

Answer 1:

Bibliographic Information

Inhibition of androgen-independent prostate cancer by estrogenic compounds is associated with increased expression of immune-related genes. Coleman, Lisa M.; Kiefer, Jeffrey A.; Brown, Lisha G.; Pitts, Tiffany E.; Nelson, Peter S.; Brubaker, Kristen D.; Vessella, Robert L.; Corey, Eva. Fred Hutchinson Cancer Research Center, Seattle, WA, USA. Neoplasia (Ann Arbor, MI, United States) (2006), 8(10), 862-878. Publisher: Neoplasia Press Inc., CODEN: NEOPFL ISSN: 1522-8002. <http://www.neoplasia.com/pdf/manuscript/neo06328.pdf> Journal; Online Computer File written in English. CAN 146:93710 AN 2006:1213429 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The clin. utility of estrogens for treating prostate cancer (CaP) was established in the 1940s by Huggins. The classic model of the anti-CaP activity of estrogens postulates an indirect mechanism involving the suppression of androgen prodn. However, clin. and preclin. studies have shown that estrogens exert growth-inhibitory effects on CaP under low-androgen conditions, suggesting addnl. modes whereby estrogens affect CaP cells and/or the microenvironment. Here the authors have investigated the activity of 17 β estradiol (E2) against androgen-independent CaP and identified mol. alterations in tumors exposed to E2. E2 treatment inhibited the growth of all four androgen-independent CaP xenografts studied (LuCaP 35V, LuCaP 23.1Al, LuCaP 49, and LuCaP 58) in castrated male mice. The mol. basis of growth suppression was studied by cDNA microarray anal., which indicated that multiple pathways are altered by E2 treatment. Of particular interest are changes in transcripts encoding proteins that mediate immune responses and regulate androgen receptor signaling. In conclusion, the authors' data show that estrogens have powerful inhibitory effects on CaP in vivo in androgen-depleted environments and suggest novel mechanisms of estrogen-mediated antitumor activity. These results indicate that incorporating estrogens into CaP treatment protocols could enhance therapeutic efficacy even in cases of advanced disease.

Answer 2:

Bibliographic Information

Early expression of the Helicase-Like Transcription Factor (HLTF/SMARCA3) in an experimental model of estrogen-induced renal carcinogenesis. Debaeve, Gael; Nonclercq, Denis; Ribaucour, Fabrice; Wiedig, Murielle; Gerbaux, Cecile; Leo, Oberdan; Laurent, Guy; Journe, Fabrice; Belayew, Alexandra; Toubeau, Gerard. Laboratory of Molecular Biology, University of Mons-Hainaut, Mons, Belg. Molecular Cancer (2006), 5 No pp. given. Publisher: BioMed Central Ltd., CODEN: MCOACG ISSN: 1476-4598. <http://www.molecular-cancer.com/content/pdf/1476-4598-5-23.pdf> Journal; Online Computer File written in English. CAN 145:207660 AN 2006:631382 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The Helicase-Like Transcription Factor (HLTF/SMARCA3) belongs to the family of SWI/SNF proteins that use the energy of ATP hydrolysis to remodel chromatin in a variety of cellular processes. Several SWI/SNF genes are disrupted in cancer, suggesting a role of tumor suppressor. Similarly, the HLTF gene was recently found to be inactivated by hypermethylation in a no. of advanced colon and gastric tumors. However, other evidences indicated a 20-fold HLTF overexpression in cell lines derived from various neoplasms (ovary, breast, cervix, kidney...). In the present study, we investigated HLTF expression by immunohistochem. in a model of kidney tumors induced by continuous administration of diethylstilbestrol to male Syrian golden hamsters. A strong labeling was already detected in small tumor buds, making HLTF an early cancer marker in this model. Although every cell stained for HLTF at this early stage, the no. of HLTF-pos. cells decreased to 10% with cancer progression, and these pos. cells were dispersed in the tumor mass. HLTF expression was conserved in the HKT-1097 cell line established from kidney tumors, but again only 10% of pos. cells were found in xenografts produced by HKT-1097 cells in nude mice. In conclusion, our data suggest that HLTF gene activation is linked to initial steps of carcinogenesis in this model and should be investigated in early stages of other neoplasms.

