

Oral Abstract

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The calcitonin receptor on osteoclasts protects against hypercalcaemia in mice

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We recently demonstrated using a genetically modified mouse model in which the calcitonin receptor (CTR) is globally deleted (Global CTRKOs), that the CTR plays a physiological role in protecting against induced hypercalcaemia (1). The aim of the present study was to investigate the mechanism by which the CTR exerts this effect. Accordingly, we generated mice in which the CTR is deleted specifically within osteoclasts (OCL-CTR KO). At 6 weeks of age, OCL-CTR KO mice were fed a low calcium diet for 2 weeks after which hypercalcaemia was induced by treatment with 0.5ug 1,25-dihydroxyvitamin D₃ on 2 consecutive mornings. Total serum calcium (Ca) levels were measured immediately prior to, and 45 and 50.5 hours post-first injection. OCL-CTR KO mice display a modest bone phenotype that is currently being examined. No differences were observed in baseline serum Ca and PTH levels between control and OCL-CTR KO genotypes, consistent with our hypothesis that the CTR on osteoclasts plays a modest physiological role in regulating bone homeostasis in the basal state.

Sex	Genotype	Hours post-first 1,25 dihydroxyvitamin D injection		
		0	45	50.5
Male	Control (n=9)	1.84+/-0.04	2.68+/-0.11	2.92+/-0.16
	OCL-CTR KO (n=5)	1.83+/-0.03	3.23+/-0.20	3.64+/-0.10
Female	Control (n=12)	1.86+/-0.03	3.09+/-0.14	3.31+/-0.14
	OCL-CTR KO (n=5)	1.87+/-0.01	3.71+/-0.09	3.84+/-0.08

Table 1: Total serum Ca levels in OCL-CTR KO mice versus controls (mM+/-SEM).

Peak serum total Ca levels at 50.5 hours following 1,25-dihydroxyvitamin D₃ induced hypercalcaemia were greater in OCL-CTR KOs compared to controls by 25% (0.73mM) (P<0.05) in males and by 16% (0.52mM) (P<0.05) in females (Table 1). In conclusion, we have demonstrated that the biological role of the CTR to protect against induced hypercalcemia in mice is primarily mediated via its action on osteoclasts.

(1) Davey RA, Turner A *et al.* The Calcitonin Receptor Plays a Physiological Role to Protect Against Hypercalcemia in Mice. *JBMR In Press*, Accepted 13th March, 2008.