Supplemental Legends

Figure S1
Numbers of marker candidate regions (DMRs) per cancer type. The cancer types without normal samples available were not tested and therefore only 23 TCGA cancer types have DMR numbers displayed. The barplots show the numbers of hypermethylated and hypomethylated DMRs per cancer type.

Figure S2
The DNA methylation of sets of 1-12 markers selected for each of 18 cancer types where respective hypermethylated marker pool was available. The plots show DNA methylation of marker CpGs in individual tumor samples in comparison to normal blood samples. Only 50 randomly chosen blood samples out of the whole control blood cohort are shown. The horizontal dashed line shows the 95^{th} percentile of the cumulative DNA methylation of each marker set in the entire control normal blood cohort (n=1,388). The AUC was calculated using the whole tumor cohort and the whole normal blood cohort (n=1,388) for each cancer type.

Figure S3
A) The universal marker set performance across all 33 TCGA cancer types. The plots show methylation of marker CpGs in individual tumor samples in comparison to normal blood samples. Only 50 randomly chosen blood samples out of the whole control blood cohort are shown. The horizontal dashed line shows the 95^{th} percentile of the cumulative DNA methylation of the universal marker set in the whole control normal blood cohort (n=1,388). The AUC was calculated using the whole tumor cohort and the whole normal blood cohort (n=1,388) for each cancer type. B) ROC curves for the universal marker set across all 33 TCGA cancer types using the normal blood cohort (n=1,388) as a control.

Supplemental Methods
Detailed description of methods

Table S1

List of 33 TCGA cancer cohorts including numbers of tumor and normal tissue samples for which Illumina HumanMethylation450 DNA methylation data were used (October 2016).

Table S2

Description of 18 cohorts of normal tissues sample Illumina HumanMethylation450 DNA methylation data obtained from the GEO that were used to filter cancer specific DMRs and test the markers. The second workbook lists Illumina HumanMethylation450 GEO cohorts that have been used for marker validation.

Table S3

List of 1,250 hypermethylated and 584 hypomethylated marker CpGs across all TCGA cancer types. Genomic coordinates are hg19. The last two columns indicate whether the marker CpG is located within polycomb locus or associated with noncoding RNA gene, respectively.

Table S4

Number of specific markers per cancer type that can identify all identifiable tumors in particular cancer type. Percentage of identifiable tumors identified by the set of 6 markers. Tumor was considered identified if at least one marker in the set had methylation larger by at least 0.3 beta than the 95^{th} percentile of the control blood cohort (n=1,388). AUCs for optimal six marker sets for individual tumor types using the normal blood cohort as a control.

Table S5

Optimal six marker CpG sets selected for each of 18 TCGA cancer types where a pool of hypermethylated marker CpGs to choose from was available. The last two columns indicate whether the marker CpG is located within polycomb locus or associated with noncoding RNA gene, respectively.

Table S6

Enrichment of polycomb loci and noncoding RNA gene associated CpGs among the marker sets.