

Gene Section

Review

DAXX (death-associated protein 6)

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Identity

Other names: BING2; DAP6; EAP1; MGC126245; MGC126246

HGNC (Hugo): DAXX

Location: 6p21.32

DNA/RNA

Description

Daxx gene has 8 exons on chromosome 6. The sizes of the exons are 66, 256, 832, 212, 214, 475, 223 and 191 bps.

Transcription

2,477 bp mRNA.

Two alternative transcripts:

1. Isoform 1 has been chosen as the canonical sequence.
2. Isoform 2 differs from the canonical sequence as follows:
696-740:SSLCIPSPARLSQTPHSQPPRPGTCKTS
VATQCDPEEIVLSDSDPAKNLGRRRSKQDQQG

Protein

Description

740 amino acids, 82.2 kDa; contains in 3 coiled coils (residues 180-217, 358-399 and 430-489), and 2 nuclear localisation signals (residues 391-395 and 628-634).

Expression

Ubiquitous.

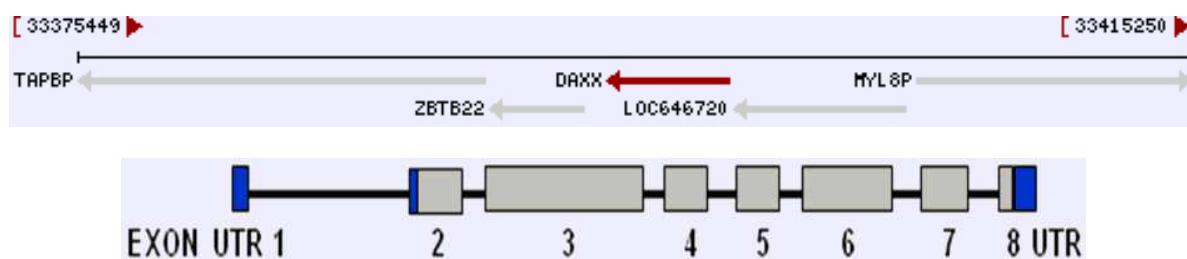
Localisation

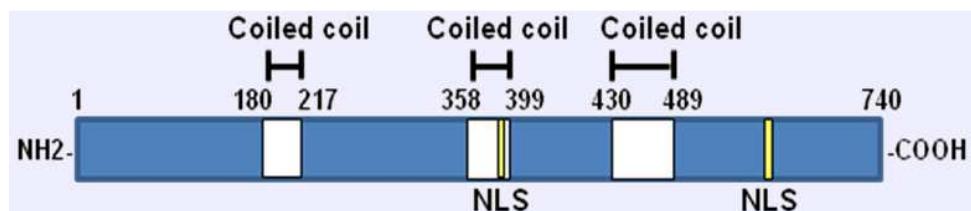
Nucleus and cytoplasm.

Note: Dispersed throughout the nucleoplasm, in PML/POD/ND10 nuclear bodies, and in nucleoli. Colocalizes with a subset of interphase centromeres, but is absent from mitotic centromeres. Detected in the cytoplasmic punctate structures. Translocated from the nucleus to the cytoplasm upon glucose deprivation or ischemic stress.

Function

Interaction with Fas death domain and induces Fas-mediated cell death.





Establishes Fas-Daxx-ASK1-JNK axis.

Implicated in ischemic cell death. Daxx translocates from the nucleus to the cytoplasm upon ischemic stress. Cytoplasmic Daxx interacts with NHE1 and stimulates the NHE1 transporter activity and suppresses the NHE1-ezrin-AKT1 pathway.

Associated with the PML body in the nucleus.

Interacts with SUMO1 and UBC9 and is sumoylated at K630 and 631. However, the sumoylation status does not determine its localization onto the PML body.

Mediates SUMO-dependent transcriptional control and subnuclear compartmentalization.

Suppresses cell death in the early embryo.

Daxx silencing sensitizes cells to Fas- and stress-induced cell death through caspase activation, cytochrome C release and JNK activation.

Homology

Holomogy with Pan troglodytes (99%); Canis lupus familiaris (89%); Bos taurus (83%); Mus musculus (70%); Rattus norvegicus (73%).

Mutations

Note

Substitutions (see the external links).

Implicated in

Promyelocytic leukemia

Disease

Daxx is a component of the promyelocytic leukemia protein (PML) nuclear bodies (NBs).

Alpha-thalassemia

Disease

Daxx complex is a novel ATP-dependent chromatin-remodeling complex, with alpha-thalassaemia syndrome protein (ATRX) being the core ATPase subunit and Daxx being the targeting subunit.

Leukemia

Disease

Daxx protein was expressed in 38.0% of 50 children with acute leukemia, which was significantly higher than that of the control group (5.0%) ($P < 0.05$). Daxx expression is abnormal in children with acute leukemia and associated with some clinical features of acute leukemia, suggesting that it may play an important role in the genesis and development of acute leukemia.

