Supplementary Information for Figures

**Supplementary information includes:**

**Supplementary Figures 1 to 6**

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**Supplementary Figure 1. Correlation analysis of clinical features and proteomic profiling of participants receiving ICI therapies. a.** Proteomic profiling correlations across participants. **b.** Correlation analysis of clinical features and proteomic profiling of patients across different irAE severity groups. **c, d.** Correlation analysis of clinical features and comparable secretory and tissue-specific proteomic profiling. The proteomic profiling was evaluated with PCA/PLS-DA scores. Statistical significance assessed using Pearson correlation coefficients for continuous variables, Fisher's exact test for categorical variables, and Wilcoxon or Kruskal-Wallis tests for continuous versus categorical variables.

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**Supplementary Figure 2. Enriched GO terms of proteins with differential abundance trends across irAE groups.** Terms are marked as decreased (blue) or increased (red) (FDR *P* < 0.05 and gene ratio > 0.1).



**Supplementary Figure 3. The consensus protein co-expression network analysis. a.** Determination of soft-threshold power in the consensus protein co-expression network analysis. Analysis of the scale-free index for various soft-threshold powers (β) and the mean connectivity for various soft-threshold powers. **b.** Dendrogram of proteins based on the measurement of dissimilarity and identification of the 17 modules. **c.** The effect of missing value threshold (10-40% missingness) on irAE network modules, assessed by Zsummary score. The dashed blue (1.96) and red (10) lines indicates a weakly and highly statistically significant, respectively. **d.** Box plots displayed the differences oforiginal module eigenprotein (the first principal components of module protein expression) across irAE groups in irAE-related modules, identified in Figure. 3a. **e.** Correlation analysis of (module explanation) original module eigenproteins and those module eigenproteins generated from hypergeometric test-selected proteins. **f.** Correlation analysis of potential biomarkers and the consensus network module eigenproteins.



**Supplementary Figure 4. GO analysis for hypergeometric test-identified proteins in irAE-related network module.** Terms are marked as decreased (blue) or increased (red) (FDR *P* < 0.05 and gene ratio > 0.1). The detail results of enrichment analysis were presented in Supplementary Table. 5.

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**Supplementary Figure 5. Associated proteins in M1/M4-specific KEGG and Reactome terms displayed in Figure 3c.** Colored proteins were those significantly change in Control vs. Mild, indicating the potential ability on early detection for patients suffering from irAEs.



**Supplementary Figure 6. Model family and link function selection for ProIRAE with 5-fold cross-validation on the discovery cohort.**