ORGANIC CHEMISTRY SEMINAR

Gold (I) Anticancer Agents: Building Blocks for the Synthesis of Heterometallic Compounds and Antibody Drug Conjugates. Preclinical Studies

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ZOOM

https://udel.zoom.us/j/92777070899

The real potential of gold (I) and (III) compounds as anticancer chemotherapeutics is now being unveiled. Gold(I)- phosphane and gold(I)-N-heterocyclic NHC-carbene complexes (like Auranofin in Chart 1) have shown promising results in advanced preclinical and clinical studies, while displaying a mode of action different from that of FDA approved platinum-based drugs. These gold(I) compounds serve as excellent building blocks for the synthesis of heterometallic complexes containing titanocenes [TiCp2] or ruthenium(II) arene derivatives [RuCl2(p- cymene)(dppm)]. In this talk, I will discuss the potential of these bimetallic Ti-Au and Ru-Au compounds against renal or prostate cancers (including studies of their efficacy in vivo, pharmacokinetics, histopathology and mechanisms).1-3 I will also report on newer Pt(IV)-Au(I) compounds described recently and their activity against triple negative breast cancer 2D and 3D models.4 Lastly, I will discuss targeting strategies for gold(I)-based cytotoxic agents in order to improve their selectivity, bioavailability and blood circulation times. More specifically I will describe the synthesis of antibody drug conjugates based on gold(I) compounds and Trastuzumab for the treatment of HER2-positive breast cancers.5,6 I will comment on the synthesis and characterization of second-generation gold-based antibody drug conjugates, and their excellent in vivo efficacy in a mouse model.

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