t(12;15)(p13;q25) ETV6/NTRK3 in solid tumors

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Published in Atlas Database: November 2019

Online updated version: http://AtlasGeneticsOncology.org/Tumors/t1215p13q25ID5267.html
Printable original version: http://documents.revuees.inist.fr/bitstream/handle/2042/70786/11-2019-t1215p13q25ID5267.pdf
DOI: 10.4267/2042/70786

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Abstract

Review on t(12;15)(p13;q25) in solid tumors, with data on clinics, and the genes involved.

Keywords
Chromosome 12; Chromosome 15; ETV6; NTRK3; Chronic eosinophilic leukemia; Acute myeloid leukemia; B-Lineage Acute lymphoblastic leukemia; Secretary ductal breast carcinoma; Congenital mesoblastic nephroma; Congenital/infantile fibrosarcoma; Papillary thyroid carcinoma; Inflammatory myofibroblastic sarcoma; Secretary carcinoma of salivary glands (mammary analogue); atypical Spitz tumors.

Clinics and pathology

A t(12;15)(p13;q25) ETV6/NTRK3 has been found: 1) in congenital/infantile fibrosarcoma and cellular mesoblastic nephroma (which may be a renal form of infantile fibrosarcoma), 2) in secretory breast (ductal) carcinoma and in it's analogue in the salivary glands, 3) in acute leukemias (both myeloid and lymphoid), 4) in papillary thyroid carcinoma, often radiation-associated, 5) in inflammatory myofibroblastic tumor, and, in few cases, in other tumors.

Equivalents of the ETV6/NTRK3 fusion was also found in rare instances in the above mentioned tumors: EML4/NTRK3, MYH9/NTRK3, MYO5A/NTRK3, LMNA/NTRK1, and ETV6/?

Disease

Congenital/infantile fibrosarcoma (WHO/OMS 8814/3) (CIF)
Congenital/infantile fibrosarcoma is a low-grade malignant spindle cell tumor of the soft tissues that usually presents before the age of 2 years (diagnosed at birth in 40%, before 6 months in 60% of cases, more common in boys than in girls), occurring 1) most often in the extremities and with a good prognosis, at times 2) in the axial skeleton with a somewhat worse prognosis.

Local recurrence is common (10 to 30% of cases) but metastases are rare. Overall 5-year survival is at least 90% (Farmakis et al., 2014).

Cytogenetics

A t(12;15)(p13;q25) ETV6/NTRK3 was found in most cases, but is not found in either infantile fibromatosis, a close but benign entity, or in fibrosarcoma of the adulthood.

The t(12;15) ETV6/NTRK3 is most often accompanied with trisomy or tetrasomy 11 (Knezevich et al., 1998; Rubin et al., 1998; Bourgeois et al., 2000; Punnett et al., 2000; Argani et al., 2001; Dubus et al., 2001; Sheng et al., 2001; Miura et al., 2002; McCahon et al., 2003; Ramphal et al., 2003; Morerio et al., 2004; Nonaka and Sun, 2004; Himori et al., 2005; Rizkalla et al., 2011).

The reciprocal NTRK3/ETV6 fusion product may also be found, with NTRK3 exon 14 fused to ETV6 exon 6 (Dubus et al., 2001).

A t(2;15)(p21;q24) EML4/NTRK3 has also been found in two cases of CIF.

One was a 9-mo-old male patient with recurrent congenital fibrosarcoma and a history of left upper extremity hemimelia without other congenital anomalies.
Exon 2 of EML4 was fused to exon 14 of NTRK3 (Tannenbaum-Dvir et al., 2015; Church et al., 2018).
A congenital infantile fibrosarcoma was found to harbor a LMNA/NTRK1 gene fusion (Wong et al., 2015).

**Disease**

**Congenital Mesoblastic Nephroma (WHO/OMS 8960/1) (CMN)**

Congenital mesoblastic nephroma is the most common kidney tumor found in infants younger than 6 months and accounts for 3-5% of all paediatric renal neoplasm. The 5-year event-free survival rate is 95%.

Histopathologically, it consist of spindled cells. There are three histologic subtypes: classic, mixed, and cellular. The cellular subtype is identical to infantile fibrosarcoma and is the form with a t(12;15) ETV6/NTRK3 and trisomy 11 (PDQ Pediatric Treatment Editorial Board, 2019). Cellular mesoblastic nephroma tends to present later in infancy than the classic form and can exhibit aggressive behavior including metastases (Bayindir et al., 2009). It has been suggested that the cellular subtype represents in fact congenital infantile fibrosarcoma occurring in the kidney (Bayindir et al., 2009; El Demellawy et al., 2016).

