Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

# Gene Section

## Mini Review

# HMGIY (high mobility group protein (non histone chromosomal) isoform I and Y)

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Published in Atlas Database: November 2000

Online updated version: http://AtlasGeneticsOncology.org/Genes/HMGIYID221.html
DOI: 10.4267/2042/37689



## Identity

**Other names:**HMG-I(Y), HMGI/Y

**HGNC (Hugo):** HMGA1

**Location:** 6p21.3

**Local order:** centromeric to HLA-A, telomeric to D6S19.


Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

## DNA/RNA

### Description

10 144 bp; 8 exons, 7 introns.

### Transcription

HMGI and HMGY are encoded by the same gene and are generated trough alternative splicing; exons 1-4 are not transcribed, exons 5-7 encode three DNA binding domains; exon 5 contains a 33 bp segment subject to alternative splicing; exon 8 encodes the acidic carboxy-terminal end; RNA length: 1.85 kb.

## Protein

### Description

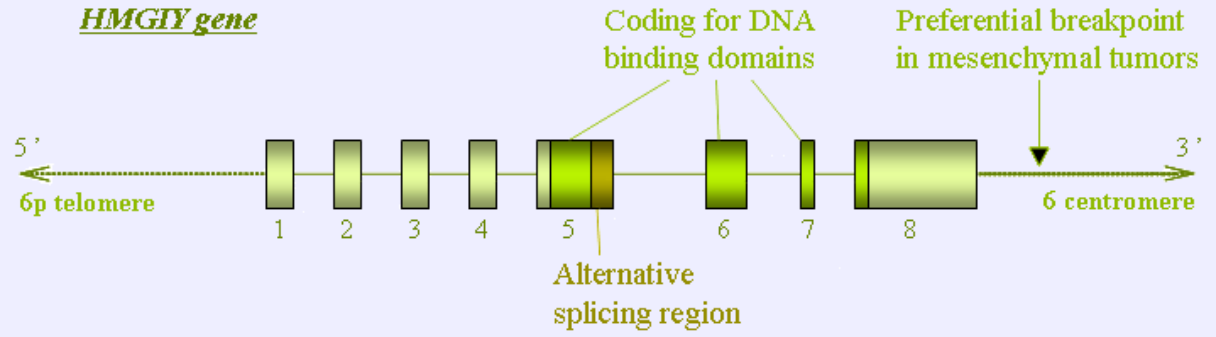
107 amino acids; three DNA binding domains (AT hooks).

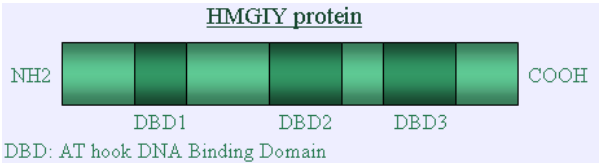
### Expression

Expressed in embryonal cells; expressed in a variety of normal human adult tissues such as heart, brain, lung, skeletal muscle, kidney, pancreas, spleen, thymus, testis, ovary, small intestine, submandibular gland and leukocytes; expressed in transformed cells with a malignant phenotype and in human malignant tumors such as prostate, thyroid carcinoma and colorectal carcinomas and a subset of benign lipomas.

### Localisation

Nuclear.






### Function

Architectural transcription, non histone, factor that binds to the minor groove of AT-rich DNA; alters DNA conformation by introducing bends and supercoils; HMGIY was shown to be an essential component of enhanceosome (higher order transcription enhancer complex); positive induction of several genes including IFN-b, E-selectin, interleukin-2 receptor a-chain, the chemokine MGSA/GRO, and the class II major histocompatibility complex gene HLA-DRA; negative regulation by binding the promoter regions of interleukin-4 and GP91-PHOX.
The precise function remains to be elucidated; probable role in regulation of chromatin structure and gene expression, and transcriptional regulation; potential oncogenic role.

