



Science

MOST NOTABLE PAPERS IN THE 2018 BIENNIAL METALS IN MEDICINE GORDON RESEARCH CONFERENCE

Yahia Z. Hamada *¹

*¹ Division of Natural Sciences and Mathematics, Lemoyne-Owen College, 807 Walker Avenue,
Memphis, TN 38126, USA

Abstract

All accounts mentioned in this paper are for and from published data only and are referenced at the end of the report. Metals in Medicine Gordon Research Conference (GRC) started in 2002 with the effort of Professor Michael J. Clark and his collaborators and it has been held biannually since then. The most recent conference was held in Proctor Academy in Andover, NH USA. We are writing this Conference Report about its most recent and vibrant activities that occurred between June 24th, and June 29th, 2018. After an immensely productive week and with a prolific number of presentations in different subfields of metals and their involvement in medicinal diagnostics and treatments, the conference met all of its objectives, one of which was that very valuable agreements for future collaborations with at least two international researchers with knowledge of Molecular Dynamics, Density Function Theory, and Molecular Mechanics Calculations have been gained. The conference had its highest number of participants and attendees since its inception. There were 50 talks and 120 poster presentations. This report is being submitted in celebration of the 85th birth year of Professor Mostafa A. El-Sayed of the Department of Chemistry and Biochemistry at Georgia Institute of Technology.

Keywords: Chemistry; Metals in Medicine; Gordon Research Conference; Inorganic Nanomaterials; and Professor Mostafa A. El-Sayed.

Cite This Article: Yahia Z. Hamada. (2018). "MOST NOTABLE PAPERS IN THE 2018 BIENNIAL METALS IN MEDICINE GORDON RESEARCH CONFERENCE." *International Journal of Research - Granthaalayah*, 6(11), 391-397. <https://doi.org/10.5281/zenodo.2228636>.

1. Introduction

A very brief History of the Metals in Medicine Gordon Research Conference is given in this introduction section. The Gordon Research Conference (GRC) was in held in 2002, 2004, 2006, 2008, 2010, 2012, 2014, 2016, and 2018. In 2002, it was chaired by Michael J. Clarke, Nicholas P. Farrell, and C. Frank Shaw. In 2004, it was chaired by Chris Orvig. In 2006, it was chaired by Peter J. Sadler and Peter Caravan. In 2008, it was chaired by Jeffrey M. Zaleski and Sonya J. Franklin. In 2010, it was chaired by Debbie C. Crans and Jan Reedijk. In 2012, it was chaired by A. Dean Sherry and Suzan J. Berners-Price. In 2014, it was chaired by Alan B. Packard and

Michael J. Hannon. In 2016, it was chaired by Katherine J. Franz and Nils Metzler-Nolte. And finally, in 2018, it was chaired by Seth M. Cohen, Kenneth Kam-Wing Lo.

I had the privilege of attending the 2018 GRC Metals in Medicine in Andover, NH between June 24th and June 29th, 2018. This was not the first time to attend this fabulous conference. The first GRC that I attended was when I received a generous invitation by one of the most prolific Inorganic Chemists-Writers, Professor Debbie C. Crans of Colorado State University to attend and present in the 2014 conference. I hesitated at the beginning, but once I saw the value and the wealth of information presented during the conference, I was amazed and had no regrets. The close interaction between top-notch scientists from all over the world gave valuable information on what research directions the scientific community is heading toward over the coming decades.

