

Turning on hormone tap could aid osteoporosis fight

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A potential new drug that 'opens the taps' for the release of useful hormones could stimulate new bone growth – and may eventually bring relief to osteoporosis sufferers.

The exciting potential of so-called negative allosteric modulators will be put under the microscope at a special symposium at The Federation of European Pharmacological Societies (EPHAR) 2008 Congress at The University of Manchester, UK, today (Wednesday, July 16).

European pharmacologists meeting in Manchester will present work that focuses on the stimulation of parathyroids – tiny glands located above the thyroids that control the release of the parathyroid (PTH) hormone into the bloodstream.

When the concentration of calcium is too low in the blood's plasma, PTH is released and acts on various tissues to increase the level of calcium in the blood. This calcium then activates the calcium sensing receptor on the parathyroid cell, which then reduces PTH release.

The first POSITIVE allosteric modulator was recently introduced into clinical practice for treating patients displaying high levels of PTH in the plasma – such as those with chronic kidney disease on dialysis and those displaying hypercalcaemia with parathyroid cancer. It mimics the effect of calcium on the receptor and so reduces PTH release.

But now attention is switching to NEGATIVE allosteric modulators,



which have been shown in pre-clinical trials to block the effect of calcium on the parathyroid cell and thus increase the release of PTH in the serum.

"Daily administration of a negative allosteric modulator of the calcium sensing receptor should promote a sustained increase of PTH in such a way that it will stimulate new bone formation," said symposium organiser Martial Ruat, a neuropharmacologist at the government funded Centre National de la Recherche Scientifique in France.

"Now clinical trials will have to demonstrate the effectiveness and suitability of negative allosteric modulators for treating osteoporosis in humans."

While pharmacologists are excited and encouraged by results so far, Dr Ruat says it will be at least another eight to 10 years before negative allosteric modulators are passed for use in patients "Osteoporosis is a complex disease and the timescale might be rather long," says Dr Ruat, who is himself carrying out research to learn more about the potential benefits of both negative and positive allosteric modulators.

He added: "The calcium sensing receptor is also found in the kidney, the intestine, in some vascular and bone cells and also in the brain. We still need to identify the roles of this receptor in these tissues before being able to specify novel applications of these drugs."

Negative and positive allosteric modulators are also being studied by European pharmacologists with a view to identifying the functions of calcium sensing receptors in the control of blood pressure.

Source: University of Manchester



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