

## Call for Applications: Two PhD fellowships

Advancing cold anticancer *facial* tricarbonylrhenium(I) compounds to their theranostic <sup>186</sup>rhenium analogues

Supervisor: Prof I. Booyesen

Co-supervisor: Dr A. Mambanda

### Abstract:

There is substantial scope for exploring the bioinorganic chemistry of the robust and physiological compatible *facial* tricarbonylrhenium(I) core towards nitrogen-donor bifunctional chelators (*viz.* terpyridine, dipyridylamine and phenanthroline) which will act as covalent anchors to various bio-vectors. These bio-vectors will allow defined biodistribution patterns of the resultant <sup>186</sup>rhenium radiopharmaceuticals to diseased sites; enhancing radio-diagnostic and –therapeutic application while limiting secondary radiation exposure to healthy cells. In fact, literature trends illustrate that these specified nitrogen-donor ligands and their derivatives display distinctive coordination modes towards the *fac*-[Re(CO)<sub>3</sub>]<sup>+</sup> core.<sup>1-3</sup> Therefore, since the fundamental coordination chemistry and synthetic routes towards <sup>186</sup>rhenium labelled precursors have been developed, particular emphasis will be placed on the design of the organic ligands covalently bonded to biovectors such as derivatives of current chemotherapeutic drugs (*e.g.* 5-fluorouracil) and biological molecules (*e.g.* biotin).<sup>4,5</sup>

During this research project, the following research activities will be undertaken:

- The synthesis, purification and characterization of the nitrogen-donor bifunctional chelators will be performed by the PhD candidates in our research laboratories in collaboration with Dr Siphamandla Sithebe.
- The synthesis, characterization, aqueous stability and biomolecular interaction studies of cold rhenium(I) compounds will be conducted by the PhD candidates in our research laboratories at UKZN.

- Subsequently, the *in vitro* anticancer screening of the cold rhenium compounds will be conducted by the PhD candidates in the research laboratory of Prof. M. Simelane based in the Department of Biochemistry at the University of Johannesburg.
- An *in vivo* toxicity study on the lead metal complex will be performed.
- 186-Rhenium production and radiolabelling experiments to form the hot lead metal compound analogue as well as the *in vivo* radiopharmaceutical studies will be conducted by the applicant under the guidance of our collaborators in the radiochemical laboratories at NECSA.

#### References:

1. Ismail, M. B.; Booyesen, I. N.; Hosten, E.; Akerman, M. P., Synthesis, characterization and DNA interaction studies of tricarbonyl rhenium(I) compounds containing terpyridine Schiff base chelates. *Journal of Organometallic Chemistry* **2017**, *833*, 1-9.
2. Causey, P. W.; Besanger, T. R.; Schaffer, P.; Valliant, J. F., Expedient Multi-Step Synthesis of Organometallic Complexes of Tc and Re in High Effective Specific Activity. A New Platform for the Production of Molecular Imaging and Therapy Agents. *Inorganic Chemistry* **2008**, *47* (18), 8213-8221.
3. Werrett, M. V.; Wright, P. J.; Simpson, P. V.; Raiteri, P.; Skelton, B. W.; Stagni, S.; Buckley, A. G.; Rigby, P. J.; Massi, M., Rhenium tetrazolato complexes coordinated to thioalkyl-functionalised phenanthroline ligands: synthesis, photophysical characterisation, and incubation in live HeLa cells. *Dalton Transactions* **2015**, *44* (47), 20636-20647.
4. Gramni, L.; Vukea, N.; Chakraborty, A.; Samson, W. J.; Dingle, L. M. K.; Xulu, B.; de la Mare, J.-A.; Edkins, A. L.; Booyesen, I. N., Anticancer evaluation of ruthenium(III) complexes with N-donor ligands tethered to coumarin or uracil moieties. *Inorganica Chimica Acta* **2019**, *492*, 98-107.
5. Ma, L.; Wang, Y.; Wang, X.; Zhu, Q.; Wang, Y.; Li, L.; Cheng, H.-B.; Zhang, J.; Liang, X.-J., Transition metal complex-based smart AIEgens explored for cancer diagnosis and theranostics. *Coordination Chemistry Reviews* **2022**, *473*, 214822.

#### Core character attributes:

The ideal candidates must be meticulous, self-motivated and dedicated. In addition, these candidates must show a high level of integrity as confidentiality is of utmost importance. Furthermore, the candidates must be dynamic individuals who can work effectively in a multidisciplinary team-orientated environment.

#### Core skills:

The candidates must be competent in common Microsoft software packages as well as have good communication and writing skills. Also, theoretical or experimental

experience in computational, bioinorganic and/ or analytical chemistry will be beneficial.

**Value of PhD studentship:**

Each PhD studentships will be R 120 000 for the first year and will be renewable subjected to satisfactory progress by all stakeholders.

**How to apply?**

Candidates must forward their detailed CVs to Prof. I Booysen ([Booysemi@ukzn.ac.za](mailto:Booysemi@ukzn.ac.za)) by 19/04/2024. Three contactable references must be included in the CV and certified copies of degree certificates must be attached. No late applications will be considered. If you are not contacted by the 24/04/2020 for an interview, please consider your application unsuccessful.