

The Design and Synthesis of an I-131 Labeled Rhodium Metalloinsertor Targeting MMR-Deficient Colorectal Cancer

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The fidelity of DNA is essential for healthy cellular development and proliferation. Mismatched base pairs can arise because of polymerase errors or exposure to genotoxic chemicals. Mismatch-repair (MMR) machinery safeguards against these errors. In patients with Lynch Syndrome (also known as Hereditary Nonpolyposis Colorectal Cancer), however, cells have damaged or lack MMR machinery and are therefore unable to repair mismatches. This can lead to the creation of single-nucleotide polymorphisms, the accumulation of mutations, and colorectal tumorigenesis. Here, a novel radiotherapeutic for Lynch syndrome was developed. Metalloinsertors, octahedral rhodium complexes bearing the sterically expansive chrysi ligand, have been shown to sensitively recognize and bind DNA mismatches in vitro, exhibiting preferential toxicity in MMR-deficient cells. To create a metalloinsertor for Lynch tumors, the tin-containing ancillary ligand PPO-Sn was coordinated to Rh(phen)(chrysi)(NH)₃ by dissolving the two components in ethanolic water under basic conditions, obtaining rac-Rh(phen)(chrysi)(PPO-Sn)+2. rac-Rh(phen)(chrysi)(PPO-Sn)+2 was synthesized at 15% yield and purified via high-performance liquid chromatography (HPLC) to >99% pure. Using HPLC data provided by my mentor, I found that the final radioiodinated product, rac-Rh(phen)(chrysi)(PPO[¹³¹I])²⁻, was produced with 30% radiochemical conversion and >98% radiochemical purity. Then I verified the identity by co-elution with a non-radioactive iodinated standard and orthogonal spectroscopy. The data validate a route to an I-131-labeled metalloinsertor suitable for biological evaluation in MMR-deficient colorectal cancer.

Awards Won:

Third Award of \$1,200

International Precious Metals Institute: First Place Award of \$5,000