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Supplementary information

The proliferative history shapes the DNA methylome of B-cell tumors and predicts clinical outcome

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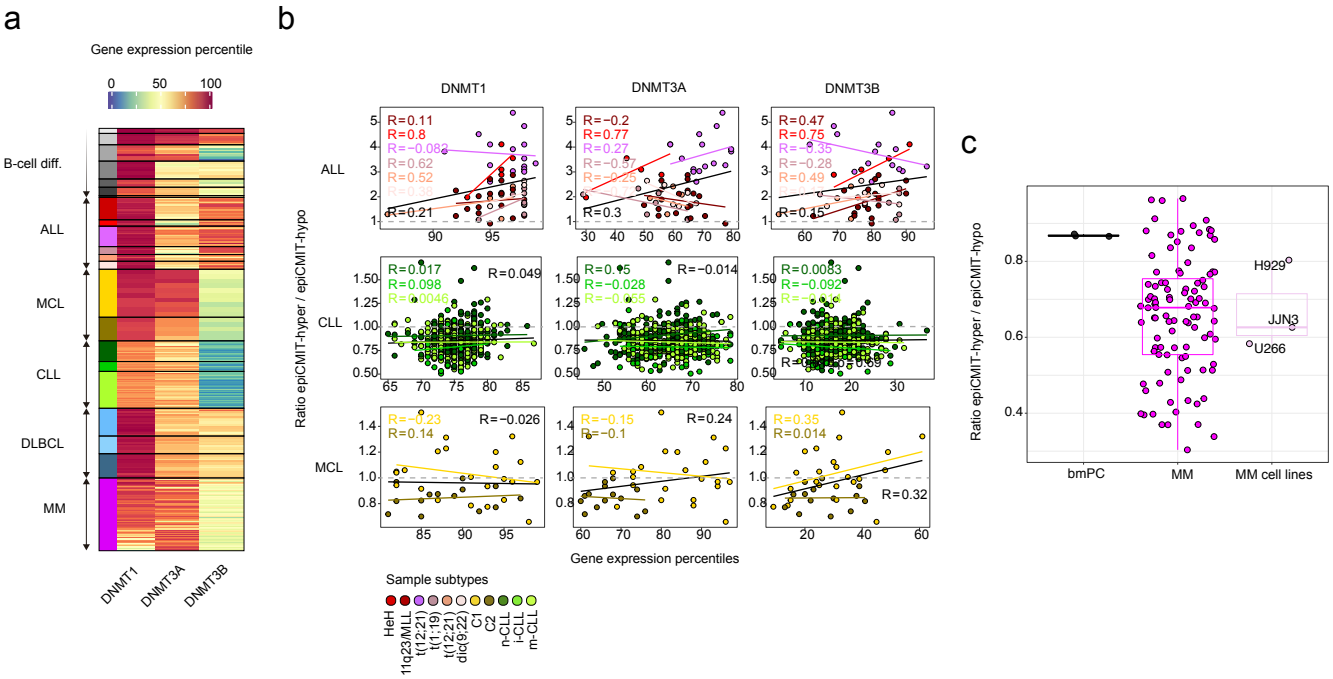

Supplementary Figure 1. Study of DNA methylation changes in relation to the DNA methyltransferase enzymes.

a, Expression of DNMT1, DNMT3A and DNMT3B in normal and neoplastic B cells. In general, DNA methyltransferase enzymes are highly expressed in neoplastic B cells, and thus their sole relative expression levels cannot account for the highly divergent tendencies for gaining or losing DNA methylation in ALL or MM subtypes.

b, ALL, MCL and CLL samples do not show differences in the epiCMIT-hyper/epiCMIT-hypo ratio due to different DNMT expression levels. If the different expression levels of DNMTs would affect the way B-cell tumors acquire DNA methylation changes, a correlation between DNMTs expression levels and the epiCMIT-hyper/epiCMIT-hypo ratio would be shown. Of note, epiCMIT-hyper and epiCMIT-hypo are highly correlated with the total number of hyper- and hypomethylated CpGs in normal and neoplastic B cells.

c, epiCMIT-hyper/epiCMIT-hypo ratio in bmPC, MM patients, and 3 MM cell lines, which show 7.7 fold increase of DNMT1 expression as compared to primary MM samples (Bollati et al., Carcinogenesis, Volume 30, Issue 8, August 2009, Pages 1330–1335). Despite this overexpression of DNMT1, these MM cell lines show the tendency of losing methylation as in the case of bmPC and MM samples, suggesting that DNA methylation loss in MM is beyond the single DNMTs expression levels.