Ferroptosis Cluster Α В consensus CDF Ferroptosis ClusterA Ferroptosis ClusterB 1.0rroptosis ClusterC and a 0.8 0.6 consensus matrix k=3 CDF 0.4 2
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9 0.2 0.0 0.8 --0.1 0.0 0.2 -С D Ε 1 2 3 3 4 5 1 2 3 4 □ 1 ■ 2 consensus matrix k=5 consensus matrix k=2 consensus matrix k=4 F Ferroptosis Cluster Project Ferroptosis Cluster Ferroptosis ClusterA Ferroptosis ClusterC Project TCGA OSCC GSE41613 GSE42743 GSVA KEGG ANTIGEN PROCESSING AND PRESENTATION KEGG B CELL RECEPTOR SIGNALING PATHWAY KEGG BASE EXCISION REPAIR KEGG CHEMOKINE SIGNALING PATHWAY KEGG CYTOKINE CYTOKINE RECEPTOR INTERACTION KEGG CYTOSOLIC DNA SENSING PATHWAY KEGG ECM RECEPTOR INTERACTION KEGG HOMOLOGOUS RECOMBINATION KEGG JAK STAT SIGNALING PATHWAY KEGG MAPK SIGNALING PATHWAY KEGG MISMATCH REPAIR KEGG NATURAL KILLER CELL MEDIATED CYTOTOXICITY KEGG NOD LIKE RECEPTOR SIGNALING PATHWAY KEGG PRIMARY IMMUNODEFICIENCY KEGG RIG I LIKE RECEPTOR SIGNALING PATHWAY KEGG T CELL RECEPTOR SIGNALING PATHWAY KEGG TGF BETA SIGNALING PATHWAY

1 Supplementary figures and figure legends



Figure S1 Unsupervised clustering of ferroptosis regulators of patients with OSCC

KEGG TOLL LIKE RECEPTOR SIGNALING PATHWAY

(A-E) Consensus matrices of 463 patients with OSCC (GSE41613, GSE42743, TCGA-OSCC) (k = 2–5). (F) GSVA enrichment analysis showing the different activation states of biological pathways associated with the ferroptosis regulation patterns. Ferroptosis cluster A vs. ferroptosis cluster C. Heat map: blue, activated pathways; red: inhibited pathways. The different cohorts served as sample annotations.



Figure S2 Characteristics of immune-cell infiltration, TME signature, immune
 checkpoint, and chemokine transcriptomes of distinct gene clusters

14	(A–E) Consensus matrices of the TCGA-OSCC data ($k = 2-5$). (F) The enrichment scores
15	of immune-cell infiltrations in three ferroptosis gene clusters. (G) The enrichment score of
16	the TME signature of three ferroptosis gene clusters. (H) Immune-checkpoint-relevant
17	genes and immune-activation-relevant genes expressed in three ferroptosis gene clusters.
18	Significant differences among of three ferroptosis clusters were assessed using the
19	Kruskal–Wallis test (ns: not significant, *P < 0.05, **P < 0.01, ***P < 0.001).
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Figure S3 Significance of the FPscore in determining the roles of the outcomes

34 (A) Kaplan–Meier PFI curves for high and low FPscore subtype in the TCGA-OSCC 35 cohort (log-rank test, P = 0.005). (B) Kaplan–Meier analysis of DSS of the high and low 36 FPscore subtypes in the TCGA-OSCC cohort (log-rank test, P = 0.003). (C, D) Kaplan– 37 Meier analysis of the OS of high and low FPscore subtype in the GES42743 cohort (log-38 rank test, P = 0.037) and GSE41613 cohort (log-rank test, P = 0.003).

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44 Figure S4 Correlation between the FPscore subtypes and somatic mutations

(A) The distributions of TMB differences in the high and low FPscore subtype (P = 0.13). (B) Boxplots showing the number of each mutation type in FPscore subtypes. (C, D) Mutational landscape of the top 20 most frequent mutated genes in the TCGA-OSCC cohort stratified according to low (blue bar) and high FPscore (red bar) subtype. Individual patients are represented in each column. The upper bar plot shows mutation number, the right bar plot shows the mutation frequency of each gene in the separate FPscore subtypes. Mutational signatures are shown as patient annotations. P values were tested using the Mann–Whitney test. (ns: not significant, *P < 0.05, **P < 0.01, ***P < 0.001).



58 Figure S5 Time-dependent ROC curve of the immunotherapy cohorts

59 (A–E) Time-dependent ROC curves for predicting OS of the independent immunotherapy

60 cohort, including IMvigor210, GSE910161, TCGA-SKCM, Gide et al. cohort, and

61 GSE78220.