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Corrigendum: Modular Medical Imaging Agents Based on Azide-Alkyne Huisgen Cycloadditions

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CORRIGENDUM

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Modular Medical Imaging Agents Based on Azide–Alkyne Huisgen Cycloadditions: Synthesis and Pre-Clinical Evaluation of ^{18}F -Labeled PSMA-Tracers for Prostate Cancer Imaging

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The published article is lacking a highly relevant reference regarding clickable PSMA-ligands with alkyne-moiety. Hence, the authors would like to acknowledge the work by Kelly et al. (2017), who already presented six alkyne-functionalized PSMA binding motifs, three triazolyl and three triazolylmethoxy variants with subsequent successful radiolabeling with ^{18}F fluoro-azide using azido-ethylene synthons. The authors would like to apologize for the oversight.

The following is the relevant section of the paper with amendments highlighted in italics:

Results and Discussion

Design of F-PSMA-MIC01.

PSMA is a well-characterized target in structure-activity-relationship (SAR) studies.^[53] The natural function of this membrane zinc-metalloproteinase is to cleave glutamate from *N*-acetyl-L-aspartyl-L-glutamate. This antigen has a glutamate-favoring S1'-pocket^[54–56] and SAR analysis revealed an adaptive, hydrophobic-favoring S1-pocket, created by an arginine patch formed by Arg463, Arg534 and Arg536 that can accommodate a variety of inhibitors.^[57] PSMA-targeting compounds with the Glu-urea-Lys motif bind to the S1-hydrophobic pocket and the S1'-pocket, as well as to the zinc ions.^[57] Interestingly, it was found that the presence of a 1,2,3-triazole motif in PSMA inhibitors enables binding to an additional arene-binding site, which has inspired us to use this moiety in developing PSMA-targeting radiotracers with high affinity.^[57] For this purpose, we designed a modular synthesis approach for PSMA-targeting radiotracers which can potentially be applied to different imaging modalities by adapting the existing Glu-urea-Lys motif^[57] so that it is able to undergo the Huisgen [3 + 2]-cycloaddition. *Even further, in 2017 it was already shown that clickable PSMA-inhibitors are valuable precursors for potent PET imaging agents.*^[C, 52]

Here, we introduce the radiotracer ^{18}F PSMA-MIC01 (Figure 2A), which is formed by alkyne-Glu-urea-Lys motif and PET-radionuclide ^{18}F , spaced from the 1,2,3-triazole by a diethylene-glycol-linker, which was shown to display the right linker length.^[51] *Compared to the previously published alkyne- PSMA binding motif,* ^[C] *our PSMA-binding motif modifies the lysine of the existing Glu-urea-Lys motif to a benzamide instead of a phenylurea. Additionally, the synthon used for the ^{18}F fluorinations is based on azido-diethylene-glycol instead of the azido-ethylene synthon used by Kelly et al.*^[C]

[c] J. Kelly, A. Amor-Coarasa, A. Nikolopoulou, D. Kim, C. Williams Jr., S. Ponnala, J. W. Babich, *Eur. J. Nuc. Med. Mol. Imaging* 2017, 44, 647–661