Institute of Biotechnology of the Czech Academy of Sciences

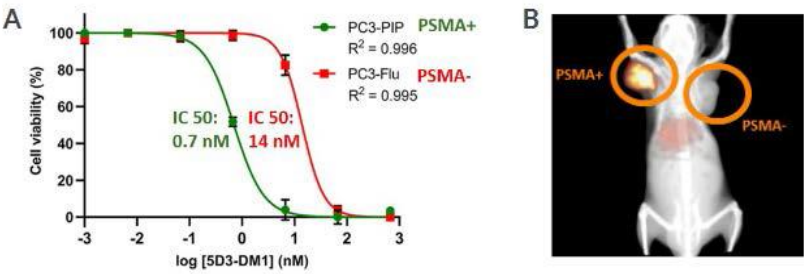
Anti-PSMA antibodies for therapeutic and diagnostic purposes

CHALENGE

Prostate cancer has the highest incidence and the second highest mortality among men in industrial countries. To improve prognosis a combination of precise diagnosis of tumor stage and specifically designed treatment plans is required. Prostate-specific membrane antigen (PSMA) is highly expressed on prostate cancer cells. Its specific presence in primary, high-grade and androgen-independent prostate cancer tumors as well as in metastases predetermines PSMA as a prime tool for prostate cancer imaging and therapy. So far, three PSMA-targeted small molecules have been approved for imaging purposes and the first PSMA-targeted radioligand-therapy gained approval by the FDA and EMA in 2022. Although progress has been made in the past years, there is a continuous high need for new prostate-cancer-specific applications, such as antibody-based therapies and diagnostics.

INNOVATION

Our humanized anti-PSMA antibody 5D3 recognizes native human PSMA and is derived from the parent murine anti-PSMA antibody reported previously1. The therapeutic and imaging potential of 5D3 has been demonstrated in vitro and in vivo. It retains its superior properties, such as sub-nanomolar affinity and high specificity for native PSMA as well as good thermal stability. In addition, it has low immunogenicity as the murine antibody constant regions and V framework are replaced by human sequences. Anticipated liabilities were removed to facilitate various applications. Its excellent binding properties make 5D3 a superior candidate for conjugation to a therapeutic or an imaging agent.



A: In vitro cytotoxicity of an antibody-drug-conjugate (ADC)2. The 5D3-based ADC was cytotoxic for PSMA+ cells at 20 times lower concentrations than for PSMA- cells proving the targeting potential of 5D3. B: In vivo imaging with 111In-DOTA-5D33

COMMERCIAL OPPORTUNITIES

The humanized anti-PSMA antibody 5D3 is suitable for prostate cancer therapy or imaging after conjugation with a therapeutic payload (a drug for ADC, radioligand for radiotherapy, photosensitizer for photodynamic therapy, etc.) or an imaging agent. “Sister” antibodies 1A11 and 3F111 are available for use in an immunohistochemistry companion diagnostic kit.

DEVELOPMENT STATUS

Optimized for developability, binding affinity and conformational stability in vitro

REFERENCES:
1 Novakova et al., The Prostate, 2017, 77(7):749-764
2 Huang et al., Mol Pharm. 2020 Sep 8; 17 (9): 3392-3402
3 Banerjee et al., J Nucl Med, 2019, 60(3):400-406

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PCT filed in 2022

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