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INHIBITOR OF ADRENOMEDULLIN TO PREVENT AND TREAT BONE DENSITY REDUCTION

ABSTRACT

The present invention is related to inhibitors of adrenomedullin or inhibitors of adrenomedullin receptors for the manufacture of a drug useful in the prevention and treatment of diseases that reduce bone density in a human or animal.

Said diseases are osteoporosis, osteomalacia, rheumatoid arthritis, chronic kidney disease, hyperparathyroidism, Cushing's disease, cystic fibrosis, eating disorders, gastric bypass and prolonged immobility.

It was developed by researchers belonging to the Rioja Salud Foundation, the University of Zaragoza, and the Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN).

DESCRIPTION

Osteoporosis is a serious problem in the elderly population.

The present invention provides the use of inhibitors of adrenomedullin or inhibitors of adrenomedullin receptors in the prevention and treatment of diseases that reduce bone density . The invention demonstrates that they are useful for the manufacture of a drug to be applied in those diseases.

An inducible knockout (KO) for adrenomedullin (AM) in adult mice has been created to test the influence of AM in bone metabolism and osteoporosis.

Bone density is higher in the KO mice than in wild type (WT) mice, indicating that AM enhances osteoporosis, and its absence leads to increased skeletal ossification.

Ovariectomized female, treated with an inhibitor of AM, showed that reduction in AM activity prevents bone loss associated with the lack of estrogen. Treated mice maintained same bone mass as non-ovariectomized group, and significantly higher than ovariectomized group.

In previous *in vitro* or *ex vivo* experiments, it was found that AM increased ossification. However, present *in vivo* data indicate the opposite. This discrepancy can be explained as follows: AM has been described as an inhibitor of insulin secretion. Glycemia regulates ghrelin levels and this, in turn, modulates bone homeostasis. Therefore, present KO mice, with diminished levels of AM, showed lower glucose levels than WT mice, and a higher concentration of ghrelin.

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APPLICATIONS

- Manufacture of a medicament.
- Prevention and treatment of diseases that reduce bone density
- Said diseases are mentioned in the abstract
- Also, in situations where bone loss depends on the decrease in gravity such as, for example, in space travel
- In humans and in farm or domestic animals

IP STATUS

Patent pending

AVAILABLE FOR

- Exclusive license agreement
- Non-exclusive license agreement
- Further research or development

INDUSTRIAL PROPERTY

European Patent Application **EP15382111.1**, filed on March 12, 2015

International Patent Application **PCT/ES2016/000035**, filed on March 12, 2016

INNOVATIVE ASPECTS AND ADVANTAGES

- An inducible knockout (KO) for adrenomedullin (AM) in adult mice has been created
- *In vivo*, AM enhances osteoporosis, absence of AM leads to increased skeletal ossification, and inhibition of AM activity prevents bone loss
- Lack of toxicity

DEVELOPMENT STATUS

Laboratory tested (*in vivo*)

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