Molecular and Physiological Roles of Estrogen Receptor

Ahed J. Al-Khatib[1*], Geir Bjørklund[2], Samir M Albalas[3]

[1]Department of legal medicine, Toxicology of Forensic Science and Toxicology, School of Medicine, Jordan University of Science and Technology, Jordan
[2]Council for Nutritional and Environmental Medicine, Mo i Rana, Norway
[3]Department of public administration, health services management, Faculty of economics and administrative sciences, Yarmouk University, Jordan

[*]**Corresponding author:** Ahed J. Al-Khatib, Department of legal medicine, Toxicology of Forensic Science and Toxicology, School of Medicine, Jordan University of Science and Technology, Irbid 22110, Jordan, E-mail: ajalkhatib@just.edu.jo

Abstract

　　Estrogen receptor (ER) has been shown to be involved in several cellular and metabolic pathways. In this study, we reviewed the literature for molecular and physiological roles of estrogen receptor in normal and pathological conditions. We discussed the expression of estrogen receptor in several tissues as well as the potential of using ERb agonists in treating proliferative hematological disorders. The function of estrogen is varied and may look contradicted. Estrogen has multiple roles under physiological conditions including signaling roles in cell growth, reproduction, development and differentiation. Estrogens exert their effects through two distinct estrogen receptors, ER-α and β to which E2 binds strongly. The expression of ERs depends mainly on the type of ER. Although estrogen mainly acts in reproductive system, its receptors are selectively expressed in different tissues. ER-β is highly expressed in the ovary, central nervous system, cardiovascular system, lung, male reproductive organs, prostate, colon, kidney and the immune system. ERb is highly expressed in lymphoid cells, and the finding of anti-proliferative roles of ERb, the potential to use ERb agonists in treating proliferative hematological disorders has been raised. Taken together, the function of estrogen seems to be determined by the estrogen receptor which is expressed in various tissues with relatively predominant forms. There is a potential to used ERb agonists in treating proliferative hematological disorders.

Keywords: Estrogen receptor; Molecular; Physiological roles

Introduction

　　Due to the importance of estrogen and its receptor, estrogen receptor (ER), we conducted this review study to bring to the reader a good source of information. In general, we may thought that ER is being of main interest in reproductive system. As will be seen in the following sections, estrogen and ER have vital roles in multiple pathways from normal physiological conditions to inflammatory conditions and carcinogenesis. This review discusses the role of ER as a signaling molecule, its variants, its role in proliferation and apoptosis, its role in immunity, its role in inflammation, autoimmunity, tumors, and its therapeutic role in treating cancer.

Signaling pathways of ER

　　Estrogens are included in regulating various physiological processes such as cell growth, reproduction, development and differentiation. Estrogen is mainly synthesized in premenopausal women by ovaries as 17b-estradiol (E2) which, in turn, exerts its effects on target organs and cells. On the other hand, the main source of E2 in postmenopausal women and in men comes from the conversion of extragonadal sites of testosterone and androstenedione into E2 by the action of cytochrome P450 aromatase enzyme[1]. However, E2 has significant roles in mediating various pathological processes such as carcinogenesis[2]. Furthermore, estrogens exert their effects through two distinct estrogen receptors, ER-α and β to which E2 binds strongly[3].

　　ERs can bind through three binding sites or domains: one is called NH2- terminal domain, another one binds the DNA, and the third one binds the ligand domain[4]. According to[5], there is a ligand-independent activation function (AF1) re-

gion in the NTD, which has a role in transcriptional activation of target genes. The AF1 region has been found to act in the recruitment of co-regulatory proteins, and its activity is prominent in ER-α in inducing gene expression, whereas its activity is less in ER-β. The DBD is characterized by being conserved between ER-α and ER-β and facilitates some forms of typical binding of the ERs to DNA in required genes, which is called "estrogen-responsive elements" (EREs). On the other hand, the LBDs of ER-α and ER-β were indicated to have a 59% of homogeneity. Furthermore, there are little differences in the structure of the binding sites of the two subtypes[6]. According to[7], small structural variations in the ligand, binding pockets permit the development of subtype selective ligands with selective affinity for and activity through ER-α and ER-β, respectively. It is worth to mention that in a study by[8], the biological roles of ER-α and ER-β as well as their target genes were shown to depend on specified ligands. The agonists of ER-β have high binding affinity for ER-β[9-11]. Other studies showed that there are three functional groups for the agonists of ERb, namely binders, activators and binders/activators[7,12]. It has been demonstrated that the LBD has an activation domain (AF2) which its activity is ligand-dependent and improves transcriptional activity[13,14]. ERs can adjust the expression of gene by binding some transcription factors including NF-jB, leading to either activation or suppression of target gene expression[15].

Multiple ER binding sites have been identified in the human genome, and these sites were found to have transcriptional regulatory mechanisms[16-18]. It has also been found that ligands have the ability to activate ER signaling independent of genomic pathways through binding to membrane-associated ERs which leads to quick cellular responses[19]. Another study has found that ERs have the ability to control transcription of target genes even if there no ligands since ERs are considered appropriate targets that can improve or impair the transcription of ER[20]. From the above discussion, the roles of ER as signaling molecule are varied and vital in various metabolic pathways. We think that further research is required to study in-depth more metabolic activities in almost cells.

Expression of the ERs and their splice variants

The expression of ERs depends mainly on the type of ER. The expression of ER α is shown particularly in reproductive system (uterus, ovary), breast, kidney, bone, white adipose tissue and liver. On the other hand, ER-β is highly expressed in the ovary, central nervous system, cardiovascular system, lung, male reproductive organs, prostate, colon, kidney and the immune system[21,22]. Numerous studies have pointed to the expression of various isoforms of both ER-α and ER-β, which are derived from alternative splices. Such splice variants have been detected in a wide range of cells from normal cells to cancer cell lines and samples from different types of cancer[15]. In this context, several studies have demonstrated ER-α mRNA splice variants in cell lines and samples from breast, endometrial, ovaries and colorectal[23-28]. ER-β has some variants that were detected in various tumors such as breast cancer[27], endometrial cancer[29,30] and thyroid cancer[31]. According to[32], wild-type ERs, splice variants of ER-α and ER-β were shown to be expressed in normal lymphoid cells. It is worth to mention that ER-α is localized in the nucleus and the cytoplasmic membrane of breast cancer cells, and it is thought that this leads to rapid signals re-

sulting in cell proliferation and survival upon ligand binding[33]. Other researchers have pointed to the membrane expression of ER-β[34,35].

Other studies are still required to correlate the expression of ER with other proteins including Bcl2, p53, and possibly others because of possible shared roles that may interact with the expression of ER.

