

## Gene Section Review

# CD44 (CD44 molecule (Indian blood group))

Yin-Ping Sen, George W Yip

Department of Anatomy, Yong Loo Lin School of Medicine, National University of Singapore, 4 Medical Drive, Block MD 10, Singapore 117597 (YPS, GWY)

Published in Atlas Database: March 2009

Online updated version: <http://AtlasGeneticsOncology.org/Genes/CD44ID980CH11p13.html>  
DOI: 10.4267/2042/44676

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.  
© 2010 Atlas of Genetics and Cytogenetics in Oncology and Haematology

### Identity

**Other names:** CD44R; CDW44; CDw44; CSPG8; ECMR-III; Epican; HCELL; HUTCH-I; IN; LHR; MC56; MDU2; MDU3; MGC10468; MIC4; MUTCH-I; PGP-1; PGP-I; Pgp1

**HGNC (Hugo):** CD44

**Location:** 11p13

### DNA/RNA

#### Description

Consists of 20 exons spanning a length of 60 kb. The first five and the last five exons are constant; Exons 1-5 and Exons 15-19 encode the N-terminal (extracellular) and C-terminal (extracellular, transmembrane, and cytoplasmic) domains respectively, and share homologous domains among all the CD44 family members. The ten exons (Exons 5a-14) located between these regions are, however, subjected to alternative splicing, resulting in the generation of CD44 variants.

### Protein

#### Description

742 amino acids.

Apart from alternative splicing, further diversity arises from post-translational modifications with N-

and O-glycosylation and glycosaminoglycanation by heparan sulphate or chondroitin sulphate to generate multiple CD44 isoforms (at least 20 are known) of different molecular sizes (85-230 kDa).

Other post-translational modifications include cleavage by specific proteinases (possibly matrix metalloproteinases) in the extracellular matrix (ECM), (de)phosphorylation (activation of protein kinase C results in dephosphorylation of Ser-706, a constitutive phosphorylation site, and the phospho-rylation of Ser-672).

N-terminal segment interacts with hyaluronan and other glycosaminoglycans, collagen, laminin and fibronectin. C-terminal segment interacts with ANK, ERM proteins (VIL2, RDX and MSN), and NF2.

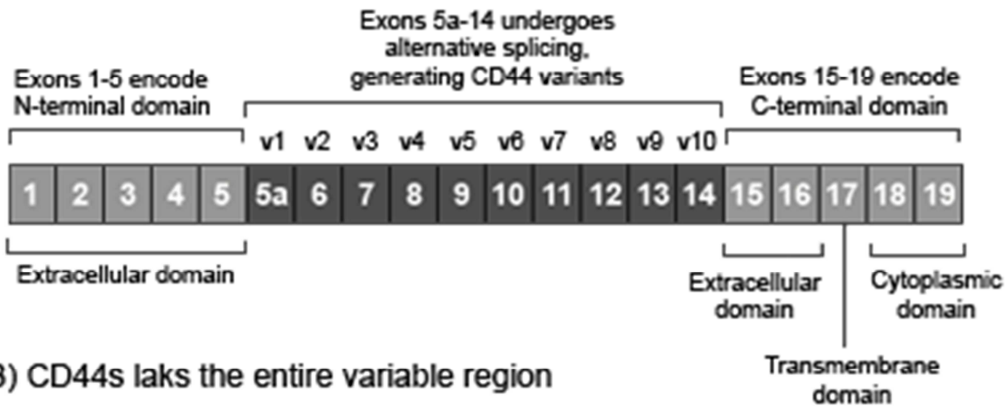
#### Expression

Standard CD44 (CD44s), which is the smallest CD44 molecule (85-95kDa), lacks the entire variable region. It is a single-chain molecule containing several domains: a distal extracellular domain (N-terminal containing the ligand-binding sites), a membrane-proximal region, a transmembrane domain, and a cytoplasmic domain. High interspecies homology among CD44 isoforms is exhibited through these basic domains (with the exception of the membrane-proximal region). As CD44s is mostly expressed on cells of lympho-haematopoietic origin, it is also known as haematopoietic CD44 (CD44H).



CD44 gene is located at chromosome 11 on the short arm (p13).

