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Frontiers in radionuclide imaging and therapy, a chemical journey from naturally radioactive elements to targeted theranostic agents

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It is with great pleasure we welcome you to this *Dalton Transactions* themed issue: *Frontiers in Radionuclide Imaging and Therapy; A chemical journey from naturally radioactive elements to targeted theranostic agents*. This themed issue recognises the contributions of Professor Isabel Santos from the Instituto Superior Técnico at the University of Lisbon, to the advancement of science in the field of radiopharmaceutical chemistry on the occasion of her recent retirement. Professor Santos has investigated the coordination chemistry of f-elements, namely actinides (U(III/IV)) and lanthanides (e.g. Sm, Ho), as well as d-transition metal compounds, mainly Re and ^{99m}Tc. Some of these metal complexes feature interesting properties for applications in molecular imaging, targeted radionuclide therapy and theranostics. She has published more than 200 publications, and has been responsible for numerous research projects. Professor Santos has been the head of the Radiopharmaceutical Sciences Group for several years, and between 2013–2015 she was the first President of the “Centre for Nuclear Sciences and Technology” (C²TN) in Lisbon, a national research facility rated as “Excellent” by the

Portuguese Science Foundation. We would like to emphasise that Professor Santos has not only made outstanding contributions to the inorganic chemistry community, but also pioneered in Portugal and Europe a move towards the inclusion of women in science, where gender equality is currently a relevant concern in the academic environment worldwide. Indeed, she has been a role model for many of her female students and co-workers, not to mention her national and international collaborators.

The recognized inter-/multi-disciplinary nature of the research domains proposed in this themed issue reflect Professor Santos’ varied scientific interests, which span basic research in inorganic/organometallic chemistry to more application oriented studies. Indeed, this issue provides a broad spectrum of studies and views on radio-metal-based molecular complexes and nanoplatfoms for molecular imaging, systemic radiotherapy and theranostics authored by well-known experts in their field. There are articles focused on the production and radiochemistry of radiometals, such as those by Abrunhosa and co-workers (DOI: 10.1039/C7DT01836C) and Jurisson and co-workers (DOI: 10.1039/C7DT02407J). Within this framework, the study presented by Oehlke and co-workers (DOI: 10.1039/C7DT01830D) is also particularly innovative as it demonstrates that microfluidic synthesis techniques can become a viable alternative to conventional, batch-

wise radiolabelling techniques. Also, in the context of new radiolabelling procedures, Reid and co-workers report on a new radiofluorination method through Cl/¹⁸F halide exchange (DOI: 10.1039/C7DT02122D).

The introduction of innovative bifunctional chelators for the stabilization of radiometals such as technetium, gallium, copper or other relevant radioisotopes for molecular nuclear imaging or targeted radiotherapy applications has been explored by the research groups of Abram (DOI: 10.1039/C7DT01834G), Maina (DOI: 10.1039/c7dt01684k), Dénat (DOI: 10.1039/C7DT01772C), Went & Blower (DOI: 10.1039/c7dt02008b) and Orvig (DOI: 10.1039/C7DT02343J).

Novel rhenium and technetium organometallic complexes potentially useful as targeted imaging probes by employing bioorthogonal chemistry or complexes useful as theranostic molecular tools using the matched pair ^{99m}Tc/Re have been introduced by the Valliant (DOI: 10.1039/C7DT01497J) and Alberto (DOI: 10.1039/C7DT02072D) groups, respectively.

Noteworthy, reports on radiometal complexes aimed at targeting organs such as the heart (Liu and co-workers, DOI: 10.1039/C7DT01292F), cell-membrane transporters (Correia and co-workers, DOI: 10.1039/C7DT01146F) and thrombus (Caravan and co-workers, DOI: 10.1039/C7DT02634J) are also included in this issue. Moreover, imaging of inflammation and infection *in vivo* is also a subject of relevant interest as

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addressed by Kniess and co-workers (DOI: 10.1039/C7DT01735A) and by Drlica and co-workers (DOI: 10.1039/C7DT01189J) in the corresponding Perspectives. One Perspective paper provides an overview on the use of metal complexes for multimodal imaging, which is currently considered a hot topic (Tóth and co-workers, DOI: 10.1039/C7DT02371E).

Apart from the molecular-based approaches, this special issue also comprises two full articles in which radio-labelled gold-based nanoparticles (AuNp) have been studied. For example, in the paper by Paulo and co-workers it has been demonstrated that thiolated bombesin-containing AuNp are potentially useful as target-specific GSH-mediated drug delivery systems (DOI: 10.1039/C7DT00864C). The work presented by Khoobchandani and co-workers (DOI: 10.1039/C7DT00383H) shows that a ^{198}Au -labeled Np (beta

emitter) promotes tumour reduction in a preclinical model of prostate cancer.

Concerning the development of novel theranostics, another hot topic, the articles by Bodio and co-workers (DOI: 10.1039/C7DT01981E) and Gomez Quiroga and co-workers (DOI: 10.1039/C7DT00043J) are exquisite examples of such a type of approach, where (bi)metallic complexes containing simultaneously a cytotoxic unit and a nuclear or optical imaging probe were synthesized and evaluated biologically with relevant results for further application.

We would also like to highlight the contributions with a higher clinical component, that is the case of the Perspective by Costa and co-workers (DOI: 10.1039/C7DT01929G), which discusses clinical applications of therapeutic radionuclides commonly used in the clinical practice of oncology; or the full article by Müller and co-workers (DOI: 10.1039/C7DT01936J), describing

the first-in-human PET/CT with ^{152}Tb -DOTATOC; and the full article by Brechbiel and co-workers (DOI: 10.1039/C7DT01819C), which reviews the use of the α -emitting radionuclides for radio-immunotherapy. These contributions were organized and written to reach the broader audience of the inorganic chemistry/organometallic community interested in biomedical applications of radiometals.

Finally, we would like to thank the editorial staff at *Dalton Transactions* for making this themed issue possible. All of the authors as well as the reviewers are also acknowledged for their effort and relevant contributions, and we hope this themed issue will encourage further developments in this exciting research field.

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Please enjoy and be inspired!