Creating & Analyzing Models of Parathyroid Hormone Bone Turnover Networks

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The parathyroid hormone (PTH) maintains calcium homeostasis by influencing bone cell activity. Less bone formation than resorption results in osteoporosis. Naturally-simulated PTH prevents disuse osteoporosis in hibernating bears, and intermittent administration of PTH is a treatment for osteoporosis in humans. During hibernation, bears maintain calcium homeostasis by increasing osteoblast differentiation (formation) and decreasing osteoblast apoptosis (death). PTH in hibernating bears may facilitate the recycling of calcium, also allowing for bone formation. Models of human bone-turnover biological networks (based on diagrams from published studies) were created using BioModel Analyzer software. The models test if each network could reach a stable and constant value, using protein functions and quantities. Concentration data of proteins involved in bone turnover for active and healthy versus hibernating or osteoporotic bears and humans was collected from published studies and inputted into the models. Model-generated protein values were compared to concentration data from published research to determine how well the model represented the data set. The networks with limited quantities of IGF-1 (insulin growth factor-1) stabilized, unlike those with more IGF-1 signaling. The models' network, not its data set, decreased the difference between model-stabilized and published protein concentrations. The models indicate the bone formation network humans likely use, highlight human versus bear bone turnover network differences, and identify which models were more suitable for each data set. Protein concentration changes are required if bear PTH is used for human osteoporosis treatments.

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