Answer 3:

Bibliographic Information

Estrogen effects on tubulin expression and taxane mediated cytotoxicity in prostate cancer cells. Montgomery, R. Bruce; Bonham, Michael; Nelson, Peter S.; Grim, Jonathan; Makary, Ekram; Vessella, Robert; Stahl, William L. Departments of Medicine and Oncology, University of Washington, Seattle, WA, USA. Prostate (Hoboken, NJ, United States) (2005), 65(2), 141-150. Publisher: Wiley-Liss, Inc., CODEN: PRSTDS ISSN: 0270-4137. Journal written in English. CAN 144:142239 AN 2005:1133517 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Background. The present study was designed to det. if estrogens change microtubule polymn. and modulate cell cycle progression in vitro, related to modulation of tubulin expression and to det. if estrogens had antagonistic or synergistic effects with microtubule active agents. **Methods.** cDNA array anal. of LNCaP cells treated with the estrogens, estradiol, estrone, diethylstilbestrol (DES), and 2-methoxyestradiol (2-ME) was carried out and the results confirmed by PCR and Western blotting. Microtubule arrays in cells treated with estrogens were assessed using indirect immunofluorescence. The effects of combining estrogens with taxane was assessed by MTT assay and flow cytometry for cell cycle kinetics. Human prostate cancer xenografts were treated with DES and docetaxel to assess the effects of combining estrogens and taxane in vivo. **Results.** Treatment of LNCaP cells with DES and 2-ME suppressed transcripts and protein for β -tubulin isotype IVa. This effect on tubulin synthesis was not blocked by estrogen or androgen receptor modulators. Other estrogens had no effect on β -tubulin expression. 2-ME and DES decreased the d. of microtubules. The administration of DES or 2-ME with paclitaxel enhanced cytotoxicity and G2-M arrest in vitro. DES enhanced tumor suppression in a human prostate cancer xenograft model when combined with the taxane docetaxel. **Conclusion.** The use of DES and 2-ME enhances the effects of taxanes and may be a novel and important means of increasing therapeutic efficacy of cytotoxic chemotherapy against prostate carcinoma.

Answer 4:

Bibliographic Information

Expression of mdm-2 oncoprotein in the primary and metastatic sites of mammary tumor (GI-101) implanted athymic nude mice. Velu, Prema Rathina; Malave, Andres; Raney, Shula R.; Hurst, Josephine; Roberson, Claire Thuning; Velu, Appu Rathina. Goodwin Institute for Cancer Research, Inc., Plantation, FL, USA. Cancer Biochemistry Biophysics (1999), 17(1-2), 133-146. Publisher: Gordon & Breach Science Publishers, CODEN: CABCD4 ISSN: 0305-7232. Journal written in English. CAN 132:164347 AN 1999:669263 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The expression of mdm-2 oncoprotein (p90) was detd. in a human breast tumor xenograft line (GI-101) that was derived from a 57 yr old female cancer patient with recurrent, infiltrating ductal adenocarcinoma (Stage IIIa, T3N2MX). Immunopptn. coupled western blot anal. of the primary tumors that have been obtained from xenograft implanted athymic nude mice, using mdm-2 (Ab-1) mouse monoclonal antibody, primarily revealed high level expression of a 90 kDa full length mdm-2 protein. In the GI-101 tumor the level of full length mdm-2 (p90) protein expression increased with the increase in the size of the tumor (100 to 2000 mm³) and a max. expression was detected in 2000 mm³ size tumors. In addn. to the expression in the primary site, a significantly high level expression of mdm-2 protein (p90) was detected in the lung and liver tissues also, which are the known metastatic sites for GI-101 xenograft tumors. However, the level of mdm-2 protein expression was undetectable in the lung and liver tissues obtained from control mice. A cell line (GI-101A) derived from the GI-101 xenograft tumor also showed a high level expression of mdm-2 protein after several generations of cell passage. When the GI-101A cells were treated with DES (Diethylstilbestrol) the mdm-2 protein expression increased after 10 min treatment and reached a peak level at 40 min. Interestingly, DES (10 and 20 μ M) treatment increased the total cell no. also after 96 h treatment compared to the non-treated cells. It appears that mdm-2 (p90) may have a significant role in supporting the tumor cell growth as well as the metastatic process of the GI-101A cells.