2. Materials and Methods

We have attended and presented our bioinorganic research to the 2018 GRC that was held in Proctor Academy in Andover, NH USA. Our poster presentation was entitled “Reactions of Malic Acid With Mo (VI) in Aqueous Solutions”

3. Results and Discussions

Keynote Speaker and the Opening Presentations

The keynote presentation was given on the first night of the program (June 24, 2018) by Professor Chad A. Mirkin of Northwestern University on nanomaterials in medicine. In his presentation, entitled “Inorganic Nanomaterials in Medicine” [1-3], Professor Mirkin showed a futuristic view of the use of the newly developed Nanomaterial in Medicine, Pharmacy, and Aerospace among other different applications. The second talk of the opening presentation was delivered by Professor Patricia Horcajada of IMDEA Energy Institute in Spain and was entitled “Engineered-Surface Metal-Organic Frameworks as Drug Nano carriers” [4-6]. The third talk was by Professor Vincent Rotello of the University of Massachusetts Amherst entitled “Bioorthogonal Catalysis Using Nanoparticle-Embedded Transition Metal Catalysts for Therapeutics and Diagnostics” [7-9]. The final talk was delivered by Michael Sailor of the UC-San Diego was entitled “Autophagic Silicon Nanoparticles for Targeted Delivery of Therapeutics” [10]. The main themes of the meeting are reported in the following sections.

Metal Homeostasis in Health and Disease

Professor Chun He of the University of Chicago, USA presented a cancer-treatment related talk entitled “Inhibiting Metal-Mediated De-methylation to Reshape Cancer Epigenetics” [11]. Professor Ann-Kathrin Duhme-Klair of University of York, UK presented a talk detailing iron-siderophores entitled “Siderophores and Their Potential Applications as Antimicrobials” [12]. Professor Debbie C. Crans of Colorado State University, USA presented a talk that resurrected the vanadium biochemistry entitled “Potention of Oncolytic Virotherapy by Vanadium Compounds” [13, 14]. Professor Raphael Rodriguez of Institute Curie, France presented a fabulous talk entitled “Reprogramming the Chemical Reactivity of Metals in Cancer” [15].

From Chemistry to Clinic

Under this subtitle, the three authors for that night gathering (Chad A. Mirkin, David Puerta, and Christine Brennan) made the connections between the real-life application of academic bench top research and how they were able to transform it into clinical applications. Professor Mirkin's talk was entitled "Ushering in the Digital Drug Design Revolution with Spherical Nucleic Acid Nanoparticle Conjugates" [16]. Dr. David Puerta of Forge Therapeutics, USA presented a talk entitled "Forge Therapeutics: Bioinorganic Directed Drug Discovery" [17]. Dr. Christine Brennan of MRL Ventures Fund, USA, presented a talk entitled "From Discovery to Company Formation: Views from a Venture Capital Investor".

Recent Development in Metallodrugs

Professor Johnathan Sessler of the University of Texas at Austin presented an entertaining, as well as very informative talk entitled "Gadolinium Texaphrins, Platinum and Gold" [18]. In this talk, he showed innovative ways of synthesis metal-containing-macromolecules. Sessler's talk was followed by a presentation by professor Valentina Gandin of the University of Padova, Italy entitled "Copper Complexes as Anticancer Agents: New Mechanistic Insights" [19]. James McKerrow of the University of California, San Diego presented a talk entitled "A Metal-Containing Drug Repurposed for Neglected Tropical Diseases", which was followed by Celine Marmion of the Royal College of Surgeons in Ireland who presented a talk entitled "Innovative Metallo-Prodrug Strategies Leading to Multimodal Cancer Therapeutics" [20]. The Metallo-Nano-Biomedicine theme within the GRC-Metals in Medicine was overwhelming during the last few GRC meetings. I will mention the most notable ones. During the presentation entitled "Photothermal Effects of Gold Nanoparticles for Therapeutic Applications" by Professor Mostafa A. El-Sayed during the 2014 GRC meeting was a great example [21, 22].

Metalloglycomics

This subsection started with a very good talk by Katelyn Arnold and ended with an excellent talk by Nicholas Farrell. Katelyn Arnold of Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, USA presented a talk entitled "Using Synthetic Heparan Sulfate to Treat Acute Liver Injury". The second talk was given by Professor Mauro Pavao of the Federal University of Rio de Janeiro, Brazil. His talk was entitled "Manganese and Glycosaminoglycans in Tumor Progression: From Cell Migration to Premetastatic Niche Formation" [23]. The last talk in this section was by Professor Nicholas P. Farrell which was entitled "Glycans as Ligands in Bioinorganic Chemistry: Chemical and Biological Studies in Metalloglycomics" [24].

