Melatonin-based strategies to treating bone disease: Focus on melatonin-mediated effects on bone cells using a novel co-culture system

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The role of melatonin in bone physiology is emerging and studies demonstrate a protective role. Melatonin is a chronobiotic molecule whose release is dependent upon the light/dark cycle and/or through an endogenous circadian clock. In sighted individuals, the release of melatonin follows the light/dark cycle where melatonin levels peak during the hours of darkness. Nocturnal levels of melatonin decrease with age and are inhibited by light. Evidence from epidemiological studies demonstrates that a blunting or loss of these nocturnal peaks through shift work impacts negatively on bone; fracture risk increases and bone mineral density decreases. In the Melatonin Osteoporosis Prevention Study (MOPS), nighttime melatonin supplementation (3mg, po) improves the balance between serum bone-resorbing osteoclasts and bone-forming osteoblasts in a population susceptible to bone loss, that is, perimenopausal women. Melatonin induces osteoblast differentiation from stem cells taken from bone marrow and some studies show that it can inhibit osteoclasts though these mechanisms need further clarification. The effect of melatonin on the modulation of bone in pre-clinical and clinical models will be discussed followed by a presentation of data describing some potential molecular mechanisms underlying these melatonin effects using a novel co-culture system consisting of human mesenchymal stem cells and human peripheral blood monocytes. Specifically, the effect of melatonin on the release of osteoblast-specific communication molecules on osteoclast differentiation will be presented. Future perspectives will also be discussed as to the clinical utility of melatonin to both regenerate new bone and to protect against bone loss in susceptible populations.

Biography

Paula Witt-Enderby received her BS degree in Biochemistry in 1988 from the University of Illinois (Urbana) and her PhD in Pharmacology and Toxicology in 1993 from the University of Arizona (Tucson). She completed her post-doctoral fellowship from 1993-1996 at Northwestern University Medical School in the Department of Molecular Pharmacology and Biological Chemistry and currently holds the rank of Professor of Pharmacology at Duquesne University. Her research interests focus on drug development and melatonin receptor-mediated signal transduction processes with an application to anti-cancer and bone-stimulating therapies. She has received 3 patents and published 12 reviews, 42 papers, and currently serves on 3 editorial boards.

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