**Supplementary Figure Legend**

**Figure S1. PD1 expression on HCC infiltrating CD8+ T cells and its clinical associations. A and B,** Flow cytometric analysis of the proportions of PD1- (**A**) and PD1Int T cells (**B**) among total CD8+ T cells from paired blood, peri-tumor and tumor of HCC patients. **C-F,** Association of patients TNM stages and tumor size with the percentage of CD8+PD1+ (**C and D**) and CD8+PD1Hi among CD8+ T cells (**E and F**) from paired blood, peri-tumor and tumor of HCC patient. Error bars indicated median with interquartile rang. Significance was assessed by Wilcoxon matched-pairs signed rank test. \*, *P*<0.05; \*\*, *P*<0.01; \*\*\*, *P*<0.001; and \*\*\*\*, *P*<0.0001.

**Figure S2. Detection of the mRNA expression levels of exhaustion related markers** **in PD1Hi CD8+ TILs.**

Therelative mRNA levels of exhaustion related markers including *PDCD1*, *HAVCR2*, *CTLA4*, *LAG3* and *ENTPD1* of CD8+PD1Hi and CD8+PD1Int TILs were determined by qRT-PCR (n=5). Significance was assessed by Wilcoxon matched-pairs signed rank test. \*, *P*<0.05; \*\*, *P*<0.01; \*\*\*, *P*<0.001; and \*\*\*\*, *P*<0.0001.

**Figure S3. Expression pattern of transcription factors, apoptotic and proliferative markers of PD1Hi CD8+ TILs.**

**A and B,** Representative flow cytometric histograms of various transcription factors (**A**) , apoptotic and proliferative markers (**B**), surface markers (**C**) and cytokine receptors (**D**) on tumor infiltrating PD1Hi (red line), PD1Int (blue line) and PD1- (black line) CD8+ TILs. One representative experiment out of three to four was shown.

**Figure S4. Expression pattern of chemokine receptors of PD1Hi CD8+ TILs and phenotypic characteristics of TIM3-PD1Hi and TIM3+PD1Hi TILs.**

**A and B,** Representative flow cytometric histograms of CCR (**A**) and CXCR (**B**) chemokine receptors on tumor infiltrating PD1Hi (red line), PD1Int (blue line) and PD1- (black line) CD8+ TILs. One representative experiment out of three to four was shown. **C**, Representative flow cytometric plot of PD1 and TIM3 expression on HCC infiltrating CD8+T cells. **D-F**, Expression of co-inhibitory receptors **(D),** exhaustion related transcription factors, apoptotic and proliferative markers **(E)** andactivation markers **(F)** on tumor infiltrating PD1-, PD1Int, TIM3-PD1Hi and TIM3+PD1Hi CD8+T cells. **G**, Representative flow cytometric histograms of cytokines and cytotoxic molecules, including IFN-γ and TNF-α (following the stimulation of PMA, ionomycin and brefeldin A for 5 hours), intracellular Granzyme B and perforin, and CD107a expression (following the overnight stimulation of anti-CD3/CD28) of tumor infiltrating PD1- (black line), PD1Int (blue line), TIM3-PD1Hi (orange line) and TIM3+PD1Hi (red line) T cells. One representative experiment out of three to four was shown.

**Figure S5. Sorting strategy of PD1Hi CD8+ TILs.**

**A and B**, Gating strategy of tumor-infiltrating CD8+ T cells based on PD1 and TIM3 expression (**A**) and post sort analysis of PD1-high, PD1-intermediate and PD1-negative CD8+ TILs subpopulation (**B**).

**Figure S6. Enriched exhausted PD1Hi CD8+ T cells in HCC tumors.**

**A**, Representative IHC images showed the staining for CD3, CD8, PD1 and TIM3 in HCC tumor and peri-tumor. Scale bar, 50μm. **B**, The 5-color multiplex immunofluorescence panel was applied on TMAs. Scale bar, 200μm. **C**, Flow cytometry alike density plot was defining “PD1Hi” and “TIM3+”-threshold based on quantitative mean pixel fluorescence intensity. **D**, Comparisons of the frequency of CD8+PD1Int T cells, CD8+PD1Hi T cells, CD8+TIM3-PD1Hi T cells and CD8+TIM3+PD1Hi T cells among CD8+PD1+ T cells between paired peri-tumor and tumor tissues in the validation cohort (n=254). Error bars indicated median with interquartile range. Significance was assessed by Wilcoxon matched-pairs signed rank test. \*, *P*<0.05; \*\*, *P*<0.01; \*\*\*, *P*<0.001; and \*\*\*\*, *P*<0.0001.

**Figure S7. Prognostic significance of the subsets of CD8+ TILs in the validation cohort.**

**A-D,** Kaplan-Meier analysis of overall survival (OS, **A** and **C**) and relapse free survival (RFS, **B** and **D**) in HCC tumors according to the proportion of CD8+PD1Int, CD8+PD1Hi **(A** and **B)**, CD8+PD1+ TILs, CD8+TIM3-PD1Hi and CD8+TIM3+PD1Hi **(C** and **D)** among CD8+PD1+ TILs in the validation cohort (n=254). **E,** Correlation analysis between the density of CD8+TIM3+PD1Hi, CD8+TIM3-PD1Hi, CD8+PD1Int and the density of PDL1+ tumor cells (PDL1+CD68-) per core respectively. Correlation was evaluated by the Spearman correlation coefficient.