New Agents for Imaging Applications

For the imaging research applications, Professor Roger Alberto of the University of Zurich, Switzerland presented a detailed talk entitled "Technetium and Rhenium Complexes with Aromatic Hydrocarbons as π -Ligands: An Entry into Biomimetic Imaging" [25]. The next presentation in this series was by Professor Carolyn J. Anderson of the University of Pittsburgh, USA. The talk was entitled "How Chelator Choice Impacts Bio-distribution of Radio-metal-Labeled Biomolecules. Her talk was in line with the work of the late professor Michael J. Welch of Washington University in St. Louis [26]. Next, Dr. Jun-Long Zhang of Peking University, China, presented an informative and a rich talk entitled "From Cell Imaging to Predrug: The Renaissance of Metallosalens in Biological Applications" [27]. The final talk in this series was presented by Professor Bengang Xing of Nanyang Technological University in Singapore. His

very informative talk was entitled “Cutting Edge Fluorescence Imaging Strategies for Precise Regulation of Cellular Functions and Localized Theranostics” [28].

Case Studies in Translational Research

The evening of that day of the conference was hosted by Nicholas P. Farrell at which three presentations were given by researchers from the same research complex in the city of Vienna. The first was presented by Dr. Walter Berger of the Medical University of Vienna, Austria. His talk was entitled “Once upon a Time in Vienna: A Story from Ruthenium to Platinum” [29]. Dr. Berger’s talk was followed by his colleague Dr. Christian Kowol of the University of Vienna, Austria, in which she also presented a talk with similar title “Once upon a Time in Vienna: The Power of Activation by Reduction” [30]. The last talk in this mini-series was a presentation by Professor Petra Heffeter in the same research group. The talk was entitled “Once upon a Time in Vienna: Tumor-Specific Accumulation of Metallodrugs” [31].

Analytical Techniques for Metals in Biological Systems

At the end of the conference, a series of presentations on the use of different analytical tools was presented. Under this analytical tools mini-series, Professor Victoria DeRose of the University of Oregon, USA presented a talk entitled “Methods for Comprehensive Analysis of Platinum Targets in Yeast and Mammalian Cancer Cells” [32]. Dr. DeRose talk was followed by a presentation by Professor Peter Lay, a chromium biochemistry expert of The University of Sydney, Australia, that was entitled “Metal Speciation in *In Vitro* and *In Vivo* Biological Activities from Drugs to Toxins” [33]. From Dr. Lay’s talk and Dr. Crans’ talks given in above, I concluded that the bioinorganic chemistry of vanadium which was once known to have potential diabetes treating effects, is being resurrected for cancer treatment [13, 32]. Following Dr. Lay’s presentation, Dr. Ryszard Lobinski of the CNRS, France presented a talk entitled “Global Approaches to Metal Speciation: Metallomics” [34]. The last presentation in this analytical tools mini-series was by Professor Samuel Meier-Menches of the University of Vienna, Austria. His talk was entitled “Emerging Proteomics Methods to Elucidate Metallodrugs' Mechanisms of Action in the Cellular Context” [35].

The last set of presentations was reserved for “Young Investigators”. Dr. Loi Do of the University of Houston, USA presented a talk entitled “Therapeutic SIMCats: In Pursuit of Catalytic Medicines” [36]. Dr. Do’s talk was followed by a presentation by Dr. Bo Li of the University of North Carolina at Chapel Hill, USA. Her talk was entitled “Metal-Chelating Antibiotics and Natural Products” [37]. The next presentation was by Dr. Anthony Grillo of the University of Washington school of Medicine, USA. His talk was entitled “A Small Molecule that Transports Iron Promotes Iron Absorption and Hemoglobinization”. The final talk in the young investigators mini-series was by Justin Wilson of the Department of Chemistry and Chemical Biology at Cornell University. His talk was entitled “Rhenium(I) Complexes as Anticancer Agents: Challenges and Opportunities” [38].