(A) CD44 gene consists of 20 exons



(B) CD44s lacks the entire variable region

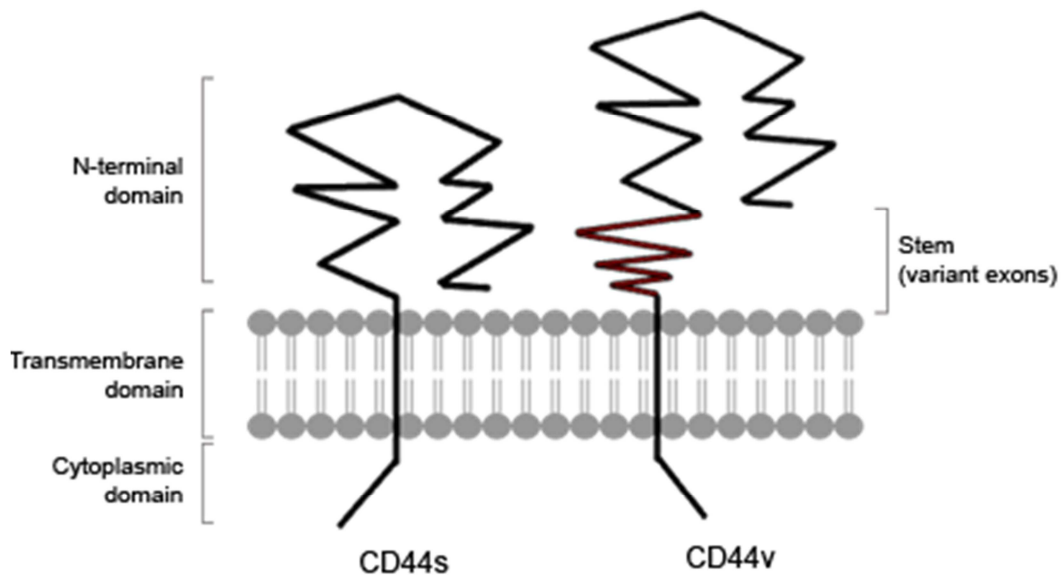


(C) CD44v6 contains variant exon 6



(A) CD44 gene consists of 20 exons. Exons 1-5 and Exons 15-19 encode homologous N-terminal and C-terminal domains respectively. Exons 5a-14 (v1 to v10) generate CD44 variants through alternative splicing. (B) CD44s consists of the homologous domains but lacks the entire variable region. (C) CD44v6 is one example of a CD44 variant isoform which contains the variant Exon 6.

CD44 molecule types and their domains



CD44s consists of the basic domains (and structure) whereas CD44v has an additional longer stem, which contains the variant exon(s).

The CD44 variant isoforms (CD44v) are identified by the presence of variant exon(s). These CD44 variant isoforms can be upregulated by T lymphocytes and other leukocytes after immunological activation. Their expression patterns are tissue specific: CD44 lacking

v2-v10 is the most common form on haematopoietic cells while larger CD44 splice variants dominate on certain normal and neoplastic epithelia, activated lymphocytes and malignant lymphomas. A CD44 isoform consisting of the last three exon products of the

variable region (CD44V8-10) is preferentially expressed on epi-thelial cells, hence it is also called epithelial CD44 or CD44E. In contrast, CD44V3-10, the longest CD44 isoform that expresses eight exons of the variable region, has been observed in keratinocytes.

### **Localisation**

Membrane; single-pass type I membrane protein.

### **Function**

CD44 is a multifunctional receptor which plays a role in cell adhesion (cell-cell and cell-ECM interactions), cell traffic, lymph node homing, presentation of chemokines and growth factors, transmission of growth signals and signals mediating haematopoiesis and apoptosis.

Ligand-binding: The principal ligand of CD44 is HA, an important component of the ECM. CD44 is involved in the uptake and intracellular degradation of HA. Other CD44 ligands include ECM components such as collagen, fibronectin, laminin, and chondroitin sulphate. ECM-unrelated ligands include mucosal addressin, serglycin, osteopontin, and the class II invariant chain.

CD44 expression in tumours: High levels of expression of CD44 have been observed in numerous cancer cell types. Some tumours, such as gliomas, express CD44s only. In contrast, other cancers, including gastrointestinal carcinoma, bladder cancer, uterine cervical cancer, breast carcinoma and non-Hodgkin's lymphomas, express CD44 variants at higher levels. In addition, results from animal studies showed that introduction of CD44s- or CD44v-specific antibodies impeded CD44-ligand interaction and led to inhibition of local tumour growth and distant metastasis. These suggest that CD44 may confer a growth advantage on some tumours and could thus be a target for cancer therapy. In addition, CD44v may be a useful diagnostic marker for some cancers, or a prognostic marker.

## **Implicated in**

### **Breast cancer**

#### **Disease**

Breast cancer is the most common cancer among women globally, with more than 1.1 million women diagnosed each year. It is also the main cause of death from cancer in females worldwide.

