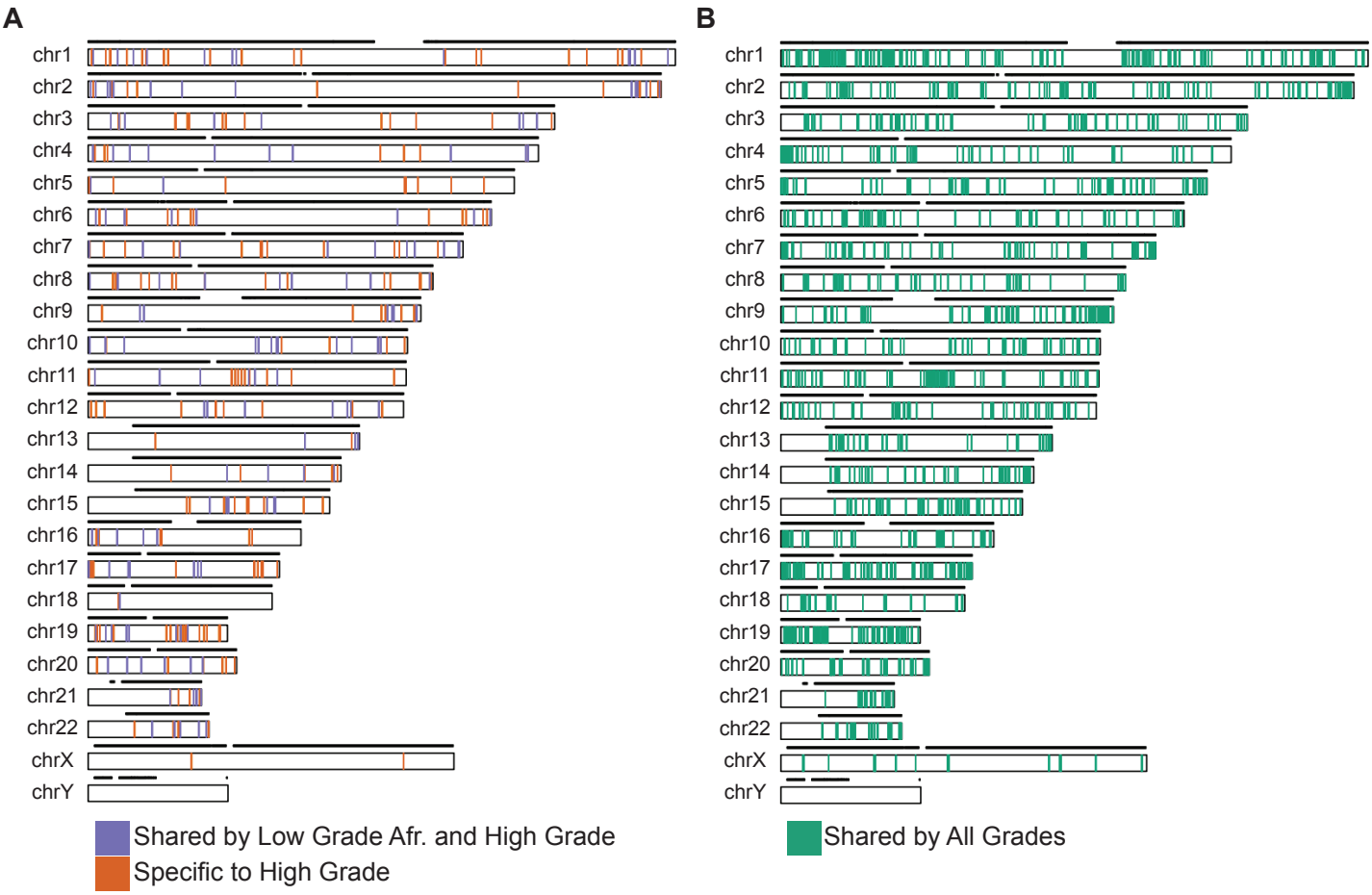
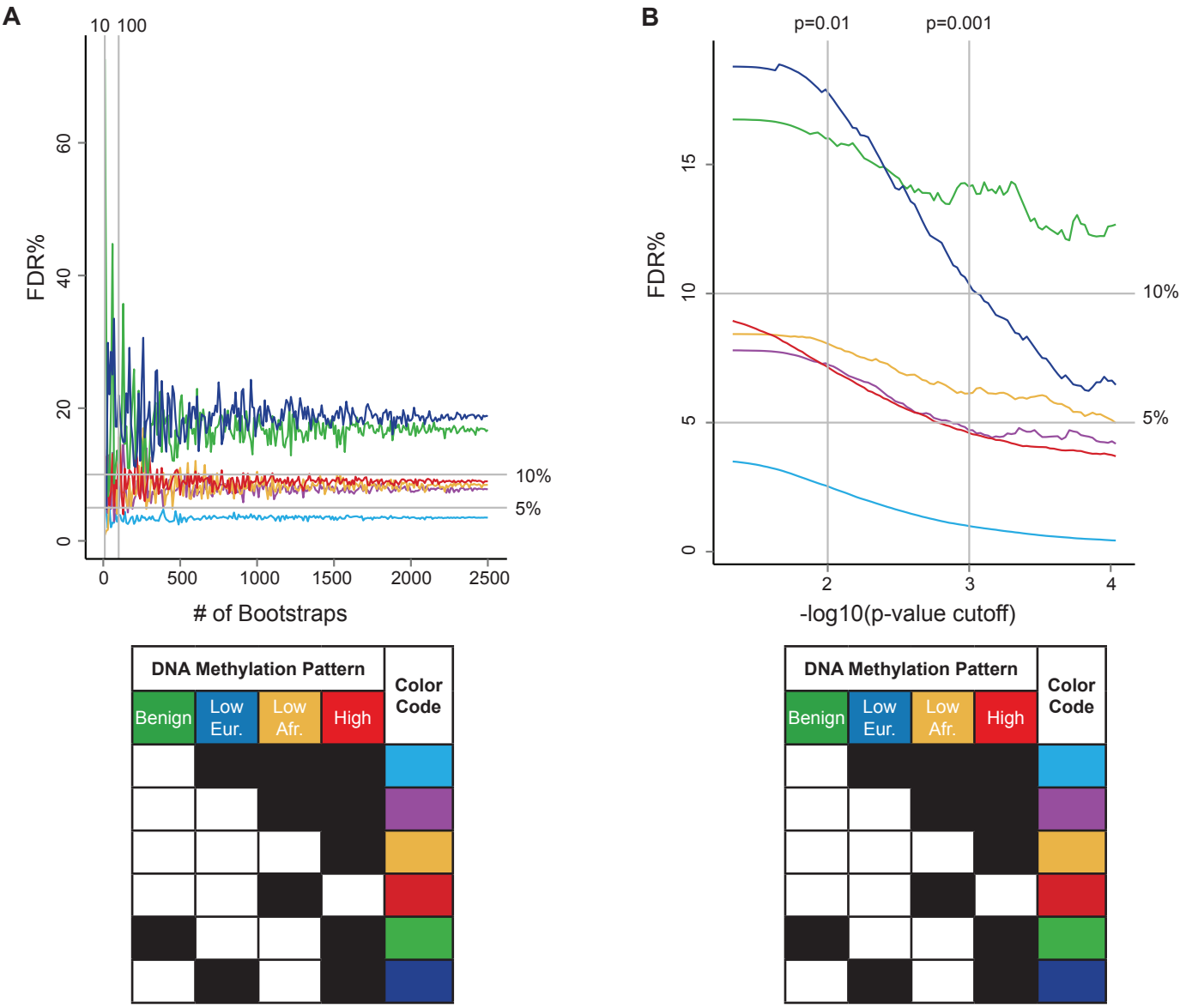
DNA Methylation Pattern					Pairwise Statistical Tests					
Benign	Low Eur.	Low Afr.	High	Pattern Code	Benign vs. Low Eur.	Benign vs. Low Afr.	Benign vs. High	Low Eur. vs. Low Afr.	Low Eur. vs. High	Low Afr. vs. High
	■	■	■	0111	SIG increase	SIG increase	SIG increase	NS	NS	NS
		■	■	0011	NS	SIG increase	SIG increase	SIG increase	SIG increase	NS
			■	0001	NS	NS	SIG increase	NS	SIG increase	SIG increase
		■		0010	NS	SIG increase	NS	SIG increase	NS	SIG decrease
■			■	1001	SIG decrease	SIG decrease	NS	NS	SIG increase	SIG increase
	■		■	0101	SIG increase	NS	SIG increase	SIG decrease	NS	SIG increase
■		■	■	1011	SIG decrease	NS	NS	SIG increase	SIG increase	NS
	■	■		0110	SIG increase	SIG increase	NS	NS	SIG decrease	SIG decrease
■	■		■	1101	NS	SIG decrease	NS	SIG decrease	NS	SIG increase
■	■			1100	NS	SIG decrease	SIG decrease	SIG decrease	SIG decrease	NS
■				1000	SIG decrease	SIG decrease	SIG decrease	NS	NS	NS
■	■	■		1110	NS	NS	SIG decrease	NS	SIG decrease	SIG decrease
	■			0100	SIG increase	NS	NS	SIG decrease	SIG decrease	NS
■		■		1010	SIG decrease	NS	SIG decrease	SIG increase	NS	SIG decrease

