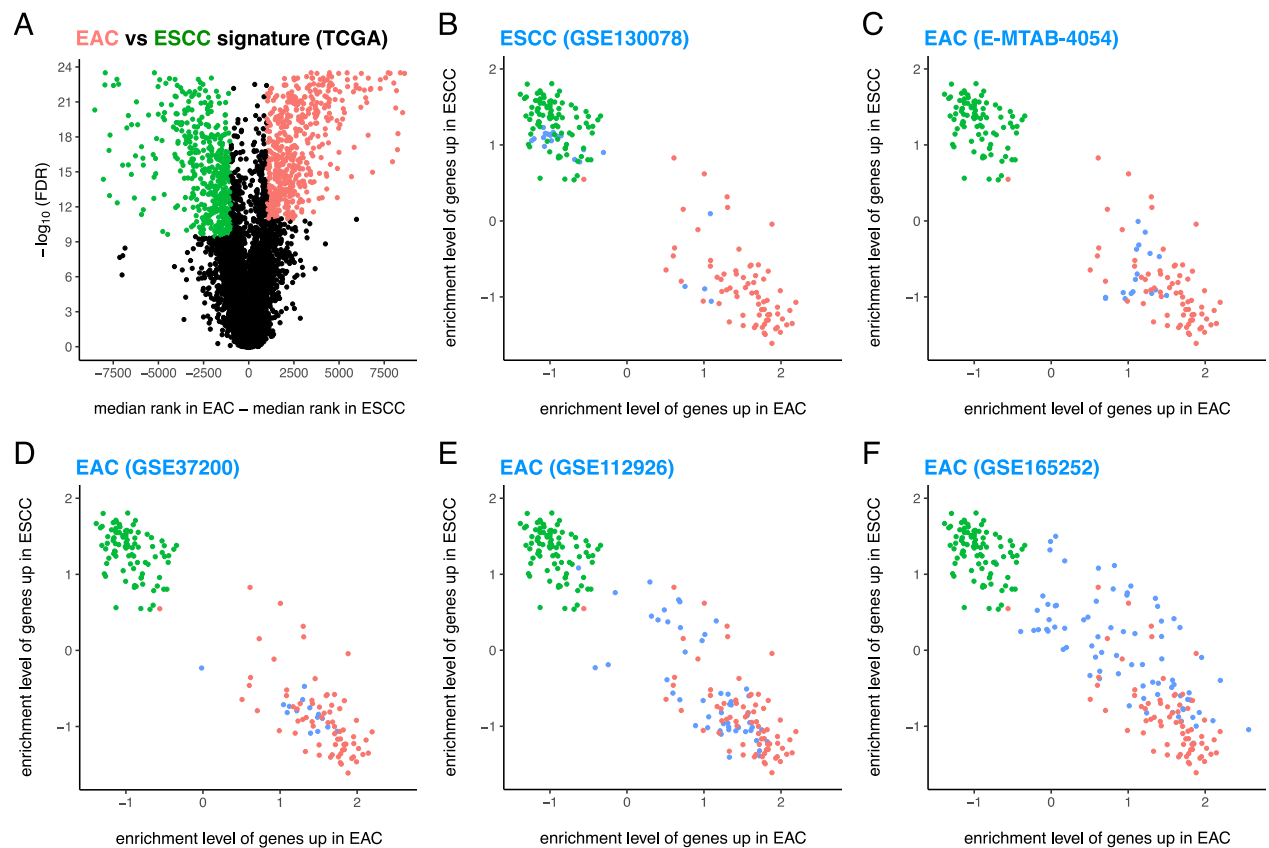
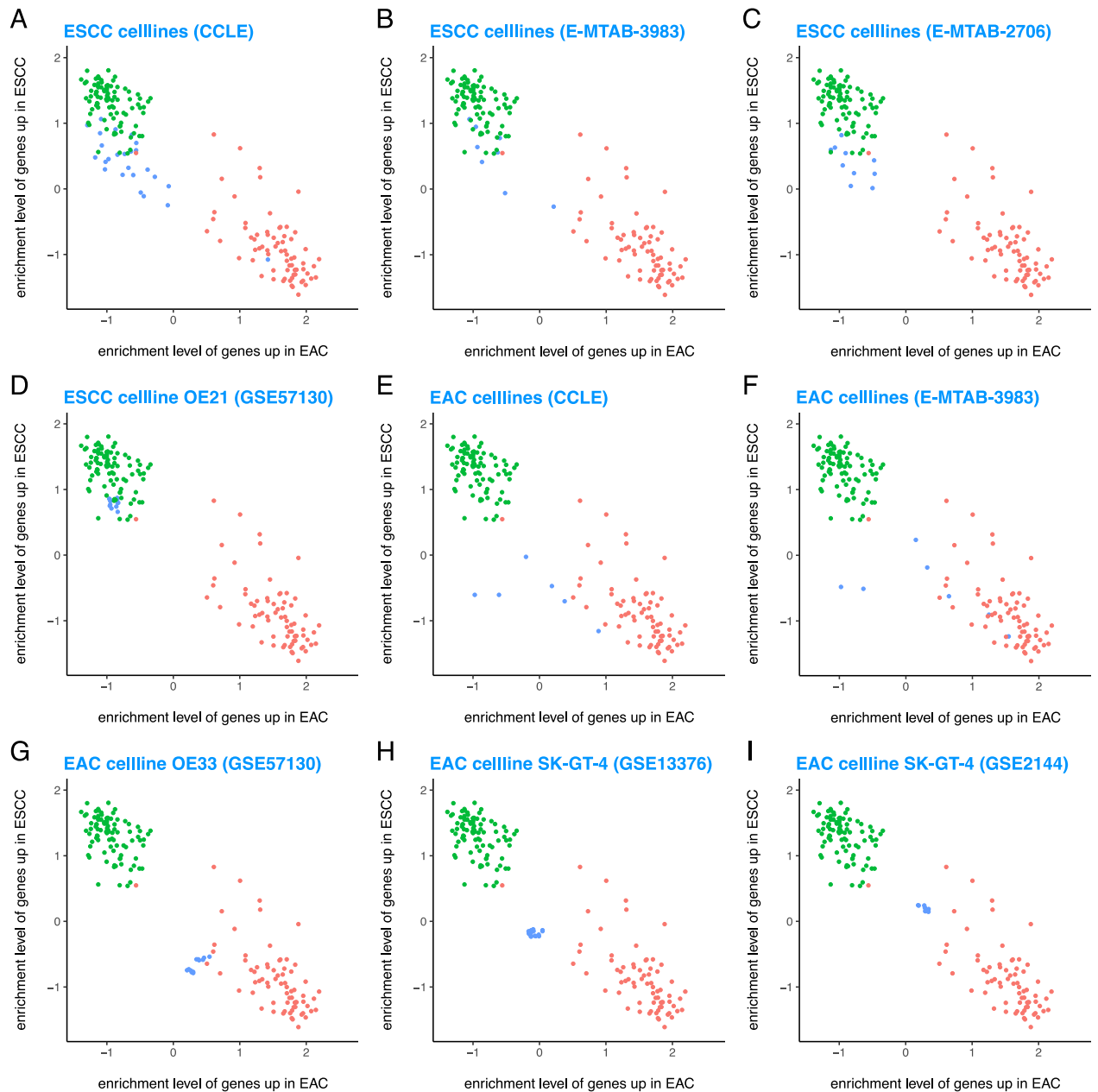


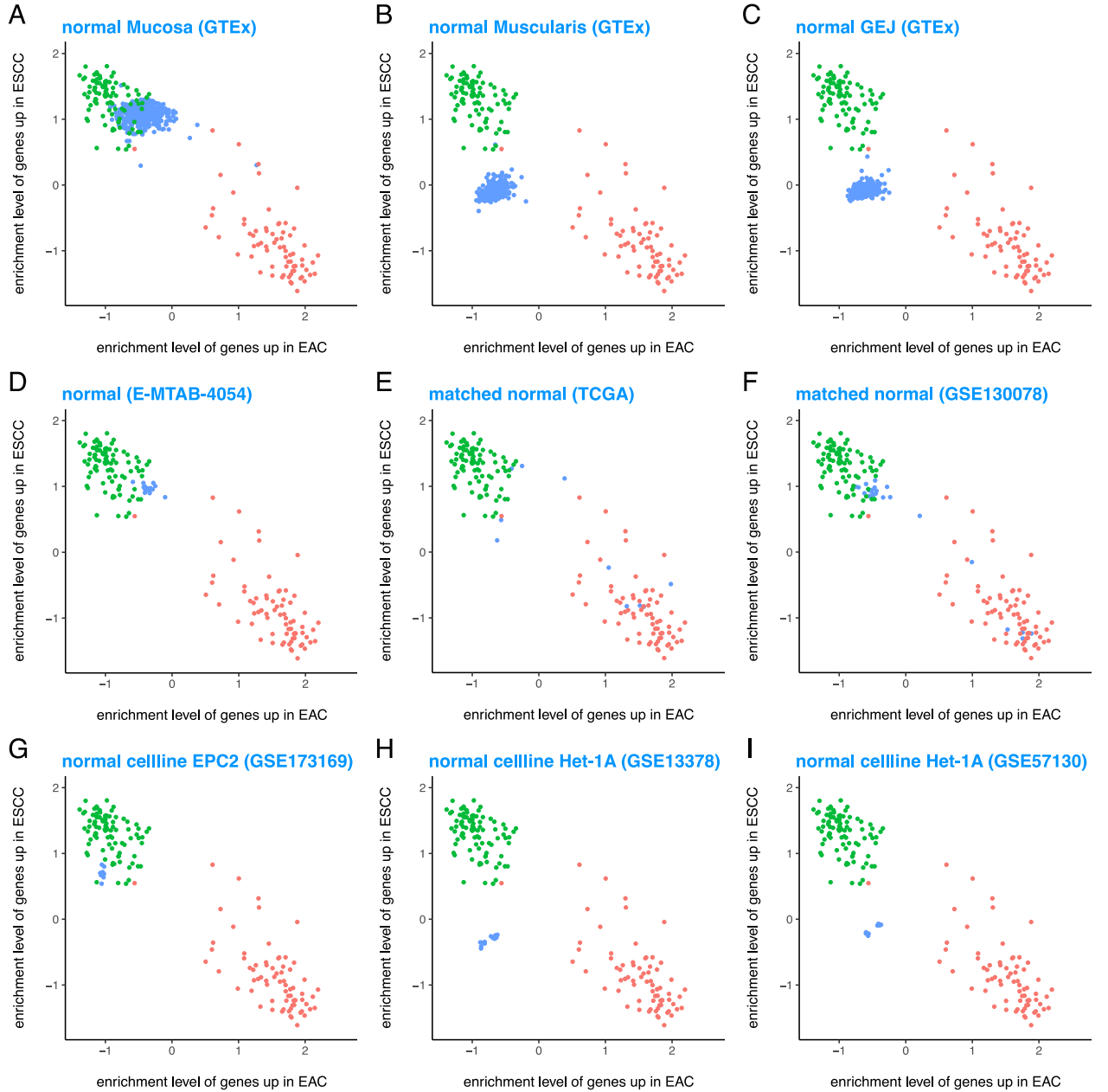
## Supplementary Figures



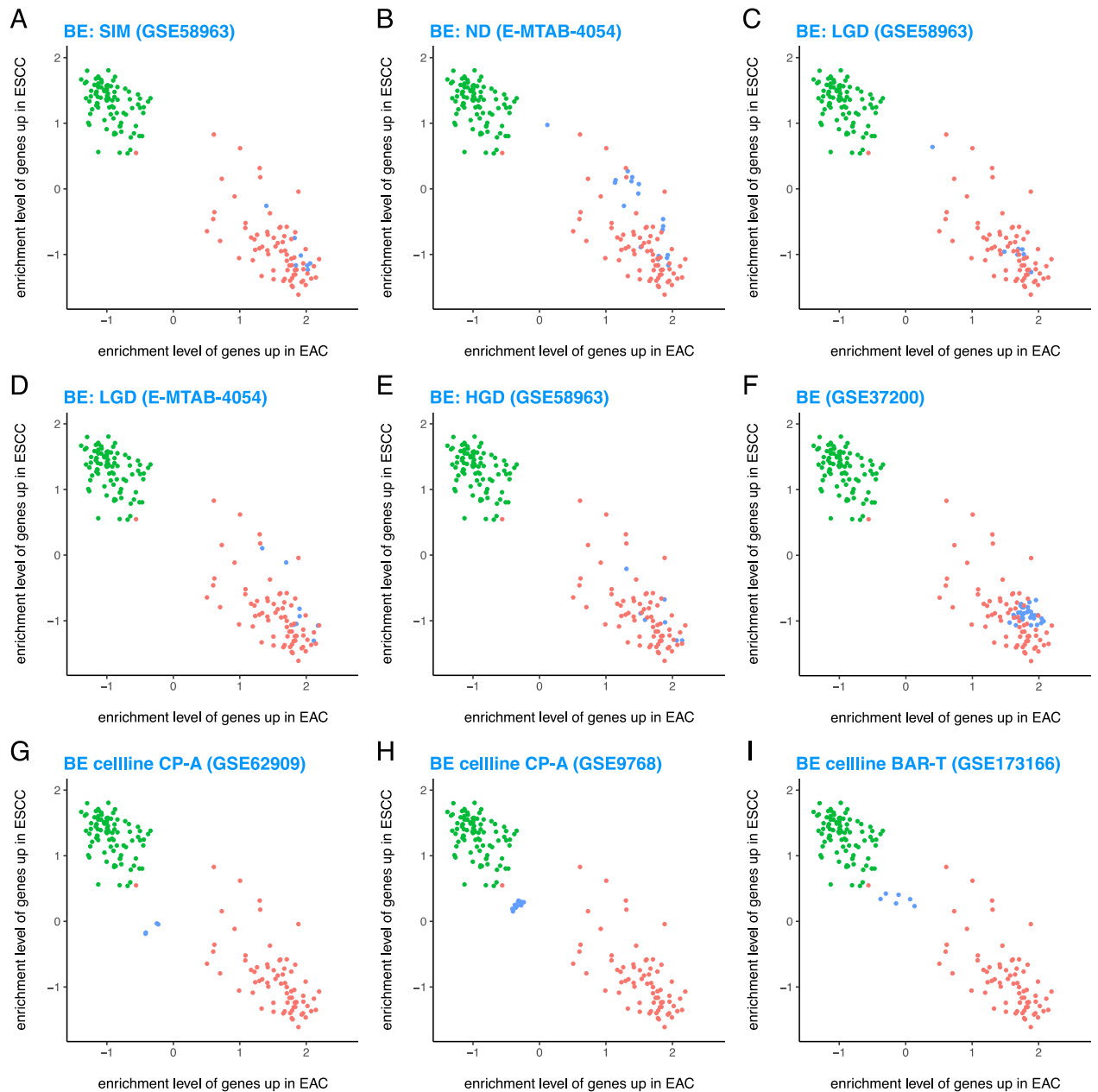
**Figure S1.** Construction and validation of gene expression signatures of esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC). (A) Gene expression signatures of EAC (consisting of 500 EAC<sup>hi</sup> genes in red) and ESCC (consisting of 500 ESCC<sup>hi</sup> genes in green) constructed from the Cancer Genome Atlas. Validation of these gene expression signatures in (B) a dataset of ESCC and (C-F) 4 datasets of EAC: red = EAC cases from TCGA, green = ESCC cases from TCGA, blue = test samples (various types of samples from datasets other than TCGA).



