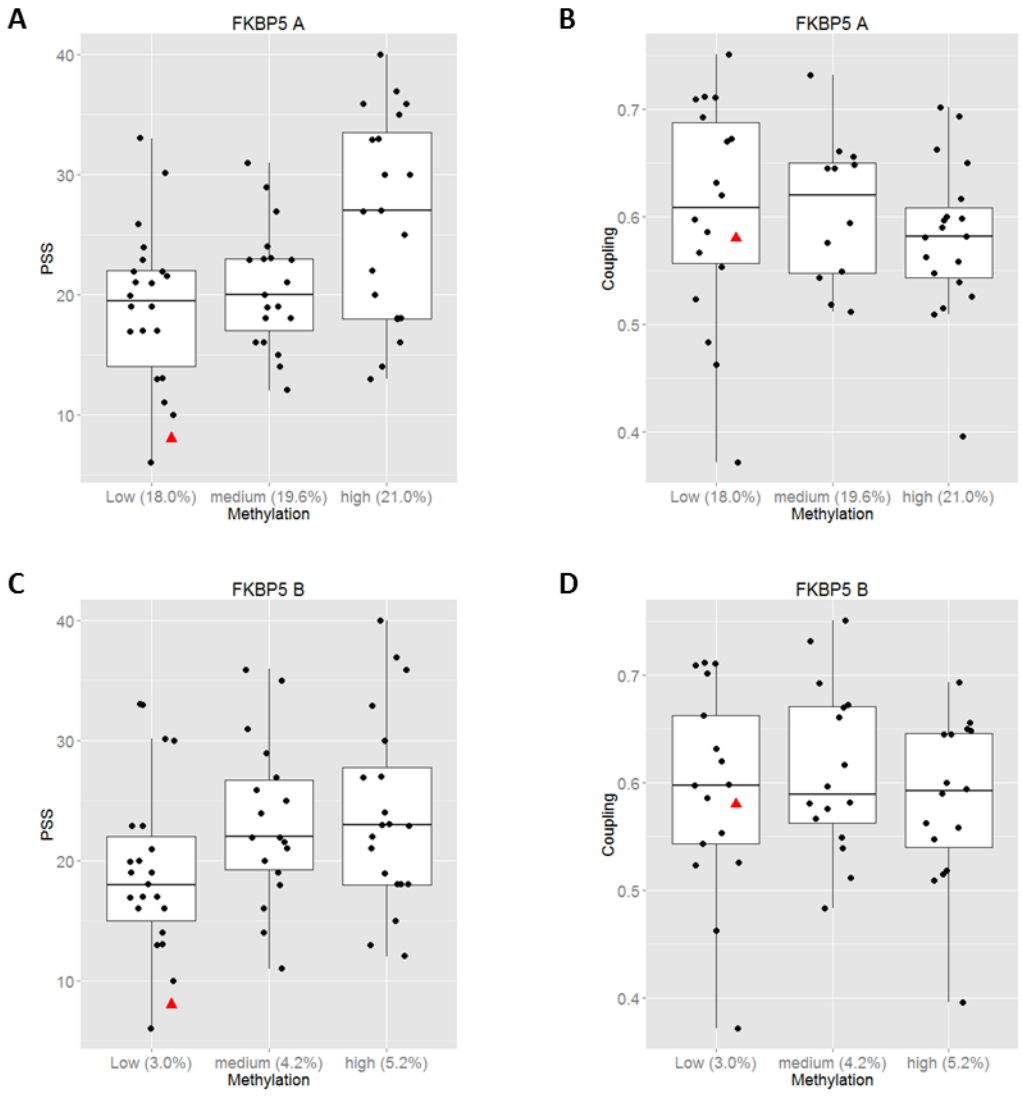
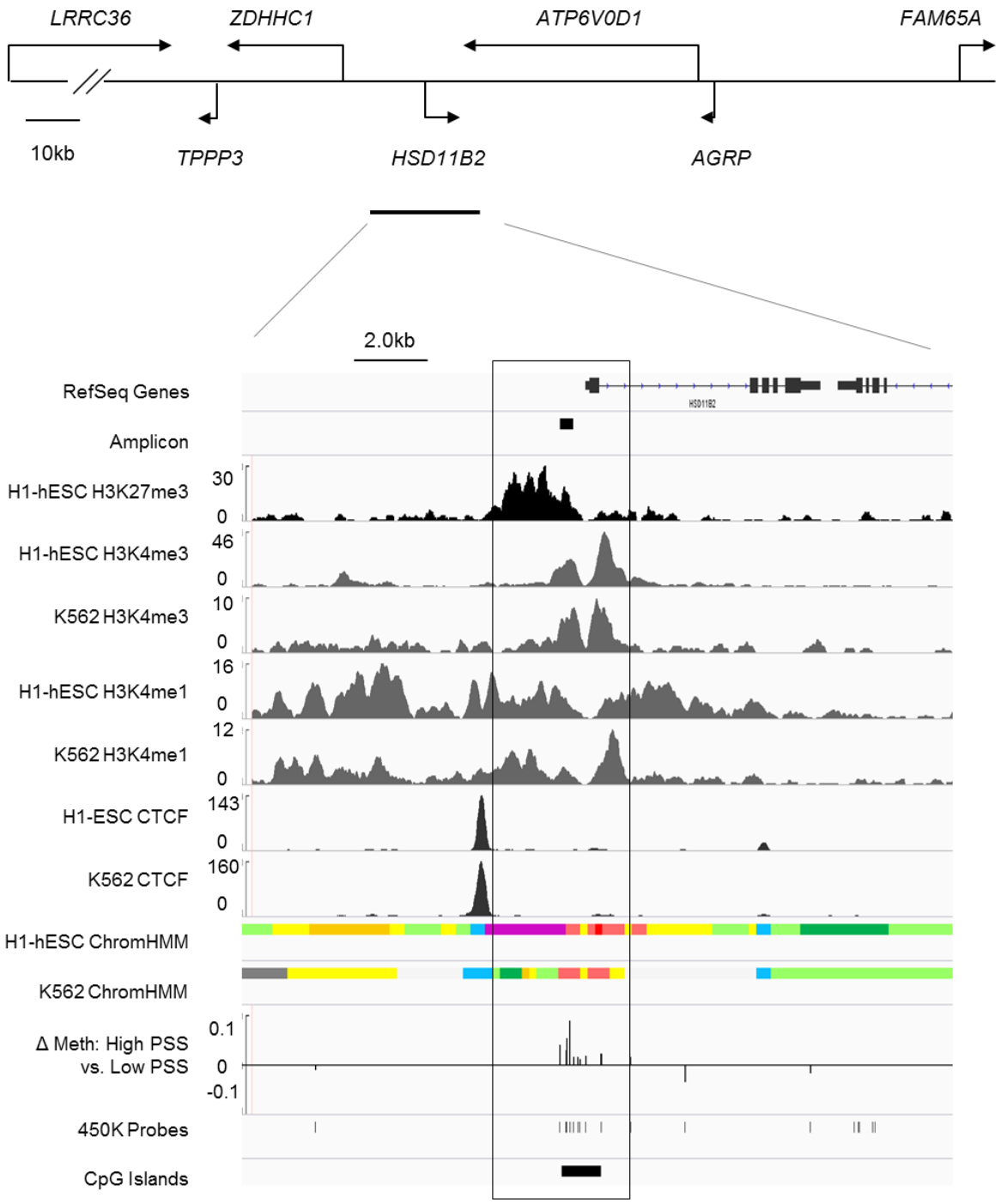


Supplemental Figure S1. Tertiles of *FKBP5* promoter methylation and internal regulatory region methylation in relation to PSS and fetal coupling. A, PSS values for participants whose placentas showed low, intermediate, or high methylation in the *FKBP5* promoter region (block A). Placentas in the lowest tertile of methylation are associated with lower mean PSS than those in the highest tertile (p=0.0012). **B,** results for fetal coupling vs. methylation in the promoter region. Placentas in the lowest

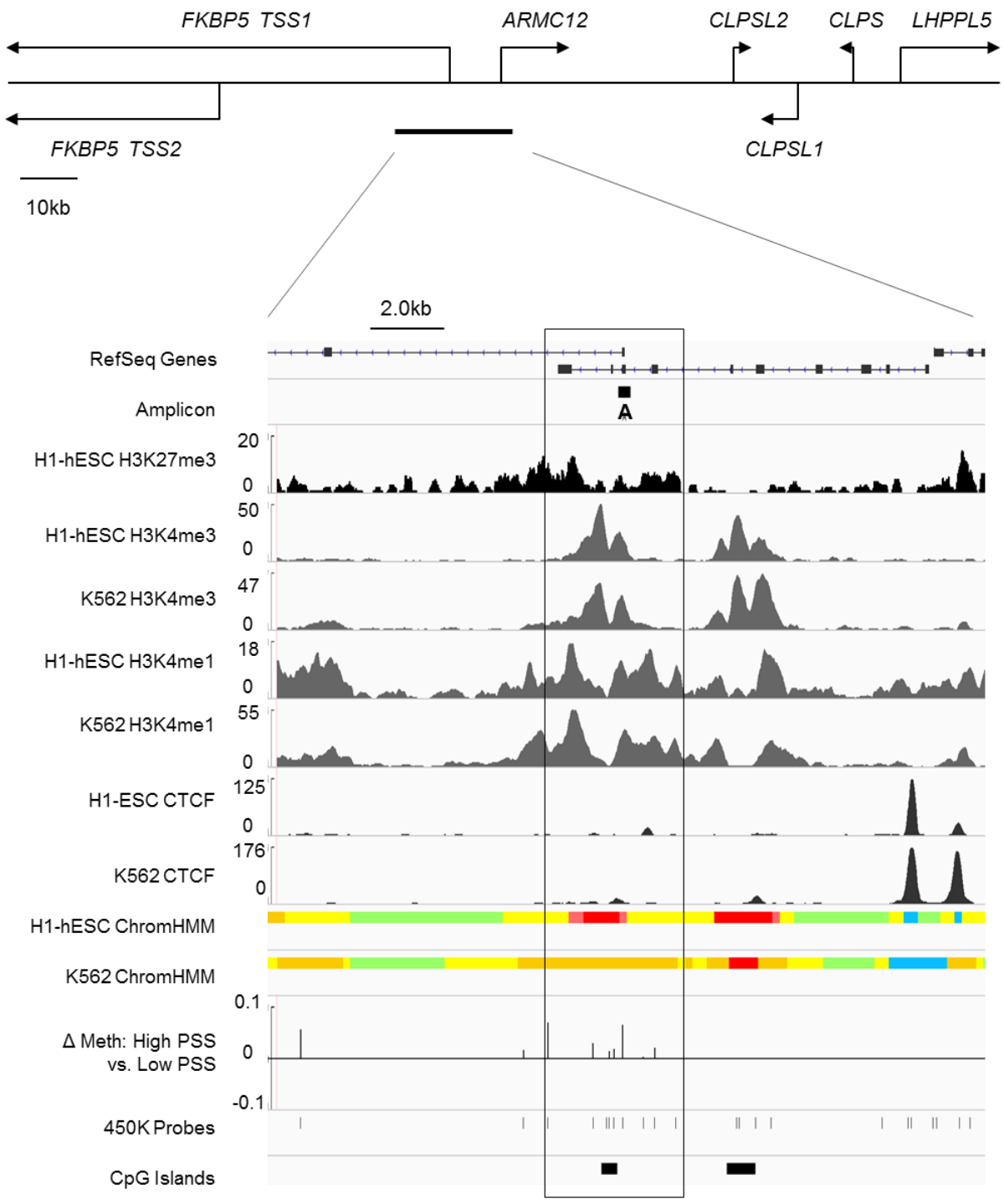
tertile of DNA methylation show a trend toward slightly higher fetal coupling (p=0.1003). For calculating mean methylation values the fractional methylation values for 6 CpGs* in the *FKBP5* promoter were averaged. **C,** PSS values for participants whose placentas showed low, intermediate, or high methylation in the *FKBP5* internal regulatory region. Placentas in the lowest tertile of methylation are associated with lower mean PSS than those in the highest tertile (p=0.0160). **D,** results for fetal coupling vs. methylation in the internal regulatory region. There is little if any correlation (p=0.4867). For calculating mean methylation values the fractional methylation values for 4 CpGs** in the *FKBP5* internal regulatory region were averaged. The red triangle denotes the donor egg participant.

