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Thematic Minireview Series: Metals in Biology 2013

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One-half of the available protein structures contain metals, explaining their roles as essential trace elements. Metals are also critical in many aspects of nucleic acid biochemistry. This prologue briefly introduces the fifth of the Thematic Series on Metals in Biology, which began in the *Journal of Biological Chemistry* in 2009. The five minireviews in this 2013 series deal with the molybdenum prosthetic group (a pterin known as Moco); the biosynthesis of the "M-cluster" molybdenum prosthetic group of nitrogenase; the biosynthesis of the nickel-based metallocenter of the enzyme urease; several of the processing, transport, and medical aspects of cobalamins; and the growing roles of heme sensor proteins.

As pointed out in the introductions to previous Thematic Series on Metals in Biology (1–4), metals play a critical role in biochemistry. A list of these for which functions are known in biology includes sodium, potassium, magnesium, vanadium, manganese, nickel, iron, cobalt, copper, zinc, selenium, and molybdenum. Chromium has been considered as a "glucose tolerance" factor, although a clear biochemical role has never been demonstrated (and the metal is a carcinogen). However, this state of knowledge of metals is undoubtedly incomplete. As pointed out in last year's series (4), a study of the "metalloproteome" of the hyperthermophile *Pyrococcus furiosus* revealed that 154 of 393 chromatographically separated metal-containing fractions did not match any known metalloproteins (5). The organism has proteins that contain tungsten, and a number of unusual metals were assimilated by this archaeon. Whether these metals are adventitious or functional is yet unknown, and the recent issue of arsenic is exemplary (6, 7).

Previous contributions to the Metals in Biology series have covered a number of issues related to metals as diverse as iron, copper, selenium, nickel, vanadium, arsenic, and manganese, considering issues related to functions, transport, toxicity, homeostasis, and other aspects. Much of the current thematic series is oriented toward the assembly of complex metal cofactors (or more appropriately called "prosthetic groups," which do not show up in the overall stoichiometry of enzyme reactions).

The series begins with two minireviews on molybdenum. In the first, Ralf R. Mendel discusses the biological assembly of the pterin-based Moco. The biosynthesis of Moco begins with GTP, involves four steps, and requires six proteins, a process that in turn requires iron and copper.

The second minireview, by Yilin Hu and Markus W. Ribbe, also deals with molybdenum, specifically the iron-molybdenum cluster of nitrogenase, a complex enzyme vital to agriculture in terms of its ability to reduce atmospheric nitrogen to ammonia. Sulfur is also involved in the form of a protein-bound cysteine persulfide as well as in the metal clusters.

In the third minireview, Mark A. Farrugia, Lee Macomber, and Robert P. Hausinger discuss the metallocenter biosynthesis of urease, a nickel-containing enzyme in bacteria and plants. Four accessory proteins are involved in a GTP-dependent insertion of nickel into the active center.

We move to cobalt in the fourth minireview, specifically aspects of cobalamin (vitamin B_{12}) treated by Carmen Gherasim, Michael Lofgren, and Ruma Banerjee. They discuss new aspects of the trafficking of cobalamin in mammals and the human diseases that result from impairments in the pathway.

The final minireview in this series, by Hazel M. Girvan and Andrew W. Munro, touches on metal center assembly but focuses on the use of a well studied prosthetic group, heme, as a biological sensor. Although hemoproteins have long been known as essential oxygen carriers and as workhorses in electron transport and the catalysis of difficult oxidations (*e.g.* cytochrome P450), there are increasing examples of heme acting as a biological sensor particularly with gaseous signals, *e.g.* $NO^{\bullet}$ and CO. These functions are found in various life forms and elegantly demonstrate the recruitment of a heavy laborer for delicate tasks.

We (the authors of the minireviews and I) hope that you learn at least something new from each of these minireviews. We plan to continue this thematic series, emphasizing it on the JBC Enzymology affinity group website, although the area involves other affinity groups, *e.g.* Protein Structure and Folding, Plant Biology, and Metabolism. There are certainly more interesting facets of the world of Metals in Biology still to explore, and I appreciate suggestions as we begin to plan the next of this series.

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