

Expression in control blood : $\Delta$ CTm (CTm)			
Sample	MAEL	SYCE1	
WB1	18.45 (>40)	12.25 (33.8)	
WB2	16.85 (>40)	10.62 (33.77)	
WB3	20.05 (>40)	15.48 (35.43)	
WB4	18.33 (>40)	10.82 (32.49)	
WB5	17.25 (>40)	15.07 (37.82)	
WB6	18.52 (>40)	18.23 (39.71)	
Median $\Delta$ CTm			
CTL	18.39	13.66	
Standard error			
CTL	1.12	3.01	
Expression in ICF1 patients : $\Delta$ CTm (CTm)			
pH	11 (32.5)	7.39 (28.88)	
pY	8.14 (30.88)	4.66 (27.39)	
P3	9.97 (30.65)	7.55 (28.24)	
<b>P4</b>	<b>9.46 (29.26)</b>	<b>9.4 (29.20)</b>	
P5	11.1 (0.06)	7.95 (28.44)	
Median $\Delta$ CTm			
ICF1	9.97	7.55	
Standard error			
ICF1	1.22	1.72	
p values			
ICF1 vs CTL		ICF1 vs CTL	
<b>9.17E-07</b>		<b>2.45E-03</b>	
ICF2 $\Delta$ CTm (CTm)			
P6	19.23 (>40)	11.1 (31.87)	
pD	20.13 (>40)	13.14 (33.01)	
pV	20.19 (>40)	12.15 (31.96)	
P8	18.57 (>40)	11.22 (32.65)	
Median $\Delta$ CTm			
ICF2	19.68	11.69	
Standard error			
ICF2	0.77	0.95	
p values			
ICF1 vs ICF2	ICF2 vs CTL	ICF1 vs ICF2	ICF2 vs CTL
<b>2.74E-06</b>	<b>0.08</b>	<b>2.29E-03</b>	<b>0.28</b>

**Additional File 6. Analysis of MAEL and SYCE1 gene expression in whole blood.** Total RNA was extracted from whole blood from healthy donors (CTL), ICF1 and ICF2 patients and subjected to RT-qPCR using primers specific for MAEL or SYCE1 mRNA. For each sample, the differences in cycle threshold (DCT) between germline gene and control U6 snRNA are indicated as a mean value of 3 independent experiments ( $\Delta$ CTm = CTm<sub>GENE</sub> - CTm<sub>U6</sub>). A mean value of the raw cycle threshold (CTm) values are indicated into brackets. For each population, median and standard error are indicated. For both genes, the differences in expression between ICF1 and CTL or ICF2 blood samples are strongly significant ( $p < 0.01$ ;  $p$  value calculated using paired, two-tailed Student's  $t$ -test) and are highlighted in blue. The values for MAEL and SYCE1 expression in whole blood from the young child diagnosed in Figure 3 are indicated in red.