A t(12;15) ETV6/NTRK3, most often accompanied with trisomy or tetrasomy 11, or a fusion ETV6/NTRK3 has been found in more than 40 cases; some cases were mixed forms; none was classical form (Rubin et al., 1998; Knezevich et al., 1998; Argani et al., 2000; Ramachandran et al., 2001; Watanabe et al., 2002; Henno et al., 2003; Anderson et al., 2006; Bayindir et al., 2009).

**Cytogenetics**

Although the t(12;15)(p13;q25) ETV6/NTRK3 was found in most cases, a t(2;15)(p21;q24) EML4/NTRK3 has also been found in one case of CMN (Church et al., 2018).

**Disease**

**Breast Ductal carcinoma - Secretory breast carcinoma subtype (WHO/OMS 8502/3) (SBC)**

Secretory breast carcinoma is a rare (less than 0.15% of all breast cancers) subtype of breast ductal carcinoma (but the most common breast cancer in the pediatric population), with a distinct morphology: eosinophilic secretion and positive periodic acid-Schiff (PAS) secretions are seen, immune-positivity for S100 and mammaglobin, most often triple negativity (ESR1/2-, PGR-, ERBB2-) and an excellent prognosis in children and adolescents. It occurs in both children and adults with a wide age range from 3 to 83 years. Most reported cases are in young women, with a median age of 25 years. There are only 120 cases published in literature, including 32 in male patients. Breast secretory carcinoma is a slow-growing, low-grade subtype of infiltrating ductal carcinoma. The disease seems slightly more aggressive in adults (Vasudev and Onuma 2011; Ghilli et al., 2018).

**Cytogenetics**

A t(12;15)(p13;q25) ETV6/NTRK3 was found in most cases (Tognon et al., 2002; Diallo et al., 2003; Stransky et al 2014).

**Genes**

ETV6/NTRK3 chimeric product can transform normal mouse mammary epithelial cells. Fusion was between ETV6 nucleotide 1033 and NTRK3 nucleotide 1601 as previously shown for sarcoma-associated fusions (Knezevich et al., 1998). This differs from the ETV6/NTRK3 gene fusion reported in a case of acute myeloid leukemia, in which ETV6 exon 5 was not present in the fusion (Eguchi et al., 1999).

The rare secretory breast carcinomas with metastases, more aggressive tumors, showed amplification of the 16p13.3 locus, a TERT promoter mutation and loss of 9p21.3 locus (Hoda et al., 2019).

**Disease**

**Mammary analogue secretory carcinoma of salivary glands (MASC)**

A t(12;15)(p13;q25) ETV6/NTRK3 was found in salivary gland tumors (mostly from the parotid gland) with histoo-morphologic and immune-histochemical features reminiscent of secretory carcinoma of the breast, with eosinophilic secretion, positivity for PAS, S-100 protein and mammaglobin (Skálová et al., 2010; Chiosea et al., 2012; Connor et al., 2012; Skálová et al., 2014; Pinto et al., 2014). More than 250 cases have been described (review in Skálová et al., 2017). Mean age was 47 years (14-78 years), there is a slight male predominance. MASC mimick other salivary tumors, most often adenocarcinoma, not otherwise specified and acinic cell carcinomas. MASC usually behaves indolently, but like other low-grade salivary gland carcinomas, there is some loco-regional recurrence and distant metastases (Skálová et al., 2017).

**Cytogenetics**

A t(12;15)(p13;q25) ETV6/NTRK3 was found in most cases. A few cases where ETV6 was fused with an unknown partner different from NTRK3 were described; these may behave more aggressively (Ito et al., 2015; Skálová et al., 2016).
**Disease**

**Thyroid: Papillary thyroid carcinoma (WHO/OMS 8260/3) (PTC)**

In an analysis of 62 radiation-associated papillary thyroid carcinomas post-Chernobyl (iodine-131 exposure), 9 (14.5%) of PTCs harbored ETV6/NTRK3 rearrangement; ETV6/NTRK3 fusion was the second most common rearrangement type after "RET/PTC". Further screening of 151 sporadic PTCs revealed three positive cases, resulting in a prevalence of 2%. The majority of post-radiation-associated PTCs with ETV6/NTRK3 rearrangement were classified as the follicular variant of PTC (Leeman-Neill et al 2014). In a study of 496 papillary thyroid carcinoma without radiation exposure, and classified as low risk, 5 cases (three "classical", one "follicular") presented with an ETV6/NTRK3 rearrangement. Ages and sex: were: 41/F, 36/F, 23/F, 17/F (The Cancer Genome 2014).

