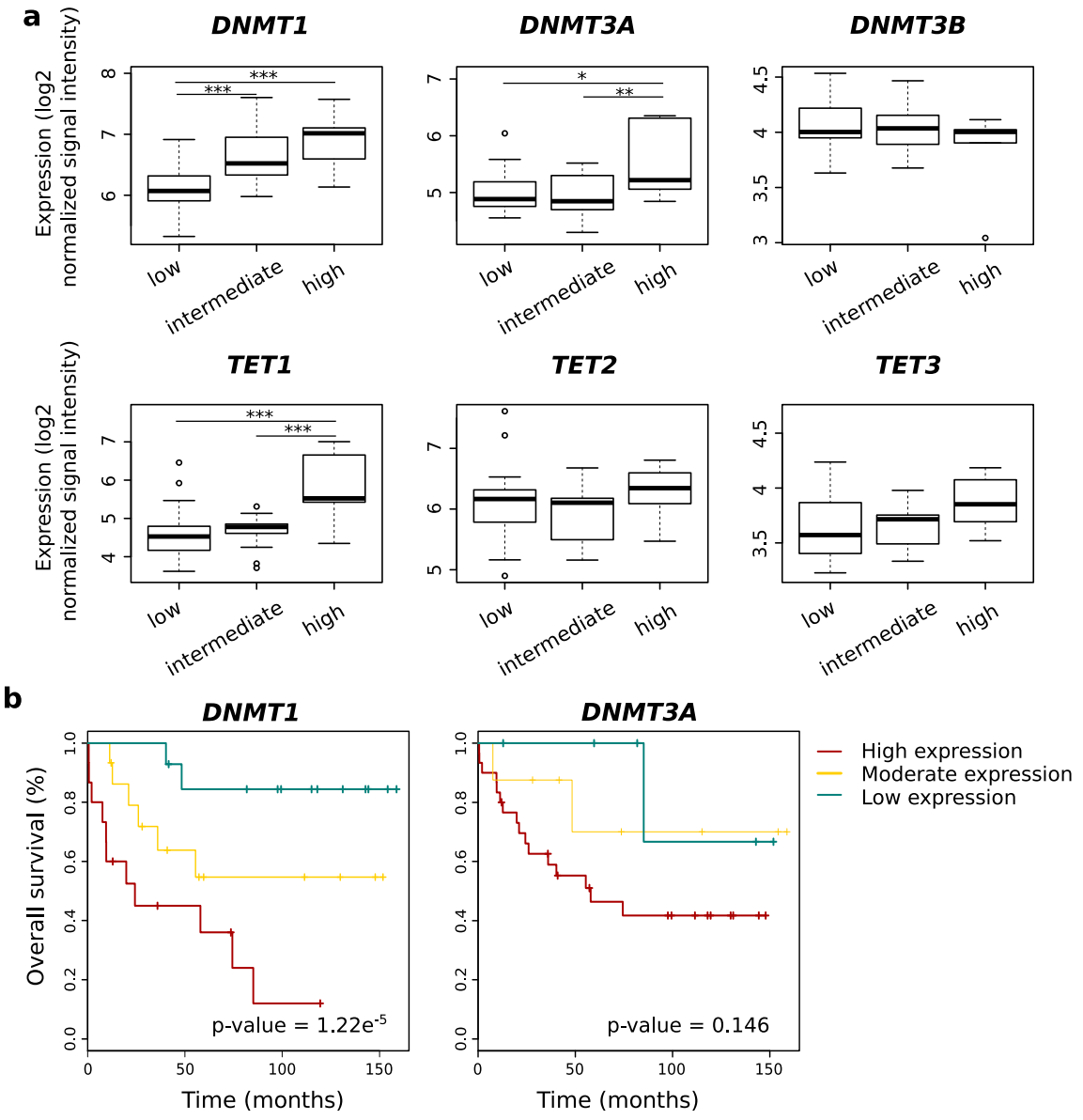

Figure S1. *DNMT1* and *DNMT3A* expression levels are upregulated in high CIMP ACC and are associated with poor clinical outcome

(**a**) Expression levels of *DNMT1*, *DNMT3A*, *DNMT3B*, *TET1*, *TET2* and *TET3* in the ENSAT patients exhibiting lCIMP, iCIMP and hCIMP (two-sided t-test, *p < 0.05, **p < 0.01, ***p < 0.005).

(**b**) Kaplan-Meier estimates of overall survival for ACC patients, as a function of DNMT1 or DNMT3A.

