*Proceedings of the Nutrition Society* (2010), **69 (OCE6)**, E474 doi:10.1017/S002966511000337X

*Summer Meeting, 28 June–1 July 2010, Nutrition and health: cell to community*

# Zinc depletion transiently retards osteogenesis and suppresses matrix mineralisation

Young-Eun Cho[1], Ria-Ann R. Lomeda[1], Hong-In Shin[2], Je-Yong-Choi[3], Young-Hee Kang[4], Young-Jin Chung[5], John H. Beattie[6] and In-Sook Kwun[1]

[1]*Department of Food Science and Nutrition, Andong National University, Kyungpook 760-749,* [2]*Department of Oral Pathology, School of Dentistry, Kyungpook National University, Daegu 700-412,* [3]*Department of Biochemistry, School of Medicine, Kyungpook National University, Daegu 700-412,* [4]*Department of Food and Nutrition, Hallym University, Chuncheon 200-70,* [5]*Department of Food and Nutrition, Chungnam National University, South Korea and* [6]*Division of Vascular Health, Rowett Institute of Nutrition and Health, University of Aberdeen, Aberdeen AB21 9SB, UK*

Retarded skeletal growth is a characteristic sign of Zn deficiency, but the role of Zn in osteoblasts is not well understood. Bone formation involves osteoblast differentiation by bone marker gene expression, which is mainly regulated by bone-specific transcription factor Runx2, and extracellular matrix (ECM) mineralisation, which involves Ca deposition and bone nodule formation. The impact of Zn depletion on bone marker gene transcription and the involvement of Runx2 in this process were investigated in osteoblastic MC3T3-E1 cells. We also investigated whether low Zn decreases ECM mineralisation. Zn depletion by addition of the Zn chelator TPEN (5 μM) with 1 μM Zn (ZnD) decreased the expression of bone marker genes (collagen type I, osteopontin, alkaline phosphatase, osteoclacin and parathyroid hormone receptor), compared to normal osteogenic medium (OSM) or Zn adequate medium (ZnA: 5 μM TPEN + 15 μM) ($P<0.05$) both at 5 d (proliferation) and 15 d (matrix maturation). Bone marker gene transcription was decreased by ZnD as was the nuclear level of Runx2 protein ($P = 0.05$) and also the cellular transcript level ($P<0.05$). Compared to OSM and ZnA treatments, a delay in maximal Runx2 gene expression and nuclear protein was observed for ZnD within the first 24 h of differentiation. ECM Ca deposition was also lower in ZnD, which was also indirectly confirmed by detection of decreased cellular (synthesized) and medium (secreted) ALP activity as well as matrix ALP activity. We propose that Zn depletion attenuates osteogenic activity by decreasing bone marker gene transcription, through reduced and delayed Runx2 expression, and by decreasing ECM mineralisation, through inhibition of ALP activity in osteoblasts. This work demonstrates a potential mechanism whereby Zn deficiency retards skeletal growth *in vivo*.