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Exploring the possibility of new ERRβ isoforms in primates and humans

It is well known that estrogen is a risk factor for breast cancer. Hence, understanding the relationship between estrogen and breast cancer is significant for physiological and disease related pathways. Traditional thought shows the effects of estrogen being transduced through estrogen receptors (ER), a nuclear receptor superfamily. Furthermore, there is a subfamily of estrogen related receptors (ERR α,β,γ) that share target genes, coregulatory proteins, ligands and sites of action with ERs. Estrogen-related receptor alpha and beta (ERR α and β,) have highly conserved amino acid sequences with estrogen receptor alpha. ERR is thought to be involved in estrogen-regulated pathways. ERR is also involved in embryo development and is also able to regulate the pS2 gene (breast cancer gene). Some ERRs are orphan nuclear receptors with no naturally occurring ligands, yet still actively influence estrogen. By studying orphan nuclear receptors (ERR α, β, γ), novel functions can be established more quickly. Although ERRα has been studied extensively, ERRβ has not. During an attempt to clone human estrogen related receptor β (ERRβ), one known isoform along with two new isoforms (unpublished data) were confirmed. The isoforms demonstrated human specificity, but revealed a unique distribution pattern, that may lead to a novel function. We checked the Cos-1 cell line which is derived from the kidney of the green monkey. The Cos-1 line is supposedly negative for ERRβ2. However, when Western Blot analysis was performed with an ERRβ2 exon 9-specific epitope, a band was produced potentially indicating an additional alternative splice form. RT-PCR characterization of the ERRβ2 gene, especially its isoforms, will lead to a clearer understanding of the exon variant splicing and providing possible breast cancer treatment targets.