ER-mediated effects on proliferation and apoptosis

ERs induce opposed effects on proliferation and apoptosis. Estrogens have been shown to increase the growth of the breast, uterus, and prostate, which implies the possibility to induce carcinogenesis[36-40]. Other studies employing ER-β knock-out mice revealed contradicting findings in which estrogens through ER-β repress proliferation and induce differentiating stem cells in various tissues[39,40,41-44].

According to[44], findings derived from ER-β knock-out mice showed prostate hyperplasia and a myeloproliferative disease which were similar to human chronic myeloid leukemia. Transfection studies involving breast and colon cancer cells that are deficient in ER-β revealed that the addition of ER-β results in reduced cell proliferation either in culture or *in vivo* in xenograft studies[45-49]. ER-β has been found in transfection studies to suppress cell proliferation in a hormone- independent way, which leads to the conclusion that ER-β may act as a tumor suppressor[45,47,48]. Various studies that target the effects of E2 on apoptosis revealed conflicting results. Some studies have pointed to inhibitory effects of E2 on growth of cells in lymphoma cells by activating apoptotic pathways[50,51]. Another study by[52] pointed to the enhanced apoptosis in osteoclasts by E2. Other studies showed contradicting findings. As an example, it has been reported that E2 has an anti-apoptotic action on T-lymphocytes and monocytes *in vitro*. Furthermore, it can inhibit apoptosis in cardiomyocytes *in vivo*[53-55]. Other researchers showed that E2 can control apoptosis pathways in cancer cells as well as normal cells[56,57]. E2 up- regulates Bcl-2 gene in ovarian epithelial cells[57].

Other studies revealed that binding of E2 to ER-β can induce apoptosis[58]. Furthermore, ER-β up- regulates Fas-L in epithelial cells of ovary[59]. Other studies reported the induction of apoptosis of ER-β in prostate and ovarian cancer cells[36,37,60]. *In vitro* study employing epithelial cell lines showed that E2 promoted cell survival through non-genomic signaling of ER-α and cell death through non-genomic signaling of ER-β[1].

According to[61], when murine lymphoma cell lines were exposed to ER-β agonist, apoptosis was more likely to be induced. Taken together, the previous context showed that ER-β has, in general, a pro-apoptotic effect, while ER-α has an anti-apoptotic effect. Furthermore, the responses depend on and to larger extent correlates with the expression of ER subtype. The existing literature does not give clear answers when the ER is likely to induce apoptosis or proliferation which opens the door for more studies. We think that future studies may point out to more diagnostic and therapeutic options which may depend on the individual context.

Expression of ERs in immune cells and their functional role

Effects of ERs in lymphocytes: Several studies have emphasized the detection of the mRNAs and proteins of ER-α and ER-β in PBMCs and neutrophils[32,62]. It has also been re-

ported that subcellular differences also exist, and CD4+ T cells express elevated concentrations of ER-α mRNA whereas B cells express largely ER-β mRNA[63]. Concerning protein level[44], reported that ER-β is the dominant ER expressed in mature leukocytes from peripheral blood, tonsils or spleen of healthy individuals. Taking into consideration that B cells are expressing more ER-β mRNA compared to ER-α mRNA, it has been found that various cell lines of lymphoma that give examples for lymphomas including Hodgkin lymphoma to greatly over express the proteins of ER-β, whereas the proteins of ER-α is either expressed in low levels or even no detectable[44,61]. In another study by[64], both ER-α and ER-β proteins were expressed in NK cells.

Effects of E2 on lymphoid cells: Estrogens have significant effects on the innate and the adaptive immune system[65]. Other studies showed the effect of estrogens on thymus and bone marrow[66-68]. Furthermore, it has been found that estrogens have a suppressive effect on both B and T lymphopoiesis. As an example, the formation of B lymphocyte selectively lowers the bone marrow of mice treated with E2[68], while other studies showed that ovariectomy of mice increased B lymphopoeisis[69,70]. Another study showed that E2 can impair the maturity of B cell maturation[71]. Other studies examining the effects of treatment with E2 on T cell populations revealed thymic involution with reduction of T lymphopoiesis[66,68,72]. Other studies depended on treatment using ER-α-selective agonist PPT showed thymic atrophy as well as important variations in the proportion of CD4/CD8 in thymus which implies that ER-α can play a principal role in atrophy of thymus induced by estrogen[73]. According to a study by[74], treatment with E2 prevented T cell-dependent immune reactions, whereas there was an improved antibody production from B cells[75]. It has been explained that how the effect of treatment with E2 is mediated on T cell immune responses by a study of[76] who proposed a mechanistic explanation in which the expression of ER-α was detected in CD4 + CD25T cells and introducing physiological doses of E2 was able to increase the expression of Foxp3 *in vitro* and converted T cells from the CD4 + CD25phenotype into regulatory CD4 + CD25 + T cells.

ERs and E2 in myeloid cells: Various studies showed the expression of ER-α and ER-β in some myeloid cells including monocytes, macrophages and dendritic cells (DC)[77-80]. The expression of ER-β has been shown to predominate in Monocytes, whereas ER-α is more expressed in macrophages[78]. The functions of estrogens are varied in cells of the myeloid cell lineage that include maturation, differentiation and migration[80]. Moreover[81], indicated that E2 has certain effects on innate immune reactivity such as improved phagocytic capacity in neutrophils and phagocytes. Within this context[82], expressed their views in explaining the large variation seen in innate immune reactivity among men and women.

Other studies have indicated that E2 can stimulate the differentiation of DCs from bone marrow DC[83,84]. It is worth to mention that E2 can improve the role of presentation of antigens of DCs through over expressing MHCII[85,86]. The differentiation of DCs is prevented in ER-α knock-out bone marrow cells which points to a predominant role for ER-α in this process[83]. Another study has further demonstrated the need for ER-α in the production of a Toll-like receptor of IFNa by plasmacytoid DCs[87].

Taking into account the previous studies, it seems that

estrogens and their receptors are

ERs and estrogens in inflammation

It is well-known that the response to inflammation is a major function of the immune system[61]. This function is under the effect of E2 because E2 has inducing influences on immune system which explains why women are more resistant to infections compared with men[65]. Under inflammatory conditions, studies pointed to up-regulation of ER-β and down-regulation of ER-α in splenocytes. This phenomenon is further confirmed under hypoxic conditions in which immune and endothelial cells are accompanying inflammation and as a result, ER-β is up-regulated while the expression of ER-α is down-regulated[65].