**Disease**

**Inflammatory myofibroblastic tumor/myofibroblastic sarcoma (WHO/OMS 8825/1) (IMT)**

Inflammatory myofibroblastic tumor is a rare visceral and soft tissue tumor (commonly seen in the lung), consisting of myofibroblastic spindle cells with inflammatory cells. Local recurrences are seen in about 25% of patient, but metastases are rare. It affects primarily children and young adults, with a slight male predominance. Favorable outcome is documented in most cases. An ETV6/NTRK3 fusion was found in at least 6 cases of inflammatory myofibroblastic tumor: in a 17-year-old girl and in 2 other cases in a subset of ALK-negative inflammatory myofibroblastic tumors, in a 7-year old child and in a 23-year-old adult patient, and in a 44-year-old female patient (Alassiri et al 2016; Yamamoto et al 2016; Takahashi et al 2018).

**Disease**

**Skin melanocytic tumors (WHO/OMS 8770/1 and 8720/3) and other skin carcinomas**

Note

A t(12;15)(p13;q25) ETV6/NTRK3 was found in 4 cases of atypical Spitz tumors (Yeh et al., 2016), a group of cutaneous melanocytic tumors (Murali et al., 2012). ETV6/NTRK3 fusion was also detected in a skin melanoma in massive data sets from genome sequencing studies from the TCGA (Stransky et al. 2014). A secretory carcinoma of the skin mimicking secretory carcinoma of the breast and the and secretory carcinoma salivary gland was found to harbor an ETV6/NTRK3 fusion gene (Huang et al., 2016).

**Cytogenetics**

Other cases presented with the following translocations/genes fusions: MYH9/NTRK3 and MYO5A/NTRK3. In all those cases, NTRK3 fusions constitutively activated the RAS/RAF/MAPK, PI3K/AKT/MTOR and PLCG pathways in melanocytes (Yeh et al., 2016).

**Disease**

**Brain tumors (WHO/OMS 9425/3 9401/3)**

Note

In a series of 149 pediatric low-grade gliomas, an ETV6/NTRK3 fusion was found in a 13-year-old girl with a pilomyxoid astrocytoma (Zhang et al 2013). An ETV6/NTRK3 fusion was also found in a high grade astrocytoma (massive data from genome sequencing) (Wu et al 2014).

**Cytogenetics**

The reciprocal NTRK3/ETV6 fusion product was also found (Zhang et al 2013).

**Disease**

**Colon adenocarcinoma (WHO/OMS 8140/3)**

At least 4 cases of colorectal carcinoma were found to have an ETV6/NTRK3 fusion, in massive data from genome sequencing studies from the TCGA (Seshagiri et al 2012; Stransky et al 2014; Hu et al 2018).

**Disease**

**Sinonasal adenocarcinoma**

Two cases of low grade sinonasal adenocarcinoma were found to have the t(12;15)(p13;q25) ET6/NTRK3 (Andreasen et al 2017).

**Cytogenetics**

Another case presented with ETV6 fused to an unknown partner (Andreasen et al 2017).

**Genes involved and proteins**

**ETV6 (ets variant 6)**

**Location** 12p13.2

**Protein**

ETV6 is a strong transcriptional repressor. ETV6 is a 452 amino acid member of the ETS family (signal-dependent transcriptional regulators, mediating cell proliferation, differentiation and tumorigenesis).
ETV6 protein contains two major domains, the HLH (helix-loop-helix) and ETS domains. The N-term HLH domain, also referred to as the pointed or sterile alpha motif domain, is responsible for hetero- and homo-dimerization. The C-term ETS domain is responsible for sequence specific DNA-binding and protein-protein interaction. A central domain, called internal domain, is involved in the recruitment of a repression complex including NCOR1, NCOR2, and SIN3A (Braekeleer et al., 2014 http://atlasgeneticsoncology.org//Genes/ETV6ID38.html).

**NTRK3 (neurotrophic tyrosine kinase, receptor, type 3)**

**Location** 15q25.3

**Protein**

NTRK3 is a transmembrane receptor tyrosine kinase which triggers PI3K/AKT, RAS/RAF/MAPK, and PLCG pathways. NTRK3 is a 839 amino acid protein with a N-term extra-cellular ligand binding domain, a transmembrane domain, and a C-term intracellular tyrosine kinase domain. Ligand for NTRK3 is NT3 (neurotrophin 3) (Knezevich 2004 http://atlasgeneticsoncology.org/Genes/NTRK3ID433.html).

**Result of the chromosomal anomaly**

**Hybrid Gene**

**Description**

In solid tumors, ETV6 exon 5 - NTRK3 exon 15 fusion is the most frequent:

The fusion was exon 4 - exon 14 in most papillary thyroid carcinoma ceases, but one exon 5 - exon 14 fusion case was also found (Leeman-Neill et al., 2014)

The fusion was exon 5 - exon 15 in: secretory ductal breast carcinoma (Tognon et al., 2002), congenital mesoblastic nephroma (Knezevich et al., 1998; Rubin et al., 1998; Argani et al., 2000; Ramachandran et al., 2001; Watanabe et al., 2002; Henno et al., 2003; Anderson et al., 2006; Bayindir et al., 2009), secretory carcinoma of salivary glands (mammary analogue) (Skálová et al., 2010; Skálová et al., 2014), atypical Spitz tumors (Yeh et al., 2016), and also in a case of colon adenocarcinoma (Seshagiri et al., 2012). The classical exon 5 - exon 15 fusion is also found in congenital/infantile fibrosarcoma (Knezevich et al., 1998; Rubin et al., 1998; Bourgeois et al., 2000; Punnett et al., 2000; Argani et al., 2001; Dubus et al., 2001; Sheng et al., 2001; Miura et al., 2002; McCahon et al., 2003; Ramphal et al., 2003; Nonaka and Sun, 2004; Himori et al., 2005), but, also, a fusion NTRK3 exon 14 - ETV6 exon 6 was found in one case (Dubus et al., 2001).

In most leukemia cases, ETV6 exon 5 was fused to NTRK3 exon 15 (Forghieri et al., 2011; Roberts et al., 2014). In one case ETV6 exon 4 was fused to NTRK3 exon 15 (Eguchi et al., 1999), and in another case, fusion transcripts contain ETV6 exons 1 through 5 fused to NTRK3 exons 13b and 14b or NTRK3 exons 13 through 18 (Kralik et al., 2011).

**Fusion Protein**

**Description**

The SAM-PNT (sterile alpha motif- pointed) domain of ETV6 is fused to the PTK (Protein Tyrosine Kinase domain) of NTRK3.

**Oncogenesis**

It leads to dimerization, and induction of CCND1 (cyclin D1) and increased cell cycle progression. ETV6/NTRK3 also leads to constitutive activation of the PI3K/AKT, RAS/RAF/MAPK, and PLCG pathways (Lannon and Sorensen, 2005).
Fusions: an integrative resource for cancer

References

Alasaari AH, Ali RH, Shen Y, Lum A, Strahlund C, Deyell R, Rassekh R, Sorensen PH, Laskin J, Marra M, Yip S, Lee CH, Ng TL. ETV6-NTRK3 Is Expressed in a Subset of ALK-Negative Inflammatory Myofibroblastic Tumors. Am J Surg Pathol. 2016 Aug;40(8):1051-61

Anderson J, Gibson S, Sebire NJ. Expression of ETV6-NTRK in classical, cellular and mixed subtypes of congenital mesoblastic nephroma. Histopathology. 2006 May;48(6):748-53

Andreasen S, Skåløv A, Agaimy A, Bishop JA, Laco J, Leivo I, Franchi A, Larsen SR, Errentaite D, Uhløe BP, von Buchwald C, Melchior LC, Michal M, Kiss K. ETV6 Gene Rearrangements: Characterize a Morphologically Distinct Subset of Sinonasal Low-grade Non-intestinal-type Adenocarcinoma: A Novel Translocation-associated Carcinoma Restricted to the Sinonasal Tract. Am J Surg Pathol. 2017 Nov;41(11):1552-1560

Argani P, Fritsch MK, Shuster AE, Perlman EJ, Coffin CM. Reduced sensitivity of paraffin-based RT-PCR assays for ETV6-NTRK3 fusion transcripts in morphologically defined infantile fibrosarcoma Am J Surg Pathol 2001 Nov;25(11):1461-4

Bayindir P, Guillerman RP, Hicks MJ, Chintagumpala MM. Cellular mesoblastic nephroma (infantile renal fibrosarcoma): institutional review of the clinical, diagnostic imaging, and pathologic features of a distinctive neoplasm of infancy Pediater Radiol 2009 Oct;39(10):1066-74

Bourgeois JM, Knezevich SR, Mathers JA, Sorensen PH. Molecular detection of the ETV6-NTRK3 gene fusion differentiates congenital fibrosarcoma from other childhood spindle cell tumors Am J Surg Pathol 2000 Jul;24(7):937-46