4. Conclusions and Recommendations

Metals in Medicine Gordon Research Conference are certainly a conference in which the bioinorganic and medicinal readers of "Inorganics" are very interested. It is worth mentioning that during the last few Metals in Medicine GRC meetings, there was a great interest from senior

faculty members of the meeting to foster young investigators' presentations. The most recent meeting had its highest number of participants and attendees since its inception. There were 50 oral presentations and 120 poster presentations. Also, the shift of the use of low molecular agent metal-containing therapeutic agents was widespread. Furthermore, chemists who have no experience with bio-related techniques (myself included) [39], such as the Kaplan-Meier Survival curves of living rodents, were eye opening. We also have learned that cancerous cells survive and flourish under conditions which 1- have high acidity, 2- high temperature environment, and 3- that are high in glutathione concentrations. We highly recommend conference loving attendees not to miss the next GRC in their area of expertise.

Acknowledgements

The author would like to thank Dr. S. Painter of LeMoyne-Owen College for reading the manuscript. Also we would like to acknowledge the financial contribution of the National Science Foundation under grant # HRD-1332459.

References

- [1] Park SY, Lytton-Jean AKR, Lee B, ET. Al. DNA-programmable nanoparticle crystallization. *Nature* 2008; 451: 553-556.
- [2] Rosi NL, Mirkin, CA. Nanostructures in Biodiagnostics. *Chem. Rev.* 2005; 105(4): 1547-1562.
- [3] Macfarlane RJ, Lee B, Jones MR, et al. Nanoparticle superlattice engineering with DNA. *Science* 2011; 334:204-208.
- [4] Bellido E, Guillevic M, Hidalgo T. Understanding the Colloidal Stability of the Mesoporous MIL-100(Fe) Nanoparticles in Physiological Media. *Langmuir* 2014; 30(20) 5911-5920.
- [5] Horcajada P, Serre C, Maurin G. et al. Flexible Porous Metal-Organic Frameworks for a Controlled Drug Delivery. *J. Am. Chem. Soc.* 2008; 130 (21): 6774-6780.
- [6] Rojas S, Baati T, Njim L, et al. Metal-Organic Frameworks as Efficient Oral Detoxifying Agents. *J. Am. Chem. Soc.* 2018; 140 (30): 9581-9586.
- [7] Tang R, Jiang Z, Ray M. et.al Cytosolic delivery of large proteins using nanoparticle-stabilized nanocapsules. *Nanoscale* 2016; 8 18038-18041.
- [8] Huo S, Gupta Y, Jiang Z. et. al. Fully Zwitterionic Nanoparticle Antimicrobial Agents through Tuning of Core Size and Ligand Structure. *ACS Nano* 2016; 10, 8732-8737.
- [9] Mumtaz S, Wang, L-S, Hussain SZ. et al. Dopamine Coated Fe₃O₄ Nanoparticles as Enzyme Mimics for the Sensitive Detection of Bacteria. *Chem. Comm.* 2017; 53, 12306-12308.
- [10] Kim D, Zuidena JM, Kang J, Pan Y, Wu L, Warther D, Arkles B, Sailor MJ. Facile Surface Modification of Hydroxylated Silicon Nanostructures Using Heterocyclic Silane. *J Am Chem Soc* 2016; 138(46): 15106-15109.
- [11] Dominissini D, Nachtergaele S, Moshitch-Moshkovitz S, et al The dynamic N1-methyladenosine methylome in eukaryotic messenger RNA. *Nature* 2016, 530, 441-446.
- [12] D. J. Raines, O. V. Moroz, E. V. Blagova, J. P. Turkenburg, K. S. Wilson, A.-K. Duhme-Klair. Bacteria in an Intense Competition for Iron: Key Component of the *Campylobacter jejuni* Iron Uptake System Scavenges Enterobactin Hydrolysis Product. *Proc. Natl. Acad. Sci. U.S.A.*, 2016; 113(21): 5850-5855.
- [13] Selman M, Rouso C, Bergeron A, Hee Son H, Krishnan R, El-Sayes N A, Varette O, Chen A, Tzelepis F, Bell J C, Crans D C, and Diallo J-S, Multi-Modal Potentiation of Oncolytic Virotherapy by Vanadium Compounds. *Molecular Therapy* 2018, 26, 1, 56-69.