Previous studies have shown that E2 has effects on pro-inflammatory transcription factors and cytokines. Furthermore, the activation of immune cells resulting from either microbial origin or signals induced by inflammation is controlled by stimulation of the nuclear factor-kappa B (NF-jB), the required pathway for the normal responses by immune cells[88]. In another study, researchers have shown that both ER-α and ER-β prevent the activity of NF-jB based on E2 in cardiac myocytes *in vitro*[89]. Furthermore, a selective ER-β agonist ERB-041 inhibits the activity of NFjB in peritoneal macrophages[90]. Taken together, both ERs inhibit NFjB activity in different cell types. Several studies have put emphasis that the expression of adhesion molecules to be regulated by E2 and the outcomes are dependent on the concentration of E2. These studies denoted that E2 levels at pregnancy suppress the expression of membrane E-selectin, and intercellular adhesion molecule-1[91,92]. Low levels of E2 up-regulate the expression of the adhesion molecules[65]. E2 can regulate expression of both pro-inflammatory and anti-inflammatory cytokines. E2 has various effects on the formation of reactive oxygene species (ROS) so that increased levels of E2 lower the formation of ROS, while either ovariectomy or low levels of E2 increase the production of ROS[65].

The effects of E2 on the expression of inflammatory (NO) synthase (iNOS) have been reported. Elevated levels of E2 have been shown to inhibit NO production stimulated by cytokine[93]. Another study pointed to the involvement of ER-α in the inflammation of vascular tissues which is associated with diabetes indicating that E2 decreases the level of (iNOS) in the aorta via ER-α[94]. The relationship between chronic inflammatory diseases and development of fibrosis has been established[95]. Other studies showed that E2 has effects on functions of fibroblasts and mechanisms of fibrosis. According to[96], E2 up-regulates basic fibroblast growth factor and the tissue inhibitor of MMPs (TIMP)[97]. Another study found that E2 could suppress a hepatic fibrosis[98,99]. Proposed an explanation of suppressed fibrosis by E2 in which hepatic stellate cells express ER-β, but not ER-α. Moreover, E2 has the ability to inhibit the fibrosis of heart through ERb *in vivo*[35]. High levels of estrogens can inhibit inflammation through making a reduction in pro-inflammatory pathways[65]. It is worth mentioning that ER subtype that is expressed in individual cell determines how the response to E2 will be by inflammatory cells.

The roles of ERs in autoimmunity

Estrogens have been shown to be one of the risk factors of autoimmunity; women are more likely to be affected by autoimmune diseases during the stages of fertility compared with

men. It is greatly considered that both B and T lymphocytes to be crucial in the initiation of autoimmune diseases[65]. E2 has its influences on lymphoid and myeloid cells which can be mediated through the expression of ERa and ERb. Various trials were made to demonstrate the roles of estrogens and ERs in autoimmune diseases. One of these trials was made in murine lupus models indicated that early removal of ovary of NZB/NZW f1 mice was able to reduce the progression of lupus. It has been shown through two studies that breeding of the ERa/genotype with three different murine lupus-prone strains provided protection against renal pathology by lacking ERa[100,101]. Also, a study showed that E2 has the ability to lower the tolerance of B-cell by ERa[71].

In another study by[44], the results showed that the deficiency of ERa led to the development of autoimmunity, whereas the use of ERa agonist PPT has therapeutic effects on some autoimmunity diseases including systemic lupus erythematosus and rheumatoid arthritis. In their study[102], showed that the removal of ovary has impacts on lupus progression which were reversed by treating with E2. The results also showed that the use of E2 or the ERa selective agonist was able to ameliorate the clinical output of arthritis compared to control group. It seems that these studies did not link the role of estrogens with infectious diseases together to participate to autoimmune diseases. Here, we would like to recommend future diseases to focus in this point because solving the estrogen problem would be an interesting area to help in autoimmune remedies.

The roles of ERs in lymphoid tumors

According to[15], numerous tumors exhibit their E2 dependency including endometrial and breast cancers. Irrespective to the fact that hematological malignancies do not depend on hormones to be initiated, it seems that lymphoid malignancies tend to be under the effect of estrogen as indicated by epidemiological studies which pointed to gender variations regarding incidence and prognosis[43,103,104]. Other studies pointed to the existence of an association between reproductive hormones and oral contraceptives with lowered risk factor among female patients with Non-Hodgkin lymphomas[4,16]. In general terms, studies showed that men are more likely to develop acute lymphocytic leukemia[43,103] and CLL[103] compared with women. Other studies showed a higher incidence of lymphoid neoplasm subtypes in males compared with females, among these examples are Burkitt lymphoma and mantle cell lymphoma, whereas in T-cell neoplasms, no significant differences were reported among females and males[43].

In the study of[61], the authors reported an evidence to show the effect of E2 on growth of lymphoma so that the mice grafted with T cell lymphoma cells, the tumor size was greater in males compared with females. The expression of ERb has been reported in both Burkitt's lymphoma cell lines[61] and PB-MCs from CLL patients[61]. Actually, it can be implied from such findings that the agonist of ERb can influence lymphoma and leukemia cells. It is believed that the consideration that wild-type ERb is expressed in lymphoid tumors as well as ERb2 in CLL patients[61]. From a clinical point of view, the expression of ERb2 may indicate poor prognosis. In another study by[31], it was found that the expression of ERb2 was able to increase the growth of cancer cells in prostate using mice model. The expression of ERb2 has been reported in low levels in mammary

glands at physiological conditions, whereas its expressed levels have been significantly increased in invasive mammary carcinomas[105]. The localization of ERb2 as either only in cytoplasm, or both cytoplasmic and nuclear plays a crucial role in evaluating the prognosis so that the involvement of cytoplasmic localization implies poor prognosis[106].

In their study[107], pointed to a very interesting finding when the ERs were found localized in membranes. The authors expressed their thoughts as ERs have a role in differentiation of hematopoietic cells. In a previous study, ERb knockout mice developed myeloproliferative disease, lymphoid proliferation, and prostate hyperplasia[44]. It can be extracted from these findings that ERb has a potential to inhibit the growth of myeloid cells and accordingly it can be considered as a tumor suppressor in hematological malignancies. The role of estrogens in lymphoid tumors looks to be independent from gender which highlights the need for future research to address the molecular aspects associated with estrogen.

The therapeutic potential of ERb agonists in treating cancers
Based on previous findings in which ERb is highly expressed in lymphoid cells, and the finding of anti-proliferative roles of ERb pointed to the possibility of using ERb agonists in treating proliferative hematological disorders. Several ERb selective agonists have been produced but not seriously tested against hematological tumors[61,108]. It was interestingly to find that no cross reactivity is found between ERB and ERa[61]. The application of ERa agonist did not exhibit any impacts on the growth of lymphoma[61]. It can be extracted from these findings that ERb agonists can be used as a therapy for lymphomas expressing ERb.

Other studies showed that some natural compounds may prefer ERb which may makes a new line of therapeutics for hematological tumors. As an example, genistein, has affinity for ERb can arrest G(2)/M cycle and increase the differentiation of acute myeloid leukemia cells[109]. It can induce apoptosis in T-cell leukemia cells[110], it can also prevent the growth of canine lymphoid cell lines[111]. The study of[12] showed that the improved expression of ERb in cell lines of breast cancer arrested a G2 cell cycle. In another study by[112], it was found that the ERb agonist DPN exhibited antigrowth impacts on breast cancer cells. Other studies have demonstrated the expression of ERb in prostate cells either normal or malignant cells, or accordingly, it is plausible to use ERb agonists in treating prostate malignancies. There is evidence from *in vitro* studies showing that treatment of prostate cancer cell lines with ERb was able to lower growth, invasiveness, and induced apoptosis in these cells[36,37,113].

