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Highlights from the 17th Workshop on Vitamin D, Chicago, IL, June 17-21, 2014

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Chicago in June was the setting for another highly successful Vitamin D Workshop – number 17 in a series that began in Frankfurt, Germany in 1973. Although historically held every three years, since 2011 the Workshop has been organized annually by a dedicated group of Vitamin D researchers. For the 17th Workshop in Chicago, which was an official satellite meeting of The Endocrine Society, the principal organizers were Dr. JoEllen Welsh (Chair), Dr. Daniel Bikle (Past Chair) and Dr. Paul Lips (Future Chair). The meeting attracted over 230 scientists from 33 countries, attesting to the continued worldwide interest in the biology of Vitamin D in relation to health. During the three day Workshop, 20 invited speakers, 36 promoted oral communications and over 100 posters were presented and discussed. A keynote lecture by Dr. David Mangelsdorf on “Nuclear receptor signaling pathways and metabolism” was co-hosted by the Vitamin D Workshop and the International Aldosterone Meeting which was meeting at the same venue. Further details of the meeting, including format, scientific sessions, speakers and sponsors are available at <http://www.vitamindworkshop.org/chicago-2014.html>.

All delegates that presented at the Vitamin D Workshop, including invited speakers, were encouraged to prepare manuscripts for this Special Issue of the Journal of Steroid Biochemistry and Molecular Biology. The manuscripts could be either in the form of a review (in the case of invited speakers) or an original research report. All papers for this Special Issue were peer reviewed according to standard journal practices by at least two reviewers. Drs. Welsh, Bikle and Lips served as Guest Editors for the Special Issue and would like to acknowledge Dr. Jerzy Adamski and the entire Elsevier support staff who worked diligently to prepare this edition. In addition, the Chairs were assisted by the Workshop Executive Committee and the Program Advisory Committee (members are listed on our website at www.vitamindworkshop.org who contributed to program planning,

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abstract ranking and manuscript peer review. We also thank the many other reviewers who assisted in manuscript review.

To provide insight into the breadth and depth of the presentations over the three day meeting, the following paragraphs briefly summarize the sessions and highlight the invited speakers, many of whom provided manuscripts for this issue. Traditionally, the Vitamin D Workshops include sessions devoted to new developments from both laboratory approaches and applied research studies. Chicago was no exception, as all three meeting days included both basic and clinical talks.

Day one began with invited talks on the *Physiology of Vitamin D*, with data presented from both human studies and mouse models. Dr. Hector DeLuca (University of Wisconsin, USA) provided an update on the enzymes that catalyze the 25-hydroxylation of vitamin D, noting that both CYP27A1 and CYP2R1 contribute substantially to circulating 25(OH)D₃ in mouse models. Dr. DeLuca also presented new data on dietary vitamin D and UV exposure in experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis. Dr. David Goltzman (McGill University, Canada) reviewed the extensive data derived from mouse correlates of the human hereditary syndromes comprising vitamin D resistant rickets (VDDR), with an emphasis on the comparative effects of VDR knockout vs CYP27B1 knockout on the skeleton. Dr Michael Kimlin from the Centre for Research Excellence in Sun and Health (Queensland University of Technology, Australia) presented his studies on UV radiation and vitamin D synthesis in humans. To round out the morning, Dr. Kevin Cashman of University College Cork (Ireland) discussed issues related to establishing dietary requirements for vitamin D and the advantages of food fortification approaches. In the afternoon, the focus shifted to *Vitamin D Receptor Biology*, with Dr. Dan Bikle (UC San Francisco, USA) reporting on the novel interactions between the VDR and the calcium sensing receptor in skin carcinogenesis and the modulation of long non-coding RNAs by 1,25(OH)₂D₃. Next, Dr. Moray Campbell (Roswell Park Cancer Center, USA) highlighted the complex networks of nuclear receptors and their ligands in prostate cancer cells and the use of global approaches to identify super-additive and sub-additive ligand-receptor interactions. Using GWAS data, Dr. Campbell also provided examples of SNPs in VDR binding sites that may be associated with chronic disease.

Complementing the basic research sessions on day one was a final session devoted to *Epidemiological Studies of Vitamin D and Disease*. Dr. Alberto Aschiero (Harvard University, USA) spoke on vitamin D and multiple sclerosis, citing compelling longitudinal studies that support an association between high vitamin D status and reduced risk of disease development. In the final invited talk on day one, Dr. Eric Orwoll (Oregon Health and Science University, USA) reported on the Male Osteoporosis study, a large prospective observational cohort study examining vitamin D status in relation to multiple end points including bone mineral density, skeletal fractures, cardiovascular disease and cancer. A unique aspect of this study is the analysis of vitamin D-binding protein (DBP) and calculation of free 25(OH)D₃ levels in relation to health outcomes.

Day two of the meeting began with Dr. John White (McGill University, Canada) who presented an overview of *Vitamin D regulation of Innate Immunity* with new data on VDR

targets, including B7-H1, that play a role in suppression of intestinal inflammation. Moving on, the lead speaker in *the Vitamin D and Cancer: Bench to Bedside* session was Dr. Roberd Bostick (Emory University, USA) who summarized his clinical studies that examined the effects of calcium and vitamin D supplementation on circulating and tissue biomarkers in patients with colonic adenomas (polyps) at high risk for colon cancer. Significant effects of vitamin D supplementation on systemic inflammation scores and tissue biomarkers relevant to cell cycle, apoptosis and wnt signaling were observed. The cancer session also included several promoted talks on the calcium sensing receptor, ovarian cancer and novel therapeutic VDR ligands.