Answer 5:

Bibliographic Information

Effects of pharmacological concentrations of estrogens on proliferation and cell cycle kinetics of human breast cancer cell lines in vitro. Reddel, Roger R.; Sutherland, Robert L. Garvan Inst. Med. Res., St. Vincent's Hosp., Sydney, Australia. Cancer Research (1987), 47(20), 5323-9. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 107:212057 AN 1987:612057 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

High dose estrogen therapy has been used effectively in the treatment of human breast cancer. To understand the mechanisms involved, the effects of high concns. (5-100 μ M) of estrogens were studied in estrogen receptor (ER) pos. (T-47D and MCF-7) and ER neg. (MDA-MB-330) human breast cancer cell lines in vitro. Inhibition of cellular proliferation was seen with the synthetic estrogen DES at concns. $>10 \mu$ M in each of the 3 cell lines. In T-47D cells, DES was shown by clonogenic survival assays to be cytotoxic. This effect was evident in both plateau phase and exponentially growing cultures, in contrast to the effects of the antiestrogen tamoxifen, which has minimal effects on plateau phase cells. The effects of DES on the proliferation of exponentially growing cultures were accompanied by changes in cell cycle parameters which included an increase in the percentages of S-phase, G2 + M, and polyploid cells and a corresponding decrease in the percentage of G0-G1 cells. These changes, which contrasted with the known effects of tamoxifen, were not seen in the non- or slowly cycling plateau phase T-47D cells. Such results are consistent with 2 mechanisms of action of high dose estrogen in vitro: a cell cycle phase-specific effect and cell cycle-independent cytotoxicity. 17α -Estradiol and 17β -estradiol had similar potency to DES in inhibiting cell proliferation and inducing the changes in cell cycle parameters in both MCF-7 and MDA-MB-330 cells. The high-dose estrogen effect was ligand specific, in that estrone and estriol were less potent than DES, 17α -estradiol, and 17β -estradiol in inhibiting cell proliferation, and the characteristic cell cycle changes were produced only by concns. of estriol $>75 \mu$ M and not at all by estrone at concns. up to 100 μ M. The androgens testosterone and dihydrotestosterone were similar in effect to estrone. The cell cycle changes assocd. with estrogen-induced growth inhibition in vitro were identical to those obsd. during regression of ER pos. but not ER neg.

human tumor xenografts in nude mice. However, the role of ER in mediating estrogen-induced regression of ER pos. tumors in vivo remains undefined.

Answer 6:

Bibliographic Information

Involvement of estrogen-related receptors in transcriptional response to hypoxia and growth of solid tumors. Ao Ada; Wang Heiman; Kamarajugadda Sushama; Lu Jianrong Department of Biochemistry and Molecular Biology, University of Florida College of Medicine, P.O. Box 103633, Gainesville, FL 32610, USA Proceedings of the National Academy of Sciences of the United States of America (2008), 105(22), 7821-6. Journal code: 7505876. E-ISSN:1091-6490. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 18509053 AN 2008360522 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The development of intratumoral hypoxia is a universal hallmark of rapidly growing solid tumors. Adaptation to the hypoxic environment, which is critical for tumor cell survival and growth, is mediated primarily through a hypoxia-inducible factor (HIF)-dependent transcriptional program. HIF activates genes that facilitate crucial adaptive mechanisms including increased glucose uptake and glycolysis and tumor angiogenesis, making it an important therapeutic target. However, the HIF-dependent transcriptional mechanism remains incompletely understood, and targeting HIF is a difficult endeavor. Here, we show that the orphan nuclear receptor estrogen-related receptors (ERRs) physically interact with HIF and stimulate HIF-induced transcription. Importantly, ERRs appear to be essential for HIF's function. Transcriptional activation of hypoxic genes in cells cultured under hypoxia is largely blocked by suppression of ERRs through expression of a dominant negative form of ERR or treatment with a pharmacological ERR inhibitor, diethylstilbestrol. Systematic administration of diethylstilbestrol severely diminished growth and angiogenesis of tumor xenografts in vivo. Because