- [14] Craig C. McLauchlan, Benjamin J. Peters, Gail R. Willsky, Debbie C. Crans. Vanadium-protein complexes: Phosphatase inhibitors favor the trigonal bipyramidal transition state geometries. *Coord. Chem. Rev.*, 2015, 301-302, 163-199.
- [15] ThiMai T, Hamai A, Hienzsch A. et al. Salinomycin kills cancer stem cells by sequestering iron in lysosomes. *Nature Chemistry* 2017; 9, 1025-1033.
- [16] Chinen AB, Guan C, Mirkin CA. Spherical Nucleic Acid Nanoparticle Conjugates Enhance G-Quadruplex Formation and Increase Serum Protein Interactions. *Angew Chem Int Ed Engl* 2015; 54(2): 527-531.
- [17] Puerta DT, Cohen SM. Examination of Novel Zinc-Binding Groups for Use in Matrix Metalloproteinase Inhibitors. *Inorg Chem* 2003; 42(11): 3423-3430.
- [18] Aydogan A, Koca A, Sener MK. et al. EDOT-Functionalized Calix [4] pyrrole for the Electrochemical Sensing of Fluoride in Water. *Org Lett* 2014; 16(14): 3764-3767.
- [19] Gandin V, Tisato F, Dolmella A. et al. (In Vitro and in Vivo Anticancer Activity of Copper(I) Complexes with Homoscorpionate Tridentate Tris(pyrazolyl)borate and Auxiliary Monodentate Phosphine Ligands. *J Med Chem* 2014; 57(11): 4745-4760.
- [20] Brabec V, Griffith DM, Kisova A. et al. Valuable Insight into the Anticancer Activity of the Platinum-Histone Deacetylase Inhibitor Conjugate, cis-[Pt(NH₃)₂malSAHA_{-2H}]. *Mol Pharmaceutics* 2012; 9(7): 1990-1999.
- [21] Jeon J-W, Zhou J, Geldmeier JA. et al. Dual-Responsive Reversible Plasmonic Behavior of Core-Shell Nanostructures with pH-Sensitive and Electroactive Polymer Shells. *Chem. Mater.*, 2016; 28 (20): 7551-7563.
- [22] Zhang S, Xiong R, Mahmoud MA. Dual-Excitation Nanocellulose Plasmonic Membranes for Molecular and Cellular SERS Detection. *ACS Appl. Mater. Interfaces*, 2018; 10 (21): 18380-18389.
- [23] Afratis N, Gialeli C, Nikitovic D. et al. Glycosaminoglycans: Key players in cancer cell biology and treatment. *The FEBS journal* 2012; 279 (7): 1177-1197.
- [24] Katner SJ, Johnson WE, Peterson EJ. et al. Comparison of Metal-Ammine Compounds Binding to DNA and Heparin. *Glycans as Ligands in Bioinorganic Chemistry. Inorg Chem* 2018; 57(6): 3116-3125.
- [25] Meola G, Braband H, Hernández-Valdés D. et al. A Mixed-Ring Sandwich Complex from Unexpected Ring Contraction in [Re(η^6 -C₆H₅Br)(η^6 -C₆R₆)](PF₆) *Inorg Chem* 2017; 56(11): 6297-6301.
- [26] Gai Y, Sun L, Hui W. et al. New Bifunctional Chelator p-SCN-PhPr-NE3TA for Copper-64: Synthesis, Peptidomimetic Conjugation, Radiolabeling, and Evaluation for PET Imaging. *Inorg.*
- [27] Ning Y, Tang J, Liu Y. et al. Highly Luminescent, Biocompatible Ytterbium (III) Complexes as Near-Infrared Fluorophores for Living Cell Imaging. *Chem Sci* 2018; 9(15): 3742-3753.
- [28] [28] Zhen X, Xie C, Jiang Y. et al. Semiconducting Photothermal Nanoagonist for Remote-Controlled Specific Cancer Therapy. *NanoLett.* 2018; 18(2): 1498-1505.
- [29] Abramkin SA, Jungawirth U, Valiahidi SM. et al. {(1R,2R,4R)-4-Methyl-1,2-cyclohexanediamine} oxalatoplatinum(II): A Novel Enantiomerically Pure Oxaliplatin Derivative Showing Improved Anticancer Activity in Vivo. *J. Med.Chem.* 2010; 53 (20): 7356-7364.
- [30] Kowol CR, Miklos W, Pfaff S. et al. Impact of Stepwise NH₂-Methylation of Triapine on the Physicochemical Properties, Anticancer Activity, and Resistance Circumvention. *J. Med. Chem.* 2016; 59 (14): 6739-6752.
- [31] Pati ML, Fanizza E, Hager S. et al. Quantum Dot Based Luminescent Nanoprobes for Sigma-2 Receptor Imaging. *Mol. Pharmaceutics*, 2018; 15 (2): 458-471.
- [32] Cunningham R, DeRose VJ. Platinum Binds Proteins in the Endoplasmic Reticulum of *S. cerevisiae* and Induces Endoplasmic Reticulum Stress. *ACS Chem. Biol.*, 2017; 12 (11): 2737-2745.

