

# Expression Profile of Human *PMS2*-like Genes: Bioinformatic and Experimental Studies

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## Abstract

The expression patterns of human *PMS2*-like sequences found on chromosome 7 of the genome of *Homo sapiens* have been studied by bioinformatic and experimental means. As a result, full-length cDNAs synthesized from all main groups of the fifteen paralogues of *PMS2* gene of *Homo sapiens* have been cloned from different human tissues and their primary sequences were established including some polymorphic variants. For the first time starting (containing ATG initiation codon) coding exons of  $\psi 5$  and  $\psi 13$  genes were identified (first predicted and then experimentally verified). This fact provide an important evidence in favor of existence of the hPMS2L proteins in human proteome.

**Keywords:** DNA mismatch repair system, chromosome 7, *PMS2*-like sequences, expression profile, *PMS2* and *PMS2L* proteins

## 1 Introduction

Mismatched nucleotides are regularly introduced by DNA polymerase during cell division and uncorrected nucleotides will result in mutations. In most cellular organisms, such replication errors are repaired mainly by the DNA mismatch repair (MMR) system that enhances replication fidelity up to 1000-folds by repairing mismatched nucleotides, and small insertions and deletions [1, 2]. The MMR system also prevents recombination between divergent sequences and repairs mismatches on heteroduplex DNA that arise during homologous recombination [3]. Therefore, defects in the MMR could lead to highly elevated mutation rates, meiotic defects and infertility [4]. Human *PMS2* protein belongs to important components of the DNA mismatch repair (MMR) system. It is a homologue of *Escherichia coli* MutL protein. In contrast to the majority of eukaryotes, not only *PMS2* gene but also the fifteen different *PMS2*-like sequences that encode numerous and various mRNAs have been found on chromosome 7 in the human genome [5-10]. The origin, exon-intron structure, and the biological role of these so-called *PMS2* pseudogenes and products of their expression remain unstudied.

## 2 Results and Discussion

Expression of the fifteen different *PMS2*-like sequences located together with the original *hPMS2* gene on human chromosome 7 produced plural mRNAs of different types. Computational analysis of all *hPMS2*-related ESTs and cDNAs available in current databases has allowed us to classify them into three main classes covering exons 1-5 (class I), 9-11 (class II) and 11-15 (class III) of the original *hPMS2* master gene, respectively. In addition, cDNAs belonging to the two first classes were further subdivided into two different subgroups each, producing five structurally distinguished subgroups of *PMS2*-like mRNAs in total. Because nucleotide sequences of the most complete members of the every subgroup have extensive coding capacities ranging at least from 190 to 240 aminoacids, we have isolated them from different sources and recloned in

suitable vectors for yeast two-hybrid system and for heterologous overexpression in *Escherichia coli*. Complete *PMS2*-like cDNAs representing four out of five subgroups have been already cloned and structurally characterized. Particularly of interest, for the first time cDNAs were isolated containing the first coding, ATG-containing exon of two *PMS2*-related human genes belonging to the class I (see above). This first exon was missing in all previously reported mRNAs [5-7]. The data obtained further support our hypothesis about existence in *Homo sapiens* special *PMS2* alike tripartite polypeptide system probably having unique, human-specific functions [11].

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