Supplementary Figure S1: Decision tables used by MethylAction to convert pairwise test results to patterns of differential DNA methylation among two or more groups. Tables are provided for a 4-group comparison, using the group names from the Figure 2 analysis. Note that MethylAction does not impose a group number limit, and can generate analogous decision tables for larger and smaller group numbers. Each digit of "pattern code" summarizes the pattern where all "1" groups are hypermethylated with respect to all "0" groups. Thus, all black squares correspond to "1" and all white correspond to "0" as also shown in Figure 2A. SIG: significant ($p < 0.05$ or user specified cutoff), NS: non-significant, "increase" and "decrease" are with respect to the mean value of the normalized read counts in each group.

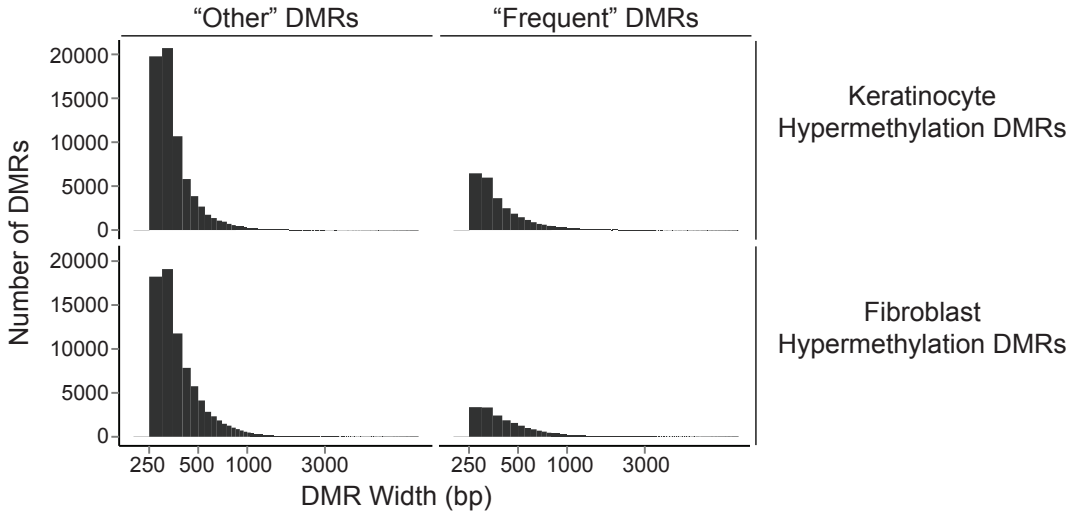


Supplementary Figure S2: Visualization of DMRs. (A) Karyogram showing the genomic locations for all "frequent" DMRs of the types represented in Figure 2C-D. Black lines indicate regions that passed initial coverage filtering. (B) Karyogram showing the genomic locations for all DMRs of the type represented in Figure 2E.

