Overlapping DNA methylation changes in enhancers in clonal cytopenia of undetermined significance and myelodysplastic neoplasm patients with *TET2*, *IDH2*, or *DNMT3A* mutations

Authors

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Supplementary data

Supplementary table 1. Clinical characteristics.

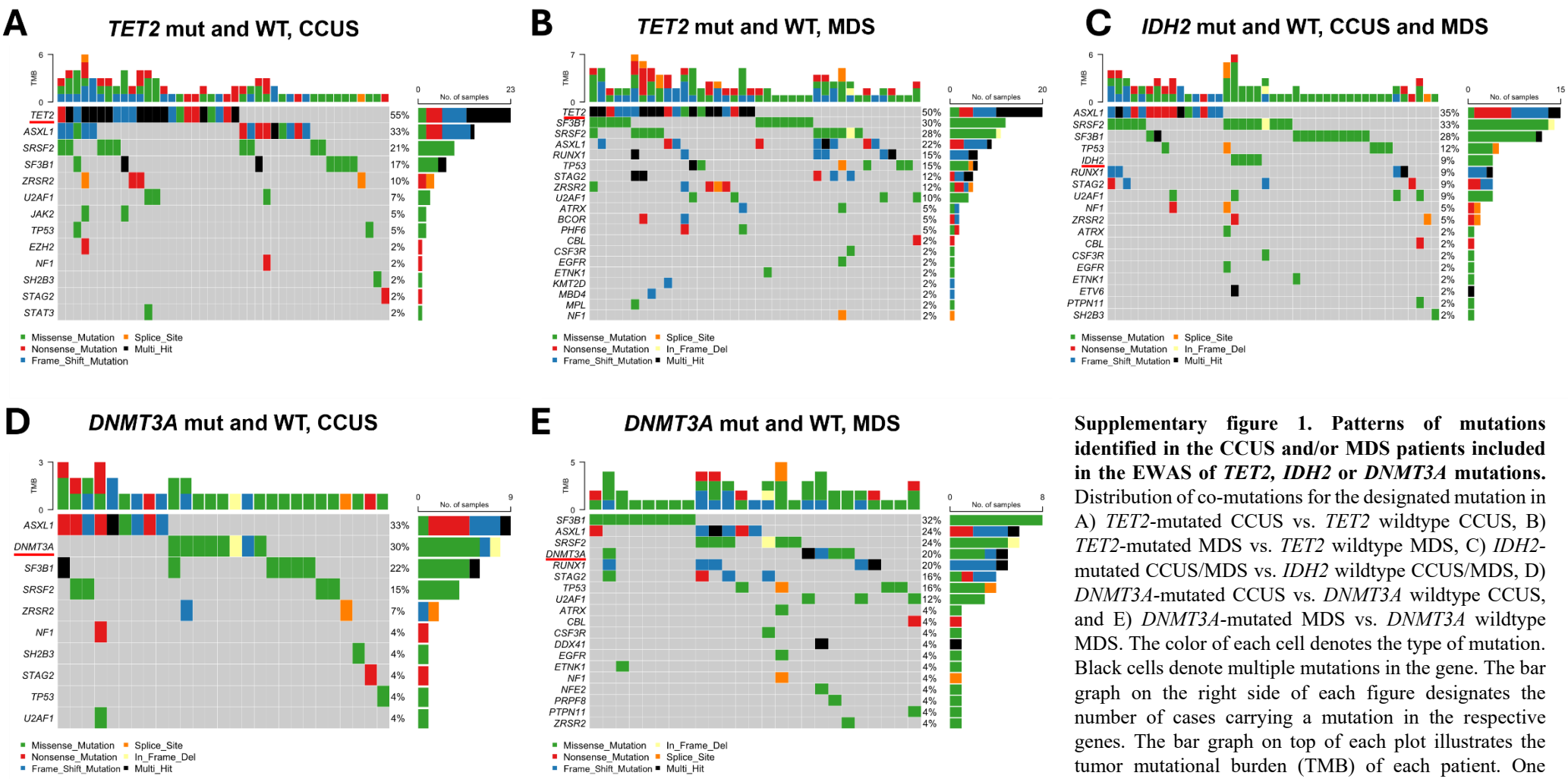
Characteristic	CCUS, n = 58 [1]	MDS, n = 59 [1]	P-value [2]
Age	75.0 (54.0, 90.0)	74.0 (41.0, 93.0)	>0.9
Sex			0.3
Female	12 (21%)	17 (29%)	
Male	46 (79%)	42 (71%)	
Hgb (mmol/L)	7.5 (4.8, 10.0)	6.3 (3.0, 9.0)	**<0.001**
ANC (cells/L)	2.2 (0.4, 11.1)	1.9 (0.3, 6.7)	0.07
Missing	1	0	
Platelets (cells/L)	135.0 (20.0, 539.0)	126.0 (25.0, 666.0)	0.6
Missing	1	0	
IPSS-R category			>0.9
Very low		13 (25%)	
Low		27 (51%)	
Intermediate		8 (15%)	
High		5 (9.4%)	
Very high		0 (0%)	
Missing		6	
Number of mutations			**0.003**
0	1 (1.7%) [3]	6 (10%)	
1	27 (47%)	10 (17%)	
2	12 (21%)	16 (27%)	
≥ 3	18 (31%)	27 (46%)	

[1] Median (range); n (%)