References

- Maruyama K, Sugano S. Oligo-capping: a simple method to replace the cap structure of eukaryotic mRNAs with oligoribonucleotides. *Gene*. 1994 Jan 28;138(1-2):171-4
- Kiriakidou M, Driscoll DA, Lopez-Guisa JM, Strauss JF 3rd. Cloning and expression of primate Daxx cDNAs and mapping of the human gene to chromosome 6p21.3 in the MHC region. *DNA Cell Biol*. 1997 Nov;16(11):1289-98
- Suzuki Y, Yoshitomo-Nakagawa K, Maruyama K, Suyama A, Sugano S. Construction and characterization of a full length-enriched and a 5'-end-enriched cDNA library. *Gene*. 1997 Oct 24;200(1-2):149-56
- Yang X, Khosravi-Far R, Chang HY, Baltimore D. Daxx, a novel Fas-binding protein that activates JNK and apoptosis. *Cell*. 1997 Jun 27;89(7):1067-76
- Chang HY, Nishitoh H, Yang X, Ichijo H, Baltimore D. Activation of apoptosis signal-regulating kinase 1 (ASK1) by the adapter protein Daxx. *Science*. 1998 Sep 18;281(5384):1860-3
- Herberg JA, Beck S, Trowsdale J. TAPASIN, DAXX, RGL2, HKE2 and four new genes (BING 1, 3 to 5) form a dense cluster at the centromeric end of the MHC. *J Mol Biol*. 1998 Apr 10;277(4):839-57
- Herberg JA, Sgouros J, Jones T, Copeman J, Humphray SJ, Sheer D, Cresswell P, Beck S, Trowsdale J. Genomic analysis of the Tapasin gene, located close to the TAP loci in the MHC. *Eur J Immunol*. 1998 Feb;28(2):459-67
- Juo P, Kuo CJ, Yuan J, Blenis J. Essential requirement for caspase-8/FLICE in the initiation of the Fas-induced apoptotic cascade. *Curr Biol*. 1998 Sep 10;8(18):1001-8
- Pluta AF, Earnshaw WC, Goldberg IG. Interphase-specific association of intrinsic centromere protein CENP-C with HDaxx, a death domain-binding protein implicated in Fas-mediated cell death. *J Cell Sci*. 1998 Jul 30;111 (Pt 14):2029-41
- Chang HY, Yang X, Baltimore D. Dissecting Fas signaling with an altered-specificity death-domain mutant: requirement of FADD binding for apoptosis but not Jun N-terminal kinase activation. *Proc Natl Acad Sci U S A*. 1999 Feb 16;96(4):1252-6
- Hollenbach AD, Sublett JE, McPherson CJ, Grosfeld G. The Pax3-FKHR oncogene is unresponsive to the Pax3-associated repressor hDaxx. *EMBO J*. 1999 Jul 1;18(13):3702-11
- Ishov AM, Sotnikov AG, Negorev D, Vladimirova OV, Neff N, Kamitani T, Yeh ET, Strauss JF 3rd, Maul GG. PML is critical for ND10 formation and recruits the PML-interacting protein daxx to this nuclear structure when modified by SUMO-1. *J Cell Biol*. 1999 Oct 18;147(2):221-34
- Michaelson JS, Bader D, Kuo F, Kozak C, Leder P. Loss of Daxx, a promiscuously interacting protein, results in extensive apoptosis in early mouse development. *Genes Dev*. 1999 Aug 1;13(15):1918-23

- Torii S, Egan DA, Evans RA, Reed JC. Human Daxx regulates Fas-induced apoptosis from nuclear PML oncogenic domains (PODs). *EMBO J.* 1999 Nov 1;18(21):6037-49
- Charette SJ, Landry J. The interaction of HSP27 with Daxx identifies a potential regulatory role of HSP27 in Fas-induced apoptosis. *Ann N Y Acad Sci.* 2000;926:126-31
- Charette SJ, Lavoie JN, Lambert H, Landry J. Inhibition of Daxx-mediated apoptosis by heat shock protein 27. *Mol Cell Biol.* 2000 Oct;20(20):7602-12
- Li H, Leo C, Zhu J, Wu X, O'Neil J, Park EJ, Chen JD. Sequestration and inhibition of Daxx-mediated transcriptional repression by PML. *Mol Cell Biol.* 2000 Mar;20(5):1784-96
- Li R, Pei H, Watson DK, Papas TS. EAP1/Daxx interacts with ETS1 and represses transcriptional activation of ETS1 target genes. *Oncogene.* 2000 Feb 10;19(6):745-53
- Rochat-Steiner V, Becker K, Micheau O, Schneider P, Burns K, Tschopp J. FIST/HIPK3: a Fas/FADD-interacting serine/threonine kinase that induces FADD phosphorylation and inhibits fas-mediated Jun NH(2)-terminal kinase activation. *J Exp Med.* 2000 Oct 16;192(8):1165-74
- Ryu SW, Chae SK, Kim E. Interaction of Daxx, a Fas binding protein, with sentrin and Ubc9. *Biochem Biophys Res Commun.* 2000 Dec 9;279(1):6-10
- Villunger A, Huang DC, Holler N, Tschopp J, Strasser A. Fas ligand-induced c-Jun kinase activation in lymphoid cells requires extensive receptor aggregation but is independent of DAXX, and Fas-mediated cell death does not involve DAXX, RIP, or RAIDD. *J Immunol.* 2000 Aug 1;165(3):1337-43
- Zhong S, Salomoni P, Ronchetti S, Guo A, Ruggero D, Pandolfi PP. Promyelocytic leukemia protein (PML) and Daxx participate in a novel nuclear pathway for apoptosis. *J Exp Med.* 2000 Feb 21;191(4):631-40
- Amin HM, Saeed S, Alkan S. Histone deacetylase inhibitors induce caspase-dependent apoptosis and downregulation of daxx in acute promyelocytic leukaemia with t(15;17). *Br J Haematol.* 2001 Nov;115(2):287-97
- Charette SJ, Lambert H, Landry J. A kinase-independent function of Ask1 in caspase-independent cell death. *J Biol Chem.* 2001 Sep 28;276(39):36071-4
- Engelhardt OG, Ullrich E, Kochs G, Haller O. Interferon-induced antiviral Mx1 GTPase is associated with components of the SUMO-1 system and promyelocytic leukemia protein nuclear bodies. *Exp Cell Res.* 2001 Dec 10;271(2):286-95
- Genini D, Sheeter D, Rought S, Zaunders JJ, Susin SA, Kroemer G, Richman DD, Carson DA, Corbeil J, Leoni LM. HIV induces lymphocyte apoptosis by a p53-initiated, mitochondrial-mediated mechanism. *FASEB J.* 2001 Jan;15(1):5-6
- Gongora R, Stephan RP, Zhang Z, Cooper MD. An essential role for Daxx in the inhibition of B lymphopoiesis by type I interferons. *Immunity.* 2001 Jun;14(6):727-37
- Ko YG, Kang YS, Park H, Seol W, Kim J, Kim T, Park HS, Choi EJ, Kim S. Apoptosis signal-regulating kinase 1 controls the proapoptotic function of death-associated protein (Daxx) in the cytoplasm. *J Biol Chem.* 2001 Oct 19;276(42):39103-6
- Lehembre F, Müller S, Pandolfi PP, Dejean A. Regulation of Pax3 transcriptional activity by SUMO-1-modified PML. *Oncogene.* 2001 Jan 4;20(1):1-9
- Perlman R, Schiemann WP, Brooks MW, Lodish HF, Weinberg RA. TGF-beta-induced apoptosis is mediated by the adapter protein Daxx that facilitates JNK activation. *Nat Cell Biol.* 2001 Aug;3(8):708-14
- Sotnikov AG, Negorev D, Ishov AM, Maul GG. [Monoclonal antibodies against protein Daxx and its localization in nuclear domains 10]. *Tsitolgiia.* 2001;43(12):1123-9
- Cermák L, Símová S, Pintzas A, Horejsí V, Andera L. Molecular mechanisms involved in CD43-mediated apoptosis of TF-1 cells. Roles of transcription Daxx expression, and adhesion molecules. *J Biol Chem.* 2002 Mar 8;277(10):7955-61
- Emelyanov AV, Kovac CR, Sepulveda MA, Birshtein BK. The interaction of Pax5 (BSAP) with Daxx can result in transcriptional activation in B cells. *J Biol Chem.* 2002 Mar 29;277(13):11156-64
- Florin L, Schäfer F, Sotlar K, Streeck RE, Sapp M. Reorganization of nuclear domain 10 induced by papillomavirus capsid protein l2. *Virology.* 2002 Mar 30;295(1):97-107
- Hofmann H, Sindre H, Stamminger T. Functional interaction between the pp71 protein of human cytomegalovirus and the PML-interacting protein human Daxx. *J Virol.* 2002 Jun;76(11):5769-83
- Hollenbach AD, McPherson CJ, Mientjes EJ, Iyengar R, Grosveld G. Daxx and histone deacetylase II associate with chromatin through an interaction with core histones and the chromatin-associated protein Dek. *J Cell Sci.* 2002 Aug 15;115(Pt 16):3319-30
- Ishov AM, Vladimirova OV, Maul GG. Daxx-mediated accumulation of human cytomegalovirus tegument protein pp71 at ND10 facilitates initiation of viral infection at these nuclear domains. *J Virol.* 2002 Aug;76(15):7705-12
- Jang MS, Ryu SW, Kim E. Modification of Daxx by small ubiquitin-related modifier-1. *Biochem Biophys Res Commun.* 2002 Jul 12;295(2):495-500
- Lalioti VS, Vergara-Jauregui S, Pulido D, Sandoval IV. The insulin-sensitive glucose transporter, GLUT4, interacts physically with Daxx. Two proteins with capacity to bind Ubc9 and conjugated to SUMO1. *J Biol Chem.* 2002 May 31;277(22):19783-91
- Li XD, Mäkelä TP, Guo D, Soliymani R, Koistinen V, Vapalahti O, Vaheri A, Lankinen H. Hantavirus nucleocapsid protein interacts with the Fas-mediated apoptosis enhancer Daxx. *J Gen Virol.* 2002 Apr;83(Pt 4):759-66
- Lin DY, Shih HM. Essential role of the 58-kDa microspherule protein in the modulation of Daxx-dependent transcriptional repression as revealed by nucleolar sequestration. *J Biol Chem.* 2002 Jul 12;277(28):25446-56
- Lopez P, Jacob RJ, Roizman B. Overexpression of promyelocytic leukemia protein precludes the dispersal of ND10 structures and has no effect on accumulation of infectious herpes simplex virus 1 or its proteins. *J Virol.* 2002 Sep;76(18):9355-67
- Lopez P, Vidal F, Martin L, Lopez-Fernandez LA, Rual JF, Rosen BS, Cuzin F, Rassoulzadegan M. Gene control in germinal differentiation: RNF6, a transcription regulatory protein in the mouse sertoli cell. *Mol Cell Biol.* 2002 May;22(10):3488-96
- Strausberg RL, Feingold EA, Grouse LH, Derge JG, Klausner RD, Collins FS, Wagner L, Shenmen CM, Schuler GD, Altschul SF, Zeeberg B, Buetow KH, Schaefer CF, Bhat NK, Hopkins RF, Jordan H, Moore T, Max SI, Wang J, Hsieh F, Diatchenko L, Marusina K, Farmer AA, Rubin GM, Hong L, Stapleton M, Soares MB, Bonaldo MF, Casavant TL, Scheetz TE, Brownstein MJ, Usdin TB, Toshiyuki S, Carninci P, Prange C, Raha SS, Loquellano NA, Peters GJ, Abramson RD, Mullany

