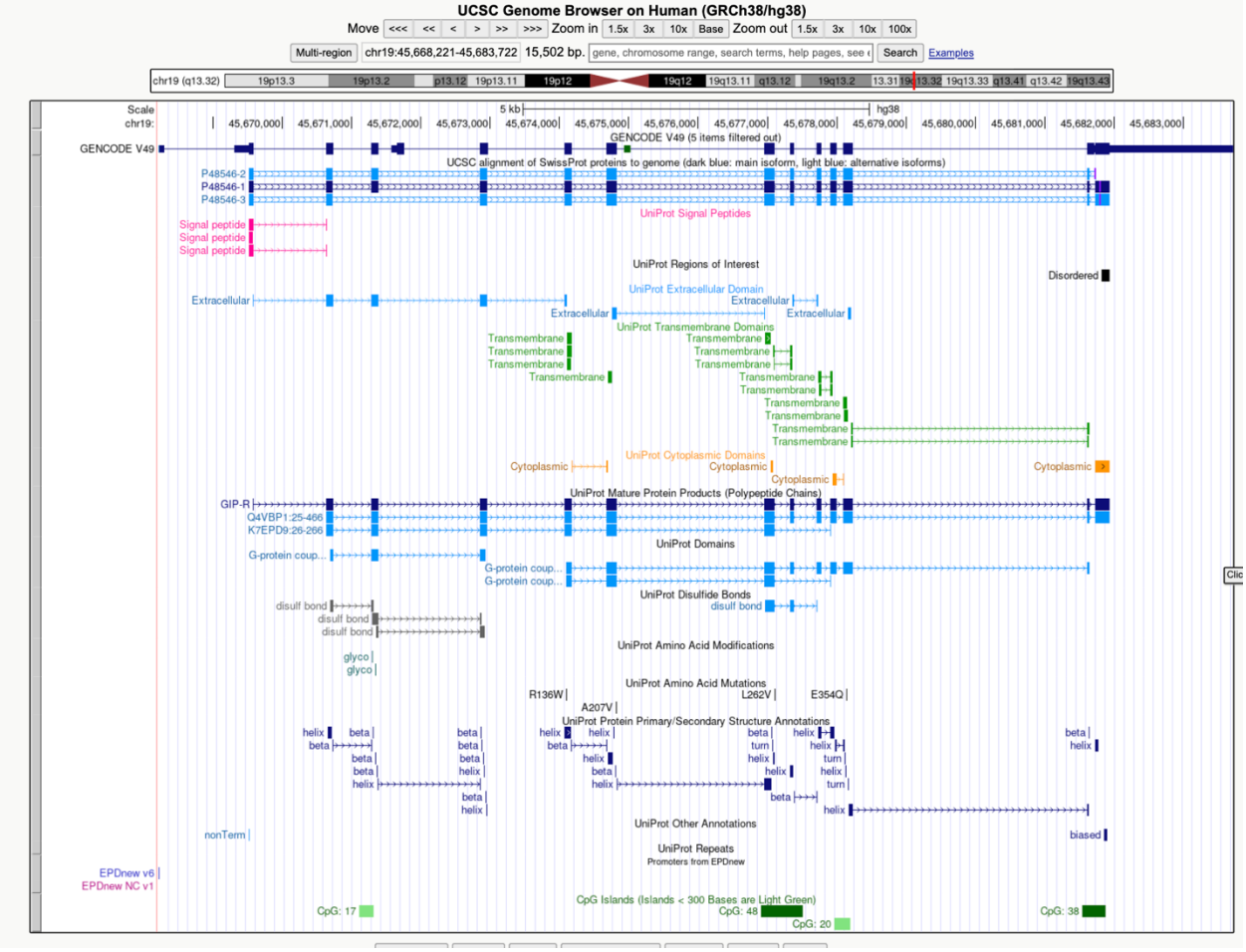
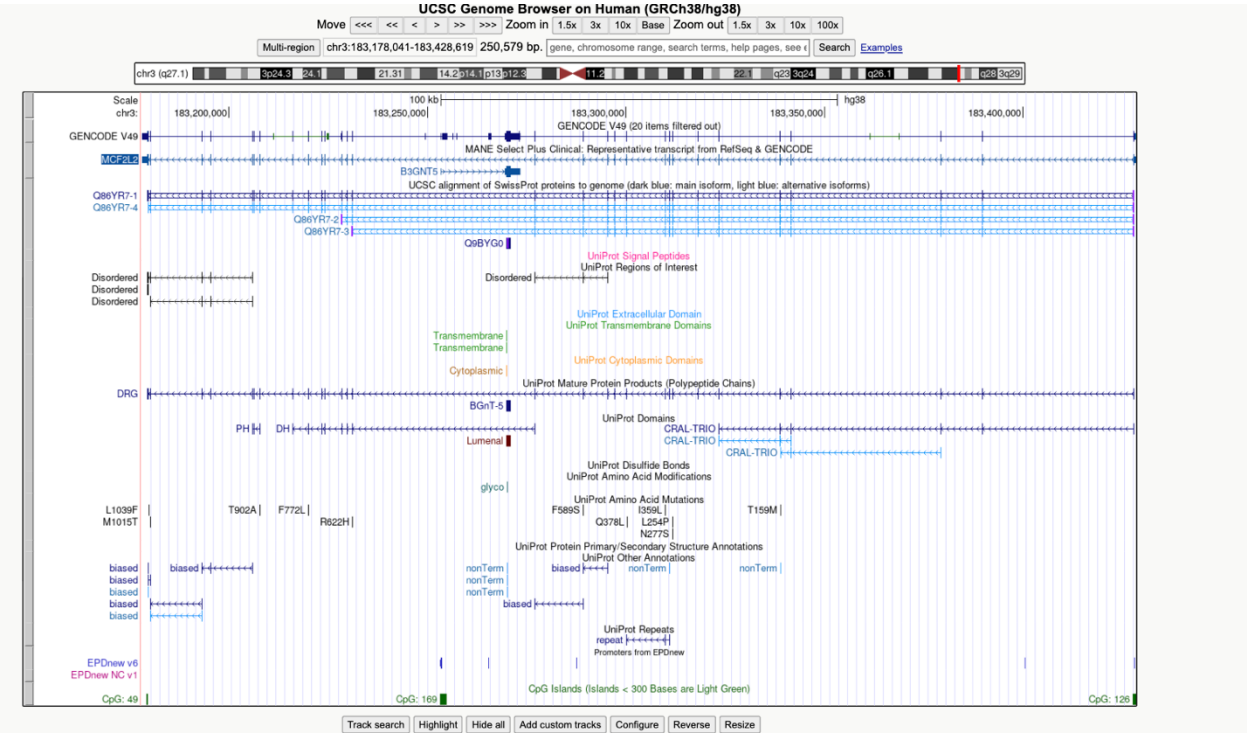
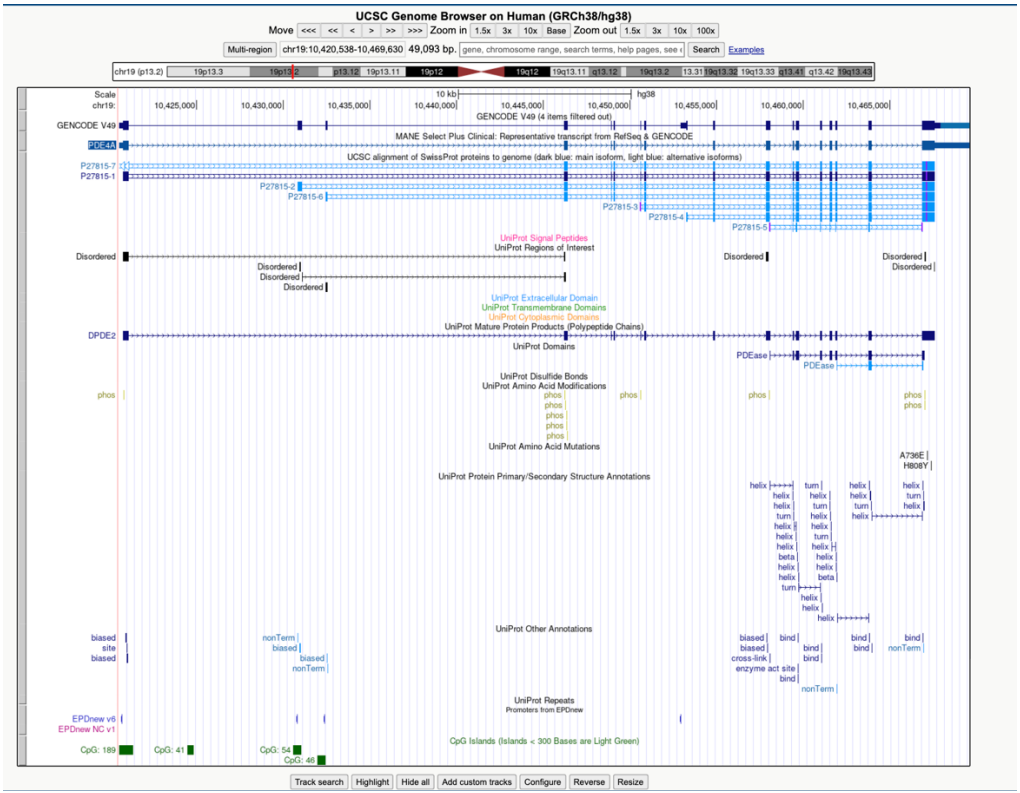


This UCSC Genome Browser view displays the GIPR locus on chromosome 19 (GRCh38). The CpG are near the promoter and 5′ regulatory region of the gene. They are positioned close to extracellular and transmembrane domain, suggesting they may influence the gene's expression through promoter or enhancer methylation. The hypomethylated and downregulated in our previous analysis could suggest that GIPR involving methylation in intragenic rather than promoter CpG regions or altered transcription factor binding. As GIPR signaling affects energy metabolism and insulin pathways, and aberrant regulation may occur via post-transcriptional control or chromatin remodeling rather than simple promoter methylation.