Other studies showed that the use of ERb agonist DPN decreased the potential of tumorigenesis of intestine using Apc(Min/+) mice[114]. Another study reported that DPN was able to prevent colon cancer cells expressing ERb[115], whereas medulloblastoma cells were inhibited from growth *in vivo* using a mouse model[116]. In another study, the ERb agonist KB9520 showed antitumorigenic impacts using rat models of cholangiocarcinoma[117]. Although the previous studies showed the potential of using ERb agonist in treating cancers, there is still a need for more studies to explore more mechanisms of action and to specify the exact pathways for optimal use of this promising line of cancer therapy.

Discussion

The present study reviewed the literature for the estrogen and ERs. Estrogen has multiple roles under physiological conditions including signaling roles in cell growth, reproduction, development and differentiation. Estrogens exert their effects through two distinct estrogen receptors, ER-α and β to which E2 binds strongly[3]. It seems that it is difficult to put the actions or roles of estrogens and ERs in one frame. There is a need in future research to identify the conditions in which the estrogens behave and what are the stimulating factors?

The expression of ERs depends mainly on the type of ER. Although estrogen mainly acts in reproductive system, its receptors are selectively expressed in different tissues. ER-β is highly expressed in the ovary, central nervous system, cardiovascular system, lung, male reproductive organs, prostate, colon, kidney and the immune system[21,22]. A debate concerning the roles of estrogen has been discussed and ended with contradicting findings in which it was thought that it increases the proliferation and growth to increase the growth of the breast, uterus, and prostate, which implies the possibility to induce carcinogenesis[36-40]. On the other hand, other contradicting findings showed that Other contradicting findings showed that estrogens through ER-β repress proliferation and induce differentiating stem cells in various tissues[39,40-44].

According to the context that ERb is highly expressed in lymphoid cells, and the finding of anti-proliferative roles of ERb, the potential to use ERb agonists in treating proliferative hematological disorders has been raised[112,114,115,117]. Estrogens through its receptors interact with the nucleus material in the cell and activate other genes such as BCL2 gene which, in turn, induces the production of BCL2 protein in cytoplasm and makes the cell ready for division and proliferation. In this context, we may ask a large question which we do not observe in studies about the source and concentration of estrogen. If estrogen comes from other sources into the body, its concentration may become more than under control in cellular processes and it is plausible to think of extra actions of estrogens which may exceed metabolic needs and makes it involved in carcinogenesis. Accordingly, we think that a lot of further research is still required to explore the role of estrogen.

Conclusions

The function of estrogen seems to be determined by the estrogen receptor which is expressed in various tissues with relatively predominant forms. The function of estrogen is varied and may look contradicted. There is a potential to use ERb agonists in treating proliferative hematological disorders.

References

1. Yakimchuk, K., Jondal, M., Okret, S. Estrogen receptor α and β in the normal immune system and in lymphoid malignancies. (2013) Mol Cell Endocrinol 375(1-2): 121-129.
Pubmed | Crossref | Others

2. Huber, J.C., Schneeberger, C., Tempfer, C.B. Genetic modelling of the estrogen metabolism as a risk factor of hormone-dependent disorders. (2002) Maturitas 42(1): 1-12.
Pubmed | Crossref | Others

3. Heldring, N., Pike, A., Andersson, S., et al. Estrogen receptors: how do they signal and what are their targets. (2007) Physiol Rev 87(3): 905-931.
Pubmed | Crossref | Others

4. Nilsson, S., Makela, S., Treuter, E., et al. Mechanisms of estrogen action. (2001) Physiol Rev 81(4): 1535-1565.
Pubmed | Crossref | Others

5. Cowley, S.M., Parker, M.G. A comparison of transcriptional activation by ER α and ER β. (1999) J Steroid Biochem Mol Biol 69(1-6): 165-175.
Pubmed | Crossref | Others

6. Kuiper, G.G., Enmark, E., Pelto-Huikko, M., et al. Cloning of a novel receptor expressed in rat prostate and ovary. (1996) Proc Natl Acad Sci USA 93(12): 5925-5930.
Pubmed | Crossref | Others

7. Leitman, D.C., Paruthiyil, S., Vivar, O.I., et al. Regulation of specific target genes and biological responses by estrogen receptor subtype agonists. (2010) Curr Opin Pharmacol 10(6): 629-636.
Pubmed | Crossref | Others

8. Stauffer, S.R., Coletta, C.J., Tedesco, R., et al. Pyrazole ligands: structure-affinity/activity relationships and estrogen receptor-alpha-selective agonists. (2000) J Med Chem 43(26): 4934-4947.
Pubmed | Crossref | Others

9. Meyers, M.J., Sun, J., Carlson, K.E., et al. Estrogen receptor-beta potency-selective ligands: structure-activity relationship studies of diarylpropionitriles and their acetylene and polar analogues. (2001) J Med Chem 44(24): 4230-4251.
Crossref | Others

10. Minutolo, F., Macchia, M., Katzenellenbogen, B.S., et al. Estrogen receptor β ligands: recent advances and biomedical applications. (2011) Med Res Rev 31(3): 364-442.
Pubmed | Crossref | Others

11. Carroll, V.M., Jeyakumar, M., Carlson, K.E., et al. Diarylpropionitrile (DPN) enantiomers: synthesis and evaluation of estrogen receptor β-selective ligands. (2012) J Med Chem 55(1): 528-537.
Pubmed | Crossref | Others

12. Paruthiyil, S., Parmar, H., Kerekatte, V., et al. Estrogen receptor β inhibits human breast cancer cell proliferation and tumor formation by causing a G2 cell cycle arrest. (2004) Cancer Res 64(1): 423-428.
Pubmed | Crossref | Others

13. Nilsson, S., Koehler, K.F. Oestrogen receptors and selective oestrogen receptor modulators: molecular and cellular pharmacology. (2005) Basic Clin Pharmacol Toxicol 96(1): 15-25.
Pubmed | Crossref | Others

14. Powell, E., Xu, W. Intermolecular interactions identify ligand-selective activity of estrogen receptor alpha/beta dimers. (2008) Proc Natl Acad Sci USA 105(48): 19012-19017.
Pubmed | Crossref | Others

15. Thomas, C., Gustafsson, J.A. The different roles of ER subtypes in cancer biology and therapy. (2011) Nat Rev Cancer 11(8): 597-608.
Pubmed | Crossref | Others

