Impact of emerging radiofluorination methods on preclinical and clinical PET imaging

Bernd Neumaier[1, 2*], **Boris Zlatopolskiy**[2]

[1]Forschungszentrum Jülich GmbH, Institute of Neuroscience and Medicine, Nuclear Chemistry (INM-5), 52428 Jülich, Germany
[2]University of Cologne, Faculty of Medicine and University Hospital Cologne, Institute of Radiochemistry and Experimental Molecular Imaging, 50937 Cologne, Germany
[*]E-mail: b.neumaier@fz-juelich.de

Keywords: [^{18}F]Fluoride, ^{18}F-labeling, PET, Cu-mediated, onium precursor

In recent years we developed the so-called "minimalist" approach to ^{18}F-fluorination. The term "minimalist" was coined by us due to the exceptional simplicity of this protocol. This ^{18}F-labeling method requires neither additives nor time-consuming azeotropic drying steps and enables not only the efficient preparation of different prosthetic groups but also clinically relevant tracers [1]. We also adopted this method to Cu-mediated radiofluorination of (aryl)(mesityl)iodonium salts [2]. Thereafter, we focused on the development of simple and efficient protocols for Cu-mediated ^{18}F-fluorination of boronated and stannyl substrates [3]. This efforts ultimately led to the discovery of alcohol-enhanced Cu-mediated radiofluorination [4]. The novel protocols enabled to produce known radiolabeled aromatic amino acids like 6-[^{18}F]fluoro-3,4-dihydroxyphenylalanine (6-[^{18}F]FDOPA), 6-[^{18}F]fluoro-3-hydroxyphenylalanine (6-[^{18}F]FMT) and 2-[^{18}F]fluorophenylalanine (2-[^{18}F]FPhe) with unmatched efficacy. Furthermore, the novel procedures allowed the preparation of the hitherto unknown but clinically highly relevant tracers like [^{18}F]fluorotryptophans ([^{18}F]FTrps), 2-[^{18F}]fluorophenethylamine ([^{18}F]FPEA) or radiolabeled muscarinic acetylcholine receptor ligands. These tracers significantly expand the diagnostic toolbox for the visualization of pathological processes in cancer and neurological disorders.

References

[1] **Neither azeotropic drying, nor base nor other additives: a minimalist approach to ^{18}F-labeling**

R. Richarz, P. Krapf, F. Zarrad, E. A. Urusova, B. Neumaier and B. D. Zlatopolskiy, *Org Biomol Chem* **2014**, *12*, 8094-9

[2] **Copper-Mediated Aromatic Radiofluorination Revisited: Efficient Production of PET Tracers on a Preparative Scale**

B. D. Zlatopolskiy, J. Zischler, P. Krapf, F. Zarrad, E. A. Urusova, E. Kordys, H. Endepols and B. Neumaier, *Chemistry* **2015**, *21*, 5972-9

[3] **A Practical Method for the Preparation of ^{18}F-Labeled Aromatic Amino Acids from Nucleophilic [^{18}F]Fluoride and Stannyl Precursors for Electrophilic Radiohalogenation**

F. Zarrad, B. Zlatopolskiy, P. Krapf, J. Zischler and B. Neumaier, *Molecules* **2017**, *22*, 2231

[4] **Alcohol-Enhanced Cu-Mediated Radiofluorination**

J. Zischler, N. Kolks, D. Modemann, B. Neumaier and B. D. Zlatopolskiy, *Chemistry – A European Journal* **2017**, *23*, 3251-3256