Title (en)

USE OF ESTROGEN RECEPTOR AGONISTS OR ANTAGONISTS FOR TREATING GROWTH, BONE DISORDERS

Title (de)

VERWENDUNG VON ÖSTROGENREZEPTOR AGONISTEN ODER ANTAGONISTEN ZUR BEHANDLUNG VON WACHSTUM UND KNOCHENSTÖRUNGEN

Title (fr)

RECEPTEUR D'OESTROGENES

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Application

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Abstract (en)

[origin: WO0076529A2] Androgens regulate the male skeleton directly via a stimulation of androgen receptors and indirectly via aromatization of androgens into estrogen and thereafter stimulation of estrogen receptors (ER). In order to investigate the relative importance of estrogen receptor subtypes in the regulation of the male skeleton, the skeletal phenotypes of wild type (WT), ER alpha , Knockout (ERKO), ER beta Knockout (BERKO) and ER alpha / beta Double Knockout (DERKO) mice were compared. ERKO and DERKO had reduced body weight as well as longitudinal bone growth. Furthermore, ERKO and DERKO but not BERKO demonstrated a pronounced decrease in bone mineral content in the long bones and in the axial skeleton. This decrease in BMC was due to cortical ostopenia as a result of decreased radial growth of the bones. Mechanical testing demonstrated that femora from ERKO were weaker as a result of the altered cortical bone dimensions. No significant change in trabecular BMD was seen in any group. ERKO demonstrated decreased serum levels of osteocalcin and IGF-I. Furthermore, serum levels of IGF-I were correlated to most of the skeletal changes seen in DERKO and ERKO. In conclusion , the skeletal phenotypes of DERKO and ERKO are similar and clearly distinguishable from WT and BERKO. Therefore, ER alpha , but not ER beta , mediates the effect of estrogen in the skeleton of male mice.

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