*(cg00052684_6_35694245_FKBP5, cg06937024_6_35695489_FKBP5, cg11845071_6_35695859_FKBP5, cg00610228_6_35695934_FKBP5, cg07485685_6_35696061_FKBP5, cg17030679_6_35696300_FKBP5)

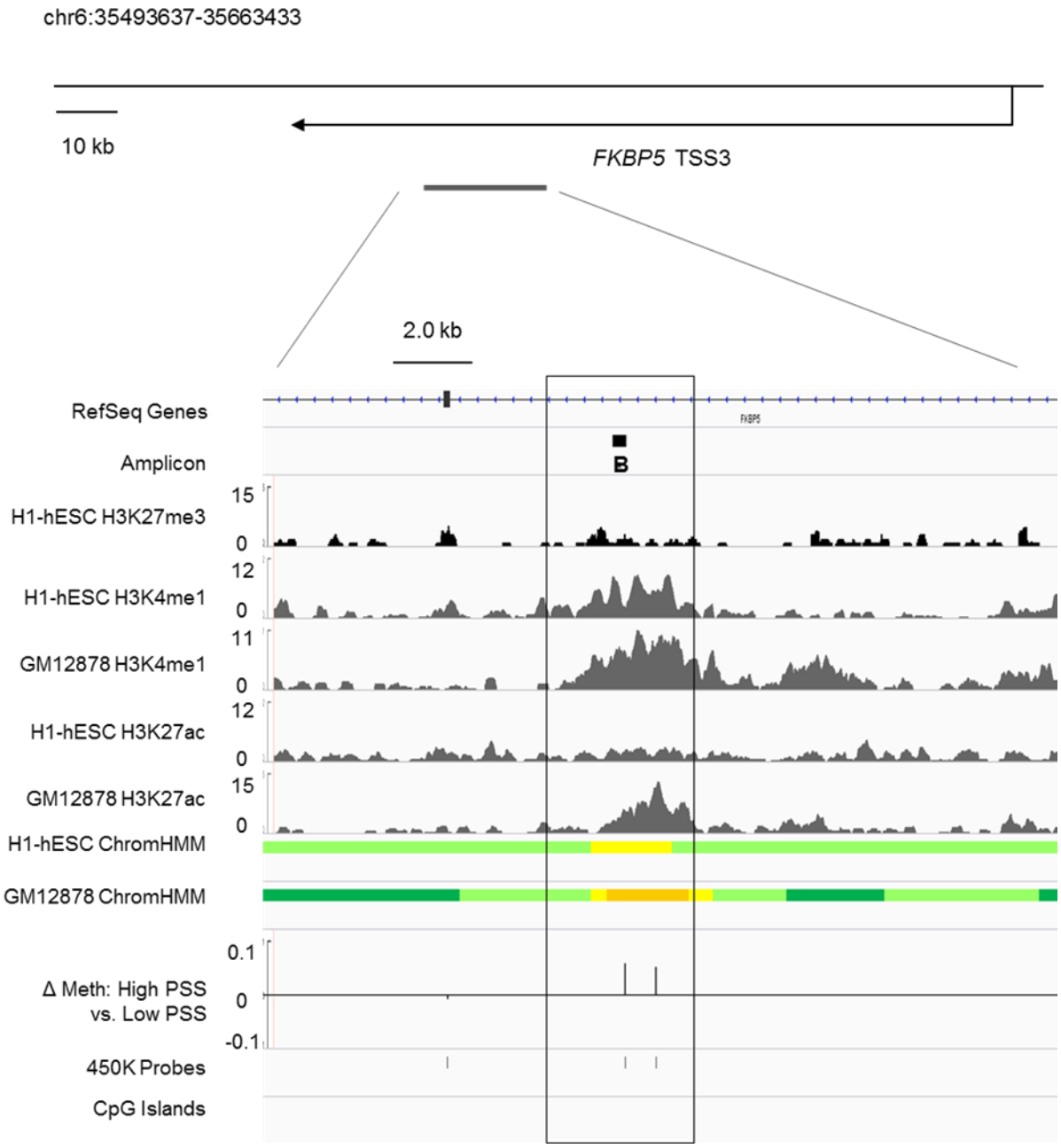
**(cg00862770_6_35655764_FKBP5, cg00140191_6_35656242_FKBP5, cg10913456_6_35656590_FKBP5, cg16012111_6_35656758_FKBP5)



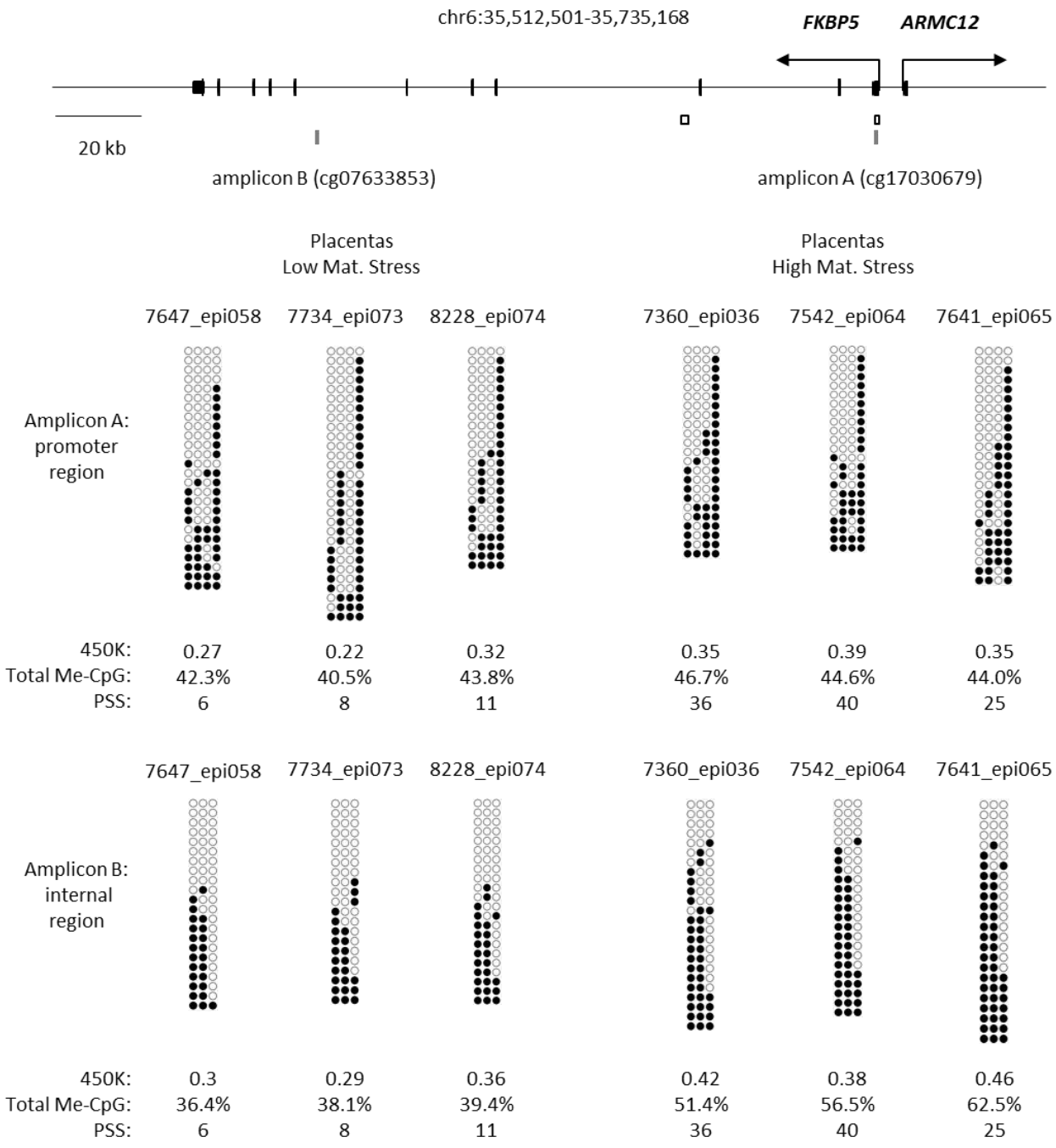
Supplemental Figure S2. Map of the differentially methylated region in the *HSD11B2* gene. Alignment of the differentially methylated region (Δ Methyl track; boxed region) with ENCODE tracks from the UCSC Genome Browser shows that the peak of differential methylation is in the promoter. This region is marked by typical promoter-associated histone modifications, including H3K4me3, and is color-coded red in the ChromHMM tracks. It is flanked upstream by poised chromatin (H3K27me3; purple in ChromHMM) and by a CTCF-bound insulator element (blue in ChromHMM).