Cancer Genome Atlas Research Network. Integrated genomic characterization of papillary thyroid carcinoma Cell 2014 Oct 23;159(3):676-90

Chiosea SI, Griffith C, Assaad A, Seethala RR. Clinicopathological characterization of mammary analogue secretory carcinoma of salivary glands Histopathology 2012 Sep;61(3):387-94

Church AJ, Calicchio ML, Nardi V, Skalova A, Pinto A, Dillon DA, Gomez-Fernandez CR, Manoj N, Haines J, Stahl JA, Dela Cruz FS, Tannenbaum-Dvir S, Glade-Bender JL, Kung AL, DuBois SG, Kozakewich HP, Janeway KA, Perez-Alayde AR, Harris MH. Recurrent EML4-NTRK3 fusions in infantile fibrosarcoma and congenital mesoblastic nephroma suggest a revised testing strategy Mod Pathol 2018 Mar;31(3):463-473

Connor A, Perez-Ordoñez B, Shago M, Skálová A, Weinreb I. Mammary analog secretory carcinoma of salivary gland origin with the ETV6 gene rearrangement by FISH: expanded morphologic and immunohistochemical spectrum of a recently described entity Am J Surg Pathol 2012 Jan;36(1):27-34

Diallo SA, Merlio JP. The leukaemia with ETV6-NTRK3 fusion transcript in an elderly patient with pancreatic carcinoma Eur J Haematol 2011 Apr;86(4):352-5

Di Domenico A, Mross K, salud AW, de Nanassy J, Paller S, Massoudian P, Sullivan KJ, de N, Santagata S, Cheetham BM, Congenital mesoblastic nephroma: a study of 39 cases using immunohistochemistry and ETV6-NTRK3 fusion gene rearrangement Pathology 2016 Jan;48(1):47-50

Farhakos SG, Herman TE, Siegel MJ. Congenital infantile fibrosarcoma J Perinatol 2014 Apr;34(4):329-30

Ferrero S, Morselli L, Potenza L, Maccarelli F, Pedrazzi L, Paolini A, Bonacorsi G, Artusi T, Gacobbi F, Corradini G, Barozzi P, Zucchini P, Marasca R, Nanni F, Crescenzi B, Mecucci C, Fatini B, Torelli G, Luppi M. Chronic eosinophilic leukemia with ETV6-NTRK3 fusion transcript in an elderly patient affected with pancreatic carcinoma Eur J Haematol 2016 Nov;97(5):445-454

Ghilli M, Marinelli MD, Scatena C, Dosa L, Traficante G, Tamburini A, Caporinali C, Buccoliero AM, Facchini F, Colizzi L, Quattrini Li A, Landucci E, Marca G, Naccarato AG, Caramella D, Favre C, Roncella M. Male secretory breast cancer: case in a 6-year-old boy with a peculiar gene duplication and review of the literature Breast Cancer Res Treat 2018 Aug;170(3):445-454

Gu Z, Churchman M, Roberts K, Li Y, Liu Y, Harvey RC, McCastlain K, Reshmi SC, Payne-Turner D, Iacobucci I, Shao Y, Chen IM, Valentine M, Pei D, Mungall KL, Mungall AJ, Ma Y, Moore R, Marra M, Stonerock E, Gastler-Foster JM, Devidas M, Dai Y, Wood B, Borowitz M, Larsen EE, Maloney K, Mattano LA Jr, Angelillo A, Salzer WL, Burke MJ, Gianni F, Spinelli O, Radich JP, Minden MD, Moorman AV, Patel B, Fielding AK, Rowe JM, Luger SM, Bhatia R, Aldoss I, Forman SJ, Kohlschmidt J, Mrózek K, Marcucci G, Bloomfield CD, Stock W, Kornblau S, Kantarjian HM, Konopleva M, Paletta E, Willman CL, Loh ML, Hunger SP, Mullighan CG. Genomic analyses identify recurrent MEF2D fusions in acute lymphoblastic leukemia Nat Commun 2016 Nov 8:7:13331

Henne S, Loueillet L, Henry C, D’Hervé D, Azzis O, Ferrer J, Poulin J, Babut JM, Merlio JP, Jouan H, Dubus P. Cellular mesoblastic nephroma: morphologic, cytogenetic and molecular links with congenital fibrosarcoma Pathol Res Pract 2003;199(1):35-40

Himori K, Hatori M, Watanabe M, Moriya T, Ogose A, Hashimoto H, Kokubun S. Infantile fibrosarcoma of thigh—a case report Ups J Med Sci 2005;110(1):85-90