### Homology

Member of the HMGI protein family, structural (but not expression pattern) homology with HMGIC.

## Mutations

### Somatic

HMGIY is found involved in chromosome rearrangements in benign tumours, mainly mesenchymal tumors.

## Implicated in

### Pulmonary chondroid hamartoma

**Disease**
Benign tumor of the lung.

**Prognosis**
Good.

**Cytogenetics**
The most frequent rearrangement is a reciprocal balanced translocation t(6;14) (p21.3; q24); the rearrangement between chromosomes 6 and 14 can sometimes be complex, identifiable by FISH; molecular results also suggest that the translocations might be more complex than shown by conventional cytogenetics, with the presence of additional cryptic rearrangements; translocations involving partner chromosomes other than chromosome 14, such as chromosomes 1, 3, 4, 5, 10, 12, 17 have also been reported; inversions inv(6)(p21q21) or inv(6)(p21.3q26) have been described.

**Hybrid/Mutated gene**
In most cases, the breakpoint was extragenic, located within a 80 kb region 3' of HMGIY; aberrant transcripts with truncation of sequences from the 3' UTR have been described; in only one case with inversion inv(6)(p21q21), a hybrid intragenic fusion has been reported: HMGIY was fused to the LAMA4 (laminin a4 chain) gene.

**Abnormal protein**
The HMGIY-LAMA4 resulted from the fusion of the three HMGIY DNA-binding domains with the LAMA4 EGF-like domain.

**Oncogenesis**
The exact role of HMGI(Y)-LAMA4 fusion is not established yet.

### Lipomas

**Disease**
Benign adipocyte tumors.

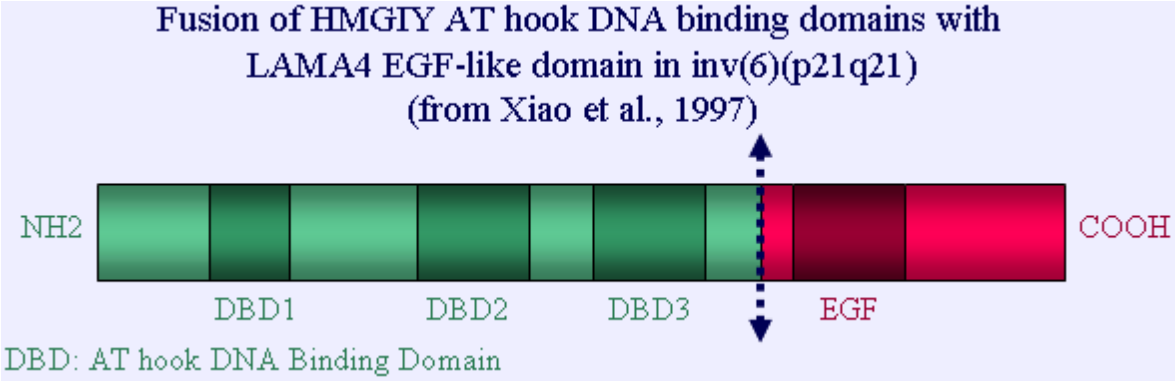
**Prognosis**
Good.

**Cytogenetics**
A small subset (5-8%) of ordinary lipomas is characterized by 6p21 rearrangements, the most frequent of which being a reciprocal translocation t(3;6)(q28;p21); in contrast to other benign mesenchymal tumors with 6p21 rearrangement, there is no evidence of HMGIY rearrangements in ordinary lipomas yet; however, to be noticed, the breakpoint on 6p21 was shown to be located whithin a 80 kb region surrounding HMGIY in one lipoma case and HMGIY expression was correlated with 6p rearrangements in two ordinary lipomas and two spindle cell lipomas

### Uterine leiomyoma

**Disease**
Benign mesenchymal tumors.

**Prognosis**
Good.




**Cytogenetics**
Approximately 40% of uterine leiomyomas present structural chromosomal rearrangements, 5% of which involve 6p abnormalities; they include t(1;6)(q23;p21), t(6;14)(p21;q24) and t(6;10)(p21;q22) as well as inversions and translocations involving other chromosomal partners; the rearrangements are sometimes complex, only identifiable by FISH analysis.

**Hybrid/Mutated gene**
No hybrid gene has been described yet; as for other mesenchymal tumors, the breakpoint was extragenic, located within a 80 kb region 3' of HMGIY; one case of aberrant transcript with truncation of 1295 bp from the 3' UTR has been described.

**Abnormal protein**
HMGIY mRNA and protein levels do not always correlate, suggesting that post-transcriptional mechanisms are involved in the regulation of HMGIY.

### *Endometrial polyps*

**Disease**
Uterine benign tumors.

**Prognosis**
Good.

**Cytogenetics**
Several chromosomal abnormalities involving the 6p21.3 region, including translocations, deletions, inversions have been described; various chromosomal partner regions, such as 14q24, 20q13, 2q35, 10q22, 8q12, 1p32, 7p15, 15q21, have been described to be associated with 6p21.3 in reciprocal translocations.

**Hybrid/Mutated gene**
No hybrid gene has been described yet; as for other mesenchymal tumors, the breakpoint is extragenic, located within a 80 kb region 3' of HMGIY.

### *Hamartoma of the breast*

**Disease**
Benign tumor-like nodule of the breast, also called adenolipoma.

**Prognosis**
Good.

**Cytogenetics**
One case with a t(1;6)(p21;21), involving the HMGIY gene has been described.

### *Microfollicular adenoma of the thyroid*

**Disease**
Epithelial tumors.

**Prognosis**
Favourable.

**Cytogenetics**
One case with a t(1;6)(p35;21) correlated with an overexpression of HMGIY has been described.

## References

Friedmann M, Holth LT, Zoghbi HY, Reeves R. Organization, inducible-expression and chromosome localization of the human HMG-I(Y) nonhistone protein gene. Nucleic Acids Res. 1993 Sep 11;21(18):4259-67

Chiappetta G, Avantaggiato V, Visconti R, Fedele M, Battista S, Trapasso F, Merciai BM, Fidanza V, Giancotti V, Santoro M, Simeone A, Fusco A. High level expression of the HMGI (Y) gene during embryonic development. Oncogene. 1996 Dec 5;13(11):2439-46

Dal Cin P, Wanschura S, Christiaens MR, Van den Berghe I, Moerman P, Polito P, Kazmierczak B, Bullerdiek J, Van den Berghe H. Hamartoma of the breast with involvement of 6p21 and rearrangement of HMGIY. Genes Chromosomes Cancer. 1997 Sep;20(1):90-2

Tallini G, Dal Cin P, Rhoden KJ, Chiapetta G, Manfioletti G, Giancotti V, Fusco A, Van den Berghe H, Sciot R. Expression of HMGI-C and HMGI(Y) in ordinary lipoma and atypical lipomatous tumors: immunohistochemical reactivity correlates with karyotypic alterations. Am J Pathol. 1997 Jul;151(1):37-43

Tkachenko A, Ashar HR, Meloni AM, Sandberg AA, Chada KK. Misexpression of disrupted HMGI architectural factors activates alternative pathways of tumorigenesis. Cancer Res. 1997 Jun 1;57(11):2276-80

Williams AJ, Powell WL, Collins T, Morton CC. HMGI(Y) expression in human uterine leiomyomata. Involvement of another high-mobility group architectural factor in a benign neoplasm. Am J Pathol. 1997 Mar;150(3):911-8

Xiao S, Lux ML, Reeves R, Hudson TJ, Fletcher JA. HMGI(Y) activation by chromosome 6p21 rearrangements in multilineage mesenchymal cells from pulmonary hamartoma. Am J Pathol. 1997 Mar;150(3):901-10