SJ, Bosak SA, McEwan PJ, McKernan KJ, Malek JA, Gunaratne PH, Richards S, Worley KC, Hale S, Garcia AM, Gay LJ, Hulyk SW, Villalon DK, Muzny DM, Sodergren EJ, Lu X, Gibbs RA, Fahey J, Helton E, Ketteman M, Madan A, Rodrigues S, Sanchez A, Whiting M, Madan A, Young AC, Shevchenko Y, Bouffard GG, Blakesley RW, Touchman JW, Green ED, Dickson MC, Rodriguez AC, Grimwood J, Schmutz J, Myers RM, Butterfield YS, Krzywinski MI, Skalska U, Smailus DE, Scherch A, Schein JE, Jones SJ, Marra MA. Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences. *Proc Natl Acad Sci U S A*. 2002 Dec 24;99(26):16899-903

Wu S, Loke HN, Rehemtulla A. Ultraviolet radiation-induced apoptosis is mediated by Daxx. *Neoplasia*. 2002 Nov-Dec;4(6):486-92

Yeoh EJ, Ross ME, Shurtleff SA, Williams WK, Patel D, Mahfouz R, Behm FG, Raimondi SC, Relling MV, Patel A, Cheng C, Campana D, Wilkins D, Zhou X, Li J, Liu H, Pui CH, Evans WE, Naeve C, Wong L, Downing JR. Classification, subtype discovery, and prediction of outcome in pediatric acute lymphoblastic leukemia by gene expression profiling. *Cancer Cell*. 2002 Mar;1(2):133-43

Becker KA, Florin L, Sapp C, Sapp M. Dissection of human papillomavirus type 33 L2 domains involved in nuclear domains (ND) 10 homing and reorganization. *Virology*. 2003 Sep 15;314(1):161-7

Chen LY, Chen JD. Daxx silencing sensitizes cells to multiple apoptotic pathways. *Mol Cell Biol*. 2003 Oct;23(20):7108-21

Chow KU, Nowak D, Boehrer S, Ruthardt M, Knau A, Hoelzer D, Mitrou PS, Weidmann E. Synergistic effects of chemotherapeutic drugs in lymphoma cells are associated with down-regulation of inhibitor of apoptosis proteins (IAPs), prostate-apoptosis-response-gene 4 (Par-4), death-associated protein (Daxx) and with enforced caspase activation. *Biochem Pharmacol*. 2003 Sep 1;66(5):711-24

