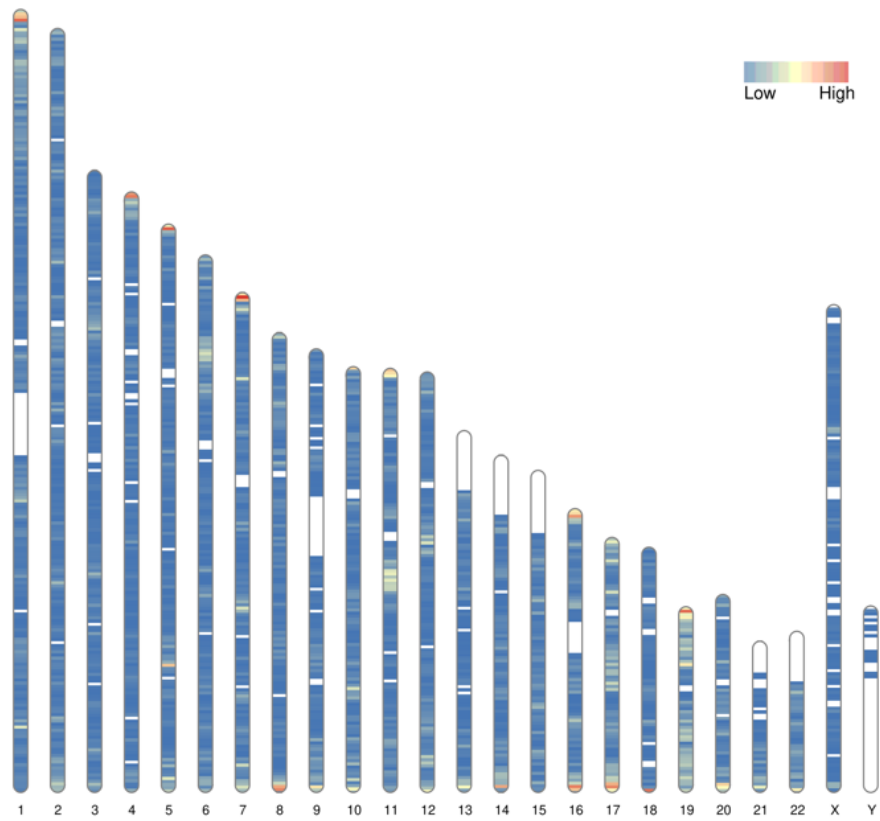
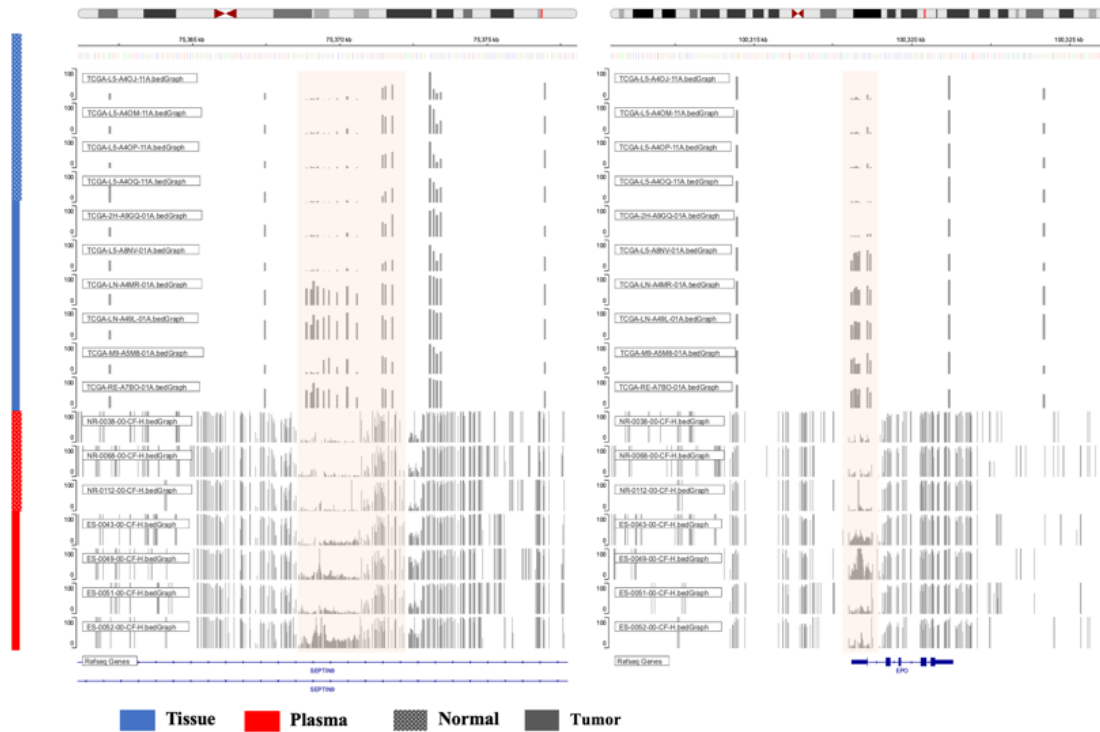