nuclear receptors are outstanding targets for drug discovery, the findings not only may offer mechanistic insights into HIF-mediated transcription but also may open new avenues for targeting the HIF pathway for cancer therapy.

Answer 7:

Bibliographic Information

Selective activation of estrogen receptor-beta transcriptional pathways by an herbal extract. Cvoro Aleksandra; Paruthiyil Sreenivasan; Jones Jeremy O; Tzagarakis-Foster Christina; Clegg Nicola J; Tatomer Deirdre; Medina Roanna T; Tagliaferri Mary; Schaufele Fred; Scanlan Thomas S; Diamond Marc I; Cohen Isaac; Leitman Dale C University of California, San Francisco, MS 1258, P.O. Box 0556, San Francisco, California 94143-0556, USA. leitmand@obgyn.ucsf.edu Endocrinology (2007), 148(2), 538-47. Journal code: 0375040. ISSN:0013-7227. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, N.I.H., EXTRAMURAL); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 17095596 AN 2007029966 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Novel estrogenic therapies are needed that ameliorate menopausal symptoms and have the bone-sparing effects of endogenous estrogens but do not promote breast or uterine cancer. Recent evidence suggests that selective activation of the estrogen receptor (ER)-beta subtype inhibits breast cancer cell proliferation. To establish whether ERbeta-selective ligands represent a viable approach to improve hormone therapy, we investigated whether the estrogenic activities present in an herbal extract, MF101, used to treat hot flashes, are ERbeta selective. MF101 promoted ERbeta, but not ERalpha, activation of an estrogen response element upstream of the luciferase reporter gene. MF101 also selectively regulates transcription of endogenous genes through ERbeta. The ERbeta selectivity was not due to differential binding because MF101 binds equally to ERalpha and ERbeta. Fluorescence resonance energy transfer and protease digestion studies showed that MF101 produces a different conformation in ERalpha from ERbeta when compared with the conformations produced by estradiol. The specific conformational change induced by MF101 allows ERbeta to bind to an estrogen response element and recruit coregulatory proteins that are required for gene activation. MF101 did not activate the ERalpha-regulated proliferative genes, c-myc and cyclin D1, or stimulate MCF-7 breast cancer cell proliferation or tumor formation in a mouse xenograft model. Our results demonstrate that herbal ERbeta-selective estrogens may be a safer alternative for hormone therapy than estrogens that nonselectively activate both ER subtypes.

Answer 8:

Bibliographic Information

Early expression of the Helicase-Like Transcription Factor (HLTF/SMARCA3) in an experimental model of estrogen-induced renal carcinogenesis. Debaue Gael; Nonclercq Denis; Ribaucour Fabrice; Wiedig Murielle; Gerbaux Cecile; Leo Oberdan; Laurent Guy; Journe Fabrice; Belayew Alexandra; Toubeau Gerard Laboratory of Molecular Biology, University of Mons-Hainaut, Mons, Belgium. gael.debaue@umh.ac.be Molecular cancer (2006), 5 23. Journal code: 101147698. E-ISSN:1476-4598. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 16762066 AN 2006490951 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

BACKGROUND: The Helicase-Like Transcription Factor (HLTF/SMARCA3) belongs to the family of SWI/SNF proteins that use the energy of ATP hydrolysis to remodel chromatin in a variety of cellular processes. Several SWI/SNF genes are disrupted in cancer, suggesting a role of tumor suppressor. Similarly, the HLTF gene was recently found to be inactivated by hypermethylation in a number of advanced colon and gastric tumors. However, other evidences indicated a 20-fold HLTF overexpression in cell lines derived from various neoplasms (ovary, breast, cervix, kidney...).