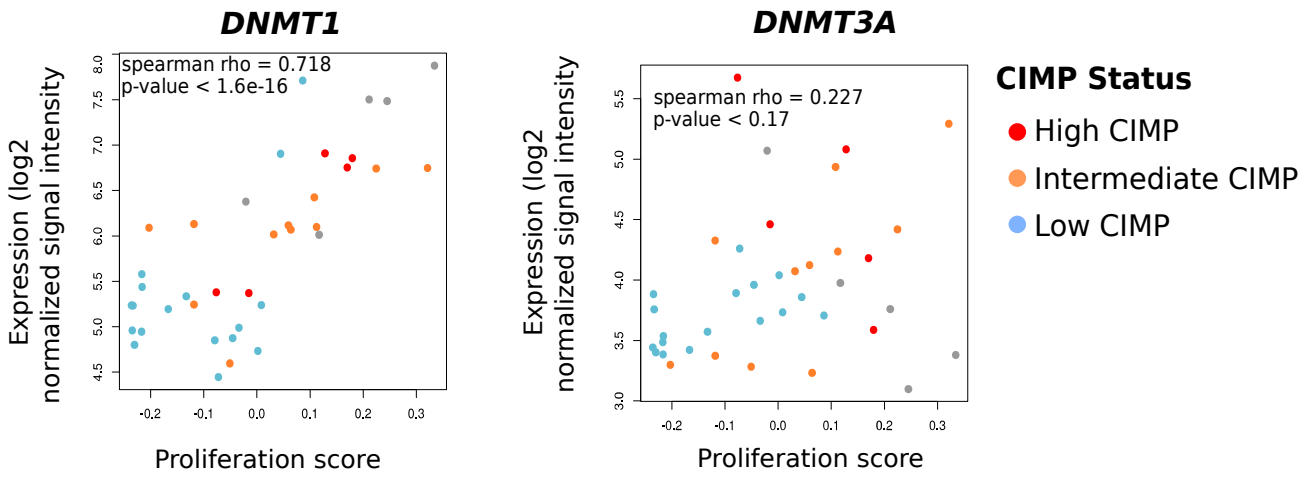

Figure S2. *DNMT1* and *DNMT3A* expression is are associated with high proliferation

Correlation between *DNMT1* and *DNMT3A* expression and cell proliferation in the ENSAT patients. hCIMP samples are represented in red, iCIMP in orange and lCIMP in blue. Patients for whom the CIMP status was not defined are represented in gray.

