Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

AKR1C3 (aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II))

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Published in Atlas Database: November 2007

Online updated version: http://AtlasGeneticsOncology.org/Genes/AKR1C3ID612ch10p15.html
DOI: 10.4267/2042/38539

Identity

Hugo: AKR1C3
Other names: DD3; HA1753; HAKRB; HAKRe; HSD17B5; KIAA0119; hluPGFS
Location: 10p15.1

DNA/RNA

Transcription

1170 bp mRNA; transcript has been detected in brain, lung, liver, small intestine, mammary gland, uterus, prostate, testis.

Protein

Description

323 amino acids, molecular weight 37 kDa.

Expression

Activated macrophage, malignant prostate epithelium, normal mammary epithelium, mature blood vessel.

Localisation

Mainly in cytoplasm.

Function

AKR1C3 metabolizes various androgen metabolites including 5a-dihydrotestosterone to 5a-androstane-3a,17b-diol, Delta^4-androstene-3,17-dione to testosterone, androstanedione to 5a-dihydrotestosterone, androsterone to 5a-androstane-3a,17b-diol.
AKR1C3 is also involved in estrogen metabolism converting estrone to 17b-estradiol as well as progesterone metabolism converting prostaglandin D_2 to 9a,11b-prostaglandin $F2_a$.
AKR1C3 has the capability of regulating the trans-activation of various nuclear receptors including androgen receptor, estrogen receptor, and peroxisome proliferator activated receptor (PPARG) by regulating the ligand availability for the nuclear receptors.

Homology

A member of the of AKR1C family proteins; AKR1C1, AKR1C2, AKR1C3, AKR1C4 in human, and AKR1C9 in rat.

Mutations

Note: Mutation of AKR1C3 has not been identified.

Implicated in

Various cancers

Note: Elevated levels of AKR1C3 expression are implicated in leukemia cell differentiation, prostate cancer (in both androgen-dependent and androgen-independent prostate cancer), and endometrial cancer. Expression of AKR1C3 was detected in a patient with myelodysplastic syndrome (MDS, refractory anemia) with progression to acute myelogenous leukemia. Overexpression of AKR1C3 in a human promyelocytic leukemia cell line, HL-60, rendered cells more resistant to all-trans retinoic acid (ATRA) and 1a,25-dihydroxyvitamin D3 induced cell differentiation.

Prostate cancer

Disease

Immunohistochemical staining of human prostate tissues detected negative or low levels of AKR1C3 expression in normal prostate epithelial cells. Strong positive AKR1C3 immunoreactivity was demonstrated in primary and androgen-independent prostate cancers.

Variable increases in AKR1C3 expression were also demonstrated in non-neoplastic changes in the prostate including chronic inflammation, atrophy, and urothelial cell metaplasia.

Endometrial cancer

Disease

Quantitative transcriptosome analysis using real-time polymerase chain reaction, AKR1C3 mRNA expression was shown to be elevated in endometrial cancer versus adjacent normal endometrium.

Breast tumor

Disease

Expression of AKR1C3 mRNA was reduced in breast tumor as compared to adjacent normal breast tissue. Immunohistochemstry revealed that the ductal epithelial cells and stromal cells of the breast express AKR1C3. In myoepithelial cells of the breast, immunoreactive AKR1C3 was absent in normal tissues, whereas strong AKR1C3 staining was apparent in cells surrounding the neoplastic epithelium of ductal carcinoma in situ.

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This article should be referenced as such:

Lin HK. AKR1C3 (aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)). Atlas Genet Cytogenet Oncol Haematol.2008;12(4):267-268.