Hoda RS, Brogi E, Pareja F, Nanjangud G, Murray MP, Weigelt B, Reis SA, Masoudian P, Sullivan KJ, de Nanassy J, Barozzi P, Zucchini P, Marasca R, Nanni F, Crescenzi B, Mecucci C, Fatini B, Torelli G, Luppi M. Congenital mesoblastic nephroma: a study of 39 cases using immunohistochemistry and ETV6-NTRK3 fusion gene rearrangement Pathology 2016 Jan;48(1):47-50

Huang S, Liu Y, Su J, Liu J, Guo X, Mei F, Zheng J, Liao G, Huang J, Zhao Y, Fan H, Wang H, Zhang Y, Zhan W, Yang X, Wang Y, Zhou Z, Du H, Fang W, Huang L, Zhan R, Pei J, Liu T, Wang D, Yuan J, Wang Y, Wu W, Liu W, Wang C, Wang C, Zhang D, Yang Z, Li M, Yu S, Chen D, Zhang Y, Sun H, Wu H, Tang S, Zhang J, Wang P, Yang W, Yang J, Sun C, Zhong J, Li M, Yang F, Wang Y, Yang Y, Zhao Q, Wang S, Li X, Wang S, Wang X. “Secretory” Carcinoma of the Skin Mimicking Secretory Carcinoma of the Breast: Case Report and Literature Review Am J Dermatopathol 2016 Sep;38(9):698-703
Histogenetic link between mesoblastic nephroma and congenital fibrosarcoma Cancer Res 1998 Nov 15;58(22):5046-9

Kralik JM, Kranewitter W, Boesmueller H, Marschon R, Tschurtschenthaler G, Rumpold H, Wiesinger K, Erdel M, Petzer AL, Webbersinke G. Characterization of a newly identified ETV6-NTRK3 fusion transcript in acute myeloid leukemia Diagn Pathol 2011 Mar 15;6:19

Lange AM, Lo HW. Inhibiting TRK Proteins in Clinical Cancer Therapy Cancers (Basel) 2018 Apr 4;10(4)

Lannon CL, Sorensen PH. ETV6-NTRK3: a chimeric protein tyrosine kinase with transformation activity in multiple cell lineages Semin Cancer Biol 2005 Jun;15(3):215-2

Leeman-Neill RJ, Kelly LM, Liu P, Brenner AV, Little MP, Bogdanova TI, Evdokimova VN, Hatch M, Zurnadzy LY, Nikitovorov YE. ETV6-NTRK3 is a common chromosomal rearrangement in radiation-associated thyroid cancer Cancer 2014 Mar 15;120(6):799-807

McCaugh E, Sorensen PH, Davis JH, Rogers PC, Schultz KR. Non-resectable congenital tumors with the ETV6-NTRK3 gene fusion are highly responsive to chemotheraphy Med Pediatr Oncol 2003 May;40(5):288-98

Miura K, Han G, Sano M, Tsutsui Y. Regression of congenital fibrosarcoma to hemangiomatous remnant with histological and genetic findings Pathol Int 2002 Sep;52(9):612-8

Moreiro C, Rapella A, Rosanda C, Tassano E, Conte M, Gambini C, Panarello C. Differential diagnosis of congenital fibrosarcoma Cancer Genet Cytogenet 2004 Jul 15;152(2):167-8

Nonaka D, Sun CC. Congenital fibrosarcoma with metastasis in a fetus Pediatr Dev Pathol 2004 Mar-Apr;7(2):187-91

PDU Pediatric Treatment Editorial Board. Wilms Tumor and Other Childhood Kidney Tumors Treatment (PDU): Health Professional Version 2020 Jan 9 PDQ Cancer Information Summaries [Internet]

Pinto A, Nosé V, Rojas C, Fan YS, Gomez Fernández C. Searching for mammary analogue [corrected] secretory carcinoma of salivary gland among its mimics Mod Pathol 2014 Jan;27(1):30-7

Punnett HH, Tomczak EZ, Pawel BR, de Chadarevian JP, Sorensen PH. ETV6-NTRK3 gene fusion in metastasizing congenital fibrosarcoma Med Pediatr Oncol 2000 Aug;35(2):137-9

Ramachandran C, Melnick SJ, Escalon E, Khatib Z, Jhabvala P, Fonseca HB, Smith S, Alamo A, Medina S. Cytogenetic and molecular characterization of a congenital mesoblastic nephroma Pediatr Dev Pathol 2001 Jul-Aug;4(4):402-11