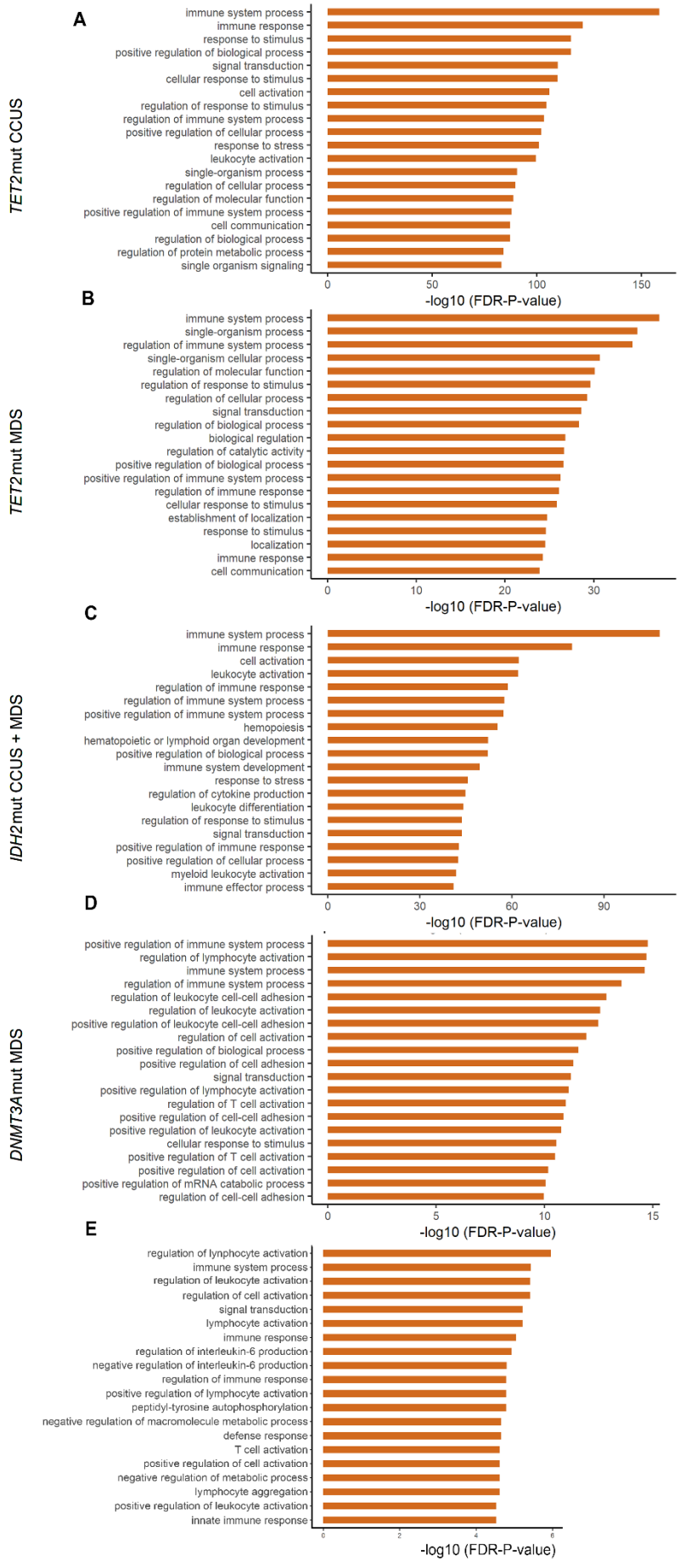
[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

[3] One patient with CCUS has no somatic mutations but present with trisomy 15

Hgb: hemoglobin; ANC: absolute neutrophil count; IPSS-R, Revised International Prognostic Scoring System; CCUS: clonal cytopenia of undetermined significance; MDS: myelodysplastic neoplasms.



Supplementary figure 1. Patterns of mutations identified in the CCUS and/or MDS patients included in the EWAS of *TET2, IDH2* or *DNMT3A* mutations. Distribution of co-mutations for the designated mutation in A) *TET2*-mutated CCUS vs. *TET2* wildtype CCUS, B) *TET2*-mutated MDS vs. *TET2* wildtype MDS, C) *IDH2*-mutated CCUS/MDS vs. *IDH2* wildtype CCUS/MDS, D) *DNMT3A*-mutated CCUS vs. *DNMT3A* wildtype CCUS, and E) *DNMT3A*-mutated MDS vs. *DNMT3A* wildtype MDS. The color of each cell denotes the type of mutation. Black cells denote multiple mutations in the gene. The bar graph on the right side of each figure designates the number of cases carrying a mutation in the respective genes. The bar graph on top of each plot illustrates the tumor mutational burden (TMB) of each patient. One CCUS patient (with trisomy 15) and six MDS patients has no mutations of the examined genes and are not included in the plots. The plots are generated using matfools, Bioconductor. EWAS: epigenome-wide association study; CCUS: clonal cytopenia of undetermined significance; MDS, myelodysplastic neoplasms; mut, mutation; TMB, tumor mutational burden; WT, wildtype.



Supplementary figure 2. Enrichment of Gene Ontology terms for genes near *TET2* and *IDH2* mutation-associated DMPs in CCUS and MDS (A, B and C), *DNMT3A* mutation-associated DMPs in MDS (D), and the 442 shared DMPs associated with *TET2*-mutated CCUS and MDS, *IDH2*-mutated CCUS and MDS, and *DNMT3A* mutated CHIP and MDS (E). Top 20 Gene Ontology terms are presented for genes near *TET2* mutation-associated hypermethylated sites in CCUS (24,365 sites; **A**) and MDS (7,139 sites; **B**), *IDH2* mutation-associated hypermethylated sites in CCUS and MDS (24,259 sites; **C**) *DNMT3A* mutation-associated hypomethylated sites in MDS (1,681 sites; **D**) and DMPs common for all three mutations (442 sites, **E**). P-values derive from hypergeometric tests performed using rGREAT v. 1.28.0 and are FDR-corrected. CCUS: clonal cytopenia of undetermined significance; MDS: myelodysplastic neoplasms; FDR: false discovery rate.