Ecsedy JA, Michaelson JS, Leder P. Homeodomain-interacting protein kinase 1 modulates Daxx localization, phosphorylation, and transcriptional activity. *Mol Cell Biol*. 2003 Feb;23(3):950-60

Hofmann TG, Stollberg N, Schmitz ML, Will H. HIPK2 regulates transforming growth factor-beta-induced c-Jun NH(2)-terminal kinase activation and apoptosis in human hepatoma cells. *Cancer Res*. 2003 Dec 1;63(23):8271-7

Kawai T, Akira S, Reed JC. ZIP kinase triggers apoptosis from nuclear PML oncogenic domains. *Mol Cell Biol*. 2003 Sep;23(17):6174-86

Kim EJ, Park JS, Um SJ. Identification of Daxx interacting with p73, one of the p53 family, and its regulation of p53 activity by competitive interaction with PML. *Nucleic Acids Res*. 2003 Sep 15;31(18):5356-67

Kim YY, Park BJ, Seo GJ, Lim JY, Lee SM, Kimm KC, Park C, Kim J, Park SI. Long form of cellular FLICE-inhibitory protein interacts with Daxx and prevents Fas-induced JNK activation. *Biochem Biophys Res Commun*. 2003 Dec 12;312(2):426-33

Lin DY, Lai MZ, Ann DK, Shih HM. Promyelocytic leukemia protein (PML) functions as a glucocorticoid receptor co-activator by sequestering Daxx to the PML oncogenic domains (PODs) to enhance its transactivation potential. *J Biol Chem*. 2003 May 2;278(18):15958-65

Michaelson JS, Leder P. RNAi reveals anti-apoptotic and transcriptionally repressive activities of DAXX. *J Cell Sci*. 2003 Jan 15;116(Pt 2):345-52

Mungall AJ, Palmer SA, Sims SK, Edwards CA, Ashurst JL, Wilming L, Jones MC, Horton R, Hunt SE, Scott CE, Gilbert JG, Clamp ME, Bethel G, Milne S, Ainscough R, Almeida JP,

Ambrose KD, Andrews TD, Ashwell RI, Babbage AK, Bagguley CL, Bailey J, Banerjee R, Barker DJ, Barlow KF, Bates K, Beare DM, Beasley H, Beasley O, Bird CP, Blakey S, Bray-Allen S, Brook J, Brown AJ, Brown JY, Burford DC, Burrill W, Burton J, Carder C, Carter NP, Chapman JC, Clark SY, Clark G, Clees CM, Clegg S, Cobley V, Collier RE, Collins JE, Colman LK, Corby NR, Coville GJ, Culley KM, Dhami P, Davies J, Dunn M, Earthrow ME, Ellington AE, Evans KA, Faulkner L, Francis MD, Frankish A, Frankland J, French L, Garner P, Garnett J, Ghori MJ, Gilby LM, Gillison CJ, Glithero RJ, Graham DV, Grant M, Gribble S, Griffiths C, Griffiths M, Hall R, Halls KS, Hammond S, Harley JL, Hart EA, Heath PD, Heathcott R, Holmes SJ, Howden PJ, Howe KL, Howell GR, Huckle E, Humphray SJ, Humphries MD, Hunt AR, Johnson CM, Joy AA, Kay M, Keenan SJ, Kimberley AM, King A, Laird GK, Langford C, Lawlor S, Leongamornlert DA, Leversha M, Lloyd CR, Lloyd DM, Loveland JE, Lovell J, Martin S, Mashreghi-Mohammadi M, Maslen GL, Matthews L, McCann OT, McLaren SJ, McLay K, McMurray A, Moore MJ, Mullikin JC, Niblett D, Nickerson T, Novik KL, Oliver K, Overton-Larty EK, Parker A, Patel R, Pearce AV, Peck AI, Phillimore B, Phillips S, Plumb RW, Porter KM, Ramsey Y, Ranby SA, Rice CM, Ross MT, Searle SM, Sehra HK, Sheridan E, Skuce CD, Smith S, Smith M, Spraggan L, Squares SL, Steward CA, Sycamore N, Tamlyn-Hall G, Tester J, Theaker AJ, Thomas DW, Thorpe A, Tracey A, Tromans A, Tubby B, Wall M, Wallis JM, West AP, White SS, Whitehead SL, Whittaker H, Wild A, Willey DJ, Wilmer TE, Wood JM, Wray PW, Wyatt JC, Young L, Younger RM, Bentley DR, Coulson A, Durbin R, Hubbard T, Sulston JE, Dunham I, Rogers J, Beck S. The DNA sequence and analysis of human chromosome 6. *Nature*. 2003 Oct 23;425(6960):805-11

Ohiro Y, Usheva A, Kobayashi S, Duffy SL, Nantz R, Gius D, Horikoshi N. Inhibition of stress-inducible kinase pathways by tumorigenic mutant p53. *Mol Cell Biol*. 2003 Jan;23(1):322-34

Reuter TY, Medhurst AL, Waisfisz Q, Zhi Y, Herterich S, Hoehn H, Gross HJ, Joenje H, Hoatlin ME, Mathew CG, Huber PA. Yeast two-hybrid screens imply involvement of Fanconi anemia proteins in transcription regulation, cell signaling, oxidative metabolism, and cellular transport. *Exp Cell Res*. 2003 Oct 1;289(2):211-21

Song JJ, Lee YJ. Effect of glucose concentration on activation of the ASK1-SEK1-JNK1 signal transduction pathway. *J Cell Biochem*. 2003 Jul 1;89(4):653-62

Song JJ, Lee YJ. Role of the ASK1-SEK1-JNK1-HIPK1 signal in Daxx trafficking and ASK1 oligomerization. *J Biol Chem*. 2003 Nov 21;278(47):47245-52

Song JJ, Lee YJ. Catalase, but not MnSOD, inhibits glucose deprivation-activated ASK1-MEK-MAPK signal transduction pathway and prevents relocalization of Daxx: hydrogen peroxide as a major second messenger of metabolic oxidative stress. *J Cell Biochem*. 2003 Oct 1;90(2):304-14

