

Description of Additional Supplementary Files

File Names: Supplementary Data 1

Description: **Clinical characteristics of 206 GC patients.** (A) Clinical characteristics of 206 GC patients. (B) GC Patient demographics and baseline characteristics.

File Names: Supplementary Data 2

Description: **Proteomic matrix of the 206 GC patients.** (A) The protein expression matrix of 12,519 proteins after match between runs. (B) The protein expression at least 1 unique peptide with 1% FDR of all 206 samples.

File Names: Supplementary Data 3

Description: **Molecular subtypes of GC.** (A) The proteomic subtype of the 206 GC patients. (B) The proteomic subtype of the 179 GC patients. (C) The association of the proteomic subtypes of 206 GC patients and 179 GC patients. (D) The significantly up-regulated expressed proteins in the proteomic subtypes of the gastric cancer cohort. (E) The pathway alterations in the proteomic subtypes of the gastric cancer cohort enriched by these signatures of these subtypes. (F) The clinical groups in an independent validation subcohorts. (G) Targeted peptides from ECM proteins. Peptides were identified from the library search result, and targeted in a PRM experiment. (H) The ECM proteins' expression by PRM assay in the DOS validation subcohort.

File Names: Supplementary Data 4

Description: **Application of FDGC subtype.** (A) The FDGC subtyping model was applied to the BPRC cohort. (B) The FDGC subtyping model was applied to the EOGC cohort. (C) The FDGC subtyping model was applied to the ACRG cohort.

File Names: Supplementary Data 5

Description: **The xCell analysis result of GC cohort.** The xCell analysis result of FDGC cohort (A), ACRG cohort (B), BPRC cohort (C). (D) Differential cell types among four subtypes of 179 proteomic subtyping. (E) The significantly down-regulated immune-related proteins in G-IV

subtype.

File Names: Supplementary Data 6

Description: **The differential analysis of DOS subcohort. (A)** The group of DOS subcohort. **(B)** The differentially expressed proteins of DSG and DNSG. **(C)** The pathway alterations of DSG and DNSG.

File Names: Supplementary Data 7

Description: **The differential analysis of XELOX subcohort. (A)** The group of XELOX subcohort. **(B)** The differentially expressed proteins of XSG and XNSG. **(C)** The pathway alterations of XSG and XNSG.

File Names: Supplementary Data 8

Description: **The differential analysis of XELOX combined with HER2 subcohort. (A)** The group of XELOX combined with HER2 subcohort. **(B)** The differentially expressed proteins of XHSG and XHNSG. **(C)** The pathway alterations of XHSG and XHNSG.

File Names: Supplementary Data 9

Description: **The differential analysis of HER2 subcohort. (A)** The group of HER2 subcohort. **(B)** The differentially expressed proteins of HSG and HNSG. **(C)** The pathway alterations of HSG and HNSG.

File Names: Supplementary Data 10

Description: **A list of signatures of the predictive classifiers in therapy subcohorts.** A list of signatures of the predictive classifiers in DOS subcohort **(A)**, XELOX subcohort **(B)**, HER2 subcohort **(C)**.

File Names: Supplementary Data 11

Description: **The PRM validation of the predictive signatures in an independent validation subcohorts. (A)** The clinical groups in an independent validation subcohorts. **(B)** Targeted

peptides from predictive signatures. Peptides were identified from the library search result, and targeted in a PRM experiment. **(C)** The signature proteins' expression by PRM assay in the DOS validation subcohort. **(D)** The signature proteins' expression by PRM assay in the XELOX validation subcohort. **(E)** The signature proteins' expression by PRM assay in the HER2 validation subcohort.

File Names: Supplementary Data 12

Description: **The differentially expressed proteins and pathway alterations in MKN45 cells overexpressing CTSE.** **(A)** The up-regulated proteins and down-regulated proteins of CTSE OE group. **(B)** KEGG pathways were obtained from enrichment analysis of differentially expressed proteins.

File Names: Supplementary Data 13

Description: **The differentially expressed proteins and pathway alterations in MKN45 cells overexpressing CTSE after DOC treatment.** **(A)** The up-regulated proteins and down-regulated proteins of CTSE OE group after DOC treatment. **(B)** KEGG pathways were obtained from enrichment analysis of differentially expressed proteins.