16. Lin, C.Y., Vega, V.B., Thomsen, J.S., et al. Whole-genome cartography of estrogen receptor alpha binding sites. (2007) PLoS Genet 3(6): e87.
Pubmed | Crossref | Others

17. Zhao, C., Gao, H., Liu, Y., et al. Genome-wide mapping of estrogen receptor-beta-binding regions reveals extensive cross-talk with transcription factor activator protein-1. (2010) Cancer Res 70(12): 5174-5183.
Pubmed | Crossref | Others

18. Grober, O.M., Mutarelli, M., Giurato, G., et al. Global analysis of estrogen receptor beta binding to breast cancer cell genome reveals an extensive interplay with estrogen receptor alpha for target gene regulation. (2011) BMC Genomics 12: 36.
Pubmed | Crossref | Others

19. Levin, E.R. Integration of the extranuclear and nuclear actions of estrogen. (2005) Mol Endocrinol 19(8): 1951-1959.
Pubmed | Crossref | Others

20. Ascenzi, P., Bocedi, A., Marino, M. Structure-function relationship of estrogen receptor alpha and beta: impact on human health. (2006) Mol Aspects Med 27(4): 299-402.
Pubmed | Crossref | Others

21. Enmark, E., Pelto-Huikko, M., Grandien, K., et al. Human estrogen receptor beta-gene structure, chromosomal localization, and expression pattern. (1997) J Clin Endocrinol Metab 82(12): 4258-4265.
Pubmed | Crossref | Others

22. Kuiper, G.G., Carlsson, B., Grandien, K., et al. Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors α and β. (1997) Endocrinology 138(3): 863-870.
Pubmed | Crossref | Others

23. Poola, I., Speirs, V. Expression of alternatively spliced estrogen receptor alpha mRNAs is increased in breast cancer tissues. (2001) J Steroid Biochem Mol Biol 78(5): 459-469.
Pubmed | Crossref | Others

24. Cavallini, A., Messa, C., Pricci, M., et al. Distribution of estrogen receptor subtypes, expression of their variant forms, and clinicopathological characteristics of human colorectal cancer. (2002) Dig Dis Sci 47(12): 2720-2728.
Pubmed | Crossref | Others

25. Kumar, V.L., Kumar, S., Srivastava, A., et al. Observations on the presence of E domain variants of estrogen receptor-alpha in the breast tumors. (2006) J Surg Oncol 94(4): 332-337.
Pubmed | Crossref | Others

26. Witek, A., Paul-Samojedny, M., Stojko, R., et al. Coexpression index of estrogen receptor alpha mRNA isoforms in simple, complex hyperplasia without atypia, complex atypical hyperplasia and adenocarcinoma. (2007) Gynecol Oncol 106(2): 407-412.
Pubmed | Crossref | Others

27. Al-Bader, M., Al-Saji, S., Ford, C.H., et al. Real-time PCR: detection of oestrogen receptor-alpha and -beta isoforms and variants in breast cancer. (2010) Anticancer Res 30(10): 4147-4156.
Pubmed | Crossref | Others

28. Lin, S.L., Yan, L.Y., Zhang, X.T., et al. ER-alpha36, a variant of ER-alpha, promotes tamoxifen agonist action in endometrial cancer cells via the MAPK/ERK and PI3K/Akt pathways. (2010) PLoS One 5(2): e9013.
Pubmed | Crossref | Others

29. Collins, F., MacPherson, S., Brown, P., et al. Expression of oestrogen receptors, ERalpha, ERbeta, and ERbeta variants, in endometrial cancers and evidence that prostaglandin F may play a role in regulating expression of ERalpha. (2009) BMC Cancer 9: 330.
Pubmed | Crossref | Others

30. Haring, J., Skrzypczak, M., Stegerer, A., et al. Estrogen receptor beta transcript variants associate with oncogene expression in endometrial cancer. (2012) Int J Mol Med 29(6): 1127-1136.
Pubmed | Crossref | Others

31. Dong, W., Li, J., Huang, Y., et al. Differential expression patterns of estrogen receptor (ER)-β splice variants between papillary thyroid cancer and nodular thyroid goiter. (2012) Med Sci Monit 18(9): BR351-BR355.
Pubmed | Crossref | Others

32. Stygar, D., Westlund, P., Eriksson, H., Sahlin, L. Identification of wild type and variants of oestrogen receptors in polymorphonuclear and mononuclear leucocytes. (2006) Clin Endocrinol (Oxf) 64(1): 74-81.
Pubmed | Crossref | Others

33. Razandi, M., Alton, G., Pedram, A., et al. Identification of a structural determinant necessary for the localization and function of estrogen receptor alpha at the plasma membrane. (2003) Mol Cell Biol 23(5): 1633-1646.
Pubmed | Crossref | Others

34. Chambliss, K.L., Yuhanna, I.S., Anderson, R.G., et al. ERbeta has nongenomic action in caveolae. (2002) Mol Endocrinol 16(5): 938-946.
Pubmed | Crossref | Others

35. Pedram, A., Razandi, M., Aitkenhead, M., et al. Estrogen inhibits cardiomyocyte hypertrophy in vitro. Antagonism of calcineurin-related hypertrophy through induction of MCIP1. (2005) J Biol Chem 280(28): 26339-26348.
Pubmed | Crossref | Others

36. Cheng, G., Weihua, Z., Warner, M., et al. Estrogen receptors ER alpha and ER beta in proliferation in the rodent mammary gland. (2004) Proc Natl Acad Sci USA 101(11): 3739-3746.
Pubmed | Crossref | Others

37. Cheng, J., Lee, E.J., Madison, L.D., et al. Expression of estrogen receptor beta in prostate carcinoma cells inhibits invasion and proliferation and triggers apoptosis. (2004) FEBS Lett 566(1-3): 169-172.
Pubmed | Crossref | Others

38. Omoto, Y., Imamov, O., Warner, M., et al. Estrogen receptor alpha and imprinting of the neonatal mouse ventral prostate by estrogen. (2005) Proc Natl Acad Sci USA 102(5): 1484-1489.
Pubmed | Crossref | Others

39. Wada-Hiraike, O., Hiraike, H., Okinaga, H., et al. Role of estrogen receptor beta in uterine stroma and epithelium: Insights from estrogen receptor beta-/-mice. (2006) Proc. Natl. Acad. Sci. USA 103(48): 18350-18355.
Pubmed | Crossref | Others

40. Wada-Hiraike, O., Imamov, O., Hiraike, H., et al. Role of estrogen receptor beta in colonic epithelium. (2006) Proc Natl Acad Sci USA 103(8): 2959-2964.
Pubmed | Crossref | Others

41. Cheng, G., Li, Y., Omoto, Y., et al. Differential regulation of estrogen receptor (ER)alpha and ERbeta in primate mammary gland. (2005) J Clin Endocrinol Metab 90(1): 435-444.
Pubmed | Crossref | Others