Bandiera A, Bonifacio D, Manfioletti G, Mantovani F, Rustighi A, Zanconati F, Fusco A, Di Bonito L, Giancotti V. Expression of HMGI(Y) proteins in squamous intraepithelial and invasive lesions of the uterine cervix. Cancer Res. 1998 Feb 1;58(3):426-31

Hess JL. Chromosomal translocations in benign tumors: the HMGI proteins. Am J Clin Pathol. 1998 Mar;109(3):251-61

Kazmierczak B, Dal Cin P, Wanschura S, Borrmann L, Fusco A, Van den Berghe H, Bullerdiek J. HMGIY is the target of 6p21.3 rearrangements in various benign mesenchymal tumors. Genes Chromosomes Cancer. 1998 Dec;23(4):279-85

Martelli AM, Riccio M, Bareggi R, Manfioletti G, Tabellini G, Baldini G, Narducci P, Giancotti V. Intranuclear distribution of HMGI/Y proteins. An immunocytochemical study. J Histochem Cytochem. 1998 Jul;46(7):863-4

Shannon MF, Himes SR, Attema J. A role for the architectural transcription factors HMGI(Y) in cytokine gene transcription in T cells. Immunol Cell Biol. 1998 Oct;76(5):461-6

Dal Cin P, Fusco A, Belge G, Chiappetta G, Fedele M, Pauwels P, Bullerdiek J, Van den Berghe H. Involvement of the HMGI(Y) gene in a microfollicular adenoma of the thyroid. Genes Chromosomes Cancer. 1999 Mar;24(3):286-9

Kazmierczak B, Meyer-Bolte K, Tran KH, Wöckel W, Breightman I, Rosigkeit J, Bartnitzke S, Bullerdiek J. A high frequency of tumors with rearrangements of genes of the HMGI(Y) family in a series of 191 pulmonary chondroid hamartomas. Genes Chromosomes Cancer. 1999 Oct;26(2):125-33

Klotzbücher M, Wasserfall A, Fuhrmann U. Misexpression of wild-type and truncated isoforms of the high-mobility group I proteins HMGI-C and HMGI(Y) in uterine leiomyomas. Am J Pathol. 1999 Nov;155(5):1535-42

Pedeutour F, Ligon AH, Morton CC. [Genetics of uterine leiomyomata]. Bull Cancer. 1999 Nov;86(11):920-8

Sornberger KS, Weremowicz S, Williams AJ, Quade BJ, Ligon AH, Pedeutour F, Vanni R, Morton CC. Expression of HMGIY in three uterine leiomyomata with complex rearrangements of chromosome 6. Cancer Genet Cytogenet. 1999 Oct 1;114(1):9-16

Yie J, Merika M, Munshi N, Chen G, Thanos D. The role of HMG I(Y) in the assembly and function of the IFN-beta enhanceosome. EMBO J. 1999 Jun 1;18(11):3074-89

Banks GC, Li Y, Reeves R. Differential in vivo modifications of the HMGI(Y) nonhistone chromatin proteins modulate nucleosome and DNA interactions. Biochemistry. 2000 Jul 18;39(28):8333-46

Tallini G, Vanni R, Manfioletti G, Kazmierczak B, Faa G, Pauwels P, Bullerdiek J, Giancotti V, Van Den Berghe H, Dal Cin P. HMGI-C and HMGI(Y) immunoreactivity correlates with cytogenetic abnormalities in lipomas, pulmonary chondroid hamartomas, endometrial polyps, and uterine leiomyomas and is compatible with rearrangement of the HMGI-C and HMGI(Y) genes. Lab Invest. 2000 Mar;80(3):359-69

*This article should be referenced as such:*

Gattas GJF, Pedeutour F. HMGIY (high mobility group protein (non histone chromosomal) isoform I and Y). Atlas Genet Cytogenet Oncol Haematol. 2001; 5(1):3-6.