

Study finds evidence that a protein, MCP-1, may determine bone loss responses to parathyroid hormone

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In a new study published in November in *Scientific Reports*, New York University College of Dentistry (NYU Dentistry) researchers investigating the catabolic effect of parathyroid hormone (PTH) in hyperparathyroidism (HPT) showed, for the first time, that monocyte chemoattractant protein-1 (MCP-1) is required for catabolic responses to PTH. HTP is a condition in which an abnormally high concentration of PTH in the blood accelerates bone loss.

The research team, led by Nicola C. Partridge, PhD, professor and chair of the Department of Basic Science and Craniofacial Biology at NYU Dentistry, had previously found that MCP-1 is important in producing an anabolic effect of PTH, in which <u>bone</u> formation is increased, and they wanted to know if it was also important in causing a catabolic <u>effect</u>, in which bone is broken down.

In the present study, the researchers focused on the role of MCP-1 in PTH-induced <u>osteoclast</u> formation. Osteoclasts are cells that break down the bone. Increased osteoclast formation causes bones to become thinner and weaker. The researchers recreated the hyperparathyroid state in mice by constantly elevating their hyperparathyroid levels. Over a two-week period, they continuously infused female wild-type and MCP-1 knockout mice with human PTH. They showed that the ability of PTH to increase osteoclast formation in vitro is markedly impaired in cells from MCP-1 knockout mice and concluded that MCP-1 is an important



chemokine, or signaling protein, in PTH-induced osteoclast formation and bone resorption.

The findings support the possibility that MCP-1 could be a marker for how PTH works in humans with hyperparathyroidism, as elevated serum MCP-1 has been shown to be correlated with elevated serum PTH levels in women. Notably, within minutes after humans undergo parathyroid adenoma surgery, MCP-1 serum levels decrease.

Because high serum levels of MCP-1 cause the white cells and osteoclasts to be stimulated, this process could have systemic effects as well as effects on bone. "MCP-1 is a chemokine, which induces cells to move along a gradient recruiting white cells and osteoclasts in tissues," says Dr. Partridge. "Accordingly, there could also be effects on adipose tissue, the heart, and inflammatory conditions."

In the United States, about 1,000 people develop HPT each year, with osteoporosis the most common manifestation. According to the National Institutes of Health, there are approximately 1.5 million osteoporotic fractures in the U.S. each year that lead to half a million hospitalizations, over 800,000 emergency room encounters, more than 2,600,000 physician office visits, and the placement of nearly 180,000 individuals in nursing homes. Hip fractures are by far the most devastating type of fracture, accounting for about 300,000 hospitalizations each year. About one in five people sustaining a hip fracture ends up in a nursing home.

Provided by New York University

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