Gene Section
Mini Review

MSH3 (mutS homolog 3 (E. coli))

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Identity

Hugo: MSH3
Other names: DUP; hMSH3; MRP1
Location: 5q11-q12
Local order: Between the DHFR and RASGRF2 genes.

DNA/RNA

Description
The MSH3 gene is composed of 24 exons spanning in a region of 222 Kb.

Transcription
There are two major transcripts of 5 kb and 3.8 kb under the control of two different polyadenilation sites.

Protein

Description
Amino acids: 1137. Molecular Weight: 127 KDa. MSH3 is a protein involved in the mismatch repair process after DNA replication.

Expression
Expression of MSH3 together with the dihydrofolate reductase (DHFR) gene appear to be regulated by a bidirectional promoter composed of multiple GC boxes and two initiator elements. MSH3 is expressed in all human tissues at low levels but with variable intensities, with higher expression in testis and pancreas and lower in small intestine and colon.

Function
MSH3 binds to MSH2 to form the MutSb heterodimer, which binds to insertion-deletion mismatches of two or more base pairs. Thereafter the MutS complex associates with the MutL complex and recruits the proteins needed for DNA excision and repair.

Homology
MSH3 is homologue to the bacterial MutS gene and to the Msh3 gene in S. cerevisiae. Homology is higher in the C-terminal region.

Mutations

Somatic
MSH3 has insertions/deletions in a A(8) repeat in tumours showing microsatellite instability (MSI). As MSH3 is a mismatch repair gene and is mutated in a microsatellite only in MSI tumours is considered to be a secondary mutator that enhances a more severe MSI.

Implicated in

MSI (MicroSatellite Instability)

Note: Tumours in which the molecular feature that leads to cancer is the lost of the mismatch repair (MMR) system.

Disease
This phenotype is present in 15% of colorectal cancer, gastric cancer and endometrial cancer, and with lower incidence in some other tissues.

Oncogenesis
The average frequencies of the microsatellite mutation reported in sporadic MSI from colorectal, gastric and endometrial cancer are 38%, 39% and 25% respectively. In hereditary MSI (or HNPCC) is 51%.

Hematological malignancies

Oncogenesis
It has been reported loss of expression of MSH3 at the mRNA level in some hematological malignancies
including chronic myelogenous leukemia and acute myelogenous leukemia, acute lymphocytic leukemia and myelodysplastic syndrome.

References


This article should be referenced as such: