Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

# Gene Section
## Mini Review

# HOXA11 (homeobox A11)

**Barbara Cauwelier, Frank Speleman**

Centrum Medische Genetica Gent- CMGG, Medical Research Building- MRB, 2 nd floor, room 120.024, De Pintelaan 185, B-9000 Ghent, Belgium

Published in Atlas Database: June 2006

Online updated version: http://AtlasGeneticsOncology.org/Genes/HOXA11ID40847ch7p15.html
DOI: 10.4267/2042/38347



## Identity

**Hugo:** HOXA11
**Other names:** HOX1I (HOMEOBOX 1I)
**Location:** 7p15-7p14.2

## DNA/RNA

### Description

Spans a 3,7 kb genomic region containing 2 exons.

### Transcription

mRNA 2295 bp.

## Protein

### Description

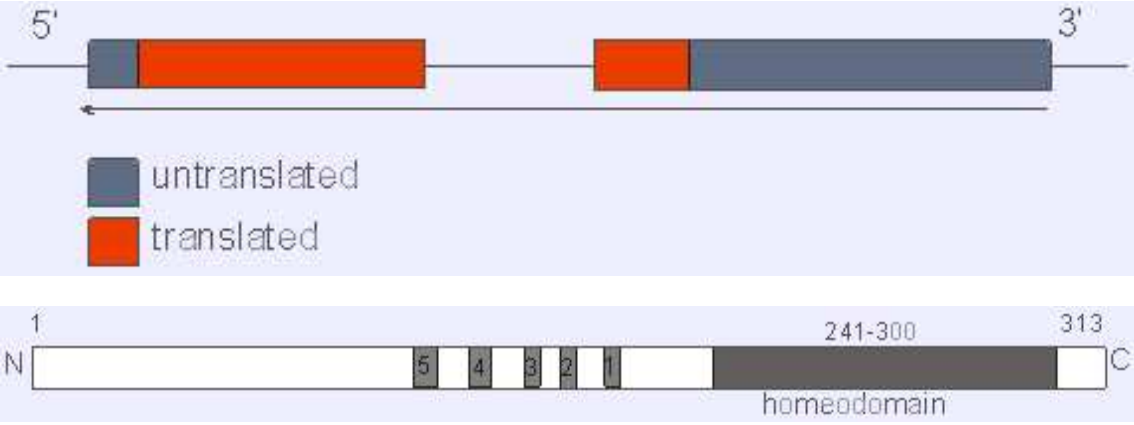
313 amino acids, 34.5 kDa, contains a homeodomain with helix-turn-helix (HTH) motif. The HTH motif Consists of approximately 20 residues and is characterised by 2 alpha-helices, which make intimate contacts with the DNA and are joined by a short turn. The second helix of the HTH motif binds to DNA via a number of hydrogen bonds and hydrophobic interactions, which occur between specific side chains and the exposed bases and thymine methyl groups within the major groove of the DNA. The first helix helps to stabilise the structure.

### Expression

In lung, bone, uterus, placenta, testis, prostate, liver, hematopoietic precursor cells, endometrium.

### Localisation

Nucleus.




Homeobox containing protein with C terminal localisation of the homedomain. N terminal several repeat regions: 1: Poly-Ser; 2: Poly-Arg; 3 :Poly-Ala; 4: Poly-Gly; 5: Poly-Ala.

### Function

Sequence-specific transcription factor which is part of a developmental regulatory system that provides cells with specific positional identities on the anterior-posterior axis. HOXA11 is involved in the regulation of uterine development and is required for female fertility. Expression of HOXA11 is detected at all differentiation stages of normal T cells in the thymus, suggesting a role in normal T cell development.

### Homology

Homolog to murine Hox-1.9; ABD-B homeobox family.

## Mutations

### Germinal

Mutation of HOXA11 in radio-ulnar synostosis with amegakaryotic thrombocytopenia; autosomal dominant inheritance; 1-bp deletion in exon 2 of the HOXA11 gene. Deletion of an adenine converted AAC (asparagine) to ACA (threonine), resulting in a premature termination codon and truncation of the remaining 22 amino acids of the HOXA11 protein.

