

CAN ESTROGEN RELATED RECEPTOR CURE CANCER?

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Orphan nuclear receptor estrogen related receptors (ERRs) share high homology with estrogen receptor(ER), and transcription co-activators. ERRs are constitutively activated without estradiol binding. ERRs involve in regulation of metabolism, ER transactivation function, anti-oxidant pathway and hypoxia induced factor target gene expression. ERR subtypes ERR-beta and ERR-gamma can decrease androgen-sensitive and androgen-insensitive prostate cell proliferation by inducing cell cycle arresting at G1-S phase. This effect is coupled with the increasing expression of cyclin-dependent kinase inhibitor p21 and p27 and the induction of p21 and p27 is ERR beta/gamma DNA binding domain (DBL) dependent. It is also seen that cyclopamine, a hedgehog pathway inhibitor that bind and inhibit Smoothed (SMO), can increase p27 level in prostate cancer cell line PC3 by decreasing the degradation of p27, and this decreased degradation is induced by decreased phosphorylation of Akt. These evidences indicate that ERR subtypes beta and gamma and hedgehog signal transduction pathway can crosstalk and regulate prostate cancer proliferation at least at the level of Akt.