



Letter to the Editor

Reply to Bingzhi Wang, Huan Deng, and Lan Cao's Letter to the Editor re: Hojjat Ahmadzadehfar, Markus Essler. Prostate-specific Membrane Antigen Imaging: A Game Changer in Prostate Cancer Diagnosis and Therapy Planning. Eur Urol. In press. <https://doi.org/10.1016/j.eururo.2019.02.028>

Despite its Slightly Limited Specificity, Prostate-specific Membrane Antigen Imaging is Still a Game Changer in Prostate Cancer Diagnosis and Therapy Planning

We read with great interest the comments of Wang et al in response to our letter [1] regarding the paper by Perera et al. [2]. Wang et al. state that prostate-specific membrane antigen (PSMA) is expressed in tissues other than the prostate and that because of this nonspecific expression, we should use more specific targets, such as PSM-9, which is a spliced variant of PSMA; according to a study published by the same group, PSM-9 is specifically overexpressed in prostate cancer [3]. It is indeed true that PSMA is not solely expressed by prostate tissue, and according to different publications, there is physiological and pathological (over)expression of PSMA in different benign and malignant conditions [4–6].

Because PSMA expression in tumours other than prostate cancer occurs mainly in vascular walls, it may be more appropriate for diagnostic imaging than for therapy. In breast cancer, vascular PSMA expression is pronounced in higher-grade, Her2-positive, and hormone receptor-negative tumours. According to Tolkach et al. [6], the highest PSMA levels have been observed in hormone receptor-negative and triple-negative breast carcinomas. In the case of renal cancer, there is higher PSMA expression in clear-cell renal carcinoma than in papillary and chromophobe renal carcinomas. Spatz et al. [5] showed that the intensity of positive versus negative endothelial PSMA expression was significantly associated with overall survival for patients with renal cancer; patients with positive PSMA expression experienced significantly shorter overall survival.

Despite the nonspecificity of PSMA expression, according to several publications and meta-analyses, PSMA-based imaging is currently the most sensitive and specific imaging modality for patients with recurrent prostate cancer [2,7].

Although we should certainly find more specific targets to increase the diagnostic accuracy of prostate cancer imaging, it should be taken into consideration that even the PSMA ligands currently used for imaging and therapy [8] are the result of more than 25 yr of hard work on different targets and ligands, which began by using the internal cellular portion of the PSMA protein as a target for imaging [9]. Conversely, it has to be considered that the rate of PSM-E expression in prostate cancer is not known. As PSM-E expression correlates with high Gleason scores, it is mostly aggressive tumours that will be positive. Therefore, imaging of prostate cancer using ligands to PSM-E may enhance specificity but reduce sensitivity when compared to PSMA imaging. A careful analysis of the expression and functional role of PSM-E is a prerequisite for the development of novel tests based on imaging of this interesting molecule.

Following the ground breaking success of colleagues at DKFZ (Heidelberg, Germany) in developing new PSMA ligands for diagnosis and therapy, we would now like to use this platform to call on all colleagues involved in theranostics and radiochemistry to conduct further work on more specific targets, such as the spliced variant of PSMA known as PSM-E.

Conflicts of interest: The authors have nothing to disclose.

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May 17, 2019