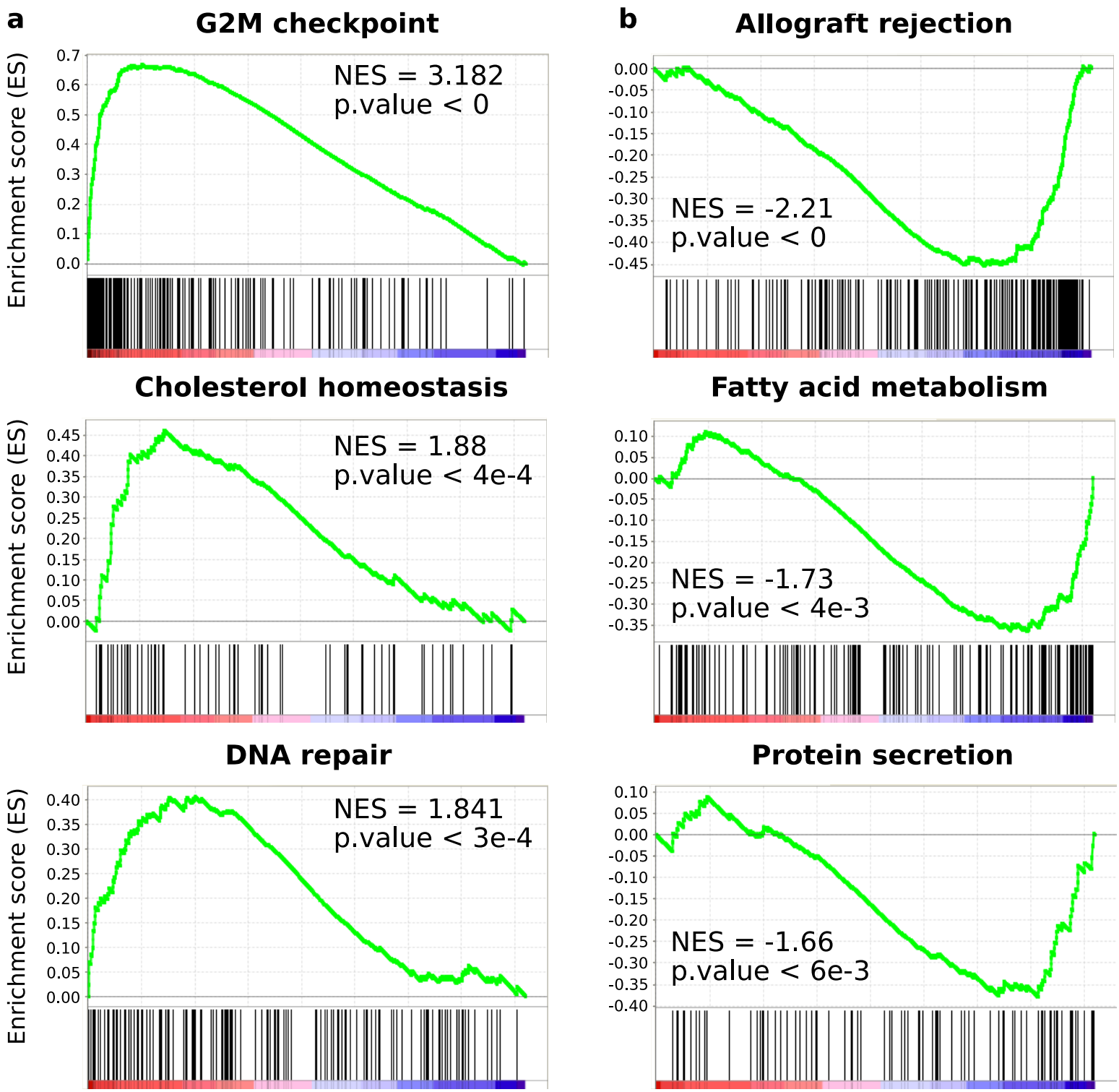

Figure S3. Gene Set Enrichment Analysis on TCGA datasets comparing hCIMP and lCIMP samples

(**a**) Representative example of gene sets enriched in hCIMP.

(**b**) Representative example of gene sets enriched in lCIMP.

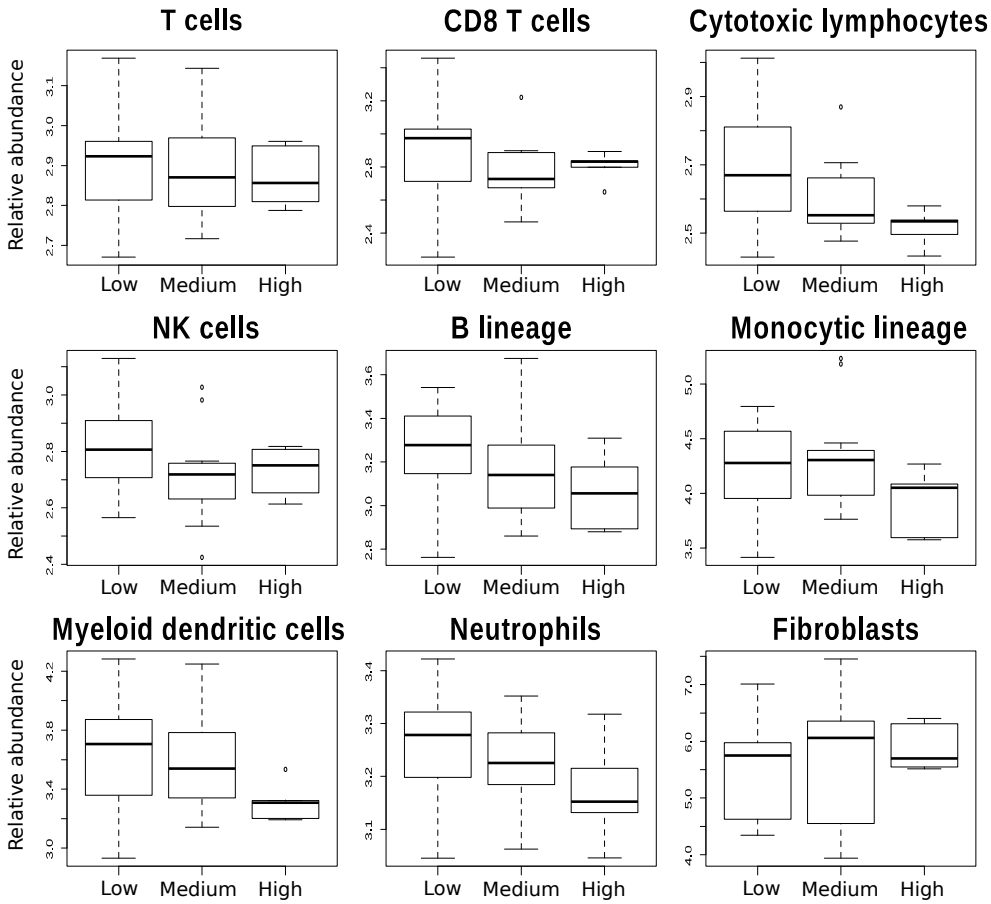

Figure S4. CIMP in ACC is characterized by lower abundance of tumor-infiltrating immune cells
Relative abundance of tumor-infiltrating immune and non-immune stromal cell populations, computed using MCP-counter, in lCIMP, iCIMP and lCIMP samples from the ENSAT dataset. Comparison of relative abundances of each population using Kruskal–Wallis test followed by Dunn's test with Benjamini–Hochberg corrections.