Breast cancer can be of the non-invasive type in which the cancer cells are confined within the mammary ducts or lobes. The non invasive type can be further divided into ductal carcinoma in situ and lobular in situ subtypes. In invasive breast carcinoma, cancer cells invade into surrounding tissues and metastasise. Invasive breast cancer constitutes up 70 to 80% of cases of breast cancer, and includes invasive ductal carcinoma and invasive lobular carcinoma.

### **Prognosis**

Depends on tumour size and grade, presence of oestrogen and progesterone receptors, occurrence of nodal/regional metastasis, peritoneal vascular invasion and rate of tumour growth.

CD44+/CD24- breast cancer stem cells have been linked to tumourigenesis and may be associated with poor patient survival rate.

The various CD44 isoforms may play a part in breast cancer prognosis. The loss of CD44s is found to be associated with an increased risk of metastasis. CD44v3 and CD44v6 are positively correlated to breast cancer tumourigenesis and metastasis, and poor patient prognosis. CD44v7-8 has also been shown to be positively associated with poor overall patient survival rate.

### **Cytogenetics**

Chr11 is involved in the chromosomal abnormalities in breast cancer. Comparative genomic hybridisation (CGH) profiles of Chr11 in breast cancer shows lack of changes on the short arm (11p) and frequent gains or losses on the long arm (11q). The distribution of loss of heterozygosity (LOH) regions on Chr11 that were consistently observed includes 11p15.5, 11q13 and 11q23.

### **Oncogenesis**

Different CD44 isoforms are associated with various stages of breast cancer progression. CD44s is downregulated in malignant breast cancer tissues compared against benign breast tissues. Nevertheless, CD44s has been reported to be essential for breast cancer invasion and metastasis to the liver. CD44 with variant exon 4 is upregulated in breast cancer and plays a role in cancer cell migration across endothelial monolayers. Soluble CD44v6 is elevated in cancerous tissues and positively correlated with larger tumour size and lymph node metastasis. Invasive cribriform breast tumours have been observed to have higher expression levels of both CD44v3 and v6, as well as reduced expression of CD44v4. In relation to hormonal receptors, a positive correlation has been reported between CD44v6 and breast carcinoma tissues with higher expression levels of estrogen and progesterone receptors. CD44s and CD44v9 expression levels are positively correlated with breast cancer tissues with elevated expression of estrogen receptors.

### **Prostate cancer**

#### **Disease**

Prostate cancer is currently ranked the fifth most common cancer worldwide. It is usually diagnosed in older men aged 50 years old and above.

Prostate cancer pathological stages range from Stage I, in which the cancer is limited to the prostate gland and the cancer cannot be felt or seen, to Stage IV, in which cancer cells have metastasised to other parts of the body such as the bladder, rectum, lymph nodes or bones.

**Prognosis**

Dependent on cancer staging, Gleason score, PSA level, patient's age and health, and the presence of recurrence.

CD44s and CD44v6 may have prognostic values in determining overall patient survival rate. Loss of CD44s expression has been found to aid in predicting cancer recurrence whereas reduced expression of CD44v6 has been positively correlated with tumour progression and reduced patient survival rate.

**Cytogenetics**

Through cytogenetic methods such as CGH and fluorescence in situ hybridization (FISH), Chr11p13 was reported to be deleted in sporadic prostate tumours. In addition, CD44 was found to be inactivated in both primary and metastatic prostate cancers.

**Oncogenesis**

Compared against benign prostate tissues, significant downregulation of CD44s occurs in prostate cancer. The promoter region of CD44 consisting of a CpG island can undergo hypermethylation at the CpG dinucleotides, leading to transcriptional repression and downregulation of CD44s. On the other hand, CD44 variant isoforms such as CD44v6 and CD44v7-10 are overexpressed in prostate cancer. Increased CD44v6 expression is positively linked with prostate tumour stage and metastasis. Upregulation of CD44v7-10 occurs in both primary and metastatic prostate carcinoma. The variant isoforms make cancer cells bind preferentially to fibronectin rather than to hyaluronan. In addition, CD44 variants can activate matrix metalloproteinase-9, an important step in prostate cancer cell migration.

**Cervical cancer****Disease**

There are two major histopathological subtypes of cervical cancer. Most cervical cancers are squamous cell carcinoma where the tumour develops from squamous cells covering the surface of the exocervix. Adenocarcinoma, originating from mucus-producing cells of the endocervix, accounts for another 10-20% of cases.

**Prognosis**

Depends on cancer stage, presence of metastasis, and the presence of recurrence.

A study showed that patients with early stage cervical cancer without involvement of pelvic lymph nodes but express CD44v6 expression have poor overall survival. Furthermore, patients with CD44v6 expression in metastatic tumours in the pelvic lymph nodes were found, more frequently, to have involvement of at least two pelvic lymph nodes and poorer patient survival rate.

