Candidate tumor suppressor gene (n = 65) screening Confirmation with DNA methylation datasets from TCGA/GEO **Criteria 1**: Mean Methylation percent (β value) > 0.25 in ESCC samples **Criteria 2**: Mean Methylation percent (β value) < 0.25 in adjacent control samples **Criteira 3**: Mean Methylation percent (β value) < 0.25 in PBMC and PBL of normals Criteria 4: At least 2 CpG sites on candidate gene fulfills criteria 1,2 and 3 Candidate tumor suppressor genes (n = 6) for further validation Four candidate biomarkers for multiplex PCR design: ADHFE1, EOMES, SALL1, TFPI2 94 pairs of ESCC tumors and adjacent control tissues for validation with targeted bisulfite sequencing Model Evaluation: Accuracy, Sensitivity, Specificity, AUC