Supplementary Figure 1

A

Overall Survival (days)

1: PD-L1 0-49% 1st line
2: PD-L1 0-49% 2nd line
3: PD-L1 0-49% 3rd line or later
4: PD-L1 50-100% 1st line
5: PD-L1 50-100% 2nd line
6: PD-L1 50-100% 3rd line or later

COX Hazard model

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<th>PD-L1 expression</th>
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<th>N</th>
<th>HR</th>
<th>95%CI</th>
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<td>0.25-5.85</td>
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<td>50-100 %</td>
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<td>17</td>
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<td>0.24-3.14</td>
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<td>0.86</td>
<td>0.24-3.14</td>
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Supplementary Figure 1

B

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<th>Response</th>
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<th>2nd line</th>
<th>3rd line</th>
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<td>Pembrolizumab</td>
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</tr>
</tbody>
</table>

Supplementary Figure 2

- **Ser**
  - Survival probability
  - OS (months)
  - P = 0.016

- **Ala**
  - Survival probability
  - OS (months)
  - P = 0.032

- **Anthranilic acid**
  - Survival probability
  - OS (months)
  - P = 0.002

- **His**
  - Survival probability
  - OS (months)
  - P = 0.001

- **Arg**
  - Survival probability
  - OS (months)
  - P = 0.008

- **Xanthurenic acid**
  - Survival probability
  - OS (months)
  - P = 0.037

- **Thr**
  - Survival probability
  - OS (months)
  - P = 0.029

- **Trp**
  - Survival probability
  - OS (months)
  - P = 0.037

- **Neopterin**
  - Survival probability
  - OS (months)
  - P = 0.037

Legend:
- Low conc.
- High conc.
- Cutoff at median
Supplementary Figure 3

A

![Survival probability vs. OS (days)]

- Low risk
- High risk
- P<0.001

B

![Risk score vs. Tumor response]

- RNAseq cases
- All cases

- Group
- PD
- PR
- SD

Risk score

- *P<0.05; Mann–Whitney–Wilcoxon test.

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**Supplementary Figure 4**

**A**
- T cell activation
- Lymphocyte differentiation
- Nuclear division
- Regulation of T cell activation
- Mitotic nuclear division
- Regulation of leukocyte cell-cell adhesion
- T cell differentiation
- Regulation of nuclear division
- Regulation of mitotic nuclear division
- T cell proliferation

**B**
Pathway enrichment

- Staphylococcus aureus infection
- Complement and coagulation cascades
- Pertussis
- Cell cycle
- NF-κB signaling pathway
- T cell receptor signaling pathway
- Hematopoietic cell lineage
- Primary immunodeficiency

**C**
- Complement cascade
  - NES=2.129; P=0.003
- Regulation of TLR by endogenous ligand
  - NES=1.903; P=0.002
- Interferon alpha beta signaling
  - NES=1.882; P=0.003
- Cell cycle checkpoints
  - NES=1.408; P=0.004
- Biological oxidations
  - NES=1.401; P=0.002
- Toll like receptor TLR1:TLR2 cascad
  - NES=1.393; P=0.003
- Cell-cell junction organization
  - NES=1.839; P=0.002
- Cell cycle checkpoints
  - NES=1.566; P=0.017

Supplementary Figure 6

The figure presents survival probability curves for various genes, each represented with different colors for low and high expression levels. The p-values for each gene's expression level are indicated, with values ranging from 0.002 to 0.05. The genes included are VAMP2, PER2, ACY1, UNC13B, SH3BP4, SFXN3, SFXN2, ASL, ASH1L, ACAA2, PSAT1, ACADS, ALDH3B1, ALDH2, and HMGCL. The x-axis represents OS (days), and the y-axis represents survival probability. The low expression group is depicted in blue, and the high expression group in red.
Supplementary Figure 7

Tumor microenvironment
- Blood vessels
- Normal cells
- Cancer cells
- Stromal cells
- CAFs
- Fibroblasts

Immune checkpoint inhibitors (ICI)

Peripheral blood
- Cytokines, etc.
- Differently expressed genes in PBMCs eg. SLC11A1, PHGDH, HAAO
- Macrophage M1
- Anti-PD-1
- CD8+ T cell
- Activate
- PD-1
- Lysosome
- Low risk
- High risk
- Difference in relative abundance and activity of immune cell subtypes. eg. CD8+ T cells, Macrophage M1

PFAAs eg. Tryptophan, Serine

Circulating immune cells