**Cytogenetics**

From an LOH study, it was observed that there were frequent losses of the short arm of Chr11 as well as fewer than expected normal Chr11.

**Oncogenesis**

Exons v6 and v7-8 are promising indicators for identifying patients with increased risk of cervical cancer at an earlier stage. Both have prognostic values, as they are associated with poorer survival rate in patients diagnosed with Stage III cervical cancer.

**Colon cancer****Disease**

Colon cancer is the third most commonly diagnosed cancer worldwide and is the fourth most frequent cause of death from cancer globally. Most colon cancers are adenocarcinomas.

**Prognosis**

Depends on the tumour growth stage, presence of metastasis.

CD44v3, v5, v6, and v8-10 are possible prognostic indicators in colon cancer.

**Cytogenetics**

Gain of Chr11 has been observed in a human colon adenocarcinoma cell line HT29, and may play a part in tumourigenesis and metastasis.

**Oncogenesis**

CD44v isoforms are overexpressed in malignant colon cancer cells. Increased CD44v6 and CD44v8-10 expression were found to enhance HA binding, tumourigenicity and distant metastasis. Co-expression of CD44v3 and heparanase is also associated with metastasis. CD44v5 can serve as an early marker for colon cancer when detected on small dysplastic polyps. Elevated CD44 with Exon v6 is associated with tumour progression and metastasis, and indicates reduced survival probability.

**Rectum cancer****Disease**

The most common form of rectal cancer is adenocarcinoma, which develops from the mucosa. The malignant tumour can metastasise to lymph nodes and other parts of the body.

**Prognosis**

CD44v6 is a promising prognostic factor which may help in predicting overall survival rate.

**Oncogenesis**

In Stage III cancer, CD44v6 is positively linked to locoregional recurrence.

**Brain cancer****Disease**

Brain cancers can generally be classified into primary

brain tumours and secondary brain tumours. Primary brain tumours occur when the tumour begins in the brain tissue and the most common type are gliomas. Secondary brain tumours occur when cancer cells spread from another part of the body to the brain. It is more common than primary brain tumours.

#### **Prognosis**

Depends on the type of brain tumour, size and location of the tumour, grade and stage of the cancer.

#### **Cytogenetics**

From trypsin-Giemsa staining and multicolour FISH, chromosomal aberrations were found on Chr11p in medulloblastoma, a subtype of brain cancer which occurs mainly in children.

#### **Oncogenesis**

In primary brain cancers, CD44 isoforms composed of single-variant Exons v3, v4, v6 or v9 were observed to be weakly expressed. In metastatic brain tumours, CD44 isoforms including those with multiple variant exons were overexpressed. However, it was observed that brain cancer cells that metastasise to the spine were negative for CD44v. Other studies showed that CD44v5/v6 was homogeneously expressed in brain cancer tissues whereas CD44v7-10 expression was upregulated in a fraction of brain tumour cells.

### **Pancreatic cancer**

#### **Disease**

About 95% of pancreatic cancer cases begin in the pancreatic. A rare type of pancreatic cancer is pancreatic islet cell cancer where the tumour occurs in the cells that make insulin and other hormones.

#### **Prognosis**

Depends on cancer stage, whether the cancer is surgically removable, presence of recurrence, and patient's general health.

CD44v2 and v6 may be useful markers of poor prognosis as their expressions were correlated with decreased overall patient survival.

#### **Cytogenetics**

Gain of Chr11q has been observed in CGH.

#### **Oncogenesis**

CD44s, CD44v3, CD44v4 and CD44v6 are expressed at moderate levels in pancreatic tumour cell lines. CD44v7 is expressed at low levels, whereas CD44v7/8 and CD44v10 are expressed in very low amounts. Additionally, CD44v2 is observed only in tumour cells and is associated with vessel invasion.

### **Lung cancer**

#### **Disease**

Lung cancer is the leading cause of cancer death worldwide. The two main types of lung cancer are small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). NSCLC is further subdivided into squamous cell lung carcinoma which originates near central bronchi, adenocarcinoma

(originating from peripheral lung tissues) and large cell lung carcinoma (found near the surface or outer edges of the lung).

#### **Prognosis**

Depends on cancer stage, type of lung cancer, presence of metastasis, presence of recurrence, and general health of the patient.

In NSCLC, high expression of CD44v6 was associated with poor prognosis.

In adenocarcinoma and large cell lung carcinoma, downregulation of CD44s, CD44v3 and v6 were linked to poor patient survival rate.

#### **Cytogenetics**

In SCLC, Chr11 has a frequent breakpoint at 11p11-12 and is often a recipient of translocated material on the short arm. Other translocations and deletions have also been observed on the long arm.

