Supplemental Table 1.

CEM no. and gender	**methylation in blood**	**clinical features**	**transmission of CEM or segregation**	**tumour diagnoses in the family**
1 m	50-60%, BS allele-specific	33 y CC. asc., 47 y CC sigma, 47 y CC rectum	n.a.	half-brother (mat. line) 51 gastric C
2 f	~20%, BS	58 y CC sigma, 59 y CC transversum + sigma MSS	n.a.	son 34 y hyperplastic polyps
3 m	~20%, BS	41 y CC rectum	no: meth. erasure in three sons with different pat. alleles, brother n.i. unmeth.	mother 59 y CC, brother 44 y adenomas
4 m	25% and *MLH1* duplication, BS	39 y CC transversum	yes: CEM of 20% and duplication also in mother with 65 y CC and in sister	mother 65 y CC, father adenomas
5 f	50%, BS allele-specific	40 y CC rectum, 41 y CC sigma	no: de novo set-up of CEM on mat. allele, brother inherited other mat. allele	mother 33 y cervix C, 64 y CC (MSS) without CEM in blood
6 m	50%, BS c.-269G meth	40 y CC asc., 44 y CC rectum	n.a., son inherited unmethylated allele	father 50 y multiple adenomas
7 m	50-60%, BS: allele-specific	33 y CC transversum	n.a.	no information
8 m	50%, BS	35 y CC asc, 42 y + 48 y skin C, 49 y cystic sebaceous gland C	n.a.	pat. uncle 72 y CC, mat. grandmother 84 y CC
9 f	BS allele-specific but partial meth.	37 y CC asc	no: de novo set-up of CEM on mat. allele	father 41 y renal C, mother healthy unmeth.
10 f	50%, BS allele-specific	30 y CC left flexure	n.a.	no information
11 m	25-35%, BS	46 y CC asc + CC transversum	n.a., both sons unmeth., but n.i.	
12 f	20-25%, BS	35 CC asc	n.a.	
13 m	50%, BS allele-specific	38 y gastic C, 51 y CC rectum, adenomas	n.a., daughter inherited unmeth allele, sister n.i. unmeth.	grandmother CC
14 m	50-60%, BS allele-specific	53 y CC coecum	no: meth. erasure in both sons with paternal meth. allele	father 73 y bladder C, sister 44 y leukemia, son 22 y adenomas
15 m	50%, BS c.-63_-58delins18 meth.	35 y CC	yes: sister also with 50% CEM and promoter variant c.-63_-58delins18 meth.	mat. grandfather 64 y CC, mother 45 y BrC, mat. aunt 54 y BrC, father healthy unmeth.
16 m	50%	30 y CC rectum, 41 y CC asc		no tumors reported

Supplemental Table 1: Details for the sixteen patients with a constitutional *MLH1* epimutation (CEM). The promoter methylation in blood is given in % if analysed by MS-MLPA, otherwise bisulphite sequencing (BS) was performed. The clinical data of the CEM carriers, transmission or segregation of CEM in family members, and family history of tumours are also listed. Diagnoses are given in years (y). Abbreviations: cancer (C), colon cancer (CC), ascendens (asc), breast cancer (BrC), maternal (mat.), methylated (meth.), paternal (pat.), not analysed (n.a.), not informative (n.i.).