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Editorial: Linking chemistry to biology and medicine via metal ions: developed from the 16th international symposium on applied bioinorganic chemistry

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Editorial on the Research Topic
Linking chemistry to biology and medicine via metal ions: developed from the 16th international symposium on applied bioinorganic chemistry

The field of bioinorganic chemistry continues to serve as a bridge between chemistry, biology, and medicine, providing fundamental insights into the roles of metal ions in biological systems. The 16th International Symposium on Applied Bioinorganic Chemistry (ISABC-16), held in Ioannina, Greece, from June 11–14, 2023, served as a platform for cutting-edge research, showcasing novel applications of metal ions in medicine, catalysis, imaging, and therapeutics. This Special Topic presents a few representative contributions inspired by ISABC-16, bringing together innovative research and reviews that demonstrate the critical role of metal ions in biological processes and medical applications.

Metal ions are indispensable in biological systems, contributing to enzyme function, electron transfer, and structural stabilization of biomolecules. Studies suggest that more than 30% of all proteins require metal ions for their biological activity. These include metalloenzymes involved in redox chemistry, hydrolysis, and energy conversion. The study of bioinorganic chemistry enables us to understand these essential biochemical functions and exploit them for medicinal and technological applications.

Recent research on transition metals, main group metals, lanthanides, and actinides has led to groundbreaking applications in medicine, including the development of metal-based drugs and imaging agents. Metal-based drugs, including cisplatin and ruthenium complexes, have significantly advanced chemotherapy, while metal nanoparticles offer promising antimicrobial applications. Additionally, metal coordination complexes are being explored for use in imaging technologies such as MRI contrast agents and radiopharmaceuticals for targeted diagnostics and therapy. All these topics were presented at the conference.

This special issue includes four articles, briefly reviewed below.

Stoltzfus and Michel, reviewed the role of cysteine-rich zinc finger (ZF) proteins in the nuclear factor kappa-B (NFκB) pathway, which is crucial for inflammation and immune regulation (Stoltzfus and Michel). The review highlights the significance of ZFs in NFκB-related signaling, their functions in pro-inflammatory and anti-inflammatory processes, and their involvement in inflammation-related diseases such as autoimmune disorders and cancer. Additionally, the article discusses how post-translational modifications (PTMs), specifically persulfidation, as well as conventional modifications such as phosphorylation and ubiquitination, influence the function of ZF proteins. Persulfidation, mediated by hydrogen sulfide (H_2S), has emerged as an important modification affecting inflammation regulation. The review summarizes the connections between ZFs and persulfidation and discusses their therapeutic implications for targeting ZF-related pathways in inflammatory diseases documenting the impact this mode of signaling can have.

Nikolaou et al., reviewed the recent advancements in the application of porphyrin derivatives in biomedical research (Nikolaou et al.). The article highlights the multifunctional role of porphyrins in biomedical applications, including:

- Photodynamic Therapy (PDT) for cancer treatment
- Wound healing using porphyrin-based hydrogels
- Drug delivery systems incorporating porphyrins for controlled release
- Bioimaging and diagnostic applications
- Peptide labeling for molecular tracking and therapeutic targeting

The review also discusses the challenges and future prospects of porphyrin-based materials, particularly in their stability, biocompatibility, and therapeutic effectiveness. It provides insights into the synthetic modifications that can improve their function and expand their potential in biomedical fields illustrating not only the many directions in this area where information is available but also new directions in the field.

Banti et al., reports on the development and evaluation of a novel palladium(II)-based metallodrug that combines an anti-metabolite nucleobase analogue (6-methyl-thiouracil, MTUC) with a mitochondriotropic agent (Tri-o-Tolyl-Phosphine, TOTP) to target breast cancer cells (Banti et al.). The study introduces a new class of mitochondria-targeted palladium(II) metallodrugs with potential for breast cancer treatment, offering a balance between cytotoxicity and selectivity. While the compound is less potent than cisplatin, higher selectivity for cancer cells over normal cells and a mitochondrial-mediated apoptotic mechanism, making it a promising candidate for further preclinical evaluation and importantly suggestive of future development and less toxic and more selective drugs.

Miller and Crans point to the fact that diagnostic agents often contain a metal ion whereas therapeutics agents with a metal ion are much less common (Miller and Crans). They suggest that the extensive use of metal-containing diagnostic agents is due to the high stability and lacking metabolism of these agents whereas therapeutic agents often are metabolized and much less stable. Then the article describes intra-tumoral delivery of therapeutics when highly reactive compounds with non-toxic decomposition products are desirable which represents a paradigm shift in the design of metal-based anticancer agents. Focusing on vanadium coordination complexes that are designed for intra-tumoral delivery have potential to target aggressive, treatment-resistant cancers such as glioblastomas, while minimizing systemic toxicity. By integrating concepts of chemical stability, pharmacokinetics, and targeted delivery, this perspective outlines a viable strategy to expand the clinical success of metal-based therapeutics beyond platinum drugs.

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