- [33] Levina A, McLeod AI, Pulte A. et al. Biotransformations of Antidiabetic Vanadium Prodrugs in Mammalian Cells and Cell Culture Media: A XANES Spectroscopic Study. *Inorg. Chem.*, 2015; 54 (14); 6707–6718.
- [34] Gutierrez Sama S, Farenc M, Barrere-Mangote C. et al. Molecular Fingerprints and Speciation of Crude Oils and Heavy Fractions Revealed by Molecular and Elemental Mass Spectrometry: Keystone between Petroleomics, Metallopetroleomics, and Petrointeractomics. *Energy Fuels*, 2018; 32 (4): 4593–4605.
- [35] Babak M, Pfaffeneder-Kmen M, Meier-Menches SM. et al. Rollover Cyclometalated Bipyridine Platinum Complexes as Potent Anticancer Agents: Impact of the Ancillary Ligands on the Mode of Action. *Inorg Chem* 2018; 57 (5): 2851–2864.
- [36] Ngo AH, Bose S, Do LH. Intracellular Chemistry: Integrating Molecular Inorganic Catalysts with Living Systems. *Chem.–Eur. J.*, 2018; 24(42): 10584-10594.
- [37] Chan AN, Shiver AL, Weaver WJ. Et al. Role for dithiolopyrrolones in disrupting bacterial metal homeostasis. *Proc. Nat. Acad. Sci. USA*, 2017; 10, 2717–2722.
- [38] Marker SC, MacMillan SN, Zipfel WR. et al. Photoactivated in Vitro Anticancer Activity of Rhenium(I) Tricarbonyl Complexes Bearing Water-Soluble Phosphines. *Inorg. Chem.* 2018; 57 (3): 1311–1331.
- [39] Hamada YZ. Prof. Mostafa A El-Sayed and Nanobiomedicine. *Nanobiomedicine* 2018; Volume 5, 1-2

*Corresponding author.

E-mail address: Yahia_hamada@ loc.edu.