



ZHER2 Affibody as a Good Candidate for Detection of Metastatic Prostate Cancer

Prostate cancer (PCa) is the second leading cause of cancer death in men. About one in 39 will die of prostate cancer and about one man out of seven is diagnosed with the problem. The expression of the Epidermal Growth Factor Receptor (EGFR) is shown in the progression of androgen independent PCa. EGFR has emerged as a promising therapeutic target for patients with castration-resistant PCa. There is an urgent need for detection of EGFR expression and monitoring the treatment in prostate cancer. Affibodies are small engineered proteins with a high affinity to a large number of target proteins or peptides. Affibodies are three-helix bundles of 58 amino acids based on Z domain of staphylococcal protein A; ZHER2 is one of them with the high-affinity to Human Epidermal growth factor Receptor 2 (HER2). Positron Emission Tomography (PET) imaging with 18F-Labeled ZHER2: 2891 affibody can be a good candidate for prostate cancer detection.

Prostate cancer is one of the most prevalent cancers in man worldwide ¹. HER2 overexpression has a significant role in the progression and metastasis of prostate cancer ²⁻⁴. Many studies have shown that HER2 expression was detected in primary and advanced androgen dependent and independent prostate cancers, respectively; therefore, it seems to be a valuable marker for detection of metastatic cancer in patients ⁵.

Affibody molecules are the class of small and stable recombinant proteins and they have the potential for therapeutic, diagnostic and other biomedical applications ⁶. Nowadays, affibody molecules are at issue as targeting vectors for PET imaging ⁷. The ZHER2 affibody demonstrates selective binding and high affinity to HER2/neo positive cancer cells ⁸. The small size of affibody makes it a good agent for tissue penetration; also, in comparison with monoclonal antibodies, the affibody provides high-contrast tumor imaging ⁹. The distribution in body and ability for targeting radio-labeled affibody molecules are controlled by four key aspects such as short length, slow penetration following the specific binding, the ability of high reabsorption in proximal tubules and long lasting effects of lipophilicity.

Taken everything into considerations, a fluorescently labeled affibody which is less affected with hemoglobin quenching can be a good candidate for prostate cancer detection and helpful in prostate surgery.

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References

1. Filippou P, Ferguson III JE, Nielsen ME. Epidemiology of prostate and testicular cancer. *S Semin Intervent Radiol* 2016;33(3):182-5.
2. Reese DM, Small EJ, Magrane G, Waldman FM, Chew K, Sudilovsky D. HER2 protein expression and gene amplification in androgen-independent prostate cancer. *Am J Clin Pathol* 2001;116(2):234-9.
3. Jorda M, Morales A, Ghorab Z, Fernandez G, Nadji M, Block N. Her2 expression in prostatic cancer: a comparison with mammary carcinoma. *J Urol* 2002;168(4):1412-4.
4. Day KC, Hiles GL, Kozminsky M, Dawsey SJ, Paul A, Broses LJ, et al. HER2 and EGFR overexpression support metastatic progression of prostate cancer to bone. *Can Res* 2017;77(1):74-85.
5. Shi Y, Brands FH, Chatterjee S, Feng A-C, Groshen S, Schewe J, et al. Her-2/neu expression in prostate cancer: high level of expression associated with exposure to hormone therapy and androgen independent disease. *J Urol* 2001;166(4):1514-9.
6. Löfblom J, Feldwisch J, Tolmachev V, Carlsson J, Ståhl S, Frejd FY. Affibody molecules: engineered proteins for therapeutic, diagnostic and biotechnological applications. *FEBS Lett* 2010;584(12):2670-80.
7. Tolmachev V, Orlova A. Affibody molecules as targeting vectors for PET imaging. *Cancers (Basel)* 2020;12(3):651.
8. Orlova A, Magnusson M, Eriksson TL, Nilsson M, Larsson B, Höidéén-Guthenberg I, et al. Tumor imaging using a picomolar affinity HER2 binding affibody molecule. *Cancer Res* 2006;66(8):4339-48.
9. Sexton K, Tichauer K, Samkoe KS, Gunn J, Hoopes PJ, Pogue BW. Fluorescent affibody peptide penetration in glioma margin is superior to full antibody. *PloS One* 2013;8(4):e60390.

Mahboobeh Nazari ^{1*} and Ramin Radmanesh ²

1. Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, Tehran, Iran

2. Department of Pharmacoeconomics and Pharmaceutical Management, Faculty of Pharmacy, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

* Corresponding author: Mahboobeh Nazari, Ph.D., Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, Tehran, Iran

Tel: +98 21 2243 2020

Fax: +98 21 2243 2021

E-mail: Ma.nazari@ari.ir, nazari1980azar@yahoo.com

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