Rampal R, Manson D, Viero S, Zielenska M, Gerstle T, Pappo A. Retropertitoneal infantile fibrosarcoma: clinical, molecular, and therapeutic aspects of an unusual tumor Pediatr Hematol Oncol 2003 Dec;20(8):835-42

Reshmi SC, Harvey RC, Roberts KG, Stonerock E, Smith A, Jenkins H, Chen IM, Valentine M, Liu Y, Li J, Shao Y, Easton J, Payne-Turner D, Gao C, Tran TH, Nguyen J, Devidas M, Dai Y, Heerema NA, Carroll AJ 3rd, Raetz EA, Borowitz MJ, Wood BL, Angiolillo AL, Burke MJ, Salzer WL, Zweidier-McKay PA, Robin KR, Carroll WL, Zhang J, Loh ML, Mullighan CG, Willman CL, Gastier-Foster JM, Hunger SP. Targetable kinase gene fusions in high-risk B-ALL: a study from the Children's Oncology Group Blood 2017 Jun 22;129(25):3352-3361

Rizkalla H, Wildgrove H, Quinn F, Capra M, O'Sullivan MJ. Congenital fibrosarcoma of the ileum: case report with molecular confirmation and literature review Fetal Pediatr Pathol 2011;30(3):156-60

Roberts KG, Li Y, Payne-Turner D, Harvey RC, Yang YL, Pei D, McCastlain K, Ding L, Lu C, Song G, Ma J, Becksfort J, Rusc H, Chen SC, Easton J, Cheng J, Boggs K, Santiago-Morales N, Iacobucci I, Fulton RS, Wen J, Valentine M, Cheng C, Paugh SW, Devidas M, Chen IM, Reshmi S, Smith A, Hedlund E, Gupta P, Nagashawatte P, Wu G, Chen X, Yergeau D, Vadodaria B, Mulder H, Winick NJ, Larsen EC, Carroll WL, Heerema NA, Carroll AJ, Grayson G, Tasion SK, Moore AS, Kelle F, Frei-Jones M, Whitlock JA, Raetz EA, White DL, Hughes TP, Guidy Avul JM, Smith MA, Marcucci G, Bloomfield CD, Mietzke K, Kohlschmidt J, Stock W, Korinblau SM, Konopleva M, Paetitia E, Pui CH, Jeha S, Relling MV, Evans WE, Gerhard DS, Gastier-Foster JM, Mardis E, Wilson RK, Loh ML, Downing JR, Hunger SP, Willman CL, Zhang J, Mullighan CG. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia N Engl J Med 2014 Sep 11;371(11):1005-15

Rubin BP, Chen CJ, Morgan TW, Xiao S, Grier HE, Kozakewich HP, Perez-Atayde AR, Fletcher JA. Congenital mesoblastic nephroma (t12;15) is associated with ETV6-NTRK3 gene fusion: cytogenetic and molecular relationship to congenital (infantile) fibrosarcoma Am J Pathol 1998 Nov;153(5):1451-8

Seshagiri S, Stawiski EW, Durinck S, Modrusan Z, Storm EE, Conboy MB, Chaudhuri S, Guan Y, Janakiraman V, Jaiswal BS, Guillory J, Ha C, Dijkgraff GJ, Stinson J, Gnad F, Huntley MA, Degenhardt JD, Haverty PM, Bourgon R, Wang W, Koeppen H, Gentleman R, Starr JK, Zhang Z, Largaespada DA, Wu TD, de Sauvage FJ, Recurrent R-spindin fusions in colon cancer Nature 2012 Aug 30;488(7413):660-4

Sheng WQ, Hsiaoaka M, Okamoto S, Tanaka A, Meis-Kindblom JM, Kindblom LG, Ishida T, Nojima T, Hashimoto H. Congenital-infantile fibrosarcoma A clinicopathologic study of 10 cases and molecular detection of the ETV6-NTRK3 fusion transcripts using paraffin-embedded tissues Am J Clin Pathol

Skalova A, Vanecik T, Simpson RH, Laco J, Majewksa H, Baneckova M, Steiner P, Michal M. Mammary Analogue Secretory Carcinoma of Salivary Glands: a clinicopathologic and molecular study including 2 cases harboring ETV6-X fusion Am J Surg Pathol 2015 May;39(5):602-10

Knezevich SR, Garnett MJ, Pysher TJ, Beckwith JB, Grundy PE, Sorensen PH. ETV6-NTRK3 gene fusions and trisomy 11 establish a histogenetic link between mesoblastic nephroma and congenital fibrosarcoma Cancer Res 1998 Nov 15;58(22):5046-9