42. Imamov, O., Morani, A., Shim, G.J., et al. Estrogen receptor beta regulates epithelial cellular differentiation in the mouse ventral prostate. (2004) Proc Natl Acad Sci USA 101(25): 9375-9380.
Pubmed | Crossref | Others

43. Morani, A., Barros, R.P., Imamov, O., et al. Lung dysfunction causes systemic hypoxia in estrogen receptor beta knockout (ERbeta -/-) mice. (2006) Proc Natl Acad Sci USA 103(18): 7165-7169.
Pubmed | Crossref | Others

44. Shim, G.J., Wang, L., Andersson, S., et al. Disruption of the estrogen receptor beta gene in mice causes myeloproliferative disease resembling chronic myeloid leukemia with lymphoid blast crisis. (2003) Proc Natl Acad Sci USA 100(11): 6694-6699.
Pubmed | Crossref | Others

45. Hartman, J., Lindberg, K., Morani, A., et al. Estrogen receptor beta inhibits angiogenesis and growth of T47D breast cancer xenografts. (2006) Cancer Res 66(23):11207–11213.
Pubmed | Crossref | Others

46. Antal, M.C., Krust, A., Chambon, P., et al. Sterility and absence of histopathological defects in nonreproductive organs of a mouse ER-beta-null mutant. (2008) Proc Natl Acad Sci USA 105(7): 2433-2438.
Pubmed | Crossref | Others

47. Hartman, J., Edvardsson, K., Lindberg, K., et al. Tumor repressive functions of estrogen receptor beta in SW480 colon cancer cells. Cancer Res 69(15): 6100–6106.
Pubmed | Crossref | Others

48. Li, H., Tu, Z., An, L., et al. Inhibitory effects of ERβ on proliferation, invasion, and tumor formation of MCF-7 breast cancer cells prognostication for the use of ERβ-selective therapy. (2012) Pharm Biol 50(7): 839-849.
Pubmed | Crossref | Others

49. Tu, Z., Ma, Y., Tian, J., et al. Estrogen receptor β potentiates the antiproliferative effect of raloxifene and affects the cell migration and invasion in HCT-116 colon cancer cells. (2012) J Cancer Res Clin Oncol 138(7): 1091-1103.
Pubmed | Crossref | Others

50. Blagosklonny, M.V., Neckers, L.M. Cytostatic and cytotoxic activity of sex steroids against human leukemia cell lines. (1994) Cancer Lett 76(2-3): 81-86.
Pubmed | Crossref | Others

51. Jenkins, J.K., Suwannaroj, S., Elbourne, K.B., et al. 17- beta-estradiol alters Jurkat lymphocyte cell cycling and induces apoptosis through suppression of Bcl-2 and cyclin A. (2001) Int Immunopharmacol 1(11): 1897-1911.
Pubmed | Crossref | Others

52. Sunyer, T., Lewis, J., Collin-Osdoby, P., et al. Estrogen's bone-protective effects may involve differential IL-1 receptor regulation in human osteoclast like cells. (1999) J Clin Invest 103(10): 1409-1418.
Pubmed | Crossref | Others

53. Patten, R.D., Pourati, I., Aronovitz, M.J., et al. 17 beta estradiol reduces cardiomyocyte apoptosis in vivo and in vitro via activation of phospho-inositide-3 kinase/Akt signaling. (2004) Circ Res 95(7): 692-699.
Pubmed | Crossref | Others

54. Cutolo, M., Capellino, S., Montagna, P., et al. Sex hormone modulation of cell growth and apoptosis of the human monocytic/ macrophage cell line. (2005) Arthritis Res Ther 7(5): R1124-R1132.
Pubmed | Crossref | Others

55. Takao, T., Kumagai, C., Hisakawa, N., et al. Effect of 17beta-estradiol on tumor necrosis factor-alpha-induced cytotoxicity in the human peripheral T lymphocytes. (2005) J Endocrinol 184(1): 191-197.
Pubmed | Crossref | Others

56. Perillo, B., Sasso, A., Abbondanza, C., et al. 17beta-estradiol inhibits apoptosis in MCF-7 cells, inducing bcl-2 expression via two estrogen-responsive elements present in the coding sequence. (2000) Mol Cell Biol 20(8): 2890-2901.
Pubmed | Crossref | Others

57. Choi, K.C., Kang, S.K., Tai, C.J., et al. Estradiol up-regulates anti-apoptotic Bcl-2 messenger ribonucleic acid and protein in tumorigenic ovarian surface epithelium cells. (2001) Endocrinology 142(6): 2351-2360.
Pubmed | Crossref | Others

58. Nilsen, J., Mor, G., Naftolin, F., Estrogen-regulated developmental neuronal apoptosis is determined by estrogen receptor subtype and the Fas/Fas ligand system. (2000) J Neurobiol 43(1): 64-78.
Pubmed | Crossref | Others

59. Sapi, E., Brown, W.D., Aschkenazi, S., et al. Regulation of Fas ligand expression by estrogen in normal ovary. (2002) J Soc Gynecol Investig 9(4): 243-250.
Pubmed | Crossref | Others

60. Bardin, A., Hoffmann, P., Boulle, N., et al. Involvement of estrogen receptor beta in ovarian carcinogenesis. (2004) Cancer Res 64(16): 5861-5869.
Pubmed | Crossref | Others

61. Yakimchuk, K., Iravani, M., Hasni, M.S., et al. Effect of ligand-activated estrogen receptor β on lymphoma growth in vitro and in vivo. (2011) Leukemia 25(7): 1103-1110.
Pubmed | Crossref | Others

62. Lamote, I., Meyer, E., De Ketelaere, A., et al. Expression of the estrogen receptor in blood neutrophils of dairy cows during the periparturient period. (2006) Theriogenology 65(6): 1082-1098.
Pubmed | Crossref | Others

63. Phiel, K.L., Henderson, R.A., Adelman, S.J., et al. Differential estrogen receptor gene expression in human peripheral blood mononuclear cell populations. (2005) Immunol Lett 97(1):107-113.
Pubmed | Crossref | Others

64. Curran, E.M., Berghaus, L.J., Vernetti, N.J., et al. Natural killer cells express estrogen receptor-alpha and estrogen receptor-beta and can respond to estrogen via a non-estrogen receptor-alphamediated pathway. (2001) Cell Immunol 214(1): 12-20.
Pubmed | Crossref | Others

65. Straub, R.H (2007). The complex role of estrogens in inflammation. Endocr Rev 28(5): 521-574.
Pubmed | Crossref | Others

66. Marotti, T., Sirotkovic, M., Pavelic, J., et al. In vivo effect of progesteron and estrogen on thymus mass and T-cell functions in female mice. (1984) Horm Metab Res 16(4): 201-203.
Pubmed | Crossref | Others

