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Editorial

Transition Metals in Catalysis: The Functional Relationship of Fe–S Clusters and Molybdenum or Tungsten Cofactor-Containing Enzyme Systems

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Following the "Molybdenum and Tungsten Enzyme conference—MoTEC2019" and the satellite meeting on "Iron–Sulfur for Life", we wanted to emphasize the link between iron–sulfur clusters and their importance for the biosynthesis, assembly, and activity of complex metalloenzymes in this Special Issue of *Inorganics*, entitled "Transition Metals in Catalysis: The Functional Relationship of Fe–S Clusters and Molybdenum or Tungsten Cofactor-Containing Enzyme Systems".

Iron–sulfur (Fe–S) centers are essential protein cofactors in all forms of life. They are involved in many of the key biological processes, including respiration, photosynthesis, metabolism of nitrogen, sulfur, carbon and hydrogen, biosynthesis of antibiotics, gene regulation, protein translation, replication and DNA repair, protection from oxidizing agents, and neurotransmission [1]. In particular, Fe–S centers are not only involved as enzyme cofactors in catalysis and electron transfer, but they are also indispensable for the biosynthesis of complex metal-containing cofactors. A prominent example is represented by the family of radical/*S*-adenosylmethionine-dependent enzymes, which were discovered in 2001 [2]. Members of this family play essential roles in the biosynthesis of metal centers as complex as the iron-molybdenum cofactor (FeMoco) of nitrogenase, the molybdenum cofactor (Moco) of various molybdoenzymes, the active sites of [Fe–Fe]- and [Fe]-hydrogenases, and the tetrapyrrole cofactors of hemes, corrins, and chlorins. In spite of the recent fundamental breakthroughs in metalloenzyme research, it has become evident that studies on single enzymes have to be transformed into the broader context of a living cell, where biosynthesis, function, and disassembly of these fascinating metal cofactors are coupled in a dynamic fashion. The various biosynthetic pathways were found to be tightly interconnected through a complex crosstalk mechanism that involves the dependence on the bioavailability of distinct metal ions, in particular, molybdenum, iron, and tungsten. The current lack of knowledge of such interaction networks is due to the sheer complexity of the metal cofactor biosynthesis with regard to both the (genetic) regulation and (chemical) metal center assembly.

This special issue intends to combine our recent knowledge on innovative model complexes and biogenesis pathways by emphasizing how they are interconnected by putting the focus on the metals, molybdenum, tungsten, and iron. In this issue, nine contributions, including four original research articles and five critical reviews, will update the reader on the broad spectrum of the role of molybdenum, tungsten, and iron in biology.

The understanding of the biological role of iron and the assembly of Fe–S clusters is reviewed in detail by Srour et al. [3]. The connection and requirement of Fe–S cluster assembly for the biosynthesis of the molybdenum cofactors is reviewed by Mendel et al. [4], while tungsten-containing enzymes and their assembly are reviewed by Seelmann et al. [5]. The review by Yang et al. [6] highlights the past work on metal–dithiolene interactions and how the unique electronic structure of the metal–dithiolene unit contributes to both the oxidative and reductive half reactions in pyranopterin molybdenum and tungsten enzymes. A more specific review focuses on the Moco and Fe–S cluster containing protein formate

dehydrogenase. The review by Hille et al. [7] reports on the recent progress in the understanding of the maturation and reaction mechanism of the cytosolic and NAD^+-dependent enzyme from *Cupriavidus necator.* The review on formate dehydrogenase is complemented by an original research article on the formate-hydrogen-lyase (FHL) complex in *Escherichia coli* by Marloth et al. [8], which is composed of the molybdenum-containing formate dehydrogenase and type-4 [NiFe]-hydrogenase. The FHL complex is phylogenetically related to respiratory complex I, and it is suspected that it has a role in energy conservation similar to the proton-pumping activity of complex I. These results indicate a coupling not only between Na^+ transport activity and H_2 production activity, but also between the FHL reaction, proton import, and cation export. The original article by Huang et al. [9] focuses on the [Fe]-hydrogenase (Hmd) that catalyzes the reversible heterolytic cleavage of H_2, and hydride transfer to methenyl-tetrahydromethanopterin (methenyl-H_4MPT^+). The article reports on the crystal structure of an asymmetric homodimer of Hmd from *Methanolacinia paynteri* (pHmd), and the results suggest that Lys150 might be involved in the FeGP-cofactor incorporation into the Hmd protein in vivo.

The theoretical investigations by Rovaletti et al. [10] focus on the only binuclear molybdoenzyme, the Mo–Cu CO dehydrogenase from *Oligotropha carboxydovorans*. This original article studies the dihydrogen oxidation catalysis by this enzyme using QM/MM calculations. The study by Ahmadi et al. [11] introduces Ni to the topic and studies tetra-nuclear nickel dithiolene complexes.

In conclusion, we hope that these open-access contributions will serve as guiding lights for future research into the biological role of molybdenum, tungsten, and iron, and their interconnection at the cellular and enzymatic level. We thank the authors for their original contributions for the special issue, and we thank the reviewers for their insightful comments on each article.

Conflicts of Interest: The author declare no conflict of interest.

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