Xue Y, Gibbons R, Yan Z, Yang D, McDowell TL, Sechi S, Qin J, Zhou S, Higgs D, Wang W. The ATRX syndrome protein forms a chromatin-remodeling complex with Daxx and localizes in promyelocytic leukemia nuclear bodies. *Proc Natl Acad Sci U S A*. 2003 Sep 16;100(19):10635-40

Zhao LY, Colosimo AL, Liu Y, Wan Y, Liao D. Adenovirus E1B 55-kilodalton oncoprotein binds to Daxx and eliminates enhancement of p53-dependent transcription by Daxx. *J Virol*. 2003 Nov;77(21):11809-21

Beausoleil SA, Jedrychowski M, Schwartz D, Elias JE, Villén J, Li J, Cohn MA, Cantley LC, Gygi SP. Large-scale characterization of HeLa cell nuclear phosphoproteins. *Proc Natl Acad Sci U S A*. 2004 Aug 17;101(33):12130-5

Becker KA, Florin L, Sapp C, Maul GG, Sapp M. Nuclear localization but not PML protein is required for incorporation of

the papillomavirus minor capsid protein L2 into virus-like particles. *J Virol.* 2004 Feb;78(3):1121-8

Boehler S, Brieger A, Schaaf S, Kukoc-Zivojinov N, Nowak D, Ruthardt M, Hoelzer D, Mitrou PS, Weidmann E, Chow KU. In the erythroleukemic cell line HEL Prostate-apoptosis-response-gene-4 (par-4) fails to down-regulate Bcl-2 and to promote apoptosis. *Leuk Lymphoma.* 2004 Jul;45(7):1445-51

Boehler S, Nowak D, Schaaf S, Bergmann M, Brieger A, Hoelzer D, Mitrou PS, Weidmann E, Chow KU. In malignant myeloid cells expression of Daxx downregulates expression of p53 and of the inhibitors of apoptosis proteins. *Hematol J.* 2004;5(6):513-8

Brieger A, Boehler S, Schaaf S, Nowak D, Ruthardt M, Kim SZ, Atadja P, Hoelzer D, Mitrou PS, Weidmann E, Chow KU. In bcr-abl-positive myeloid cells resistant to conventional chemotherapeutic agents, expression of Par-4 increases sensitivity to imatinib (ST1571) and histone deacetylase-inhibitors. *Biochem Pharmacol.* 2004 Jul 1;68(1):85-93

Cho S, Ko HM, Kim JM, Lee JA, Park JE, Jang MS, Park SG, Lee DH, Ryu SE, Park BC. Positive regulation of apoptosis signal-regulating kinase 1 by hD53L1. *J Biol Chem.* 2004 Apr 16;279(16):16050-6

Gerhard DS, Wagner L, Feingold EA, Shenmen CM, Grouse LH, Schuler G, Klein SL, Old S, Rasooly R, Good P, Guyer M, Peck AM, Derge JG, Lipman D, Collins FS, Jang W, Sherry S, Feolo M, Misquitta L, Lee E, Rotmistrovsky K, Greenhut SF, Schaefer CF, Buetow K, Bonner TI, Haussler D, Kent J, Kiekhaus M, Furey T, Brent M, Prange C, Schreiber K, Shapiro N, Bhat NK, Hopkins RF, Hsie F, Driscoll T, Soares MB, Casavant TL, Scheetz TE, Brown-Stein MJ, Usdin TB, Toshiyuki S, Carninci P, Piao Y, Dudekula DB, Ko MS, Kawakami K, Suzuki Y, Sugano S, Gruber CE, Smith MR, Simmons B, Moore T, Waterman R, Johnson SL, Ruan Y, Wei CL, Mathavan S, Gunaratne PH, Wu J, Garcia AM, Hulyk SW, Fuh E, Yuan Y, Snead A, Kowis C, Hodgson A, Muzny DM, McPherson J, Gibbs RA, Fahey J, Helton E, Ketteman M, Madan A, Rodrigues S, Sanchez A, Whiting M, Madari A, Young AC, Wetherby KD, Granite SJ, Kwong PN, Brinkley CP, Pearson RL, Bouffard GG, Blakesley RW, Green ED, Dickson MC, Rodriguez AC, Grimwood J, Schmutz J, Myers RM, Butterfield YS, Griffith M, Griffith OL, Krzywinski MI, Liao N, Morin R, Palmquist D, Petrescu AS, Skalska U, Smailus DE, Stott JM, Schnurch A, Schein JE, Jones SJ, Holt RA, Baross A, Marra MA, Clifton S, Makowski KA, Bosak S, Malek J. The status, quality, and expansion of the NIH full-length cDNA project: the Mammalian Gene Collection (MGC). *Genome Res.* 2004 Oct;14(10B):2121-7

Gostissa M, Morelli M, Mantovani F, Guida E, Piazza S, Collavin L, Brancolini C, Schneider C, Del Sal G. The transcriptional repressor hDaxx potentiates p53-dependent apoptosis. *J Biol Chem.* 2004 Nov 12;279(46):48013-23

Ishov AM, Vladimirova OV, Maul GG. Heterochromatin and ND10 are cell-cycle regulated and phosphorylation-dependent alternate nuclear sites of the transcription repressor Daxx and SWI/SNF protein ATRX. *J Cell Sci.* 2004 Aug 1;117(Pt 17):3807-20

La M, Kim K, Park J, Won J, Lee JH, Fu YM, Meadows GG, Joe CO. Daxx-mediated transcriptional repression of MMP1 gene is reversed by SPOP. *Biochem Biophys Res Commun.* 2004 Jul 30;320(3):760-5

Lin DY, Fang HI, Ma AH, Huang YS, Pu YS, Jenster G, Kung HJ, Shih HM. Negative modulation of androgen receptor transcriptional activity by Daxx. *Mol Cell Biol.* 2004 Dec;24(24):10529-41

Mo YY, Yu Y, Ee PL, Beck WT. Overexpression of a dominant-negative mutant Ubc9 is associated with increased sensitivity to anticancer drugs. *Cancer Res.* 2004 Apr 15;64(8):2793-8

Muromoto R, Sugiyama K, Takachi A, Imoto S, Sato N, Yamamoto T, Oritani K, Shimoda K, Matsuda T. Physical and functional interactions between Daxx and DNA methyltransferase 1-associated protein, DMAP1. *J Immunol.* 2004 Mar 1;172(5):2985-93