#### **Oncogenesis**

CD44v6 expression is positively linked to metastasis in NSCLC. However, the variant 6 isoform and CD44v3 are negatively correlated with invasion in lung adenocarcinoma. Additionally, both CD44v3 and v6 mRNAs are not always translated into functional proteins due to post-translational disruption in cancer cells.

### **Liver cancer**

#### **Disease**

Liver cancer is ranked among the top ten cancer types worldwide. Hepatocellular carcinoma is the most common type of liver cancer. Other forms include intrahepatic cholangiocarcinoma and fibro-lamellar carcinoma.

#### **Prognosis**

In poorly differentiated hepatocellular carcinoma, CD44 isoforms such as CD44s, v5, v6, v7-8 and v10 are upregulated and associated with poorer overall patient survival rate.

#### **Oncogenesis**

Upregulated CD44v6 expression is coupled with the presence of vascular invasion.

### **Stomach cancer**

#### **Disease**

The most common form of gastric cancer is adenocarcinoma, where the tumour arises from the gastric glands. The malignant cells can invade through the stomach wall and spread to nearby organs and lymph nodes.

#### **Prognosis**

CD44v6 and sCD44v6 are positively correlated with tumour progression in the diffuse type of gastric cancer and lower patient survival rate.

#### **Cytogenetics**

Chr11 is involved in chromosomal abnormalities in gastric carcinoma and correlated with poor prognosis. It was observed in a CGH study that the 11p11.2-14

region, containing the CD44 gene at Chr11p13, was highly amplified.

### Oncogenesis

Serum concentration of soluble CD44 variant 6 isoform is correlated with the depth of invasion and presence of metastatic tumour cells as well as cancer stage in patients with diffuse type gastric cancer. Thus, sCD44v6 may be a valuable prognostic indicator. The ratio of CD44E to CD44H expression in gastric cancer tissues was also observed to be significantly

higher than in non-cancerous tissues. Patients with elevated E/H ratio have reduced survival rates.

CD44v3 showed no association with cancer spread or patient survival.

### Non-Hodgkin Lymphoma (NHL)

#### Disease

NHL is the most common cancer of the lymphatic system with at least 61 subtypes. It is generally divided into B-cell lymphoma and T-cell lymphoma. NHL may occur in lymph nodes, specialised lymphatic organs (such as the spleen) or lymphatic tissues (such as those in the stomach), and is able to spread via the lymphatic vessels and blood stream.

#### Prognosis

The International Prognostic Index (IPI) is a useful method in determining survival outcome of patients with fast-growing lymphomas. The index consists of five factors: the patient's age, lymphoma stage, presence of metastasis, patient's performance status, and serum level of lactate dehydrogenase.

Expressions of serum soluble CD44 at diagnosis as well as CD44 with Exon variant 6 are correlated with lower patient survival rate.

#### Oncogenesis

CD44 with variant Exons 6-10 are elevated in NHL. In vivo studies have indicated that CD44 containing directly-spliced Exon 10 is more highly associated with local tumour development and distant metastasis compared against larger Exon 10-containing variants (for example, CD44ex10-14 and CD44ex7-14) and CD44H.

## References

Wurster-Hill DH, Cannizzaro LA, Pettengill OS, Sorenson GD, Cate CC, Maurer LH. Cytogenetics of small cell carcinoma of the lung. *Cancer Genet Cytogenet.* 1984 Dec;13(4):303-30

Muleris M, Salmon RJ, Dutrillaux B. Cytogenetics of colorectal adenocarcinomas. *Cancer Genet Cytogenet.* 1990 Jun;46(2):143-56

Friedrichs K, Franke F, Lisboa BW, Kügler G, Gille I, Terpe HJ, Hölzel F, Maass H, Günthert U. CD44 isoforms correlate with cellular differentiation but not with prognosis in human breast cancer. *Cancer Res.* 1995 Nov 15;55(22):5424-33

Herrlich P, Pals S, Ponta H. CD44 in colon cancer. *Eur J Cancer.* 1995 Jul-Aug;31A(7-8):1110-2

Kainz C, Kohlberger P, Tempfer C, Sliutz G, Gitsch G, Reinthaller A, Breitenecker G. Prognostic value of CD44 splice variants in human stage III cervical cancer. *Eur J Cancer.* 1995 Sep;31A(10):1706-9

Li H, Liu J, Hofmann M. [Immunohistochemical characterization of CD44 molecules expressed in human brain metastases]. *Zhonghua Zhong Liu Za Zhi.* 1995 Sep;17(5):325-7

