Strontium and osteoblast function

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Dear Editor,

We thank Drs. Xie and Ye [1] for their interest in our paper [2] and address their main comments below.

Firstly, we were careful to acknowledge the contrasting findings of other published studies, both in vitro and in vivo. We do not know of any evidence to support the assertion of Drs. Xie and Ye that “ Sr^{2+} concentrations in biological micro-environment(s) play essential roles in bone formation”.

Secondly, Drs. Xie and Ye are concerned that we did not study sufficiently high concentrations of Sr^{2+} in our osteoblast experiments. We chose Sr^{2+} concentrations that spanned the maximum circulating Sr^{2+} level (about 0.1 mM), measured in patients treated with 2 g/day strontium ranelate [3]. We emphasise that this concentration of Sr^{2+} was already sufficient to cause near-total inhibition of bone mineralisation in our cell cultures, and thus, no additional effect was observed at the highest dose tested (1 mM). No data are available for local, extravascular concentrations of Sr^{2+} in patients or animals—but to us, it seems extremely unlikely that they would reach levels as high as the 9 mM Sr^{2+} used in the paper cited by Xie and Ye [4]. Moreover, it seems inconceivable that such a large amount of Sr^{2+} could somehow trigger bone formation (a process that involves mineralisation) when a 90-fold lower

concentration was able to block bone mineralisation so convincingly.

Thirdly, Drs. Xie and Ye are troubled that we did not include Ca^{2+} in our culture system. The formulation of the standard DMEM cell culture medium we used is widely available but we are happy to confirm that it does indeed contain Ca^{2+} , added to a concentration of 1.8 mM. This calcium is, of course, required for the abundant matrix mineralisation evident in our control cultures.

Lastly, we certainly did not state in our paper that Sr^{2+} is a “foe of bone formation”. Rather, as we suggest in the discussion, Sr^{2+} could potentially exert beneficial effects on bone by acting to limit secondary mineralisation, thus reducing stiffness or brittleness.

References

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