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Abstract for poster:

"Hypercalcemia Produced by Parathyroid Hormone Suppresses Experimental Autoimmune Encephalomyelitis In Female But not Male Mice"

Besides its role in regulating serum levels of calcium and phosphorus, 1α,25-dihydroxyvitamin D_3 (1,25-$(OH)_2D_3$) has potent effects on the immune system and suppresses disease in several animal models of autoimmune disorders including experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis. While the amount of 1,25-$(OH)_2D_3$ needed to prevent EAE is dependent on the gender of the mouse and amount of calcium available in the diet, the minimum levels of 1,25-$(OH)_2D_3$ sufficient to prevent disease cause hypercalcemia. To test if hypercalcemia independent of high levels of 1,25-$(OH)_2D_3$ can suppress EAE, we used a 25-hydroxyvitamin D_3-1α-hydroxylase (1α-hydroxylase) knockout mouse strain. Because these 1α-hydroxylase knockout mice lack the parathyroid hormone (PTH)-regulated enzyme that synthesizes 1,25-$(OH)_2D_3$, hypercalcemia from increased bone turnover was created by continuous administration of PTH without changing the circulating levels of 1,25-$(OH)_2D_3$. This PTH-mediated hypercalcemia generated after EAE induction prevented disease in female mice but not male mice. Circulating levels of interleukin-6, a potent pro-inflammatory cytokine involved in bone turnover, were elevated in control female mice compared to male mice and were significantly depressed in female mice that were hypercalcemic. In order to evaluate the role of estrogen in the protection against EAE by hypercalcemia, EAE was induced in 1α-hydroxylase knockout mice that had undergone ovariectomy or sham surgery. PTH-mediated hypercalcemia

prevented EAE in the sham-operated but not the ovariectomized mice. We conclude that the combination of estrogen and hypercalcemia is able to prevent EAE after disease induction.