

BACKGROUND

MLH1 (MutL Homolog 1, colon cancer, nonpolyposis type 2 (*E. coli*)) is a protein involved in the mismatch repair process after DNA replication. MLH1 is homologue to the bacterial MutL gene, especially in the N-terminal region, and MLH1 homologues are also present in eukaryotes (for example in *Mus musculus*, *Drosophila melanogaster*, *Caenorhabditis elegans* or *Saccharomyces cerevisiae*). It contains an ATPase domain and two interaction domains, one for MutS homologs (MSH2, MSH3, MSH6) and the other for PMS2, MLH3 or PMS1. MLH1 has no known enzymatic activity. MLH1 forms a heterodimerizer with PMS2 to form MutL alpha, a component of the post-replicative DNA mismatch repair system (MMR). DNA repair is initiated by MutS alpha (MSH2-MSH6) or MutS beta (MSH2-MSH6) binding to a dsDNA mismatch, then MutL alpha is recruited to the heteroduplex. Assembly of the MutL-MutS-heteroduplex ternary complex in presence of RFC and PCNA is sufficient to activate endonuclease activity of PMS2. It introduces single-strand breaks near the mismatch and thus generates new entry points for the exonuclease EXO1 to degrade the strand containing the mismatch. DNA methylation would prevent cleavage and therefore assure that only the newly mutated DNA strand is going to be corrected. MutL alpha (MLH1-PMS2) interacts physically with the clamp loader subunits of DNA polymerase III, suggesting that it may play a role to recruit the DNA polymerase III to the site of the MMR.¹ MLH1 is also implicated in DNA damage signaling, a process which induces cell cycle arrest and can lead to apoptosis in case of major DNA damages. MLH1 heterodimerizes with MLH3 to form MutL gamma which plays a role in meiosis.²

There are over 300 MLH1 germline mutations described all along the gene that cause hereditary non-polyposis colorectal cancer (HNPCC). These mutations are not present in any particular hotspot or zone of the gene and include either nucleotide substitutions (missense, nonsense or splicing errors) or insertions/deletions (gross or small). In most of these mutations the resulting protein is truncated. There are also founding mutations which account for a high proportion of the HNPCC tumors in some specific populations (for example there are two Finnish mutations that delete the exons 16 or 6). Some germline genetic changes have also been described in both exons and introns as non pathogenic. There are described some sporadic mismatch repair deficiency cases (sporadic MSI) with somatic MLH1 mutations, although most of them have MLH1 promoter hypermethylation.³

References:

1. Schofield, M.J. & Hsieh, P.: Ann. Rev. Microbiol. 57:579-609, 2003
2. Lipkin, S.M. et al: Nature Genet. 31:385-90, 2002
3. Bronner, C.E. et al: Nature 368:258-61, 1994

TECHNICAL INFORMATION

Source:

MLH1 antibody is a mouse monoclonal antibody raised against purified recombinant human MLH1 fragment expressed in *E. coli*.

Specificity and Sensitivity:

This antibody detects endogenous MLH1 proteins without cross-reactivity with other family members.

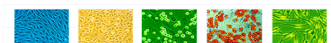
Storage Buffer: PBS and 30% glycerol

Storage:

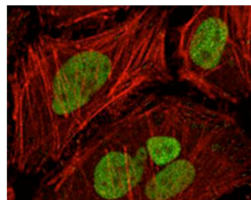
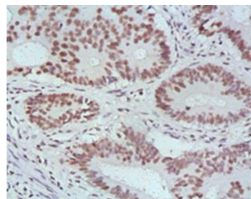
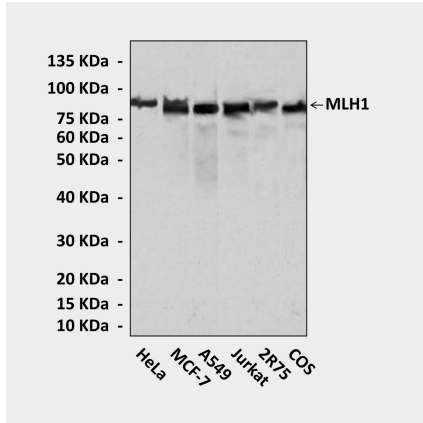
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	1:50
IHC	1:200
ICC	1:200
FACS	n/d
*Optimal dilutions must be determined by end user.	



QUALITY CONTROL DATA



Top: Western Blot detection of MLH1 proteins in various cell lysates using MLH1 Antibody. **Middle:** This antibody stains paraffin-embedded human rectum cancer tissue in immunohistochemical analysis. **Bottom:** It also stains HeLa cells in confocal immunofluorescent testing (MLH1 antibody: Green; Actin filaments: Red; DRAQ5 DNA dye: Blue).

