Anticancer approach by a gold artificial metalloenzyme-catalyzed synthesis of quaternary ammonium derivatives via hydroamination

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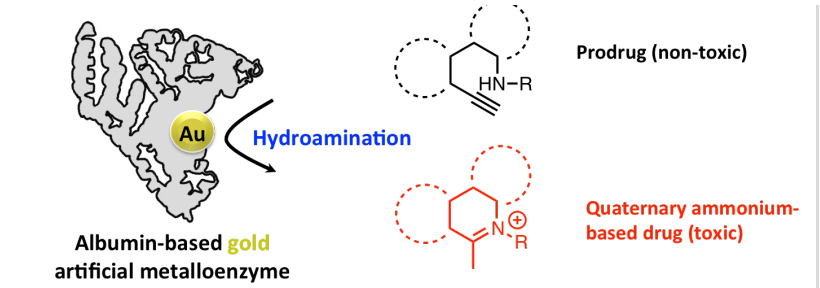
One of the most common treatments for cancer is chemotherapy, which is defined as the use of drugs to destroy cancer cells. This approach has demonstrated significant curative effects. However, because chemotherapy is not perfectly specific for cancer cells, it has significant side effects on rapidly dividing healthy cells.[1] An emerging approach in the field of targeted drug delivery is establishment of abiotic metal-triggered prodrug mechanisms that can control the release of bioactive drugs.[2] This approach is advantageous because of the bioorthogonality of abiotic metals. Currently, design of prodrugs that use abiotic metals as a trigger relies heavily on uncaging strategies.

This work introduce a strategy based on a gold-catalyzed synthesis of a quaternary ammonium-based anticancer drug from a prodrug in good turnover number (over 100) via hydroamination under physiological conditions. To make the prodrug strategy biocompatible, a human serum albumin-based gold artificial metalloenzyme[3,4] (ArM), rather than of the free gold metal complex, was used as a trigger for prodrug activation. The albumin-based gold ArM protected the catalytic activity of a bound gold metal even in the presence of up to 1 mM glutathione *in vitro*. The synthesized drug via the gold ArM exerted a therapeutic effect in cell-based assays, highlighting the potential usefulness of the gold ArM in anticancer approachs.



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