Supplemental Figure S3. Map of the differentially methylated region in the *FKBP5* promoter (amplicon A). Alignment of the differentially methylated region (Δ Methyl track; boxed region) with ENCODE tracks from the UCSC Genome Browser shows a peak of differential methylation in the promoter of this gene. This region is marked by typical promoter-associated histone modifications, including H3K4me3, and is color-coded red in the ChromHMM tracks.



Supplemental Figure S4. Map of the differentially methylated region in the *FKBP5* internal transcribed region (amplicon B). Alignment of the differentially methylated region (Δ Methyl track; boxed region) with ENCODE tracks from the UCSC Genome Browser shows a peak of differential methylation in an internal enhancer region of this gene. This region is marked by H3K4me1, and is color-coded yellow in the ChromHMM tracks.



Supplemental Figure S5. Validation of the Beadchip data and additional mapping of CpG methylation in the *FKPB5* promoter region and internal regulatory region using bis–seq. As is seen in the 450K data (On line supplement Figure S1), the gains of methylation in high vs. low PSS are weak

in the promoter region and stronger in the internal regulatory region. In bis–seq each row is a clone corresponding to one genomic DNA molecule, and thus is derived initially from one cell in the placenta. (Each subject's study number is listed, e.g., 7647_epi058.) About half of all placental cells have substantial DNA methylation in the internal regulatory region regardless of maternal stress, and a minor additional percentage of placental cells have gained methylation in this region with stress. PCR primer sequences for amplicon A were For: GGTTTTGTTTATTTGGGAGAAGTATT , Rev: AAAAATCTTCAAAAACCTAATAATTTTAAA, and for amplicon B were For: TGGTTTTTAAATTTGGAATATTGATG, Rev: ACCCTACAAACTACACTCCCAATAA.