Reinthaller A, Kainz C, Kohlberger P, Tempfer C, Gitsch G, Kölbl H, Breitenecker G. [CD44 splice variants as prognostic factors in invasive cervix carcinoma]. *Gynakol Geburtshilfliche Rundsch.* 1995;35(1):16-9

Jones PA. DNA methylation errors and cancer. *Cancer Res.* 1996 Jun 1;56(11):2463-7

Kainz C, Tempfer C, Kohlberger P, Janisch S, Koelbl H, Gitsch G, Breitenecker G. Immunohistochemical detection of adhesion molecule CD44 splice variants in lymph node metastases of cervical cancer. *Int J Cancer.* 1996 Jun 21;69(3):170-3

Atkin NB. Cytogenetics of carcinoma of the cervix uteri: a review. *Cancer Genet Cytogenet.* 1997 May;95(1):33-9

Speiser P, Wanner C, Tempfer C, Mittelböck M, Hanzal E, Bancher-Todesca D, Gitsch G, Reinthaller A, Kainz C. CD44 is an independent prognostic factor in early-stage cervical cancer. *Int J Cancer.* 1997 Apr 22;74(2):185-8

Gotoda T, Matsumura Y, Kokawa A, Kondo H. [The prognostic factors of pancreatic cancer--adhesion molecule CD44]. *Gan To Kagaku Ryoho.* 1998 Nov;25(13):2036-42

Page DL, Jensen RA, Simpson JF. Routinely available indicators of prognosis in breast cancer. *Breast Cancer Res Treat.* 1998;51(3):195-208

Ropponen KM, Eskelinen MJ, Lipponen PK, Alhava E, Kosma VM. Expression of CD44 and variant proteins in human colorectal cancer and its relevance for prognosis. *Scand J Gastroenterol.* 1998 Mar;33(3):301-9

Saito H, Tsujitani S, Katano K, Ikeguchi M, Maeta M, Kaibara N. Serum concentration of CD44 variant 6 and its relation to prognosis in patients with gastric carcinoma. *Cancer.* 1998 Sep 15;83(6):1094-101

Shibuya Y, Okabayashi T, Oda K, Tanaka N. Ratio of CD44 epithelial variant to CD44 hematopoietic variant is a useful prognostic indicator in gastric and colorectal carcinoma. *Jpn J Clin Oncol.* 1998 Oct;28(10):609-14

Yakushijin Y, Steckel J, Kharbanda S, Hasserjian R, Neuberger D, Jiang W, Anderson I, Shipp MA. A directly spliced exon 10-containing CD44 variant promotes the metastasis and homotypic aggregation of aggressive non-Hodgkin's lymphoma. *Blood.* 1998 Jun 1;91(11):4282-91

Yamaguchi A. [Expression of variant CD44 in colorectal cancer and its relationship to liver metastasis]. *Nippon Geka Gakkai Zasshi.* 1998 Jul;99(7):409-14

Bertrand V, Couturier-Turpin MH, Louvel A, Panis Y, Couturier D. Relation between cytogenetic characteristics of two human colonic adenocarcinoma cell lines and their ability to grow locally or metastasize or both: an experimental study in the nude mouse. *Cancer Genet Cytogenet.* 1999 Aug;113(1):36-44

Lou W, Krill D, Dhir R, Becich MJ, Dong JT, Frierson HF Jr, Isaacs WB, Isaacs JT, Gao AC. Methylation of the CD44 metastasis suppressor gene in human prostate cancer. *Cancer Res.* 1999 May 15;59(10):2329-31

Resnick DK, Resnick NM, Welch WC, Cooper DL. Differential expressions of CD44 variants in tumors affecting the central nervous system. *Mol Diagn.* 1999 Sep;4(3):219-32