67. Erlandsson, M.C., Ohlsson, C., Gustafsson, J.A., et al. Role of oestrogen receptors alpha and beta in immune organ development and in oestrogen mediated effects on thymus. (2001) Immunology 103(1): 17-25.
Pubmed | Crossref | Others

68. Kouro, T., Medina, K.L., Oritani, K., et al. Characteristics of early murine B-lymphocyte precursors and their direct sensitivity to negative regulators. (2001) Blood 97(9): 2708-2715.
Pubmed | Crossref | Others

69. Masuzawa, T., Miyaura, C., Onoe, Y., et al. Estrogen deficiency stimulates B lymphopoiesis in mouse bone marrow. (1994) J Clin Invest 94(3): 1090-1097.
Pubmed | Crossref | Others

70. Wilson, C.A., Mrose, S.A., Thomas, D.W. Enhanced production of B lymphocytes after castration. (1995) Blood 85(6): 1535-1539.
Pubmed | Crossref | Others

71. Hill, L., Jeganathan, V., Chinnasamy, P., et al. Differential roles of estrogen receptors α and β in control of B-cell maturation and selection. (2011) Mol Med 17(3-4): 211-220.
Pubmed | Crossref | Others

72. Rijhsinghani, A.G., Thompson, K., Bhatia, S.K., et al. Estrogen blocks early T cell development in the thymus. (1996) Am J Reprod Immunol 36(5): 269-277.
Pubmed | Crossref | Others

73. Li, J., McMurray, R.W. Effects of estrogen receptor subtype-selective agonists on immune functions in ovariectomized mice. (2006) Int Immunopharmacol 6(9): 1413-1423.
Pubmed | Crossref | Others

74. Carlsten, H., Holmdahl, R., Tarkowski, A., et al. Oestradiol- and testosterone-mediated effects on the immune system in normal and autoimmune mice are genetically linked and inherited as dominant traits. (1989) Immunology 68(2): 209-214.
Pubmed | Crossref | Others

75. Erlandsson, M.C., Jonsson, C.A., Islander, U., et al. Oestrogen receptor specificity in oestradiol-mediated effects on B lymphopoiesis and immunoglobulin production in male mice. (2003)Immunology 108(3): 346-351.
Pubmed | Crossref | Others

76. Polanczyk, M.J., Carson, B.D., Subramanian, S., et al. Cutting edge: estrogen drives expansion of the CD4+CD25+ regulatory T cell compartment. (2004) J Immunol 173(4): 2227-2230.
Pubmed | Crossref | Others

77. Komi, J., Lassila, O. Nonsteroidal anti-estrogens inhibit the functional differentiation of human monocyte-derived dendritic cells. (2000) Blood 95(9): 2875- 2882.
Pubmed | Crossref | Others

78. Mor, G., Sapi, E., Abrahams, V.M., et al. Interaction of the estrogen receptors with the Fas ligand promoter in human monocytes. (2003) J Immunol 170(1): 114-122.
Pubmed | Crossref | Others

79. Mao, A., Paharkova-Vatchkova, V., Hardy, J., et al. Estrogen selectively promotes the differentiation of dendritic cells with characteristics of Langerhans cells. (2005) J Immunol 175(8): 5146-5151.
Pubmed | Crossref | Others

80. Harkonen, P.L., Vaananen, H.K. Monocyte-macrophage system as a target for estrogen and selective estrogen receptor modulators. (2006) Ann. NY Acad Sci 1089: 218-227.
Pubmed | Crossref | Others

81. Bouman, A., Heineman, M.J., Faas, M.M. Sex hormones and the immune response in humans.(2005) Hum Reprod Update 11(4): 411-423.
Pubmed | Crossref | Others

82. Pennell, L.M., Galligan, C.L., Fish, E.N. Sex affects immunity. (2012) J Autoimmun 38(2-3): J282-J291.
Pubmed | Crossref | Others

83. Paharkova-Vatchkova, V., Maldonado, R., Kovats, S. Estrogen preferentially promotes the differentiation of CD11c+ CD11b(intermediate) dendritic cells from bone marrow precursors. (2004) J Immunol 172(3): 1426-1436.
Pubmed | Crossref | Others

84. Carreras, E., Turner, S., Paharkova-Vatchkova, V., et al. Estradiol acts directly on bone marrow myeloid progenitors to differentially regulate GM-CSF or Flt3 ligand-mediated dendritic cell differentiation. (2008) J Immunol 180(2): 727-738.
Pubmed | Crossref | Others

85. Nalbandian, G., Paharkova-Vatchkova, V., Mao, A., et al. The selective estrogen receptor modulators, tamoxifen and raloxifene, impair dendritic cell differentiation and activation. (2005) J Immunol 175(4): 2666-2675.
Pubmed | Crossref | Others

86. Siracusa, M.C., Overstreet, M.G., Housseau, F., et al. 17beta-estradiol alters the activity of conventional and IFN-producing killer dendritic cells. (2008) J Immunol 180(3): 1423-1431.
Pubmed | Crossref | Others

87. Seillet, C., Laffont, S., Tremollieres, F., et al. The TLR-mediated response of plasmacytoid dendritic cells is positively regulated by estradiol in vivo through cell-intrinsic estrogen receptor α signaling. (2012) Blood 119(2): 454-464.
Pubmed | Crossref | Others

88. Karin, M., Lin, A. NF-kappaB at the crossroads of life and death. (2002) Nat Immunol 3(3): 221-227.
Pubmed | Crossref | Others

89. Pelzer, T., Neumann, M., de Jager, T., et al. Estrogen effects in the myocardium: inhibition of NF-kappaB DNA binding by estrogen receptor alpha and -beta. (2001) Biochem Biophys Res Commun 286(5): 1153-1157.
Pubmed | Crossref | Others

90. Xiu-li, W., Wen-jun, C., Hui-hua, D., et al. ERB-041, a selective ER beta agonist, inhibits iNOS production in LPS-activated peritoneal macrophages of endometriosis via suppression of NF-kappaB activation. (2009) Mol Immunol 46(11-12): 2413-2418.
Pubmed | Crossref | Others

91. Caulin-Glaser, T., Watson, C.A., Pardi, R., et al. Effects of 17betaestradiol on cytokine-induced endothelial cell adhesion molecule expression. (1996) J Clin Invest 98(1): 36-42.
Pubmed | Crossref | Others

92. Mukherjee, T.K., Nathan, L., Dinh, H., et al. 17-epiestriol, an estrogen metabolite, is more potent than estradiol in inhibiting vascular cell adhesion molecule 1 (VCAM-1) mRNA expression. (2003) J Biol Chem 278(14): 11746-11752.
Pubmed | Crossref | Others

93. Wen, Y., Yang, S., Liu, R., et al. Estrogen attenuates nuclear factor-kappa B activation induced by transient cerebral ischemia. (2004) Brain Res 1008(2): 147-154.
Pubmed | Crossref | Others

