Supplemental Figure Legends

Supplemental Figure 1. McrBC methodology recommends dye-swaps. This implies an extra hybridization for each sample. We found that dye-swaps do not provide enough of an improvement to justify the costs. By averaging the dye-swaps the precision assessment, reported for the case that did not use dye-swaps in Table 3, yielded SDs of 0.30 and 0.35 for the DKO and HCT116 samples respectively. The correlation with Illumina ranged from 0.65 to 0.68. These results provide only a slight improvement over those obtained without the use of dye-swaps. The plot shown here is like Figure 2 but uses *M* values that are averages of the dye-swaps.

Supplemental Figure 2. Box-plots of the differences between replicate M values for each method. The first four orange box-plots compare the McrBC when dye-swaps are used. The first two are from DKO and the latter two are from HCT116. The next four orange box-plots compare McrBC when dye-swaps are not used. The first two are from DKO and the latter two are from HCT116. The last two orange box-plots compare McrBC using the promoter tiling array. The first is from DKO and the second is from HCT116. The first two green box-plots compare the HELP method on the canonical array design. The first is from DKO and the second is from HCT116. The next two green box-plots compare the HELP method using the promoter tiling array. The first is from DKO and the second is from HCT116. The purple box-plots compare the MeDIP method. The first is from DKO and the second is from HCT116.

Supplemental Figure 3. Pyrosequencing analysis of regions showing differences between the tested methods and the Illumina reference standard. The Illumina data were correct in all cases.

Supplemental Figure 4. Results for all the hybridizations in our experiment that used the canonical arrays. Data format is te same as Figure 2.

Supplemental Figure 5. As Figure 4 for five other regions.

Supplemental Figure 6. As Figure 5, but we divide the Illumina regions into those with observed to expected CpG above 6 (inside CpG island) and below 6 (outside CpG island).