Correction: Identification of Novel Pathogenic Sequence Variants of the Mismatch Repair Genes During Screening for Lynch Syndrome in a Single Centre of Eastern Hungary

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The original version of this article unfortunately contained a mistake. The variants listed in Table 3 of the original version of this article are not in line with the latest HGVS (Human Genome Variation Society) nomenclature (version 19.01). The correct variants are listed in the corrected Table 3 below. The relevant corrected sections:

Mutations Identified in the hMLH1 Gene

A pathogenic sequence variant of hMLH1 gene was found in 2 patients (Table 3). In patient #1, a missense mutation in codon 48, exon 2 (c.143A>C) was identified. This mutation results in an amino acid change: from glutamine to proline (p.Q48P). We have previously published this mutation as it was found in our several screened families [26,

27]. It has also been reported by others as a pathogenic sequence variant of the MMR genes causing Lynch syndrome [30], and can be found in multiple databases, such as ClinVar, dbSNP, and OMIMdatabases (<https://www.ncbi.nlm.nih.gov/clinvar/variation/89739>, <https://www.ncbi.nlm.nih.gov/snp/587778914>). Based on these circumstances, we suspect that this is a European founder mutation. During the DNA sequencing of the second patient, an ins>frameshift>STOP mutation of the exon 11 of hMLH1 gene was identified. This is a one-nucleotide insertion which causes a frameshift when an extra cytosine is inserted into the 901 position. During translation, a proline will be inserted instead of glutamine at the 301 position, and behind 4 more amino acids there will be a STOP codon. Altogether, 5 new amino acids will be expressed and then the translation will be stopped (P-X-X-X-X-STOP). This mutation cannot be found in any of the databases and was not published yet by other groups. We believe that it is a new pathogenic sequence variant of the

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MMR genes, which is responsible for the development of Lynch syndrome in this patient.

Mutations Identified in the hMSH2 Gene

MSI-H status and absence of nuclear expression of the hMSH2 and hMSH6 proteins were found in the third patient's tumor in Table 3. DNA sequencing revealed a pathogenic nonsense mutation in exon 13 at codon 680 in the hMSH2 gene. An arginine to STOP codon change was caused by this mutation, which results in a cytosine-thymine change at 2038 position, thus leading to premature protein chain termination. It is a well-known pathogenic sequence variant of the MMR genes causing Lynch syndrome and has been reported several times in the literature. It can also be found in dbSNP and ClinVar databases (<https://www.ncbi.nlm.nih.gov/snp/63749932>, <https://www.ncbi.nlm.nih.gov/clinvar/variation/36572/#summary-evidence>). Patient #6 had a simultaneous hMLH1 promoter hypermethylation and hMSH2 gene mutation on exon 14 showing double deletion→frameshift→STOP mutation. This mutation

involves multiple nucleotide (c.[2366_2367del;2370_2375del]), which causes a frameshift. As a consequence, the frameshift starts at the 789 position in the protein, where valine is expressed instead of alanine. Five more codons then follow and the sixth is a STOP codon (V-X-X-X-X-STOP). Based on the ClinVar database, this region is very variable and multiple mutations have been published, most of which were associated with Lynch syndrome ([https://www.ncbi.nlm.nih.gov/clinvar?term=609309\[MIM\]](https://www.ncbi.nlm.nih.gov/clinvar?term=609309[MIM])). To the best of our knowledge, this mutation has not been published so far. We believe that this is a new pathogenic sequence variant from an unstable region in the hMSH2 gene associated with Lynch syndrome.

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Table 3 The locations of the variants and the 2 hMLH1 promoter hypermethylation

	Sex	Age at diagnosis	Amsterdam II	Bethesda	MSI	MLH1 promoter hyper-methylation	Affected gene	Type of the variant	Variant*	Effect on protein level*
1	F	44	No	yes	H	no	MLH1	Probably Founder	c.143A>C	p.Q48P
2	M	40	No	yes	H	no	MLH1	New mutation	c.901dup	p.Q301Pfs*6
3	M	43	No	yes	H	no	MSH2	Probably Founder	c.2038C>T	p.R680*
4	M	32	Yes	no	H	no	EPCAM	Large deletion	g.(47601138_47612316)_ (47617251_47627529)del	Uncertain
5	M	43	No	yes	H	yes		No mutation hyper-methylation	—	
6	F	30	Yes	no	H	yes	MSH2	New mutation with hyper-methylation	c.[2366_2367del;2370_2375del] or c.2366_2375delinsTT	p.A789Vfs*7

* NCBI RefSeq accession numbers: NM_000249.4 for MLH1 and NM_000251.3 for MSH2 and NC_000002.12 for EPCAM