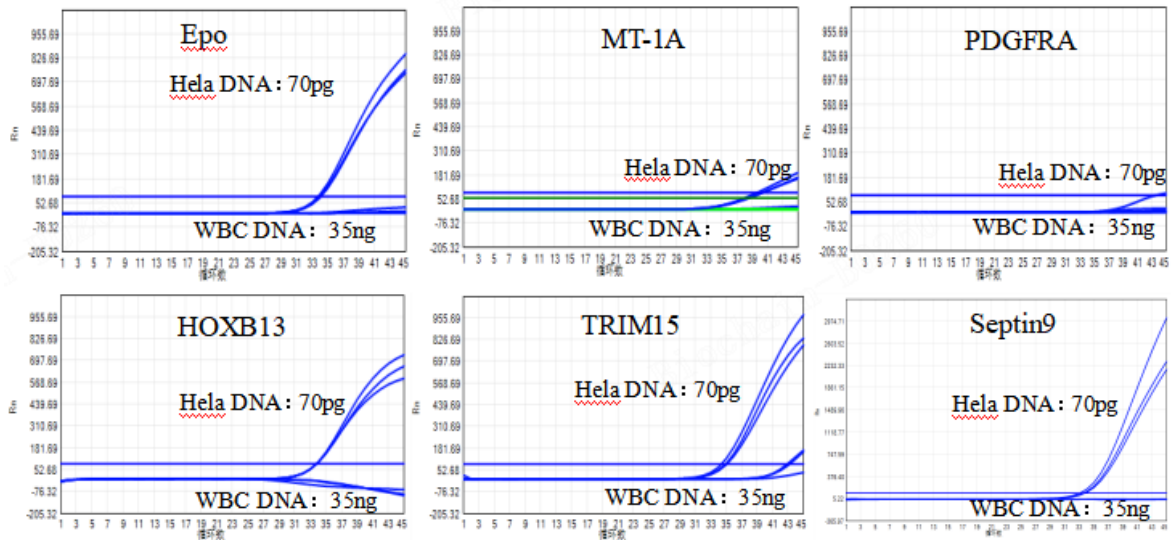
## Supplementary Figures



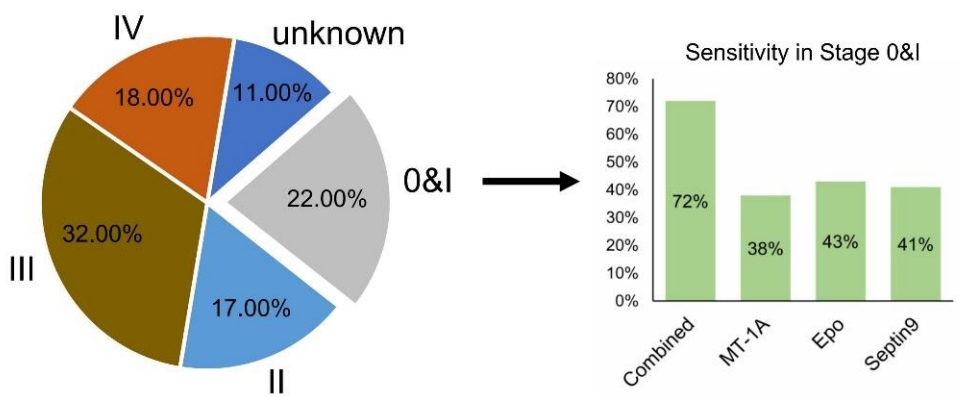
**Supplementary Figure 1.** Overall methylation level in different chromosomes. The high methylation regions were shown in orange and red.