Muromoto R, Sugiyama K, Yamamoto T, Oritani K, Shimoda K, Matsuda T. Physical and functional interactions between Daxx and TSG101. *Biochem Biophys Res Commun.* 2004 Apr 9;316(3):827-33

Song JJ, Lee YJ. Tryptophan 621 and serine 667 residues of Daxx regulate its nuclear export during glucose deprivation. *J Biol Chem.* 2004 Jul 16;279(29):30573-8

Song JJ, Lee YJ. Daxx deletion mutant (amino acids 501-625)-induced apoptosis occurs through the JNK/p38-Bax-dependent mitochondrial pathway. *J Cell Biochem.* 2004 Aug 15;92(6):1257-70

Takahashi Y, Lallemand-Breitenbach V, Zhu J, de Thé H. PML nuclear bodies and apoptosis. *Oncogene.* 2004 Apr 12;23(16):2819-24

Tang J, Wu S, Liu H, Stratt R, Barak OG, Shiekhattar R, Picketts DJ, Yang X. A novel transcription regulatory complex containing death domain-associated protein and the ATR-X syndrome protein. *J Biol Chem.* 2004 May 7;279(19):20369-77

Alkan S, Huang Q, Ergin M, Denning MF, Nand S, Maududi T, Paner GP, Ozpuyan F, Izban KF. Survival role of protein kinase C (PKC) in chronic lymphocytic leukemia and determination of isoform expression pattern and genes altered by PKC inhibition. *Am J Hematol.* 2005 Jun;79(2):97-106

Boehler S, Nowak D, Hochmuth S, Kim SZ, Treppohl B, Afkir A, Hoelzer D, Mitrou PS, Weidmann E, Chow KU. Daxx overexpression in T-lymphoblastic Jurkat cells enhances caspase-dependent death receptor- and drug-induced apoptosis in distinct ways. *Cell Signal.* 2005 May;17(5):581-95

Boehler S, Nowak D, Kukoc-Zivojinov N, Hochmuth S, Kim SZ, Hoelzer D, Mitrou PS, Weidmann E, Chow KU. Expression of Daxx sensitizes Jurkat T-cells to the apoptosis-inducing effect of chemotherapeutic agents. *Pharmacol Res.* 2005 Apr;51(4):367-74

Cantrell SR, Bresnahan WA. Interaction between the human cytomegalovirus UL82 gene product (pp71) and hDaxx regulates immediate-early gene expression and viral replication. *J Virol.* 2005 Jun;79(12):7792-802

Chang CC, Lin DY, Fang HI, Chen RH, Shih HM. Daxx mediates the small ubiquitin-like modifier-dependent transcriptional repression of Smad4. *J Biol Chem.* 2005 Mar 18;280(11):10164-73

Greger JG, Katz RA, Ishov AM, Maul GG, Skalka AM. The cellular protein daxx interacts with avian sarcoma virus integrase and viral DNA to repress viral transcription. *J Virol.* 2005 Apr;79(8):4610-8

Hwang JR, Zhang C, Patterson C. C-terminus of heat shock protein 70-interacting protein facilitates degradation of apoptosis signal-regulating kinase 1 and inhibits apoptosis signal-regulating kinase 1-dependent apoptosis. *Cell Stress Chaperones.* 2005 Summer;10(2):147-56

Ishida N, Oritani K, Shiraga M, Yoshida H, Kawamoto S, Ujii H, Masaie H, Ichii M, Tomiyama Y, Kanakura Y. Differential effects of a novel IFN-zeta/limitin and IFN-alpha on signals for Daxx induction and Crk phosphorylation that couple with growth control of megakaryocytes. *Exp Hematol.* 2005 Apr;33(4):495-503

Junn E, Taniguchi H, Jeong BS, Zhao X, Ichijo H, Mouradian MM. Interaction of DJ-1 with Daxx inhibits apoptosis signal-