The UCSC Genome Browser visualization of the MCF2L2 gene located on chromosome 3q27.1shows a long coding region with multiple exons and several CpG islands distributed near the promoter and intragenic regions. The annotated protein domains, including CRAL-TRIO, DH and PH domains, suggest a role in Rho GTPase signaling and membrane-cytoskeletal regulation. These domains are critical for intracellular signal transduction and may contribute to cancer cell migration and invasion. In our BRCA dataset, MCF2L2 appeared hypomethylated and downregulated in metastatic tumors, suggesting possible epigenetic deregulation leading to altered transcriptional activity.



The UCSC Genome Browser visualization of PDE4A, located on chromosome 19, reveals multiple CpG islands concentrated near the promoter and 5′ untranslated region of the gene. These CpG-rich regions indicate potential sites of transcriptional regulation via methylation. In the context of our BRCA dataset, PDE4A was found to be hypomethylated and downregulated in metastatic samples. This suggests that reduced methylation is not driving increased expression, implying other mechanisms, such as transcriptional repression or altered enhancer accessibility might be responsible.

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The review highlights that inhibition of PDE4A in breast cancer stem cells increases cAMP levels and PKA activity, which up-regulates PTEN and induces cell-cycle arrest. This result supports that PDE4A plays a functional role in breast cancer progression, and thus alterations in its regulation, including methylation. However, in my analysis PDE4A is hypomethylated and downregulated in metastatic BRCA, which is the opposite than the paper suggests. This discrepancy shows that for PDE4A, other regulatory mechanisms may dominate over CpG methylation in controlling its expression.