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Vitamin D and Metabolomics

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Vitamin D is a fat-soluble secosteroid. Among the several forms of metabolites-vitamers, the two physiologically relevant forms are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol): the side chain of D2 contains a double bond between carbons 22 and 23 and a methyl group on C-24. Pre-vitamin D3 is formed in the skin and is photolyzed by ultraviolet light (UV) in a six-electron conrotatory electrocyclic reaction; it spontaneously isomerizes to vitamin D3 in an antarafacial hydride sigmatropic shift. Small quantities of vitamin D also are present in foods. Vitamin D is transported to the liver and hydroxylated into prohormone 25-hydroxycholecalciferol [25(OH)D], calcidiol. In the proximal renal tubules, it is hydroxylated (A) via parathyroid hormone (PTH)-driven, C1-hydroxylation to active vitamin D [1,25$(OH)_2$D], calcitriol; and (B) via 24-hydroxylase, inactive vitamin D [24,25$(OH)_2$D]. When 1, 25$(OH)_2$D is synthesized by extra renal cells, including monocyte-macrophages, it acts as a paracrine-cytokine factor, defending against invading microbial pathogens. Other molecular forms of vitamin D include lumisterol (D1), 22-dihydroergocalciferol (D4), and sitocalciferol (D5). However, there are a number of intermediary metabolites whose actions are yet to be discovered. Hormone 1,25$(OH)_2$D regulates blood calcium and phosphate, promoting mineralization and the growth and remodeling of bone. Thus, vitamin D insufficiency leads to poorly calcified brittle bones, whereas sufficiency prevents these, including rickets and osteomalacia. Vitamin D also modulates neuromuscular functions, damps inflammation, and modulates actions of several key genes that regulate cell proliferation, differentiation, and apoptosis. Thus, deficiency status leads to exacerbation of a variety of human disorders, including cancer and cardiovascular diseases. The metabolomics and the metabolic diagnostic tools can now be applied to diagnosis and management.

Biography

Sunil Wimalawansa, MD, Ph.D., MBA, is a Professor of Medicine, Endocrinology, Metabolism, and Nutrition, former chief at the UMDNJ-RWJMS, Professor of Physiology and Integrative Biology, and Director, Regional Osteoporosis Center, New Jersey. He has published more than 200 scientific articles, 45 scientific book chapters, and 8 books. He has received several awards, including Clinical Excellence in Metabolic Bone Diseases; multiple young-investigator scientific awards, Glen Foundation Endocrinology/Aging awards; the Dr. Oscar Gluck Humanitarian award; and a prestigious Lifetime Achievement Award for his worldwide contributions to science, philanthropic work, and humanity. He is the founder-president of several charitable organizations worldwide.

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