Description of Additional Supplementary Files

Supplementary Data 1. Clinical characteristics of all patients.

A. Clinical information of 861 patients for discovery. Age at diagnosis, date of operation, residual tumor, histological type, grade, FIGO stage, metastasis of lymph, frequency of chemotherapy, recurrence free survival, recurrent disease, chemoresistance, follow-up time, CA125 before the treatment, HE4 before the treatment, CA125 at the last cycle of chemotherapy, additional Bevacizumab or PARP inhibitor, sampling location, tissue or plasma proteome are listed. For residual tumor, 0 represents no residual disease; 1 represents residual size less than 1 cm; 2 represents residual size greater than 1 cm. For frequency of chemotherapy, A represents no more than two cycles of chemotherapy; B represents three to five cycles of chemotherapy; C represents six to eight cycles of chemotherapy; D represents more than eight cycles of chemotherapy. For sampling location, A represents uterine appendages; B represents pelvic cavity; C represents abdominal cavity; D represents distant metastasis.

B. Sample information for tissue proteome.

C. Sample information for plasma proteome.

D. The effects of lymphatic metastasis, FIGO stage, platinum status, residual tumor and frequency of chemotherapy between primary HGSOC and other histotypes analyzed by Fisher's exact test.

E. Clinical information of 49 patients for validation.

F. Sample information for tissue proteome of the validation set.

G. Sample information for plasma proteome of the validation set.

Supplementary Data 2. Global proteome.

A. Protein matrix of tissue samples by PulseDIA after quality control.

B. Protein matrix of plasma samples by TMTpro-labeled proteome after quality control.

Supplementary Data 3. Malignancy associated biomarkers.

A. Statistic difference of quantified protein numbers between carcinoma groups and each other three groups, namely normal, benign, borderline groups by two-sided unpaired

Welch's t-test.

B. Differentially expressed proteins of tissue samples across five groups using ANOVA. 8741 proteins have been shortlisted with B-H adjusted p value less than 0.05.

C. Protein clusters of tissue samples across five groups using mFuzz.

D. Differentialy expressed proteins of tissue samples between primary carcinoma and normal groups. 2934 proteins have been shortlisted with fold change larger than 2 and B-H adjusted p value less than 0.05.

E. Pathway enrichment for 2551 differentially expressed proteins of tissue samples between primary carcinoma and normal groups using IPA, related to Figure 2C. P values are derived from one-sided Fisher's Exact Test for pathway enrichment. The pathways for Figure 2C were mannually checked and those with unavaliable Z scores were exluded.

F. Differentialy expressed proteins between each histotypes and benign/borderline samples by two-sided unpaired Welch's t-test. 5464 proteins have been shortlisted with fold change larger than 1.5 and B-H adjusted p value less than 0.05.

G. Differentialy expressed proteins of plasma samples between carcinoma and non-carcinoma groups by two-sided unpaired Welch's t-test. 287 proteins have been shortlisted with fold change larger than 1.2 and B-H adjusted p value less than 0.05.

H. Statistic difference of the performance between eight-protein model and each other models to distinguish carcinoma and non-carcinoma groups by bootstrap method.

Supplementary Data 4. Histotype specific differentially expressed proteins.

A. Differentially expressed proteins between HGSOC and other four histoypes in PDS-EOC cohort by two-sided unpaired Welch's t-test.

B. Differentially expressed proteins between normal groups and each histological type in PDS-EOC cohort by two-sided unpaired Welch's t-test.

C. Differentially expressed proteins among five histotypes of PDS-EOC cohort by two-sided unpaired Welch's t-test.

D. Histotype specific DEPs by two-sided unpaired Welch's t-test.

E. Pathway enrichment for major histotype specific DEPs in each cluster using Ward's minimum variance method. P values are derived from one-sided Fisher's Exact Test for pathway enrichment.

Supplementary Data 5. Prognostic proteins.