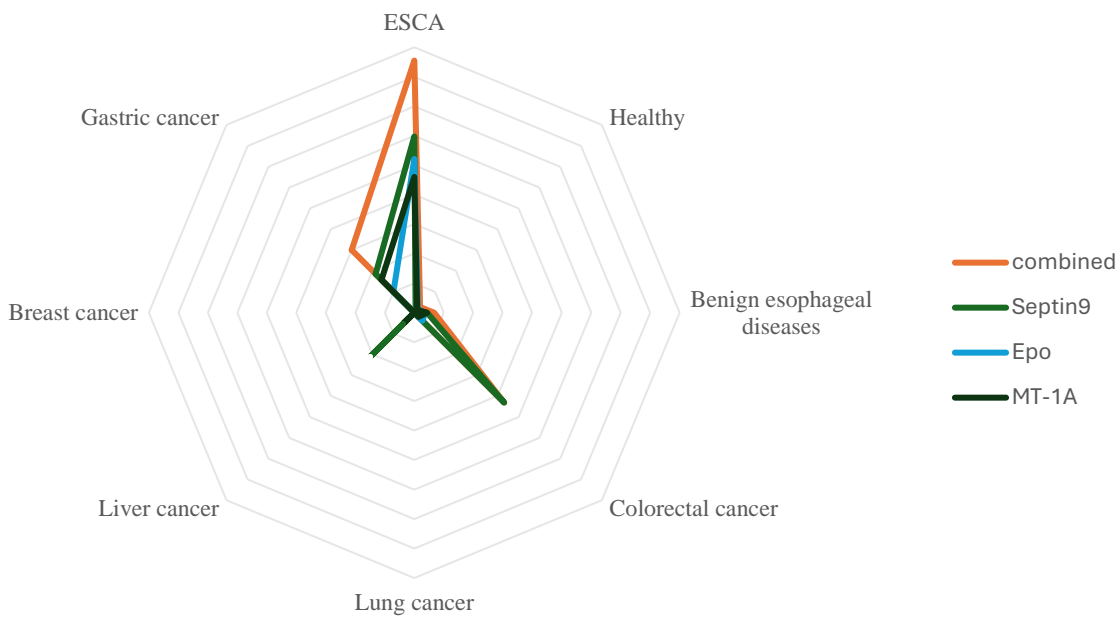
**Supplementary Figure 2.** Genome browser view of methylation level in selected genes between normal and tumor patients with tissue or plasma samples.



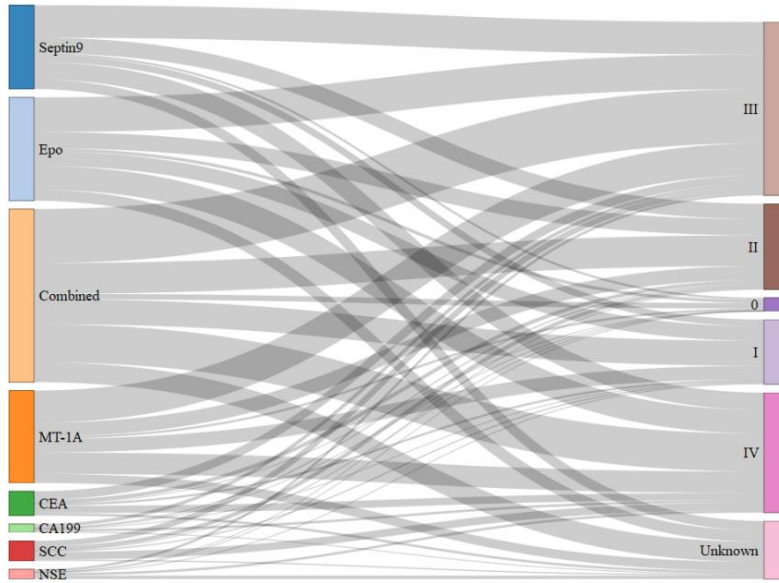
**Supplementary Figure 3.** Results of qMSP testing for six esophageal cancer differential methylation genes in HeLa cells and WBC cell DNA. EPO, MT-1A, HOXB13, TRIM15, and Septin9 showed relatively standard amplification curves and higher signal values in the qMSP testing of HeLa cells, while EPO, MT-1A, PDGFRA, HOXB13, and Septin9 genes exhibited no significant amplification curves in the qMSP testing of WBC cell DNA.



**Supplementary Figure 4.** The proportion of each stage in clinical validation and the positive rate of MDM panel and combined detection of MDM in early esophageal cancer (stage 0&I).



**Supplementary Figure 5.** The specificity of MDM panel with healthy control, benign esophageal diseases, and other cancer types in radar plot.



**Supplementary Figure 6.** The Sankey plot showed comparison of identification EC patients by tumor protein marker (CEA CA199, SCC, NSE) or methylation markers in 0 to IV stages.