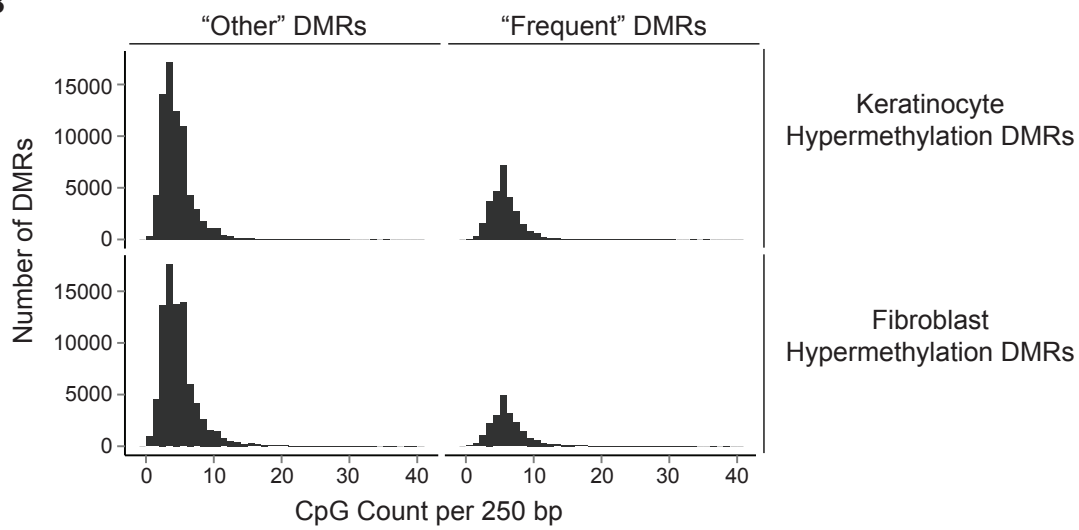


Supplementary Figure S3: Analysis of Bootstrap False Discovery Rates (FDRs). (A) FDRs for "frequent" DMRs as a function of number of bootstraps performed. Each color represents a specific pattern of DNA methylation differences between the four groups as indicated in the table below. (B) FDRs for "frequent" DMRs as a function of ANODEV p-value cutoff used.