- Choi SH, Takahashi K, Eto H, Yoon SS, Tanabe KK. CD44s expression in human colon carcinomas influences growth of liver metastases. *Int J Cancer*. 2000 Feb 15;85(4):523-6
- Endo K, Terada T. Protein expression of CD44 (standard and variant isoforms) in hepatocellular carcinoma: relationships with tumor grade, clinicopathologic parameters, p53 expression, and patient survival. *J Hepatol*. 2000 Jan;32(1):78-84
- Fukuda Y, Kurihara N, Imoto I, Yasui K, Yoshida M, Yanagihara K, Park JG, Nakamura Y, Inazawa J. CD44 is a potential target of amplification within the 11p13 amplicon detected in gastric cancer cell lines. *Genes Chromosomes Cancer*. 2000 Dec;29(4):315-24
- Pirinen R, Hirvikoski P, Böhm J, Kellokoski J, Moisio K, Virén M, Johansson R, Hollmén S, Kosma VM. Reduced expression of CD44v3 variant isoform is associated with unfavorable outcome in non-small cell lung carcinoma. *Hum Pathol*. 2000 Sep;31(9):1088-95
- Vis AN, Noordzij MA, Fitoz K, Wildhagen MF, Schröder FH, van der Kwast TH. Prognostic value of cell cycle proteins p27(kip1) and MIB-1, and the cell adhesion protein CD44s in surgically treated patients with prostate cancer. *J Urol*. 2000 Dec;164(6):2156-61
- Aaltomaa S, Lipponen P, Ala-Opas M, Kosma VM. Expression and prognostic value of CD44 standard and variant v3 and v6 isoforms in prostate cancer. *Eur Urol*. 2001 Feb;39(2):138-44
- Ringel J, Jesnowski R, Schmidt C, Ringel J, Köhler HJ, Rychly J, Batra SK, Löhr M. CD44 in normal human pancreas and pancreatic carcinoma cell lines. *Teratog Carcinog Mutagen*. 2001;21(1):97-106
- Setälä L, Lipponen P, Tammi R, Tammi M, Eskelinen M, Alhava E, Kosma VM. Expression of CD44 and its variant isoform v3 has no prognostic value in gastric cancer. *Histopathology*. 2001 Jan;38(1):13-20
- Taçyildiz N, Cavdar AO, Yavuz G, Gözdaşoglu S, Unal E, Ertem U, Duru F, İkinçioğulları A, Babacan E, Kuzu I, Cin S. Serum levels and differential expression of CD44 in childhood leukemia and malignant lymphoma: correlation with prognostic criteria and survival. *Pediatr Int*. 2001 Aug;43(4):354-60
- Tsukuda H, Matsumura Y, Inoue T, Kobayashi Y, Ookawa K, Aoki T, Nebiki H, Yamazaki O, Kondo H, Kakizoe T. Diagnostic application of CD44 variant expression in pancreatic juice for detection of pancreatic neoplasm. *Anticancer Res*. 2001 May-Jun;21(3C):2175-83
- Xin Y, Grace A, Gallagher MM, Curran BT, Leader MB, Kay EW. CD44V6 in gastric carcinoma: a marker of tumor progression. *Appl Immunohistochem Mol Morphol*. 2001 Jun;9(2):138-42
- Akisik E, Bavbek S, Dalay N. CD44 variant exons in leukemia and lymphoma. *Pathol Oncol Res*. 2002;8(1):36-40
- Gao H, Chen H, Zhang Z, Jiang T. [Levels and clinical significance of CD44 (intron 9) and CD44v6 in malignant cerebroma]. *Zhonghua Wai Ke Za Zhi*. 2002 Feb;40(2):94-6
- Kuniyasu H, Chihara Y, Kubozoe T, Takahashi T. Co-expression of CD44v3 and heparanase is correlated with metastasis of human colon cancer. *Int J Mol Med*. 2002 Sep;10(3):333-7
- Popescu NC, Zimonjic DB. Chromosome and gene alterations in breast cancer as markers for diagnosis and prognosis as well as pathogenetic targets for therapy. *Am J Med Genet*. 2002 Oct 30;115(3):142-9
- Qin LX, Tang ZY. The prognostic molecular markers in hepatocellular carcinoma. *World J Gastroenterol*. 2002 Jun;8(3):385-92
- Suzuki H, Yamashiro K. Reduced expression of CD44 v3 and v6 is related to invasion in lung adenocarcinoma. *Lung Cancer*. 2002 Nov;38(2):137-41
- Ryś J, Kruczek A, Lackowska B, Jaszcz-Gruchała A, Brandys A, Stelmach A, Reinfuss M. The role of CD44v3 expression in female breast carcinomas. *Pol J Pathol*. 2003;54(4):243-7
- Yamada Y, Itano N, Narimatsu H, Kudo T, Hirohashi S, Ochiai A, Tohno I, Ueda M, Kimata K. CD44 variant exon 6 expressions in colon cancer assessed by quantitative analysis using real time reverse transcriptase-polymerase chain reaction. *Oncol Rep*. 2003 Nov-Dec;10(6):1919-24
- Zuo W, Li H. [Relationship of the expression of CD44v6 and paxillin to the prognosis of non-small cell lung carcinoma]. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2003 Jul;34(3):484-5
- Lopez JI, Camenisch TD, Stevens MV, Sands BJ, McDonald J, Schroeder JA. CD44 attenuates metastatic invasion during cancer progression. *Cancer Res*. 2005 Aug 1;65(15):6755-63
- Tse GM, Tan PH, Ma TK, Gilks CB, Poon CS, Law BK. CD44s is useful in the differentiation of benign and malignant papillary lesions of the breast. *J Clin Pathol*. 2005 Nov;58(11):1185-8
- Watanabe O, Kinoshita J, Shimizu T, Imamura H, Hirano A, Okabe T, Aiba M, Ogawa K. Expression of a CD44 variant and VEGF-C and the implications for lymphatic metastasis and long-term prognosis of human breast cancer. *J Exp Clin Cancer Res*. 2005 Mar;24(1):75-82
- Götte M, Yip GW. Heparanase, hyaluronan, and CD44 in cancers: a breast carcinoma perspective. *Cancer Res*. 2006 Nov 1;66(21):10233-7
- Le QT, Chen E, Salim A, Cao H, Kong CS, Whyte R, Donington J, Cannon W, Wakelee H, Tibshirani R, Mitchell JD, Richardson D, O'Byrne KJ, Koong AC, Giaccia AJ. An evaluation of tumor oxygenation and gene expression in patients with early stage non-small cell lung cancers. *Clin Cancer Res*. 2006 Mar 1;12(5):1507-14
- Desai B, Rogers MJ, Chellaiiah MA. Mechanisms of osteopontin and CD44 as metastatic principles in prostate cancer cells. *Mol Cancer*. 2007 Mar 7;6:18
- Griffin CA, Morsberger L, Hawkins AL, Haddadin M, Patel A, Ried T, Schrock E, Perlman EJ, Jaffee E. Molecular cytogenetic characterization of pancreas cancer cell lines reveals high complexity chromosomal alterations. *Cytogenet Genome Res*. 2007;118(2-4):148-56
- Holland H, Koschny R, Krupp W, Meixensberger J, Bauer M, Schober R, Kirsten H, Ganten TM, Ahnert P. Cytogenetic and molecular biological characterization of an adult medulloblastoma. *Cancer Genet Cytogenet*. 2007 Oct 15;178(2):104-13
- Ouhtit A, Abd Elmageed ZY, Abdraboh ME, Lioe TF, Raj MH. In vivo evidence for the role of CD44s in promoting breast cancer metastasis to the liver. *Am J Pathol*. 2007 Dec;171(6):2033-9
- Afify A, McNiel MA, Braggin J, Bailey H, Paulino AF. Expression of CD44s, CD44v6, and hyaluronan across the spectrum of normal-hyperplasia-carcinoma in breast. *Appl Immunohistochem Mol Morphol*. 2008 Mar;16(2):121-7
- Gong JF, Yuan YH, Song GH, Yu J, Han Y, Jia J, Ren J. [Pilot study on the correlation between high incidence of