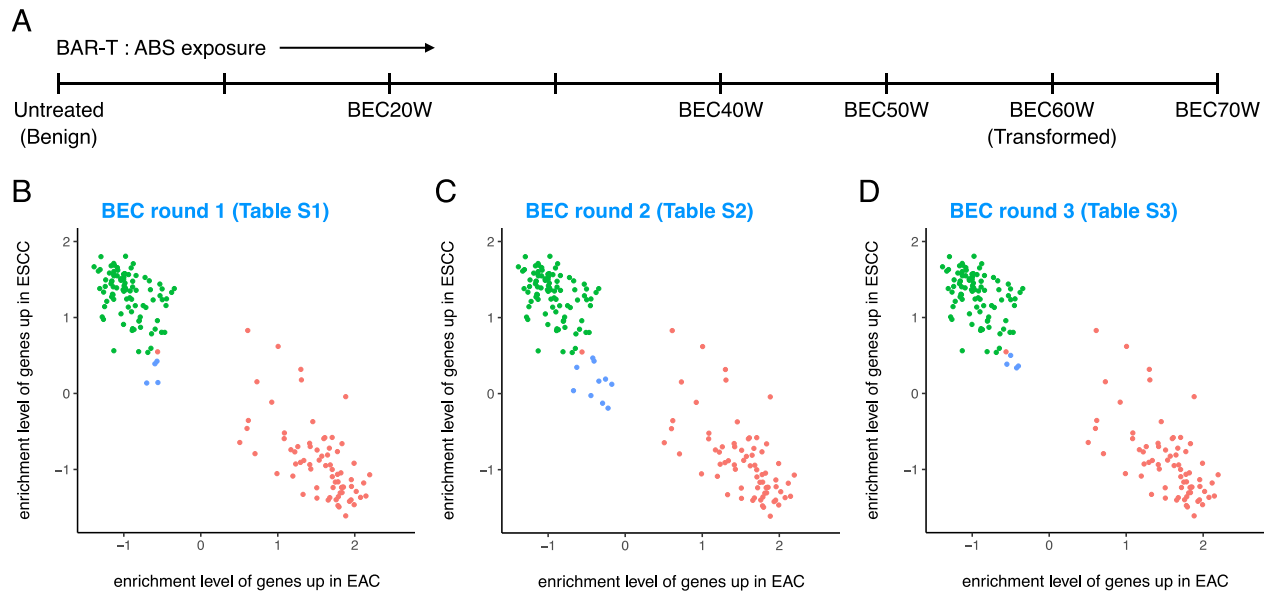
**Figure S2.** ESCC cell-lines are quite similar to primary ESCC tumors, but EAC cell-lines (although EAC-like) are considerably different from primary EAC tumors. Enrichment level of 500 EAC<sup>hi</sup> and 500 ESCC<sup>hi</sup> genes shows that (A-D) ESCC cell-lines cluster with primary ESCC tumors, but (E-I) EAC cell-lines often cluster near primary EAC tumors. red = EAC cases from TCGA, green = ESCC cases from TCGA, blue = test samples (various types of samples from datasets other than TCGA).



**Figure S3.** Normal esophageal cell-lines are quite similar to tissues derived from various parts of the normal esophagus. Enrichment levels of 500 EAC<sup>hi</sup> and 500 ESCC<sup>hi</sup> genes show that (A) normal esophagus mucosa is ESCC-like, (B) normal esophagus muscularis and (C) normal gastro-esophageal junction are neither EAC-like nor ESCC-like, (D) normal squamous esophagus is ESCC-like similar to normal esophagus mucosa, (E,F) matched normal esophagus from esophageal cancer patients are all over the place, (G) normal esophageal cell-line EPC2 is similar to normal esophagus mucosa (ESCC-like), (H,I) normal esophageal cell-line Het-1A is similar to normal esophagus muscularis and normal gastro-esophageal junction (neither EAC-like nor ESCC-like). red = EAC cases from TCGA, green = ESCC cases from TCGA, blue = test samples (various types of samples from datasets other than TCGA).



**Figure S4.** Barrett's Esophagus (BE) cell-lines were ESCC-like and extremely different from EAC-like primary BE tissues. Enrichment levels of 500 EAC<sup>hi</sup> and 500 ESCC<sup>hi</sup> genes show that (A-F) primary BE tissues are EAC-like at all stages (SIM = specialized intestinal metaplasia, ND = non-dysplastic, LGD = low grade dysplasia, HGD = high grade dysplasia), (G-I) BE cell-lines (CP-A, BAR-T) are surprisingly ESCC-like, and extremely different from primary BE tissues. red = EAC cases from TCGA, green = ESCC cases from TCGA, blue = test samples (various types of samples from datasets other than TCGA).



**Figure S5.** ABS exposure was not sufficient to induce EAC-like GEP in the BE cell line BAR-T and it remained ESCC-like even after malignant transformation. **(A)** Outline of the various time points at which BAR-T samples were collected from a previously established in-vitro model of BE carcinogenesis. Several untreated BAR-T samples were also included in the analysis. **(B-D)** Enrichment levels of 500 EAC<sup>hi</sup> and 500 ESCC<sup>hi</sup> genes showed that BAR-T samples remain ESCC-like despite ABS exposure and do not become EAC-like even after malignant transformation. red = EAC cases from TCGA, green = ESCC cases from TCGA, blue = test samples (various types of samples from datasets other than TCGA).