PhD13

Bioconjugation kits for multi-metal use and multi-organ targeting

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Application Area: Cancer, Cardiovascular **Modality:** SPECT, PET **Related:** PhD 3, 12, 14, 15

Background

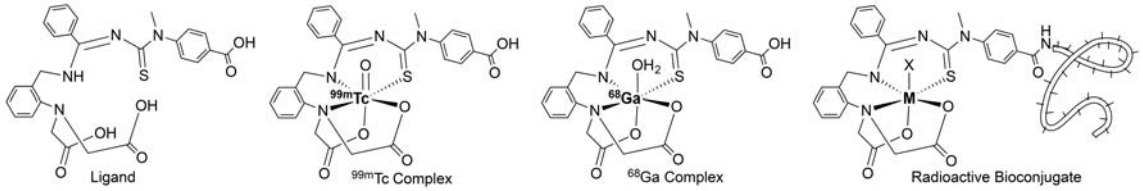
The chemical structure of radioactive compounds is the basis for their effective operation in the delivery of biochemical and biophysical-structural information.[1-5] During recent years, hybrid imaging tools and bioconjugation approaches in tracer chemistry generated a need for modular tracers based on different radioactive nuclides.[3,5,6] This concept allows the combination of different tracer-specific imaging techniques. Furthermore, modular tracer chemistry could support theranostic approaches,[5] which require the quantification of therapeutic isotopes or non-radioactive drugs by medical imaging techniques.

Hypothesis

Novel multi-metal chelators[7,8] will facilitate the development of bioconjugation kits based on various radiometals for PET and SPECT and the combination thereof.

Methods

Advanced chemical synthesis methods will give access to the novel compounds, which are first tested for their chemical structure and stability with spectroscopic and diffraction methods (IR, NMR, MS, UV/Vis, X-ray diffraction). Stability of the new compounds in biological media will be tested by typical *in vitro* methods as followed by SPECT and PET studies.



Work Packages

WP1: Ligands: synthesis & characterization

WP2: Non-radioactive complexes: synthesis & characterization

WP3: Transformation to n.c.a. compounds, in-vitro tests

WP4: Peptide coupling, in-vitro tests

WP5: Kit formulation

year 1 — *year 2* — *year 3*

WP1: Novel chelator systems will be designed in a way to make them suitable for the formation of stable complexes with various radioactive isotopes of the SPECT and PET nuclide families. Tri- to hexadentate ligands are scheduled to be synthesized on the basis of thiocarbamoylbenzimide chlorides, aroylthioureas or aminoalcohols.

WP2: The ligands are selected in a way that orthogonal bioconjugation is possible. Methods of computational chemistry will be applied for the optimization of the ligand design. After full analytical and spectroscopic characterization of the ligands, their complex formation behavior will be checked for non-radioactive or long-lived nuclides of the targeted metal ions and the structures and the chemical stability of the products will be investigated.

WP3: Transformation to the n.c.a. concentrations of the metal ions will be performed for the conjugated as well as for the non-conjugated ligand systems.

WP4: Concentration-independent analytical data will be derived and *in vitro* data of the complexes will be recorded in order to find candidates suitable for biodistribution PET and SPECT studies.

WP5: Based on the bioconjugation approach for labeling, labeling kits will be developed, which allow the coupling of arbitrary target-seeking biomolecules to one unique chelator system via peptide coupling or ‘click chemistry’.

Clinical Translation

The proposed chemistry is intended to deliver proof-of-principle solutions for the development of prospective radiopharmaceuticals. In the follow-up of this PhD project, transformation of the in vivo results to clinically applicable solutions in intended.

Literature

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