

## Invited Speaker Abstract

ISI7

### Theoretical investigation of the role of the RANK-RANKL-OPG system in bone remodeling

Pivonka P<sup>1</sup>, Zimak J<sup>1</sup>, Smith DW<sup>1</sup>, Gardiner BS<sup>1</sup>, Dunstan CR<sup>2</sup>, Sims NA<sup>3</sup>, Martin TJ<sup>3</sup> and Mundy GR<sup>4</sup>

<sup>1</sup>Dept. of Civil and Environmental Engineering, University of Melbourne, VIC, Australia.

<sup>2</sup>Biomedical Engineering, University of Sydney, NSW, Australia.

<sup>3</sup>Dept. of Medicine at St. Vincent's Hospital, University of Melbourne, VIC, Australia.

<sup>4</sup>Center for Bone Biology, Vanderbilt University, Nashville, USA.

The RANK-RANKL-OPG system constitutes a major signaling pathway in bone remodeling. It has been demonstrated experimentally that any modification of its components, such as for example, changes of receptor/ligand expression, knockout of signal transduction pathways, and modification of cell receptors, have major impacts on bone turnover and bone homeostasis. In this paper we apply a recently developed bone cell population dynamics model describing the action of basic multicellular units (BMUs) responsible for bone resorption and formation [1]. This mathematical model incorporates the RANK-RANKL-OPG signaling cascade together with the action of TGF- $\beta$  on bone cells. Given this simple yet powerful model we address the following two questions: (i) Can the proposed bone cell population dynamic model reproduce commonly observed disease states related to changes of RANK, RANKL, and/or OPG? and then (ii) What are the most efficient therapeutic strategies to restore bone homeostasis given various disease states related to the RANK-RANKL-OPG pathway. It turns out that the numerical model predictions are in good (qualitative) agreement with the experimentally observed disease states related to particular modification of the RANK-RANKL-OPG pathway. Secondly, different therapeutic strategies need to be applied in order to restore bone homeostasis for different changes of RANK/RANKL/OPG expressions due to bone diseases.

### Reference

[1] P. Pivonka, J. Zimak, D.W. Smith, B.S. Gardiner, C.R. Dunstan, N.A. Sims, T.J. Martin, G.R. Mundy. Model structure and control of bone remodeling: a theoretical study. *BONE*, 2008. (available online 15 April 2008)