at increasing concentrations by flow cytometry.

Specificity for prostate epithelial cells was tested on frozen tissues of human prostate, brain, kidney, colon, heart, lung and liver.

### PET-Imaging

The three mAbs were conjugated with the chelating agent DOTA and radio-labelled with  $^{64}\text{Cu}$ . PET imaging was performed with SCID mice bearing PSMA-positive C4-2 or PSMA-negative DU 145 xenografts. Each animal received 20 to 30  $\mu\text{g}$  of  $^{64}\text{Cu}$ -3/A12 corresponding to 7.6 to 11.5 MBq. PET scans were taken 3, 24, and 48 h after injection.

After the last scan the biodistribution was measured by gamma-counting.

## Results

→ 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 three different extracellular epitopes of PSMA.

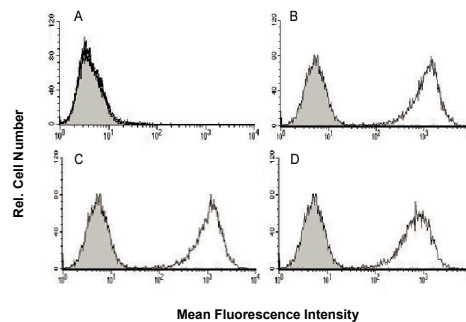


Fig. 1: Binding of mAbs 3/E7 (B), 3/F11 (C) and 3/A12 (D) to PSMA-positive LNCaP cells and PSMA-negative DU 145 cells (A).

→ 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.

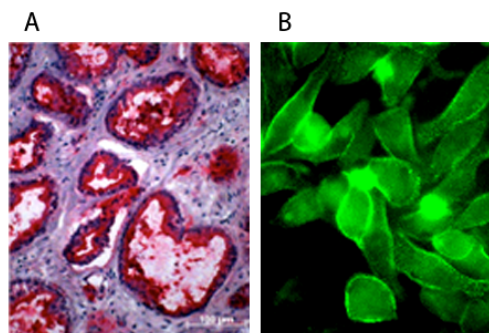


Fig. 2: (A) Immunohistochemistry with the mAb 3/F11 on human prostate cancer tissue. (B) Immunofluorescence with mAb 3/A12 on LNCaP cells.

→ Small animal PET Imaging with the  $^{64}\text{Cu}$ -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.

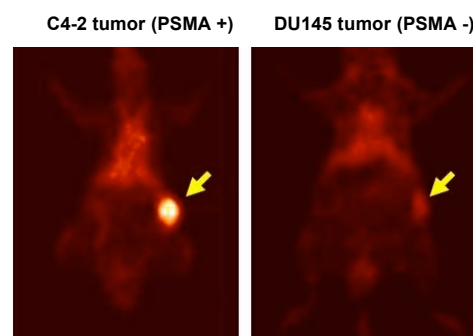


Fig. 3: PET-Images of mice bearing PSMA-positive C4-2 and PSMA-negative DU 145 tumors 24 h post injection of  $^{64}\text{Cu}$ -DOTA-3/A12. Arrows indicate position of tumors.

## Conclusions

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

- Elsässer-Beile, U. et al. (2006). *Prostate* **66** (13): 1359-70.  
Bühler et al. (2007). *Tumor Biol* **28** (Suppl 1): 90.