Supplemental Figure Legends

Supplemental Figure 1: Bisulfite kit testing. (**A**) Bisulfite kit yields. (**B**) Jurkat genomic DNA was left untreated (U) or bisufite treated with the QIAGEN EpiTect (Q), Sigma Imprint DNA Modification (S) or Zymo EX DNA Methylation Gold (Z) kit. Samples were run on a 6% TBE gel and visualized with SYBRGold.

Supplemental Figure 2: Coverage achieved at various melting temperatures (x-axis), 250 bp amplicons (blue), 350 bp amplicons (green), and 450 bp amplicons (yellow), with no CpGs allowed in the primer (**A**) or 1 CpG allowed per primer (**B**).

Supplemental Figure 3: Coverage achieved along amplicons with and without concatenation.

Supplemental Table 1: List of the 69 genomic loci derived from the Sequenom Standard EpiPanel for *in silico* testing of the primer design algorithm.

Supplemental Table 2: Genomic loci, sequences, CpG content and amplicon length for each of the primers targeting the 50 genes of interest.

Supplemental Table 3: Primer3 conditions used for primer design.

Supplemental Table 4: Sanger-based validation of RainDance microdroplet PCR CpG methylation analysis. One amplicon from each of 8 analyzed CGI-containing genes (four

with high CpG methylation (grey) and corresponding low mRNA expression, four with low CpG methylation (white) and corresponding high mRNA expression) was PCR amplified from bisulfite-treated wild-type Jurkat DNA, TA cloned, and Sanger sequenced. Total CpGs represent the number of CpGs per amplicon multiplied by the number of clones sequenced. Total non-CpG cytosine conversion was calculated across all amplicons and clones, and Sanger CpG conversion was normalized based upon the calculated percent conversion (97.2%).