News from the National Institute of General Medical Sciences (NIGMS)

MEETING ANNOUNCEMENT: *Metals in Medicine: Targets, Diagnostics, and Therapeutics*, June 28–29, 2000, Natcher Conference Center, NIH, Bethesda, Maryland

For many scientists, the idea of metals as drugs is a non-starter: too toxic, too unstable, non-specific, not bioavailable. Yet, the success of cisplatin and its congeners, and the successes of metal complexes in imaging and radiotherapy, suggest that metal-containing agents can have desirable therapeutic activities and can exhibit clinically useful pharmacokinetic properties. Furthermore, advances in understanding and controlling the chemistry of inorganic complexes present new opportunities to exploit a fuller range of materials as therapeutic leads.

NIGMS is pleased to invite AAPS members and other interested *Pharmaceutical Research* readers to attend a meeting on the NIH campus this summer to explore the role of bioinorganic chemistry in the pharmaceutical industry and the potential for development of metal-containing agents as pharmaceuticals.

Why metals and why now? Recent discoveries in basic science have led to an increased understanding of the roles of metals in cell regulation (e.g., redox state, oxygen, NO, and CO sensors, and transcription modulators); the complexities of metal metabolism (e.g., metal chaperones and metal sequestering vesicles); and mechanisms of metalloenzymes and principles for the design of inhibitors to control them (e.g., matrix metalloproteases, NO synthase, heme oxygenase). The ability to synthesize sophisticated metal complexes has been well advanced in recent years, and there is a growing understanding of principles governing their chemistry *in vivo*. Both *in vitro* and *in vivo* experiments have pointed to new potential modes of therapy utilizing metal-containing agents for DNA/RNA cleavage, enzyme inhibition, membrane transport inhibition, and as receptor ligands.

Metals in Medicine: Targets, Diagnostics, and Therapeutics will feature invited speakers from academia, industry, and the government. The main objective, in addition to presenting state-of-the-art research, is to identify areas of emerging research opportunity in bioinorganic chemistry with high potential for application to drug development. It is hoped that this meeting will increase communication and lead to new collaborative research efforts.

Leaders in drug discovery and development will discuss their experiences in testing metal-containing agents as anticancer, antiviral, antidiabetic, and antioxidant drugs. It would be useful to hear from additional industry leaders about the inclusion of metals in their current libraries of compounds—volunteered abstracts and contributions during discussion are most welcome.

A second focus will be on current methods for studying drug development targets that are themselves metal-containing enzymes and regulatory proteins. How good are methods for modeling metal centers? How much does our present understanding of inorganic chemistry contribute to the drug design process?

Also featured at the meeting will be recent discoveries in the area of metal metabolism, and the opportunities they may present for new drug discovery. Developments in treatments for abnormal metal metabolism (e.g., metal supplementation, metal chelation therapy) will be presented and discussed.

To date, some of the most successful applications of metal-containing agents have been in the areas of imaging and radiation therapy. A session has been included to highlight lessons learned during the development of these agents, such as factors controlling toxicity, stability, and pharmacokinetics, that may hopefully carry over to the future development of metal complexes for other indications.

As a result of this meeting, it is hoped that an enunciation of principles for the medicinal chemistry of metals can be distilled. Issues such as the stability and toxicity of metals complexes need to be put into perspective--not all metals are "heavy metals" and not all metal complexes immediately fall apart. The unique regulatory issues that may be encountered for metallopharmaceuticals will be discussed by representatives from the Food and Drug Administration. Selected examples of how regulatory hurdles were successfully overcome in the development of cisplatin and other drugs currently in the pipeline will be presented by academic and industrial speakers.

SESSION TITLES:

- Molecular and Cellular Targets of Metal Action
- Metal-Containing Targets of Drug Action
- Imaging, Radiology, and Photodynamic Therapy
- Metal Metabolism as a Therapeutic Target
- Metallotherapeutics and Disease
- Medicinal Chemistry of Metallopharmaceuticals

Each session will include talks by invited speakers, followed by short presentations selected from volunteered poster abstracts, and an open discussion. Specific research accomplishments, contributions on the role of inorganic chemistry in industry, and comments on areas of research opportunity are encouraged. The complete meeting agenda can be found at the URL listed below.

Poster Session and Reception: A poster session and reception will be held the evening following the first day's sessions. If you are interested in presenting a poster or a short talk, please contact Dr. Peter C. Preusch (contact information is provided at the end of this article).

Meeting Sponsors: The meeting is sponsored by the National Institute of General Medical Sciences; the Center for Scientific Review (NIH); the National Cancer Institute; the National Institute of Diabetes and Digestive and Kidney Diseases; the National Institute of Allergy and Infectious Diseases; the National Institute of Environmental Health Sciences; and the Office of Dietary Supplements (NIH).

Registration for the meeting is FREE, but pre-registration is requested. For meeting information and to register online, visit the meeting Web site at http://www.nih.gov/nigms/news/meetings/metals.html, or contact Dr. Peter C. Preusch: Division

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