RESULTS: In the present study, we investigated HLTF expression by immunohistochemistry in a model of kidney tumors induced by continuous administration of diethylstilbestrol to male Syrian golden hamsters. A strong labeling was already detected in small tumor buds, making HLTF an early cancer marker in this model. Although every cell stained for HLTF at this early stage, the number of HLTF-positive cells decreased to 10% with cancer progression, and these positive cells were dispersed in the tumor mass. HLTF expression was conserved in the HKT-1097 cell line established from kidney tumors, but again only 10% of positive cells were found in xenografts produced by HKT-1097 cells in nude mice.

CONCLUSION: In conclusion, our data suggest that HLTF gene activation is linked to initial steps of carcinogenesis in this model and should be investigated in early stages of other neoplasms.

Answer 9:

Bibliographic Information

Towards functional glycomics by localization of binding sites for tissue lectins: lectin histochemical reactivity for galectins during diethylstilbestrol-induced kidney tumorigenesis in male Syrian hamster. Saussez Sven; Lorfevre Francois; Nonclercq Denis; Laurent Guy; Andre Sabine; Journe Fabrice; Kiss Robert; Toubeau Gerard; Gabius Hans-Joachim Laboratory of Histology, Faculty of Medicine and Pharmacy, University of Mons-Hainaut, Avenue du Champ de Mars, 6-Pentagone 1B, 7000, Mons, Belgium. sven.saussez@umh.ac.be Histochemistry and cell biology (2006), 126(1), 57-69. Journal code: 9506663. ISSN:0948-6143. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 16435123 AN 2006355530 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Endogenous lectins act as effectors of cellular activities such as growth regulation, migration, and adhesion. Following their immunohistochemical localization in our previous study (Saussez et al. in *Histochem Cell Biol* 123:29-41, 2005) we purified several galectins and used them as tools for monitoring accessible binding sites. Herein, we report the use of galectin histochemistry for the analysis of diethylstilbestrol (DES)-induced renal tumors in male Syrian hamster kidney (SHKT). Sections of normal kidney and DES-treated kidney were analyzed with biotinylated galectins-1, -3 (full-length and truncated), and -7. Accessible binding sites were detected, localization was predominantly extracellular and confined to medium-sized and large tumors. Monitoring the SHKT-derived HKT-1097 line, processed in vitro or as xenograft material, cytoplasmic and nuclear staining for galectins-1, -3, and -3tr could be observed. Adaptation of SHKT cells to long-term growth in culture is thus associated with emergence of this signal. Our data set illustrates the feasibility to complement immunohistochemical data by application of the tissue lectins as probes, and to detect regulation of galectin reactivity with differential characteristics within tumor progression in vivo and unique features of the tumor cell line in vitro and in vivo.

Answer 10:

Bibliographic Information

Temporal and spatial factors in diethylstilbestrol-induced squamous metaplasia in the developing human prostate. II. Persistent changes after removal of diethylstilbestrol. Yonemura C Y; Cunha G R; Sugimura Y; Mee S L Department of Anatomy, University of California, School of Medicine, San Francisco, CA 94143, USA *Acta anatomica* (1995), 153(1), 1-11. Journal code: 0370272. ISSN:0001-5180. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 8560954 AN 96105052 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

