

## Introduction

# Neurotransmitter functions in bone remodeling

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Bone strength and therefore its resistance to fracture are strongly correlated with the mass and orientation of the load-bearing extracellular matrix. The matrix is in turn the result of the orchestrated activity of osteoblasts and osteoclasts that form and model/remodel the tissue. Changes in bone mass and architecture are therefore linked directly to the regulated activity of those cells, and therefore the endocrine, paracrine and autocrine influences on them. An ability to influence intercellular communication would provide the basis for novel therapeutic strategies for bone diseases, but conventional approaches to the discovery of novel targets, and the search for and development of compounds capable of influencing them can be protracted.

One way in which this process can be shortened is by the identification of a signalling pathway in bone that is known in another tissue, in which case, agents already developed for that tissue could have utility in bone. Such approaches have one drawback though, in that side effects of treatment of bone diseases may arise in the original target organ or tissue, limiting the usefulness of putative new osteotropic drugs. In this respect, the central nervous system has a major advantage in that the blood-brain barrier exists to protect the brain from numerous circulating factors that would be deleterious to its function. The identification of signalling systems in bone that are known to have functions in the CNS may therefore present exciting therapeutic opportunities, as drugs that regulate bone and CNS cell function but are

unable to cross the blood-brain barrier would have innate tissue specificity.

For some years it has been known that neurotransmitters such as bradykinin CGRP and VIP influence osteoblast activity, but recent studies focusing on the roles of glutamate, dopamine and serotonin in bone are the subject of this session. While it is not simple to move from basic studies to new drugs, the vast array of agents that modulate neurotransmission already includes some that are incapable of entering the brain, and could therefore regulate bone mass. Modification of others by addition of charged groupings for example could decrease their ability to enter the CNS, so reducing the normal scale of drug development time considerably. Whether this approach becomes a clinical reality is not yet clear, but the data of the three presenters provide rational targets for further work.

The three speakers and their talks are as follows:

**Chantal Chenu**, "Regulation of bone resorption by osteoclastic glutamate receptors"

**Amanda Taylor**, "Osteoblastic glutamate receptor function regulates bone formation and resorption"

**Michael Blizotes**, "The role of dopamine and serotonin in regulating bone mass and strength - Studies on dopamine and serotonin transporter knockout mice"

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