Day two also highlighted the well-known association between *Vitamin D, Calcium and Bone Homeostasis*, with invited talks by Dr. Sylvia Christakos (Rutgers New Jersey Medical School, USA) and Dr. Rajiv Kumar (Mayo Clinic, USA). Dr. Christakos described extensive studies in mouse models that demonstrated the importance of VDR in the distal intestine for calcium absorption and the interactive functions of TRPV6 and calbindin-D_{9k} in promoting this process, particularly under conditions of low dietary calcium. Dr. Kumar reported on a newly discovered role for the bone-derived protein sclerostin in suppressing renal 1-hydroxylation of 25(OH)D₃. He also described the phenotype of sclerostin null mice, who exhibit increased bone density and abnormal circulating levels of vitamin D metabolites and FGF23.

One of the most novel sessions at the Chicago meeting centered on *Vitamin D and Stem Cells*. Dr. Marie Demay (Massachusetts General Hospital, USA) spoke on the complex interactions required for keratinocyte stem cell lineage progression and how these are disrupted in the absence of the VDR. Pathways regulated by VDR in this context include hedgehog and wnt signaling, and this regulation appears to be independent of both 1,25(OH)₂D₃ and calcium. The other talk in this session, by Dr. Nanjoo Suh (Rutgers School of Pharmacy, USA), focused on cancer stem cells. Dr. Suh's studies demonstrated that 1,25(OH)₂D₃ and a synthetic Gemini analog strongly suppress CD44 and Notch signaling in aggressive triple negative breast cancer stem cells, reducing tumor growth in vitro and in vivo.

The final day of the meeting kicked off with the Keynote session *Nuclear Receptor Signaling Pathways and Metabolism* featuring Dr. David Mangelsdorf (UT Southwestern Medical Center, USA), who presented an outstanding lecture to a joint audience of the Vitamin D Workshop and the Aldosterone Society. Dr. Mangelsdorf reported on the complex endocrine control of adiposity, metabolism and aging by FGF21 in mouse models and the possibility for pharmacologic targeting of this system for weight loss and longevity. Directly following the Keynote was a session focused on *Vitamin D, Energy Metabolism and Adiposity*. Data from in vitro models of adipogenesis and tissue specific VDR knockout mouse strains was discussed by Dr. JoEllen Welsh (University at Albany Cancer Research Center, USA), who used genomic approaches to identify VDR targets associated with adipocyte differentiation. Dr. Anthony Hanley (University of Toronto, Canada) then reported on epidemiological studies linking vitamin D status with type 2 diabetes and metabolic syndrome. Both speakers identified multiple research gaps in this rapidly evolving area.

The final afternoon of the workshop started with a session on ***Vitamin D Supplementation Trials***. Dr. Rolf Jorde (University of Tromsø, Norway) summarized existing randomized controlled trials of vitamin D supplementation, pointing out the difficulties in design and interpretation of such studies given the unique biology of vitamin D. Following Dr. Jorde, Dr. Joanne Manson (Harvard Medical School, USA) reported on VITAL, a large randomized controlled trial of vitamin D supplementation with end points of cardiovascular disease and cancer. VITAL has completed recruitment of over 26,000 men and women who will be followed until 2017. A large subset of the participants will provide blood samples for 25(OH)D₃ analysis and there are 18 funded ancillary studies with this cohort. It is anticipated that over the next five years VITAL, together with other large scale ongoing randomized trials of vitamin D supplementation worldwide, will provide crucial data on the ability of vitamin D supplementation to impact disease development in human populations.

The final session of the workshop was devoted to ***New Insights into Vitamin D Biology***, which included talks on vitamin D and the brain (Dr. John McGrath, Queensland Brain Institute, Australia) and the origin and metabolism of vitamin D in fish (Dr. David Fraser, University of Sydney, Australia). Dr. McGrath described the expression of the VDR in neurons and glial cells throughout the brain and reported on potential correlations of vitamin D status with neuropsychiatric outcomes, as supported by both human and animal studies. Dr. Fraser gave a fascinating talk on the unique vitamin D metabolic pathways in rainbow trout, which unexpectedly produce and store large amounts of 1,25(OH)₂D₃ in liver. He also described studies that clarified the origin of vitamin D in fish, which is not dietary as previously thought but via skin synthesis. Details are described in Dr. Fraser's manuscript in this Special Issue.

A final note on the generous sponsors of the 17th Vitamin D Workshop in Chicago. The Workshop was fortunate to be awarded a Conference Grant from the National Institute on Aging¹ which funded invited speakers and young investigator awards. Corporate sponsors of the meeting included Chugai Pharmaceutical Co., Ltd. (Japan), Heartland Assays (USA), Biotech Pharmaceutical (USA), Teijin Inc. (Japan), Diasorin (Italy), Merck (USA), Cerbios (Switzerland), OPKO Health (USA), Cerbios-Pharma SA (Switzerland), DSM Nutritional Products Ltd. (Switzerland) and Everidis (USA). Thanks to the generous support of our sponsors, the Vitamin D Workshop continues to thrive after 40 years.

Please enjoy this Special Issue highlighting the diverse and intriguing science presented at the 2014 Vitamin D Workshop.

Acknowledgments

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