**Gene Section**

Mini Review

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

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### Identity

**Other names:** HMGI-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 through 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.

![HMGIY gene](image-url)
**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-β, E-selectin, interleukin-2 receptor α-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 α4 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 within 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


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


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