Public Abstract
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Technetium and rhenium have radioactive isotopes that are clinically useful for diagnostic (Tc-99m) or therapeutic (Re-186/188) purposes. This makes them attractive candidates for incorporation into pharmaceuticals. One way to incorporate radioactive metals into pharmaceuticals is through the use of a bifunctional chelating agent (BFCA), which inertly traps the metal while also attaching it to a targeting biomolecule.

Technetium-99m is an attractive radionuclide not only because of its diagnostic capabilities, but also because it is a widely available and relatively affordable option. Two Tc-99m radiopharmaceuticals were created that seek to target somatostatin receptors (SSTRs), which are commonly overexpressed on neuroendocrine tumor tissues. Two different histidine-derived BFCAs were used to chelate a technetium-99m tricarbonyl core while simultaneously tethering it to an antagonist peptide with a high affinity for somatostatin receptor subtype two (SSTR2).

Due to the fact that non-radioactive Re is in the same group as Tc, the analogous macroscale Re compounds were synthesized. This helped to determine the identity of the products made on the radio-tracer level (nano- to picomolar) as well as determine receptor affinity through competitive binding assays in SSTR2-expressing cells. Both Re compounds, exhibited very good, low nanomolar affinities for SSTR2. The Tc-99m radiotracer products both exhibited high *in vitro* stability during challenges in cysteine, histidine, and mouse serum. Biodistribution and imaging studies in mice were also performed.

The complexation of Re using a tetradentate diphosphinedithiol (DPDT) ligand was also explored. Rhenium is more readily oxidized than technetium, which can cause complications when seeking to use Re-186/188 radiopharmaceuticals in the body. Complexation with more reducing ligands (such as DPDT) may help stabilize Re(V) in the body. Thus, the initial chemistry of Re- and Tc-DPDT complexes was explored. This led to the creation of a highly stable Re(V)-DPDT complex, which remained stable in oxidative environments over a period of several months. Macroscale reactions using the DPDT ligand to synthesize the Tc-99 counterpart led to the formation of Tc(III) complexes from Tc(VII), without the need for additional reducing agents.