To determine if the metaplastic effects of diethylstilbestrol (DES) on prostatic development are reversible, human fetal prostates (obtained from abortus specimens 6-22 weeks old) were bisected mid-sagittally; one half was grafted under the

renal capsule of untreated, athymic, male nude mice and the contralateral half was similarly grafted into DES-treated hosts. Severe squamous metaplasia seen in the prostatic ducts after 1 month of continuous DES exposure either disappeared entirely or became reduced in extent and degree after retransplantation of the DES-treated specimens to untreated, intact male hosts and 2 additional months of growth. However, 14 of 21 DES-treated prostates harvested after a 2-month recovery period without DES revealed ductal dilatation (ectasia) and persistent distortion of ductal architecture. Ectasia was most severe in the proximal ducts near the urethra and in prostates 17 weeks or older at the end of 1 month of DES treatment. The clinical consequences of early alteration of prostatic ductal architecture and development are potentially deleterious, as men who were prenatally exposed to DES may be at increased risk for the development of prostatic disease.

Answer 11:

Bibliographic Information

Tumor-inhibiting potential of ZK 112.993, a new progesterone antagonist, in hormone-sensitive, experimental rodent and human mammary tumors. Schneider M R; Michna H; Nishino Y; Neef G; el Etreby M F Research Laboratories of Schering AG, Berlin, F.R.G Anticancer research (1990), 10(3), 683-7. Journal code: 8102988. ISSN:0250-7005. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 2369083 AN 90314324 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The progesterone antagonists Onapristone (ZK 98.299) and Mifepristone (RU 486) proved to be strong inhibitors of various rodent mammary tumors. Therefore, a further potent antiprogesterin, ZK 112.993, and 11 beta-(4-acetyl-phenyl)-analog of Mifepristone, with a high progesterone receptor affinity was tested in experimental rodent and human breast cancer models. In the hormone-dependent MXT(+) mammary tumor of the mouse, treatment of tumors immediately after implantation with 5 mg/kg for 6 weeks led to an inhibition of growth by 95%, being significantly superior to that caused by tamoxifen, diethylstilbestrol and Onapristone. Treatment of established MXT(+) tumors by ZK 112.993 at doses of 0.5, 1.0 and 2.0 mg/kg led to a strong inhibition that equalled that of ovariectomy and surpassed that of Onapristone in the lower doses. In the human, receptor positive mammary carcinoma T61 implanted in male, castrated nude mice, ZK 112.993 (10 mg/kg) significantly retarded tumor growth. Its effect was again superior to Onapristone though weaker than that of tamoxifen. The NMU-induced mammary carcinoma of the rat (established tumors) was inhibited by ZK 112.993 (5 and 10 mg/kg) in a dose-dependent manner slightly superior to Onapristone but weaker than after ovariectomy. Due to its strong antitumor activity and because of the innovative mechanism of action of antiprogesterones in tumor treatment, ZK 112.993 could be of great value for the treatment of breast cancer.

Answer 12:

Bibliographic Information

Effect of steroid hormones on human colorectal adenocarcinoma xenografts, of known steroid-receptor status, in nude mice. Stebbings W S; Vinson G P; Farthing M J; Balkwill F; Wood R F Professional Surgical Unit, St. Bartholomew's Hospital, London, U.K Journal of cancer research and clinical oncology (1989), 115(5), 439-44. Journal code: 7902060. ISSN:0171-5216. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 2808482 AN 90037143 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The effect of hormone therapy on the growth of human colonic adenocarcinoma xenografts in nude mice was evaluated. Primary xeno-transplantation for ten different human colorectal adenocarcinomas into nude mice yielded a tumour take of 50%. One of these host tumours was found to contain androgen receptors (8 fmol/mg cytosol protein; Kd 0.73 x 10⁻⁹)

M), which were maintained in the xenograft at the third and ninth passages, but not expressed at the tenth and twelfth passages. The host tumour and its xenograft did not express either oestrogen or progesterone receptors. Administration of dihydrotestosterone led to inhibition of xenograft growth at the ninth passage compared with untreated controls (P less than 0.05), but had no effect on xenograft growth at the tenth and twelfth passages when androgen receptors were absent. Stilboestrol and progesterone failed to influence xenograft growth. In conclusion, dihydrotestosterone administration led to inhibition of xenograft growth only in the presence of androgen receptor, suggesting that some colorectal cancers might be considered steroid-hormone-sensitive tumours.