CD44+/CD24 -/low/ABCG2- cells and poor prognosis in breast cancer]. Beijing Da Xue Xue Bao. 2008 Oct 18;40(5):465-70

Hurt EM, Kawasaki BT, Klarmann GJ, Thomas SB, Farrar WL. CD44+ CD24(-) prostate cells are early cancer progenitor/stem cells that provide a model for patients with poor prognosis. Br J Cancer. 2008 Feb 26;98(4):756-65

Mayer S, zur Hausen A, Watermann DO, Stamm S, Jäger M, Gitsch G, Stickeler E. Increased soluble CD44 concentrations are associated with larger tumor size and lymph node metastasis in breast cancer patients. J Cancer Res Clin Oncol. 2008 Nov;134(11):1229-35

Panani AD. Cytogenetic and molecular aspects of gastric cancer: clinical implications. Cancer Lett. 2008 Aug 8;266(2):99-115

Peng J, Lu JJ, Zhu J, Xu Y, Lu H, Lian P, Cai G, Cai S. Prediction of treatment outcome by CD44v6 after total mesorectal excision in locally advanced rectal cancer. Cancer J. 2008 Jan-Feb;14(1):54-61

Robbins EW, Travanty EA, Yang K, Iczkowski KA. MAP kinase pathways and calcitonin influence CD44 alternate isoform expression in prostate cancer cells. BMC Cancer. 2008 Sep 15;8:260

Saleh F, Reno W. Invasive cribriform breast carcinomas in patients with grade 1 and stage IIA (T2 N0 M0) breast cancer strongly express the v3 and v6, but not the v4 isoforms of the metastatic marker CD44. Neoplasma. 2008;55(3):246-55

Zen K, Liu DQ, Guo YL, Wang C, Shan J, Fang M, Zhang CY, Liu Y. CD44v4 is a major E-selectin ligand that mediates breast cancer cell transendothelial migration. PLoS One. 2008 Mar 19;3(3):e1826

---

*This article should be referenced as such:*

Sen YP, Yip GW. CD44 (CD44 molecule (Indian blood group)). Atlas Genet Cytogenet Oncol Haematol. 2010; 14(2):95-102.

---