- regulating kinase 1 activity and cell death. *Proc Natl Acad Sci U S A.* 2005 Jul 5;102(27):9691-6
- Khelifi AF, D'Alcontres MS, Salomoni P. Daxx is required for stress-induced cell death and JNK activation. *Cell Death Differ.* 2005 Jul;12(7):724-33
- Kim KS, Hwang HA, Chae SK, Ha H, Kwon KS. Upregulation of Daxx mediates apoptosis in response to oxidative stress. *J Cell Biochem.* 2005 Oct 1;96(2):330-8
- Kuo HY, Chang CC, Jeng JC, Hu HM, Lin DY, Maul GG, Kwok RP, Shih HM. SUMO modification negatively modulates the transcriptional activity of CREB-binding protein via the recruitment of Daxx. *Proc Natl Acad Sci U S A.* 2005 Nov 22;102(47):16973-8
- Song JJ, Lee YJ. Dissociation of Akt1 from its negative regulator JIP1 is mediated through the ASK1-MEK-JNK signal transduction pathway during metabolic oxidative stress: a negative feedback loop. *J Cell Biol.* 2005 Jul 4;170(1):61-72
- Tang J, Chang HY, Yang X. The death domain-associated protein modulates activity of the transcription co-factor Skip/NcoA62. *FEBS Lett.* 2005 May 23;579(13):2883-90
- Cantrell SR, Bresnahan WA. Human cytomegalovirus (HCMV) UL82 gene product (pp71) relieves hDaxx-mediated repression of HCMV replication. *J Virol.* 2006 Jun;80(12):6188-91
- Chen A, Wang PY, Yang YC, Huang YH, Yeh JJ, Chou YH, Cheng JT, Hong YR, Li SS. SUMO regulates the cytoplasmomonuclear transport of its target protein Daxx. *J Cell Biochem.* 2006 Jul 1;98(4):895-911
- Chen JZ, Ji CN, Xu GL, Pang RY, Yao JH, Zhu HZ, Xue JL, Jia W. DAXX interacts with phage PhiC31 integrase and inhibits recombination. *Nucleic Acids Res.* 2006;34(21):6298-304
- Chen XH, Gao RL, Zhen ZY, Qian XD, Xu WH. [Expression of apoptosis-related proteins in the human bone marrow hematopoietic cells treated by Panax Notoginsides]. *Zhongguo Shi Yan Xue Ye Xue Za Zhi.* 2006 Apr;14(2):343-6
- Croxton R, Puto LA, de Belle I, Thomas M, Torii S, Hanai F, Cuddy M, Reed JC. Daxx represses expression of a subset of antiapoptotic genes regulated by nuclear factor-kappaB. *Cancer Res.* 2006 Sep 15;66(18):9026-35
- Ha WY, Li XJ, Yue PY, Wong DY, Yue KK, Chung WS, Zhao L, Leung PY, Liu L, Wong RN. Gene expression profiling of human synovial sarcoma cell line (HS701.T) in response to IL-1 β stimulation. *Inflamm Res.* 2006 Jul;55(7):293-9
- Kitagawa D, Kajihara H, Negishi T, Ura S, Watanabe T, Wada T, Ichijo H, Katada T, Nishina H. Release of RASSF1C from the nucleus by Daxx degradation links DNA damage and SAPK/JNK activation. *EMBO J.* 2006 Jul 26;25(14):3286-97
- Kwon JE, La M, Oh KH, Oh YM, Kim GR, Seol JH, Baek SH, Chiba T, Tanaka K, Bang OS, Joe CO, Chung CH. BTB domain-containing speckle-type POZ protein (SPOP) serves as an adaptor of Daxx for ubiquitination by Cul3-based ubiquitin ligase. *J Biol Chem.* 2006 May 5;281(18):12664-72
- Lemos TA, Kobarg J. CGI-55 interacts with nuclear proteins and co-localizes to p80-coilin positive-coiled bodies in the nucleus. *Cell Biochem Biophys.* 2006;44(3):463-74
- Leroy C, Deheuninck J, Revenueau S, Foveau B, Ji Z, Villenot C, Quieff S, Tulasne D, Kerckaert JP, Fafeur V. HGF/SF regulates expression of apoptotic genes in MCF-10A human mammary epithelial cells. *Ann N Y Acad Sci.* 2006 Dec;1090:188-202
- Li XJ, Yue PY, Ha WY, Wong DY, Tin MM, Wang PX, Wong RN, Liu L. Effect of sinomenine on gene expression of the IL-1 beta-activated human synovial sarcoma. *Life Sci.* 2006 Jul 10;79(7):665-73
- Lin DY, Huang YS, Jeng JC, Kuo HY, Chang CC, Chao TT, Ho CC, Chen YC, Lin TP, Fang HI, Hung CC, Suen CS, Hwang MJ, Chang KS, Maul GG, Shih HM. Role of SUMO-interacting motif in Daxx SUMO modification, subnuclear localization, and repression of sumoylated transcription factors. *Mol Cell.* 2006 Nov 3;24(3):341-54
- Murakami Y, Yamagoe S, Noguchi K, Takebe Y, Takahashi N, Uehara Y, Fukazawa H. Ets-1-dependent expression of vascular endothelial growth factor receptors is activated by latency-associated nuclear antigen of Kaposi's sarcoma-associated herpesvirus through interaction with Daxx. *J Biol Chem.* 2006 Sep 22;281(38):28113-21
- Muromoto R, Ishida M, Sugiyama K, Sekine Y, Oritani K, Shimoda K, Matsuda T. Sumoylation of Daxx regulates IFN-induced growth suppression of B lymphocytes and the hormone receptor-mediated transactivation. *J Immunol.* 2006 Jul 15;177(2):1160-70
- Muromoto R, Nakao K, Watanabe T, Sato N, Sekine Y, Sugiyama K, Oritani K, Shimoda K, Matsuda T. Physical and functional interactions between Daxx and STAT3. *Oncogene.* 2006 Mar 30;25(14):2131-6
- Nery FC, Rui E, Kuniyoshi TM, Kobarg J. Evidence for the interaction of the regulatory protein Ki-1/57 with p53 and its interacting proteins. *Biochem Biophys Res Commun.* 2006 Mar 17;341(3):847-55
- Olsen JV, Blagoev B, Gnad F, Macek B, Kumar C, Mortensen P, Mann M. Global, in vivo, and site-specific phosphorylation dynamics in signaling networks. *Cell.* 2006 Nov 3;127(3):635-48
- Preston CM, Nicholl MJ. Role of the cellular protein hDaxx in human cytomegalovirus immediate-early gene expression. *J Gen Virol.* 2006 May;87(Pt 5):1113-21
- Saffert RT, Kalejta RF. Inactivating a cellular intrinsic immune defense mediated by Daxx is the mechanism through which the human cytomegalovirus pp71 protein stimulates viral immediate-early gene expression. *J Virol.* 2006 Apr;80(8):3863-71
- Salomoni P, Khelifi AF. Daxx: death or survival protein? *Trends Cell Biol.* 2006 Feb;16(2):97-104
- Tzeng SL, Cheng YW, Li CH, Lin YS, Hsu HC, Kang JJ. Physiological and functional interactions between Tcf4 and Daxx in colon cancer cells. *J Biol Chem.* 2006 Jun 2;281(22):15405-11
- Woodhall DL, Groves IJ, Reeves MB, Wilkinson G, Sinclair JH. Human Daxx-mediated repression of human cytomegalovirus gene expression correlates with a repressive chromatin structure around the major immediate early promoter. *J Biol Chem.* 2006 Dec 8;281(49):37652-60
- Everett RD, Murray J, Orr A, Preston CM. Herpes simplex virus type 1 genomes are associated with ND10 nuclear substructures in quiescently infected human fibroblasts. *J Virol.* 2007 Oct;81(20):10991-1004
- Groves IJ, Sinclair JH. Knockdown of hDaxx in normally non-permissive undifferentiated cells does not permit human cytomegalovirus immediate-early gene expression. *J Gen Virol.* 2007 Nov;88(Pt 11):2935-40
- Hwang J, Kalejta RF. Proteasome-dependent, ubiquitin-independent degradation of Daxx by the viral pp71 protein in human cytomegalovirus-infected cells. *Virology.* 2007 Oct 25;367(2):334-8
- Jung YS, Kim HY, Lee YJ, Kim E. Subcellular localization of Daxx determines its opposing functions in ischemic cell death. *FEBS Lett.* 2007 Mar 6;581(5):843-52

