

Oral Abstract

OR12

PYY deletion increases bone formation in mice

Wong IPL¹, Enriquez R¹, Boey D², Sainsbury A², Herzog H², Eisman JA¹ and Baldock PA¹

¹Bone and Mineral Program, ²Neuroscience Program, Garvan Institute of Medical Research, St Vincent's Hospital, NSW 2010, Australia.

The neuropeptide Y (NPY) system regulates bone anabolism through hypothalamic Y2 and non-hypothalamic Y1 receptors. Over-expression of NPY in the hypothalamus is known to decrease anabolism. Another NPY receptor ligand, the peripherally produced peptide YY (PYY), is an important satiety hormone. Recently, PYY was shown to have an inverse correlation with BMD in anorexia nervosa patients.

The aims of our study were to examine the bone phenotype of PYY knockout mice (PYY^{-/-}) and to investigate if NPY is involved in PYY signalling to bone, by assessing NPY/PYY double knockout mice (NPY/PYY^{-/-}).

Body weight and adiposity were not altered in PYY^{-/-}. Whole body BMD was greater in PYY^{-/-} compared to wildtype (p=0.03). PYY^{-/-} exhibited greater cancellous bone volume (15.9 ±1.9 vs 11.3 ±0.9 %, p=0.03) in the distal femur, accompanied by greater mineral apposition rate (MAR) (1.75 ±0.07 vs 1.41 ±0.05 µm/d, p=0.002) with no change in osteoclast surface. Endocortical MAR of PYY^{-/-} was also greater (2.95 ±0.24 vs 2.03 ±0.11 µm/d, p=0.002), consistent with the µCT analysis showing reduced endocortical circumference (p=0.03) and thicker cortical bone (p=0.02) in PYY^{-/-}.

The anabolic phenotype evident in NPY^{-/-} and PYY^{-/-} mice was absent or greatly attenuated in NPY/PYY^{-/-}.

PYY regulates bone mass through suppression of osteoblast activity in cancellous and cortical bone. These effects appear independent of energy homeostatic signalling. Greater understanding of the role of PYY signalling in bone may reveal novel links between bone mass and diet.