Answer 13:

Bibliographic Information

Induction of progesterone receptor with 17 beta-estradiol in human ovarian cancer. Hamilton T C; Behrens B C; Louie K G; Ozols R F. *The Journal of clinical endocrinology and metabolism* (1984), 59(3), 561-3. Journal code: 0375362. ISSN:0021-972X. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 6746867 AN 84265099 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

We utilized a xenograft model of human ovarian cancer to study the ability of estrogen to induce progesterone receptor. Tumor cytosol from 17 beta-estradiol treated oophorectomized animals, but not oophorectomized controls, contained a [3H]ORG 2058 binding moiety of sedimentation coefficient 6-9S. This component showed specificity for the progestagens: progesterone, ORG 2058, and R5020 and for the antiprogestagen cyproterone acetate. At 1000-fold molar excess, 5 alpha-dihydrotestosterone competed partially for these sites while diethylstilbestrol, dexamethasone, and the antiandrogen, SCH 16423, were ineffective competitors. The dissociation constant for this progestagen binding entity was 0.14 nM using [3H]ORG 2058 as labeled ligand and R5020 as competitor. In addition, saturation analysis demonstrated that approximately 400 fmol of progestagen specific binding capacity was available per mg of cytosol protein. These data suggest that estrogen can induce progesterone receptor in human ovarian carcinoma.

Answer 14:

Bibliographic Information

Experimental study of the effect of diethylstilbestrol on the development of the human female reproductive tract. Taguchi O; Cunha G R; Robboy S J. *Biological research in pregnancy and perinatology* (1983), 4(2), 56-70. Journal code: 8302758. ISSN:0724-438X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 6882849 AN 83283665 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Female genital tracts from human embryos and fetuses 5-17 weeks post fertilization were grown for 1-3 months in vivo as grafts to athymic female nude mice. The nude mice were either untreated or treated with diethylstilbestrol (DES). In control (untreated) hosts, anticipated normal development occurred with a high degree of precision. Mullerian ducts fused and proliferated, forming a solid uterovaginal canal that later canalized and formed a normal vaginal mucosa. Uterine glands appeared, and the uterine tube developed its highly plicated mucosa. Under the influence of DES, many of these normal developmental processes were adversely affected. Mullerian epithelium was largely obliterated in the fallopian tube and uterine corpus, mesenchymal stratification into endometrial stroma and myometrium was suppressed, plical development in the fallopian tube was inhibited, cervicovaginal epithelial development was abnormal, and vaginal adenosis was observed in several specimens. This in vivo model of human development is discussed in terms of its potential for resolving the mechanisms of normal human genital development and understanding the teratogenic action of DES on the developing human genital tract.

Answer 15:

Bibliographic Information

Accretion of biopsy specimens of vaginal adenosis from patients exposed in utero to diethylstilbestrol, when transplanted to athymic nude mice. Pienkowski M M; Mann L C; Rosloniec E F Jr; Welsch C W Journal of the National Cancer Institute (1979), 62(3), 521-3. Journal code: 7503089. ISSN:0027-8874. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 283281 AN 79112606 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Vaginal adenosis biopsy specimens from 10 patients exposed in utero to diethylstilbestrol were transplanted for 30 days into athymic (nude) mice. Almost all grafts were recovered, and they had morphologic features closely resembling those of the original biopsy specimens, i.e., cystic, complex, and simple occult glands covered mainly with an endocervical type of epithelium showing extensive squamous metaplasia. Autoradiographic analysis of these grafts after pulse administration of [3H]thymidine into the mice revealed extensive labeling of epithelial cells. These results imply that female athymic (nude) mice are compatible hosts for accretion of the human adenosis.