## Implicated in

### inv(7)(p15q34), t(7;7)(p15;q34)

**Disease**

T-cell acute lymphoblastic leukemia.

**Cytogenetics**

inv(7)(p15q34) or t(7;7)(p15;q34) places 5'HOXA cluster genes (7p15) under the influence of strong enhancers within the TCRB locus (7q34) resulting in ectopic expression of especially HOXA10 and HOXA11.

**Abnormal Protein**

No fusion protein but ectopic expression of HOXA10 and HOXA11.

### t(7;11)(p15;p15)

**Disease**

CML, only once reported.

**Prognosis**

Unknown

**Cytogenetics**

This rearrangement fuses the 5' NUP98 gene in frame to the 3' HOXA11 gene generation a chimeric fusion transcript.

**Hybrid/Mutated Gene**

5' NUP98 - 3' HOXA11.

## References

Small KM, Potter SS. Homeotic transformations and limb defects in HOXA11 mutant mice. Genes Dev 1993;7(12A):2318-2328.

Davis AP, Witte DP, Hsieh-Li HM, Potter SS, Capecchi MR. Absence of radius and ulna in mice lacking Hoxa-11 and Hoxd-11. Nature 1995;375(6534):791-795.

Hsieh-Li HM, Witte DP, Weinstein M, Branford W, Li H, Small K, Potter SS,. HOXA11 structure, extensive antisense transcription, and function in male and female fertility. Development 1995;121(5):1373-1385.

Gendron RL, Paradis H, Hsieh-Li HM, Lee DW, Potter SS, Markoff E. Abnormal uterine stromal and glandular function associated with maternal reproductive defects in Hoxa-11 null mice. Biol Reprod 1997;56(5):1097-1105.

Branford WW, Benson GV, Ma L, Maas RL, Potter SS. Characterization of HOXA10/HOXA11 transheterozygotes reveals functional redundancy and regulatory interactions. Dev Biol 2000;224(2):373-387.

Thompson AA, Nguyen LT. Amegakaryocytic thrombocytopenia and radio-ulnar synostosis are associated with HOXA11 mutation. Nat Genet 2000;26(4):397-398.

Fujino T, Suzuki A, Ito Y, Ohyashiki K, Hatano Y, Miura I, Nakamura T. Single-translocation and double-chimeric transcripts: detection of NUP98-HOXA9 in myeloid leukemias with HOXA11 or HOXA13 breaks of the chromosomal translocation t(7;11)(p15;p15). Blood 2002;99(4):1428-1433.

Taghon T, Thys K, De Smedt M, Weerkamp F, Staal FJ, Plum J, Leclercq G. Homeobox gene expression profile in human hematopoietic multipotent stem cells and T-cell progenitors: implications for human T-cell. Leukemia 2003;17(6):1157-1163.

Wellik DM, Capecchi MR. HOX10 and HOX11 genes are required to globally pattern the mammalian skeleton. Science 2003;301(5631):363-367.

Soulier J, Clappier E, Cayuela JM, Regnault A, García-Peydró M, Dombret H, Baruchel A, Toribio ML, Sigaux F. HOXA genes are included in genetic and biologic networks defining human acute T-cell leukemia (T-ALL). Blood 2005;106(1):274-286.

Speleman F, Cauwelier B, Dastugue N, Cools J, Verhasselt B, Poppe B, Van Roy N, Vandesompele J, Graux C, Uyttebroeck A, Boogaerts M, De Moerloose B, Benoit Y, Selleslag D, Billiet J, Robert A, Huguet F, Vandenberghe P, De Paepe A, Marynen P, Hagemeijer A. A new recurrent inversion, inv(7)(p15q34), leads to transcriptional activation of HOXA10 and HOXA11 in a subset of T-cell acute lymphoblastic leukemias. Leukemia 2005;19(3):358-366.

*This article should be referenced as such:*
Cauwelier B, Speleman F. HOXA11 (homeobox A11). Atlas Genet Cytogenet Oncol Haematol.2006;10(4):234-235.