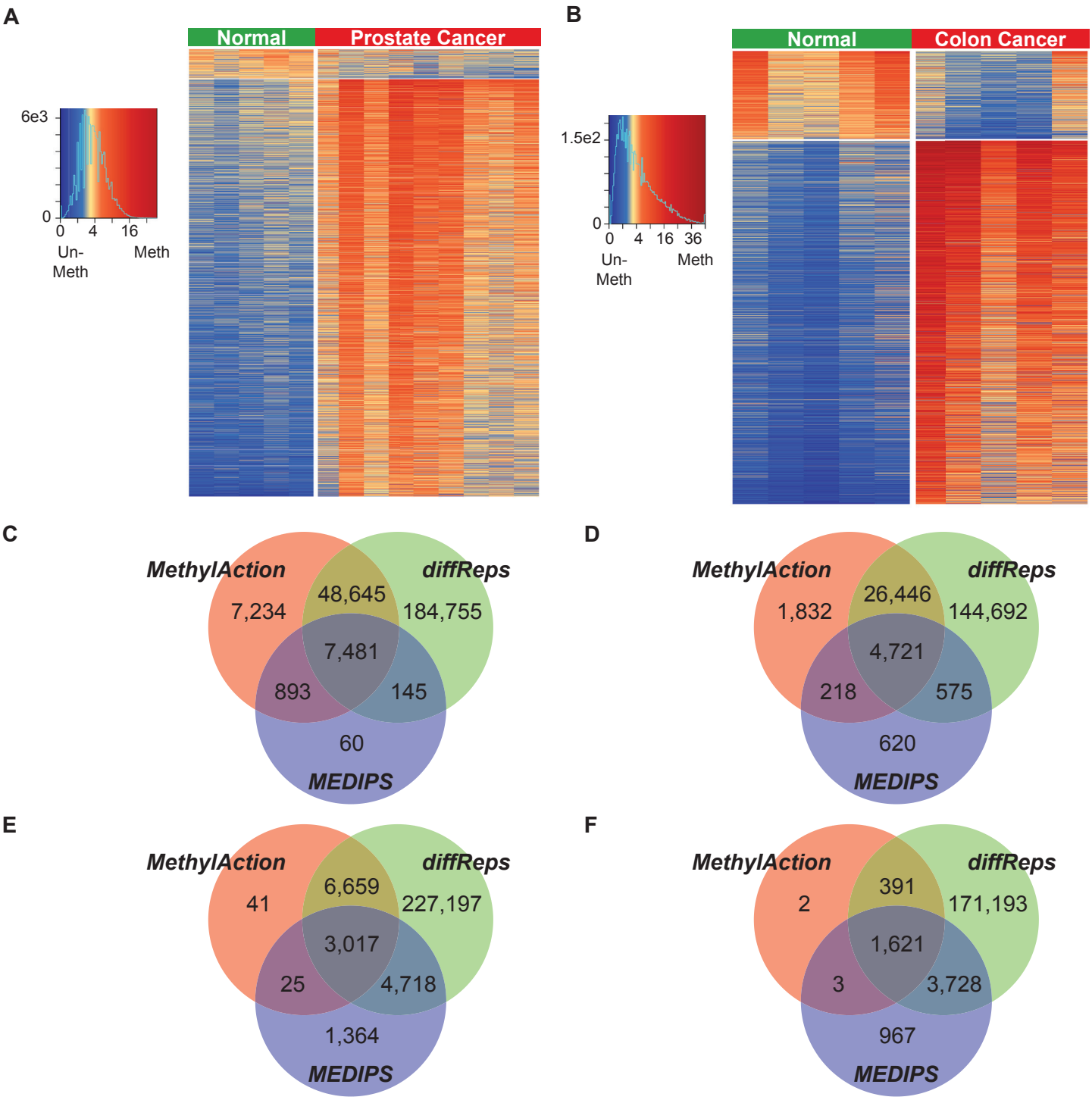
A



B



Supplementary Figure S4: Descriptive statistics of skin DMRs. (A) Histogram of DMR widths for the skin DMRs presented in Figure 3. Histogram bars represent 50 bp increments (same as window size used for the analysis). X-axis has been $\log_{10}$ scaled. (B) Histogram of CpG density within the skin DMRs from Figure 3. Values are presented as the number of CpGs per 250 bp increment (the minimum DMR width) within a DMR to normalize for DMR width.



Supplementary Figure S5: Detection of DMRs in prostate cancer and colon cancer enrichment sequencing data. (A) Heatmap of "frequent" DMRs detected by MethylAction between benign prostatic tissue and prostate tumor tissue. Columns represent samples, and rows represent DMRs. Normalized read counts have been divided by the window size and square root-transformed for visualization purposes. (B) Heatmap of "frequent" DMRs detected by MethylAction between matched benign colon and colon tumor tissue (Illingworth, 2010). (C) Venn diagram of the number of consensus regions unique to each or in common among all three tools for the prostate cancer dataset. The DMR sets from all three analysis results were reduced into a set of consensus regions to enable the comparison. Both the "frequent" and the "other" DMRs from MethylAction were used. (D) Venn diagram as in (C) for the colon cancer dataset. (E) Venn diagram comparing the three tools, where only the "frequent" DMRs from MethylAction are considered for the prostate cancer dataset. (F) Venn diagram as in (E) for the colon cancer dataset.