

# ***0668 Estrogen Receptor Alpha-36 Expression and Function in Osteoblast Plasma Membranes***

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Objective: Estrogen receptors (ERs) belong to the class of steroid hormone receptors that canonically function as transcriptional regulators in the nucleus upon binding of ligand in the cytosol. Human articular chondrocytes exhibit sexual dimorphism in their responses to 17 $\beta$ -estradiol (E2), which are membrane-mediated and do not follow traditional pathways of estrogen signaling. Nuclear ERs are present in both male and female chondrocytes, suggesting that membrane-associated ERs are responsible for the sex-specific differences.

Methods: Plasma membranes from male-derived MG63 osteoblast cell-line and from the female-derived SAOS-2 cell-line were examined for the presence of the ER $\alpha$ 36 variant of the traditional receptor, ER $\alpha$ 66, based on the finding that it mediated the membrane-response to E2 in breast cancer cells lacking ER $\alpha$ 66. Flow cytometry of non-permeabilized cells using anti-human ER $\alpha$ 36 antibodies assessed whether the receptors were expressed on the cell surface of the two cell-lines, and on normal human osteoblasts isolated from maxillary bone of three female and three male donors. ER $\alpha$ 36 was also assessed using immunocytochemistry. Receptor function was determined as a function of E2-dependent PKC using blocking antibodies to ER $\alpha$ 36.

Results: Western blots showed ER $\alpha$ 36 in plasma membranes from both cell-lines. Flow cytometry exhibited a two-fold increase in membrane ER $\alpha$ 36 in female SAOS-2 cells compared to male MG63 cells and this correlated with ER $\alpha$ 36-mediated PKC. ER $\alpha$ 36 was also present on normal human osteoblasts but a distinct sexual dimorphism was not determined due to the small sample size. Immunocytochemistry confirmed its membrane location and demonstrated that it was not present in the nucleus.

Discussion: These preliminary results did not definitively show differences in the expression of ER $\alpha$ 36 in healthy females versus healthy males, however it is of note that both sexes expressed the variant receptor.

Conclusion: ER $\alpha$ 36 does not function in the classical steroid hormone receptor pathway but may actually function through membrane-mediated signaling.

[Seq #89 - Bone Cell Signaling](#)

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