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Perspective Article



# The Perspective for Luminescent Transition Metal-based Theranostic Probes

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## Short Communication

Transition metal-based chemotherapy drugs became one of the workhorses in the clinic since cisplatin was approved as an anticancer drug in 1970s [1]. The wide medical use of other related platinum drugs including carboplatin and oxaliplatin further spurred the intense interests of the scientists in the development of metallodrugs. However, it is aware that tumors can be evolved to be resistant to platinum drugs, prompting to develop non-platinum-based metallodrugs. Nowadays, a variety of metal-based complexes have been investigated as agents for various diseases ranging from cancers to neurodegenerative diseases [2]. However, it should be noted that no new non-radioactive metallodrug was approved for medical use after the platinum drugs [3].

The development of new metallodrugs is facing some challenges. Most metallodrugs failed to enter clinical trials due to their related adverse side-effects. These side-effects are mainly contributed by unclear interaction mechanisms, high toxicity and low biocompatibility. Frankly, pharmaceutical agents are mainly small organic compounds and naturally derived molecules, metallodrugs remain attractive due to their unique properties [1]. Firstly, transition metal complexes generally display rich chemical geometries, such as square planar Pt (II) complexes, octahedral ruthenium (II)/iridium (III)/rhodium (III) complexes. This rich chemical space provides the possibility of additional interaction with biological macromolecules, especially for protein-protein interactions which are generally difficult to be targeted by traditional small molecule-based agents as these targets lack well-defined interaction pockets. Secondly, many metal centers display multiple oxidation states, endowing the complexes with a new mechanism of action during interaction with biological targets. For example, ferrocene and ferrocene derivatives are known to reversibly go through oxidation-reduction, which can be harnessed to provide additional modes of action, such as ROS generation and interference with redox homeostasis in living systems [3]. Fascinatingly, many transition metal complexes show desirable photophysical properties, especially for d6, d8 and d10 transition metal complexes. These complexes generally show highly strong room-temperature phosphorescence, long emission lifetime, high photostability etc. These excellent properties enable them to be potential diagnostic probes. Therefore, there is an increasing trend that the scientists are exploring the theranostic potential of luminescent transition metal complexes since these probes are more cost-effective, and are capable of real-time monitoring therapeutic process, even realizing imaging-guide surgery [4].

To out delighted, the first Ru (II) polypyridyl complex-based photosensitizer TLD1433 has completed phase Ib clinical trial for the treatment of bladder cancer [5], shedding light on the theranostic potential of luminescent transition metal complexes. However, the low specificity of the metal complexes to tumor tissues leads to off off-target accumulation in the body, causing unwanted side effects. At the same time, most complexes also suffer from low water solubility, hampering them to be orally administered. In addition, near-infrared (NIR) transition metal complexes for deep tissue penetration are relatively rare, and the development of NIR complexes generally involves high aromatically conjugated ligands, which are not favorable for biological applications.

To address these problems, I think there are three main promising strategies in future. One is to conjugate biologically compatible molecules to metal complexes, such as biotin or

other cancer specifically targeted natural products, peptides and carbohydrates. For example, we have developed galactose [6], peptide WKYMVm [7] and natural product oridonin [8] conjugated iridium (III) complex-based luminescence probes, which displays high specificity to cancer cells with highly improved compatibility. With the immense interest in luminescent nanomaterials, metal complexes-based nanomaterials offer new opportunities to develop biocompatible and multifunctional theranostic probes. For example, the Ru (II) polypyridyl complex was used to serve as a building block to develop phosphorescent nanoscale coordination polymers, which surface can be further factionalized for biological applications [9]. Another strategy is to develop NIR complexes, which use traditional organic dyes to be ligands, such as coumarin, BODIPY etc. These organic dye-based ligands not only possibly enable the complexes to emit in the NIR region, but also show high extinction coefficient [10]. At last, I believe that more luminescent transition metal-based theranostic probes will advance into clinical trials if bioinorganic chemists tightly collaborate with other area scientists, such as materials, medicine.

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## Conflicts of Interest

Author declare no conflict of interest.

## References

1. Wang X, Wang X, Jin S, Muhammad N, Guo Z (2018) Stimuli-Responsive Therapeutic Metallodrugs. Chem Rev 119(2): 1138-1192.
2. Murray BS, Dyson PJ (2020) Recent progress in the development of organometallics for the treatment of cancer. Current Opinion in Chemical Biology 56: 28-34.
3. Patra M, Gasser G (2017) The medicinal chemistry of ferrocene and its derivatives. Nature Reviews Chemistry 1: 0066.
4. Fernández-Moreira V, Gimeno MC (2018) Frontispiece: Heterobimetallic Complexes for Theranostic Applications. Chemistry A European Journal 24(14): 3345.
5. Monro S, Colón KL, Yin H, Roque J, Konda P, et al. (2019) Transition Metal Complexes and Photodynamic Therapy from a Tumor-Centered Approach: Challenges, Opportunities, and Highlights from the Development of TLD1433. Chem Rev 119(2): 797-828.
6. Wang W, Vellaisamy K, Li G, Wu C, Ko CN, et al. (2017) Development of a Long-Lived Luminescence Probe for Visualizing β-Galactosidase in Ovarian Carcinoma Cells. Analytical Chemistry 89(21): 11679- 11684.
7. Vellaisamy K, Li G, Wang W, Leung CH, Ma DL (2018) A long-lived peptide-conjugated iridium(iii) complex as a luminescent probe and inhibitor of the cell migration mediator, formyl peptide receptor 2. Chem Sci 9(43): 8171- 8177.
8. Wang W, Yang C, Lin S, Vellaisamy K, Li G, et al. (2017) First Synthesis of an Oridonin-Conjugated Iridium(III) Complex for the Intracellular Tracking of NF-κB in Living Cells. Chemistry A European Journal 23(20): 4929-4935.
9. Liu D, Huxford RC, Lin W (2011) Phosphorescent nanoscale coordination polymers as contrast agents for optical imaging. Angew Chem Int Ed Engl 50(16): 3696-3700.
10. Feng Z, Yu Y, Yang X, Zhong D, Song D, et al. (2019) Isomers of Coumarin-Based Cyclometalated Ir(III) Complexes with Easily Tuned Phosphorescent Color and Features for Highly Efficient Organic Light-Emitting Diodes. Inorganic Chemistry 58(11):7393-7408.