CONTROL ID: 1718577

TITLE: Investigating Cell Entry of Cisplatin and Anticancer Platinum(IV) Prodrugs Using Fluorescence Microscopy

AUTHORS/INSTITUTIONS: W. Ang, D. Montagner, S. Yap, Chemistry, National University of Singapore, Singapore, SINGAPORE|

CURRENT CATEGORY: Metals in Medicine and Health

ABSTRACT BODY:

Abstract Body: Since the discovery of its potent antitumoral activity, the inorganic drug cisplatin has become one of the most important anticancer agents used in the clinic. Together with carboplatin and oxaliplatin, they formed a class of highly effective platinum(II)-based chemotherapeutic drugs. Despite their clinical success, these drugs are limited by high toxicity, severe side-effects and incidences of drug resistance. In recent years, attention has been turned to the development of platinum(IV) carboxylate complexes as prodrugs to classical platinum(II) agents. Understanding how these anticancer platinum complexes are being processed by cancer cells is important towards exploiting this prodrug strategy to develop the next generation of platinum drugs. Currently, there are limited analytical tools that are capable of directly visualizing the localization of these important platinum anticancer compounds. With the goal of understanding their mechanism of action, we engineered a rhodamine-based probe that can be applied to image cis-amineplatinum(II) complexes within a complex cellular environment using fluorescence microscopy. By design, fluorescence turn-on was achieved by binding of platinum complex at the probe, followed by ring opening of the rhodamine spirolactam motif. The probe was selective towards platinum(II) complexes against the backdrop of intracellular metal ions. The probe was also able to discriminate between platinum(IV) and platinum(II) species by taking advantage of the limited chemical reactivity of platinum(IV) complexes. We investigated the mechanism by which recognition of specific platinum drugs was achieved by the probe leading to fluorescence turn-on. We also applied the probe in live mammalian cells to show intracellular conversion of platinum(IV) prodrugs to platinum(II) species upon cell entry.