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Harnessing the power of microbial siderophores for nuclear imaging

Under iron-deficient conditions most aerobic microorganisms secret low molecular-weight chelating compounds –siderophores, which actively transport ferric ions into the cells via specific transporters in the microbial membranes [1, 2]. The biomimetic approach allowed us to diversify the arsenal of siderophore-type molecules, introduce additional desired chemical and/or physical properties, and provide means to identify general motifs governing an interplay between structure and function in biological activity [1-5].
Taking into account, that siderophores are absent in the host cells, they are tempting targets for microbial imaging, for example with Ga-68 or Zr-89 using positron emission tomography (PET) [6]. Of the evaluated siderophores, 68Ga-ferrioxamine E and its close biomimetic analogues were shown as the most promising for possible applications in PET imaging of *S. aureus* and *A. fumigatus* species [7]. Currently we are working on other bacterial (*P. aeruginosa*) and fungal species, to better understand the in vivo speciation and differences in the biological recognition and uptake.
On the other hand, desferrioxamine B (DFO) is currently the most commonly used chelator to radiolabel biomolecules with 89Zr [6]. However, its *in vivo* stability has proven insufficient, and transchelation has been observed. Our Zr(IV) –DFO solution studies provided information on the actual chemical form of the complex in biological media [8], and this can contribute to a better understanding of the *in vivo* speciation and differences in the biological activity of this and other chelators [5-7].
Overall, mimics of siderophores hold potential as inert and stable carriers for Fe(III), Ga(III) and Zr(IV) ions for diagnostic medical applications. They also allow identifying critical microbial compartments in which siderophores accumulate and thus illuminate key targets for specific drugs against microbial diseases.

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Primary author: GUMIENNA-KONTECKA, Elbieta (University of Wroclaw)

Co-authors: Prof. SHANZER, Abraham (Weizmann Institute of Science, Rehovot, Israel); Dr MULAR, Andrzej (University of Wroclaw, Faculty of Chemistry, Wroclaw, Poland); Prof. DECRISTOFORO, Clemens (Medical University of Innsbruck, Department of Nuclear Medicine, Innsbruck, Austria); Prof. KOZLOWSKI, Henryk (University of Opole, Department of Health Sciences, Opole, Poland); Prof. HAAS, Hubertus (Medical University of Innsbruck, Department of Molecular Biology, Innsbruck, Austria); Mrs SZCZERBA, Klaudia (University of Wroclaw, Faculty of Chemistry, Wroclaw, Poland); Dr PETRIK, Milos (Palacký University Olomouc, Institute of Molecular and Translational Medicine, Olomouc, Czech Republic)

Presenter: GUMIENNA-KONTECKA, Elbieta (University of Wroclaw)

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