Itô Y, Ishibashi K, Masaki A, Fujii K, Fujiyoshi Y, Hattori H, Kawakita D, Matsumoto M, Miyabe S, Shimozato K, Nagao T, Inagaki H. Mammary analogue secretory carcinoma of salivary glands: a clinicopathologic and molecular study including 2 cases harboring ETV6-X fusion Am J Surg Pathol 2015 May;39(5):602-10
NTRK3 fusion gene: a case report J Int Med Res 2018 Aug;46(8):3496-3503
Tognon C, Knezevich SR, Huntsman D, Roskelley CD, Melnyk N, Mathers JA, Becker L, Carneiro F, MacPherson N, Horsman D, Poremba C, Sorensen PH. Expression of the ETV6-NTRK3 gene fusion as a primary event in human secretory breast carcinoma Cancer Cell 2002 Nov;2(5):367-76
Vasudev P, Onuma K. Secretory breast carcinoma: unique, triple-negative carcinoma with a favorable prognosis and characteristic molecular expression Arch Pathol Lab Med 2011 Dec;135(12):1606-10
Watanabe N, Kobayashi H, Hirama T, Kikuta A, Koizumi S, Tsuru T, Kaneko Y. Cryptic t(12;15)(p13;q26) producing the ETV6-NTRK3 fusion gene and no loss of IGF2 imprinting in congenital mesoblastic nephroma with trisomy 11: fluorescence in situ hybridization and IGF2 allelic expression analysis Cancer Genet Cytogenet 2002 Jul 1;136(1):10-6
Wong V, Pavlick D, Brennan T, Yelensky R, Crawford J, Ross JS, Miller VA, Malicki D, Stephens PJ, Ali SM, Ahn H. Evaluation of a Congenital Infantile Fibrosarcoma by Comprehensive Genomic Profiling Reveals an LMNA-NTRK1 Gene Fusion Responsive to Crizotinib J Natl Cancer Inst 2015 Nov 12;108(1)
Wu G, Diaz AK, Paugh BS, Rankin SL, Ju B, Li Y, Zhu X, Qu C, Chen X, Zhang J, Easton J, Edmonson M, Ma X, Lu C, Nagahawatte P, Hedlund E, Rusch M, Pounds S, Lin T, Onar-Thomas A, Huether R, Kriwacki R, Parker M, Gupta P, Beckford J, Wei L, Mulder HL, Boggs K, Vadodaria B, Yergeau D, Russell JC, Ochoa K, Fulton RS, Fulton LL, Jones C, Boop FA, Broniscer A, Wetmore C, Gajjar A, Ding L, Mardis ER, Wilson RK, Taylor MR, Downing JR, Ellison DW, Zhang J, Baker SJ. The genomic landscape of diffuse intrinsic pontine glioma and pediatric non-brainstem high-grade glioma Nat Genet 2014 May;46(5):444-450
Yamamoto H, Yoshida A, Taguchi K, Kohashi K, Hatanaka Y, Yamashita A, Mori D, Oda Y. ALK, ROS1 and NTRK3 gene rearrangements in inflammatory myofibroblastic tumours Histopathology 2016 Jul;69(1):72-83
Yeh I, Tee MK, Botton T, Shain AH, Sparatta AJ, Gagnon A, Vemula SS, Garrido MC, Nakamaru K, Isoyama T, McCallmont TH, LeBoit PE, Bastian BC. NTRK3 kinase fusions in Spitz tumours J Pathol 2016 Nov;240(3):282-290
Zhang J, Wu G, Miller CP, Tatevosssian RG, Dalton JD, Tang B, Orisme W, Punchiweha C, Parker M, Qaddoumi I, Boop FA, Lu C, Kandoth C, Ding L, Lee R, Huether R, Chen X, Hedlund E, Nagahawatte P, Rusch M, Boggs K, Cheng J, Beckford J, Ma J, Song G, Li Y, Wei L, Wang J, Shurtleff S, Easton J, Zhao D, Fulton RS, Fulton LL, Dooling DJ, Vadodaria B, Mulder HL, Tang C, Ochoa K, Mullighan CG, Gajjar A, Kriwacki R, Sheer D, Gilbertson RJ, Mardis ER, Wilson RK, Downing JR, Baker SJ, Ellison DW; St. Jude Children's Research Hospital-Washington University Pediatric Cancer Genome Project Whole-genome sequencing identifies genetic alterations in pediatric low-grade gliomas Nat Genet

This article should be referenced as such:
Huret JL. t(12;15)(p13;q25) ETV6/NTRK3 in solid tumors. Atlas Genet Cytogenet Oncol Haematol. 2020; 24(9):351-356.