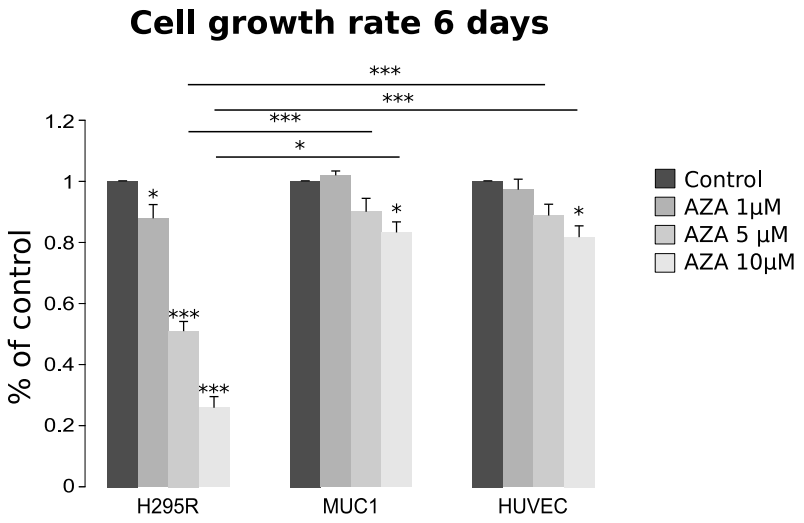

Figure S5. Impact of demethylating agent on cell proliferation in ACC cell lines

Effect of a 6-day treatment with the DNA methylation inhibitor 5-azacytidine (AZA) at 1, 5, or 10µM in the H295R (n=4), MUC1 (n=5) cell lines and the non-tumor HUVEC cell line (n=5). Cell growth was estimated by neutral red proliferation assay. *P*-values of the Kruskal–Wallis test and Dunn's test for stochastic dominance are reported: * p-value < 0.05; ** p-value < 0.01; *** p-value < 0.005

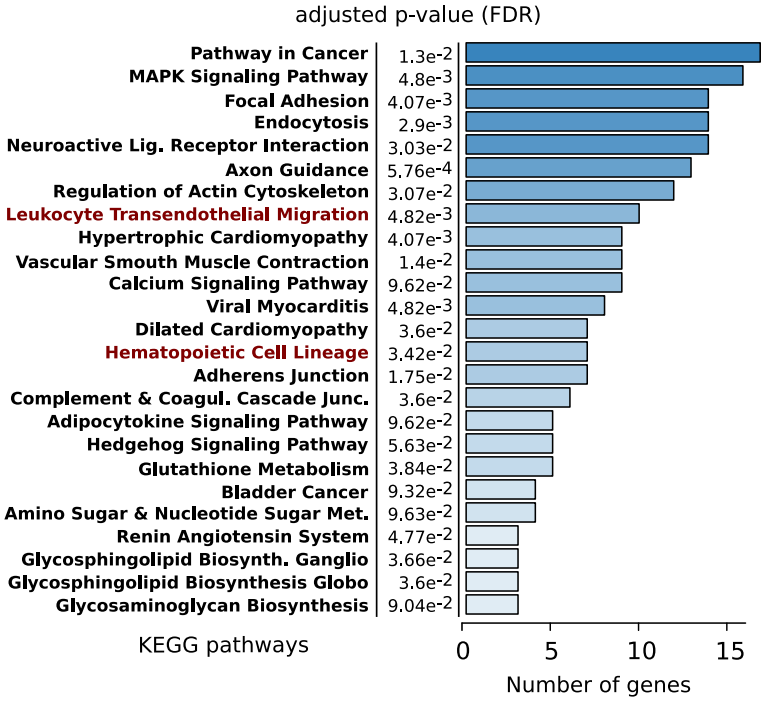

Figure S6. Gene pathways differentially active in H295R compared to MUC-1 cells due to DNA hypermethylation

Pathway enrichment analysis on genes that exhibit a significantly hypermethylated DMR in their promoter and significantly lower expression in H295R than in MUC-1 cells. Pathways related to the immune response are highlighted in red.