94. Cignarella, A., Bolego, C., Pelosi, V., et al. Distinct roles of estrogen receptor-alpha and beta in the modulation of vascular inducible nitric-oxide synthase in diabetes. (2009) J Pharmacol Exp Ther 328(1): 174-182.
Pubmed | Crossref | Others

95. Wynn, T.A., Ramalingam, T.R. Mechanisms of fibrosis: therapeutic translation for fibrotic disease. (2012) Nat Med 18(7): 1028-1040.
Pubmed | Crossref | Others

96. Fujimoto, J., Hori, M., Ichigo, S., et al. Ovarian steroids regulate the expression of basic fibroblast growth factor and its mRNA in fibroblasts derived from uterine endometrium. (1997) Ann Clin Biochem 34(Pt 1): 91-96.
Pubmed | Crossref | Others

97. Sato, T., Ito, A., Mori, Y., et al. Hormonal regulation of collagenolysis in uterine cervical fibroblasts. Modulation of synthesis of procollagenase, prostromelysin and tissue inhibitor of metalloproteinases (TIMP) by progesterone and oestradiol-17 beta. (1991) Biochem J 275(Pt 3): 645-650.
Pubmed | Crossref | Others

98. Yasuda, M., Shimizu, I., Shiba, M., et al. Suppressive effects of estradiol on dimethylnitrosamine-induced fibrosis of the liver in rats. (1999) Hepatology 29(3): 719-727.
Pubmed | Crossref | Others

99. Zhou, Y., Shimizu, I., Lu, G., et al. Hepatic stellate cells contain the functional estrogen receptor beta but not the estrogen receptor alpha in male and female rats. (2001) Biochem Biophys Res Commun 286(5): 1059-1065.
Pubmed | Crossref | Others

100. Balwierz, W. In: Oncology and pediatric hematology. (2008) Wydawnictwo Lekarskie PZWL Warsaw 290.
Pubmed | Crossref | Others

101. Svenson, J.L., EuDaly, J., Ruiz, P., et al. Impact of estrogen receptor deficiency on disease expression in the NZM2410 lupus prone mouse. (2008) Clin Immunol 128(2): 259-268.
Pubmed | Crossref | Others

102. Engdahl, C., Jochems, C., Windahl, S.H., et al. Amelioration of collagen-induced arthritis and immune-associated bone loss through signaling via estrogen receptor alpha, and not estrogen receptor beta or G protein-coupled receptor 30. (2010) Arthritis Rheum 62(2): 524-533.
Pubmed | Crossref | Others

103. Forsythe, A., Breland, T., Majumdar, S., et al. Gender differences in incidence rates of childhood B-precursor acute lymphocytic leukemia in Mississippi. (2010)J Pediatr Oncol Nurs 27(3): 164-167.
Pubmed | Crossref | Others

104. Parkin, D.M., Stiller, C.A., Draper, G.J., et al. The international incidence of childhood cancer. (1988) Int J Cancer 42(4): 511-520.
Pubmed | Crossref | Others

105. Esslimani-Sahla, M., Kramar, A, Simony-Lafontaine, J., et al. Increased estrogen receptor betacx expression during mammary carcinogenesis. (2005) Clin Cancer Res 11(9): 3170-3174.
Pubmed | Crossref | Others

106. Shaaban, A.M., Green, A.R., Karthik S, et al. Nuclear and cytoplasmic expression of ERbeta1, ERbeta2, and ERbeta5 identifies distinct prognostic outcome for breast cancer patients. (2008) Clin Cancer Res 14(16): 5228-5235.
Pubmed | Crossref | Others

107. Kauss, M.A., Reiterer, G., Bunaciu, R.P., et al. Human myeloblastic leukemia cells (HL-60) express a membrane receptor for estrogen that signals and modulates retinoic acid-induced cell differentiation. (2008) Exp Cell Res 314(16): 2999-3006.
Pubmed | Crossref | Others

108. Mohler, M.L., Narayanan, R., Coss, C.C., et al. Estrogen receptor β selective nonsteroidal estrogens: seeking clinical indications. (2010) Expert Opinion on Therapeutic Patents 20(4): 507-534.
Pubmed | Crossref | Others

109. Sánchez, Y., Amrán, D., de Blas, E., et al. Regulation of genistein-induced differentiation in human acute myeloid leukaemia cells (HL60, NB4) Protein kinase modulation and reactive oxygen species generation. (2009) Biochem Pharmacol., 77(3): 384-96.
Pubmed ׀ Crossref ׀ Others

110. Yamasaki, M., Mukai, A., Ohba, M., et al. Genistein induced apoptotic cell death in adult T cell leukemia cells through estrogen receptors. (2010) Biosci Biotechnol Biochem 74(10): 2113-2115.
Pubmed ׀ Crossref ׀ Others

111. Jamadar-Shroff, V., Papich, M.G., Suter, S.E. Soy-derived isoflavones inhibit the growth of canine lymphoid cell lines. (2009) Clin Cancer Res 15(4): 1269-1276.
Pubmed ׀ Crossref ׀ Others

112. Sotoca, A.M., Van den Berg, H., Vervoort, J., et al. Influence of Cellular ERa/ERb Ratio on the ERa-Agonist Induced Proliferation of Human T47D Breast Cancer Cells. (2008) Toxicol Sci 105(2): 303-311.
Pubmed ׀ Crossref ׀ Others

113. Prins, G.S., Korach, K.S. The role of estrogens and estrogen receptors in normal prostate growth and disease. (2008) Steroids 73(3): 233-244.
Pubmed ׀ Crossref ׀ Others

114. Giroux, V., Bernatchez, G., Carrier, J.C. Chemopreventive effect of ERβ-Selective agonist on intestinal tumorigenesis in Apc(Min/+) mice. (2011) Mol Carcinog 50(5): 359-369.
Pubmed ׀ Crossref ׀ Others

115. Motylewska, E., Stasikowska, O., Melen-Mucha, G. The inhibitory effect of diarylpropionitrile, a selective agonist of estrogen receptor beta, on the growth of MC38 colon cancer line. (2009) Cancer Lett 276(1): 68-73.
PMid:19101081
Pubmed ׀ Crossref ׀ Others

116. Mancuso, M., Leonardi, S., Giardullo, P., et al. The estrogen receptor beta agonist diarylpropionitrile (DPN) inhibits medulloblastoma development via anti-proliferative and pro-apototic pathways. (2011) Cancer Lett 308: (2): 197-202.
Pubmed ׀ Crossref ׀ Others

117. Marzioni, M., Torrice, A., Saccomanno, S., et al. An oestrogen receptor beta-selective agonist exerts anti-neoplastic effects in experimental intrahepatic cholangiocarcinoma. (2012) Dig Liver Dis 44(2): 132-142.
Pubmed ׀ Crossref ׀ Others