- Limjindaporn T, Netsawang J, Noisakran S, Thiemmeca S, Wongwiwat W, Sudsaward S, Avirutnan P, Puttikhunt C, Kasinerk W, Sriburi R, Sittisombut N, Yenchitsomanus PT, Malasit P. Sensitization to Fas-mediated apoptosis by dengue virus capsid protein. *Biochem Biophys Res Commun.* 2007 Oct 19;362(2):334-9
- Lin SC, Li Q. Axin bridges Daxx to p53. *Cell Res.* 2007 Apr;17(4):301-2
- Lindsay CR, Scholz A, Morozov VM, Ishov AM. Daxx shortens mitotic arrest caused by paclitaxel. *Cell Cycle.* 2007 May 15;6(10):1200-4
- Liu J, Zhang LQ, Hu Q, Lin HH, Liu AG, Tao HF, Song YQ, Zhang XL. [Expression of Daxx in children with acute leukemia]. *Zhongguo Dang Dai Er Ke Za Zhi.* 2007 Feb;9(1):33-6
- Meinecke I, Cinski A, Baier A, Peters MA, Dankbar B, Wille A, Drynda A, Mendoza H, Gay RE, Hay RT, Ink B, Gay S, Pap T. Modification of nuclear PML protein by SUMO-1 regulates Fas-induced apoptosis in rheumatoid arthritis synovial fibroblasts. *Proc Natl Acad Sci U S A.* 2007 Mar 20;104(12):5073-8
- Park J, Lee JH, La M, Jang MJ, Chae GW, Kim SB, Tak H, Jung Y, Byun B, Ahn JK, Joe CO. Inhibition of NF-kappaB acetylation and its transcriptional activity by Daxx. *J Mol Biol.* 2007 Apr 27;368(2):388-97
- Ryo A, Hirai A, Nishi M, Liou YC, Perrem K, Lin SC, Hirano H, Lee SW, Aoki I. A suppressive role of the prolyl isomerase Pin1 in cellular apoptosis mediated by the death-associated protein Daxx. *J Biol Chem.* 2007 Dec 14;282(50):36671-81
- Saffert RT, Kalejta RF. Human cytomegalovirus gene expression is silenced by Daxx-mediated intrinsic immune defense in model latent infections established in vitro. *J Virol.* 2007 Sep;81(17):9109-20
- Shih HM, Chang CC, Kuo HY, Lin DY. Daxx mediates SUMO-dependent transcriptional control and subnuclear compartmentalization. *Biochem Soc Trans.* 2007 Dec;35(Pt 6):1397-400
- Su B, Yang YB, Tuo QH, Zhu BY, Lei XY, Yin W, Liao DF. Anti-apoptotic effects of probucol are associated with downregulation of Daxx expression in THP-1 macrophage. *Cardiovasc Drugs Ther.* 2007 Feb;21(1):37-45
- van der Slik AR, van den Eng I, Eerligh P, Doxiadis II, Koeleman BP, Roep BO, Giphart MJ. Sequence variation within the major histocompatibility complex subregion centromeric of HLA class II in type 1 diabetes. *Tissue Antigens.* 2007 Apr;69(4):348-53
- Awasthi YC, Sharma R, Sharma A, Yadav S, Singhal SS, Chaudhary P, Awasthi S. Self-regulatory role of 4-hydroxynonenal in signaling for stress-induced programmed cell death. *Free Radic Biol Med.* 2008 Jul 15;45(2):111-8
- Chen YC, Kappel C, Beaudouin J, Eils R, Spector DL. Live cell dynamics of promyelocytic leukemia nuclear bodies upon entry into and exit from mitosis. *Mol Biol Cell.* 2008 Jul;19(7):3147-62
- Jia L, Yu W, Wang P, Li J, Sanders BG, Kline K. Critical roles for JNK, c-Jun, and Fas/FasL-Signaling in vitamin E analog-induced apoptosis in human prostate cancer cells. *Prostate.* 2008 Mar 1;68(4):427-41
- Jung YS, Kim HY, Kim J, Lee MG, Pouysségur J, Kim E. Physical interactions and functional coupling between Daxx and sodium hydrogen exchanger 1 in ischemic cell death. *J Biol Chem.* 2008 Jan 11;283(2):1018-25
- Kaspari M, Tavalai N, Stamminger T, Zimmermann A, Schilf R, Bogner E. Proteasome inhibitor MG132 blocks viral DNA replication and assembly of human cytomegalovirus. *FEBS Lett.* 2008 Mar 5;582(5):666-72
- Maul GG, Negorev D. Differences between mouse and human cytomegalovirus interactions with their respective hosts at immediate early times of the replication cycle. *Med Microbiol Immunol.* 2008 Jun;197(2):241-9
- Nieto-Miguel T, Gajate C, González-Camacho F, Mollinedo F. Proapoptotic role of Hsp90 by its interaction with c-Jun N-terminal kinase in lipid rafts in edelfosine-mediated antileukemic therapy. *Oncogene.* 2008 Mar 13;27(12):1779-87
- Poleshko A, Palagin I, Zhang R, Boimel P, Castagna C, Adams PD, Skalka AM, Katz RA. Identification of cellular proteins that maintain retroviral epigenetic silencing: evidence for an antiviral response. *J Virol.* 2008 Mar;82(5):2313-23
- Puto LA, Reed JC. Daxx represses RelB target promoters via DNA methyltransferase recruitment and DNA hypermethylation. *Genes Dev.* 2008 Apr 15;22(8):998-1010
- Sharma R, Sharma A, Dwivedi S, Zimniak P, Awasthi S, Awasthi YC. 4-Hydroxynonenal self-limits fas-mediated DISC-independent apoptosis by promoting export of Daxx from the nucleus to the cytosol and its binding to Fas. *Biochemistry.* 2008 Jan 8;47(1):143-56
- Tavalai N, Papirer P, Rechter S, Stamminger T. Nuclear domain 10 components promyelocytic leukemia protein and hDaxx independently contribute to an intrinsic antiviral defense against human cytomegalovirus infection. *J Virol.* 2008 Jan;82(1):126-37
- Tuo QH, Liang L, Zhu BY, Cao X, Liao DF. Effect of Daxx on cholesterol accumulation in hepatic cells. *World J Gastroenterol.* 2008 Jan 21;14(3):435-40
- Yeung PL, Chen LY, Tsai SC, Zhang A, Chen JD. Daxx contains two nuclear localization signals and interacts with importin alpha3. *J Cell Biochem.* 2008 Feb 1;103(2):456-70

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