

Estrogen receptor alpha

Estrogen receptor alpha (ER α), also known as NR3A1 (nuclear receptor subfamily 3, group A, member 1), is one of two main types of estrogen receptor, a **nuclear receptor** that is activated by the sex hormone **estrogen**. In humans, ER α is encoded by the gene ESR1 (EStrogen Receptor 1).

The estrogen receptor (ER) is a ligand-activated **transcription factor** composed of several domains important for hormone binding, DNA binding, and activation of transcription.

Alternative splicing results in several ESR1 mRNA transcripts, which differ primarily in their 5-prime untranslated regions. The translated receptors show less variability.

Agonists of ER α selective over ER β include:

Propylpyrazoletriol (PPT)

16 α -LE2 (Cpd1471)

16 α -IE2

SKF-82,958 – also a D1-like receptor full agonist

(R,R)-Tetrahydrochrysene (R,R-THC) – not actually selective over ER β , but rather an antagonist instead of an agonist of ER β

Antagonists of ER α selective over ER β include:

Methylpiperidinopyrazole (MPP)

Estrogen insensitivity syndrome is a very rare condition characterized by a defective ER α that is insensitive to estrogens.

The clinical presentation of a female was observed to include absence of breast development and other female secondary sexual characteristics at puberty, hypoplastic uterus, primary amenorrhea, enlarged multicystic ovaries and associated lower abdominal pain, mild hyperandrogenism (manifested as cystic acne), and delayed bone maturation as well as an increased rate of bone turnover.

The clinical presentation in a male was reported to include lack of epiphyseal closure, tall stature, osteoporosis, and poor sperm viability.

Both individuals were completely insensitive to exogenous estrogen treatment, even with high doses.

Park et al investigated the association between degenerative **lumbar scoliosis** (DLS) and **estrogen receptor alpha** (ER α) gene polymorphisms in 184 patients with a diagnosis of DLS, by determining the presences of the Pvu II and Xba I polymorphisms, measuring bone mineral densities at the lumbar spine (LSBMD) and femoral neck (FNBMD), and by investigating biochemical markers of bone turnover and comparing these results with those of 220 healthy normal controls.

Genotype frequencies in DLS patients and controls revealed a significant difference for the Pvu II

polymorphism only ($p = 0.0287$). No significant difference was found between the DLS and control groups with respect to the Xba I polymorphism, bone mineral density (BMD), or biochemical markers. Furthermore, no significant association was observed between the Pvu II polymorphism and BMD, lumbar scoliosis, lateral listhesis, or biochemical markers in patients with DLS.

These results suggest that the ER α Pvu II polymorphism influences the prevalence of DLS ¹⁾.

¹⁾

Park YS, Suh KT, Shin JK, Lee JS. Estrogen receptor gene polymorphism in patients with degenerative lumbar scoliosis. Br J Neurosurg. 2016 Jul 11:1-4. [Epub ahead of print] PubMed PMID: 27399961.

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