A. Prognostic proteins of advanced HGSOC tissue samples from PDS-EOC cohort in RFS by Univariate Cox analysis.

B. Prognostic proteins of advanced HGSOC tissue samples from RLP-EOC cohort in RFS by Univariate Cox analysis.

C. Prognostic proteins of advanced HGSOC tissue samples from NACT-EOC cohort in RFS by Univariate Cox analysis.

D. Pathway enrichment for prognostic proteins of advanced HGSOC tissue samples from each cohort in RFS using IPA. P values are derived from one-sided Fisher's Exact Test for pathway enrichment.

E. 150 prognostic proteins validated in any of the four cohorts in CPTAC and Chowdury cohorts.

F. Prognostic proteins of HGSOC tissue samples from PDS-EOC cohort in RFS by Univariate Cox analysis.

G. Prognostic proteins of HGSOC plasma samples from PDS-EOC cohort in RFS by Univariate Cox analysis.

H. Pathway enrichment for prognostic proteins of HGSOC plasma samples from PDS-EOC cohort in RFS using Metascape. P values are derived from one-sided Fisher's Exact Test for pathway enrichment.

I. Univariate Cox analysis of clinical factors across plasma samples.

J. Multivariate Cox analysis of significantly prognostic proteins (B-H adjusted p value < 0.05) in plasma samples to adjust the effect from four potentially cofounding clinical factors. All 18 significantly prognostic proteins were independent of clincial factors.

K. Multivariate Cox analysis of overlapped prognostic proteins between tissue and plasma samples from PDS-EOC cohort to adjust the effect from four potentially cofounding clinical factors. All 17 overlapped prognostic proteins were independent of clincial factors. The statistical significance determined by the univariate or multivariate Cox proportional hazards analysis throughout Supplementary Table 5 is established using the log-rank test.

Supplementary Data 6. Verification of prognostic proteins by MRM and machine learning

model.

A. Protein matrix of prognostic proteins of PDS-HGSOC tissue samples quantified by MRM.

B. Prognositic proteins of tissue samples verified by MRM. The t-test_p value was calcualted by two-sided unpaired Welch's t-test.

C. Protein matrix of prognostic proteins of PDS-HGSOC plasma samples quantified by MRM.

D. Prognositic proteins of plasma samples verified by MRM. The t-test_p value was calcualted by two-sided unpaired Welch's t-test.

E. CiRT for MRM assay of tissue and plasma samples.

F. The predictive result of ZZOV cohort by Model A. 0, patients with RFS ≤ 12 months; 1, those with RFS > 12 months.

G. The predictive result of ZZOV cohort by Model B.

H. The predictive result of ZZOV cohort by Model C.

I. The predictive result of CPTAC cohort by revised Model B.

Supplementary Data 7. Integrative analysis of target region sequencing and proteomic data between chemo-sensitive and -resistant EOC patients.

A. 295-gene panel for target genome.

B. Germline variants in targeted genomic data across 96 patients.

C. Target genomic data of somatic mutations across 96 patients.

D. Quality control for genomic data.

E. Copy number alteration data.

F. Two-sided Fisher’s exact test for potential drivers of chemoresistance in PDS-HGSOC and RLP-HGSOC patients.

G. Differentially expressed proteins (DEPs) between chemosensitive HGSOC patients with HRR mutations and chemoresistant ones without any HRR mutations. P values were calculated by two-sided unpaired Welch's t-test.

H. Pathway enrichment for 33 DEPs which were annotated to have direct interactions with 14 genes in the HRR pathway. P values are derived from one-sided Fisher’s Exact Test for

pathway enrichment.

I. Differentially expressed proteins between chemosensitive and chemoresistant HGSOC patients of the relapsing cohort. P values were calculated by two-sided unpaired Welch's t-test.

J. Pathway enrichment for 356 DEPs associated with chemoresistance in relapsing cohort using Metascape. P values are derived from one-sided Fisher’s Exact Test for pathway enrichment.