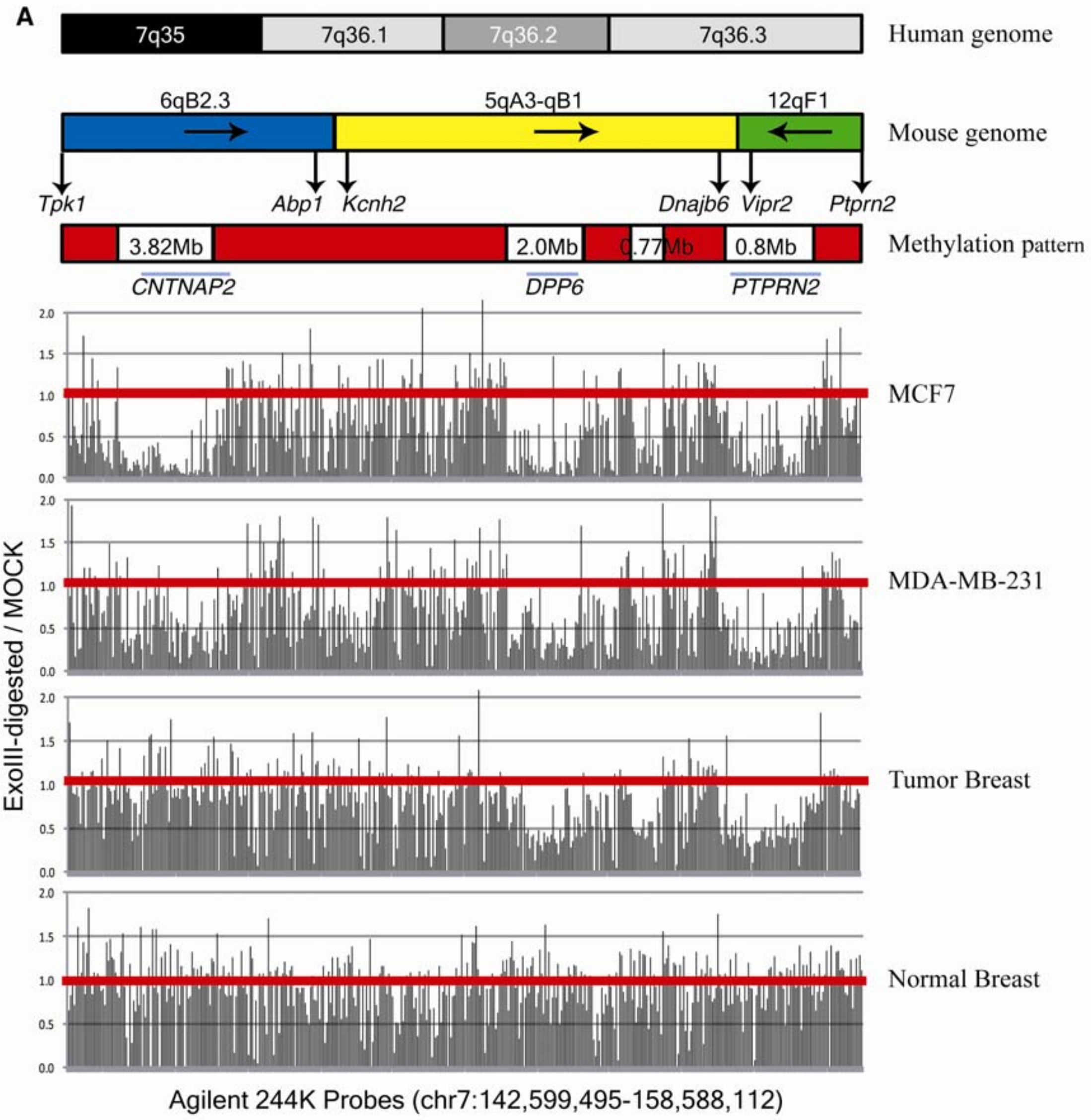
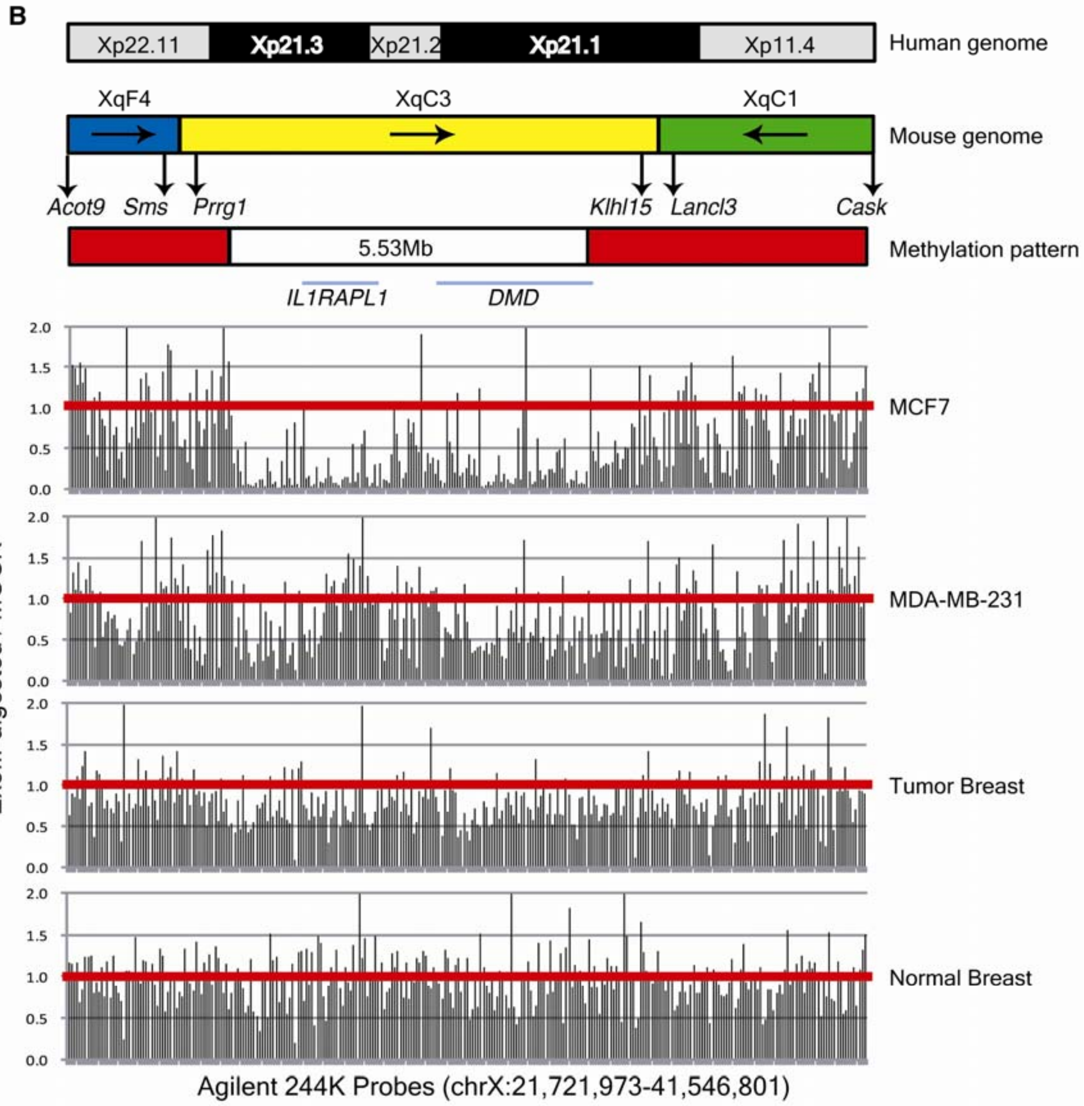
Supplemental Figure 4.




B
Xp22.11
Xp21.3
Xp21.2
Xp21.1
Xp11.4
Human genome
XqF4
XqC3
XqC1
Mouse genome
Acot9
Sms
Prrg1
Klhl15
Lancl3
Cask
5.53Mb
Methylation pattern
IL1RAPL1
DMD
ExoIII-digested / MOCK
2.0
1.5
1.0
0.5
0.0
MCF7
MDA-MB-231
Tumor Breast
Normal Breast
Agilent 244K Probes (chrX:21,721,973-41,546,801)

Supplemental Figure 4. Megabase-size hypomethylation zones in tumor cells. The majority of large hypomethylated zones in MCF7 genome occur in genomic region with low gene density. (A) The hypomethylated regions (white bars) in 7q35-36 are found in the genomes of MCF-7 (*P* < 0.01, Fisher's exact test), MDA-MB-231 (*P* < 0.01, Fisher's exact test) and primary breast tumor (*P* < 0.05, Fisher's exact test) as compared with normal breast genome. An example is shown for the *FRA7I* region at the telomere of chromosome 7 with three large hypomethylated zones in MCF-7 (*P* < 0.01), MDA-MB-231 (*P* < 0.01) and primary tumor (*P* < 0.05). This region coincides with three extensively hypomethylated large genes: *CNTNAP2* (2.3Mb), *DPP6* (1.1Mb) and *PTPRN2* (1.05Mb) in the MCF-7 and MDA-MB-231 genomes. Primary tumor only exhibits the *DPP6* and *PTPRN2* hypomethylated zones. Several novel genes, mRNA or EST (e.g. eye-specific *C7ORF33*) with no homologous mouse sequence are found