## **Description of Additional Supplementary Files**

File Name: Supplementary Data 1

Description: Clinical characteristics of patients in the scRNA-seq cohort, Discovery cohort,

Validation cohort 1 and Validation cohort 2

File Name: Supplementary Data 2

Description: Quality measures of scRNA-seq experiments in CD45- and CD45+ cells

File Name: Supplementary Data 3

Description: Cell type counts

File Name: Supplementary Data 4

Description: Down-sampling analysis of changed cell types between adjacent normal tissues and

**ESCC** tumors

File Name: Supplementary Data 5

Description: Eight epithelial expression program gene lists

File Name: Supplementary Data 6

Description: Cell subtype markers for T cells, B cells, myeloid cells, fibroblasts and endothelial cells

derived from the analysis of scRNA-seq data

File Name: Supplementary Data 7

Description: T cell clones in ESCC tumors shared with adjacent normal tissues

File Name: Supplementary Data 8

Description: Associations between program gene expression levels and ESCC survival in Discovery

cohort (N = 139) and Validation cohort 1 (N = 94)