downstream from *CNTNAP2*. Similarly, a 1.03Mb gene poor region is situated next to *DPP6* gene and harbors novel genes (mammary-gland gene *AK131514*, brain-specific gene *FLJ16734*) without mouse homologs. In the hypomethylated zone containing *PTPRN2*, a gene situated at the evolutionary breakpoint, *DNAJB6*, has homolog copies located either in the hypomethylated zones of MCF-7 or at evolutionary breakpoints of six other human chromosomes. The 7q35-ter fragile site region is frequently deleted or rearranged in myeloid malignancy. (B) The hypomethylated region (white bar) in Xp22.11-11.4 is found in the genomes of MCF-7 (*P* < 0.01, Fisher's exact test), and less prominently in MDA-MB-231 and primary breast tumor genomes as compared with normal breast genome. This region is situated between two evolutionary breakpoints, joining different segments of mouse X chromosome. A 3.5Mb gene poor region is situated upstream of *IL1RAPL1* and contains novel testis-specific genes or cDNA (*AK057304, BC024027, MAGEB6, WDR42B*) with no or low homology with mouse sequence. A 4Mb gene poor region is also found between *DMD* and the evolutionary breakpoint and contains three novel testis-specific genes (*FAM47A, B, C*) and two novel trachea-enriched genes (*CXORF22, 59*). The red horizontal line represents ratio of 1 between signals of *Exo*III digested and mock digested DNA.