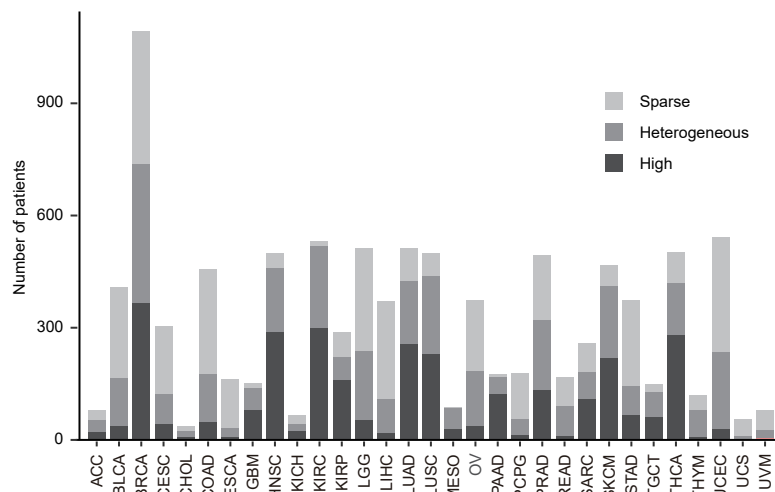
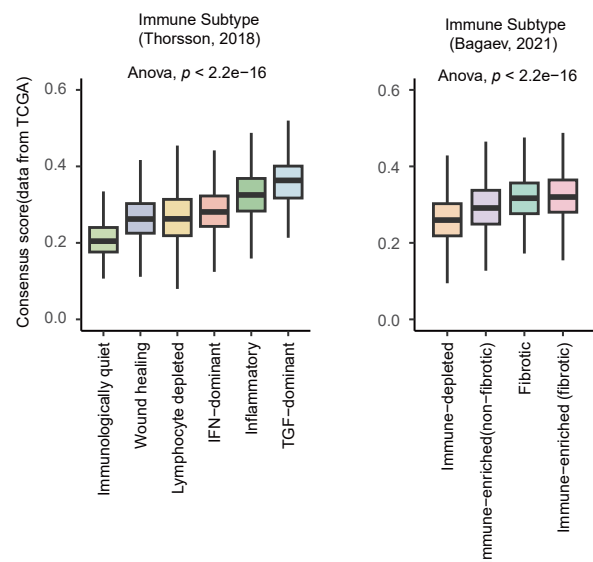


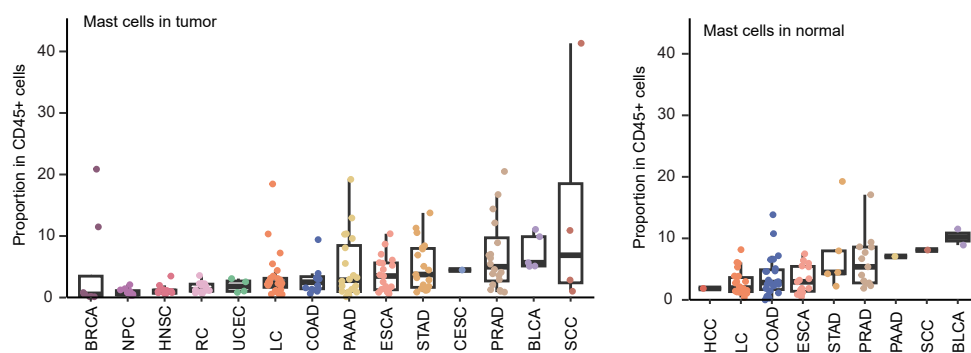
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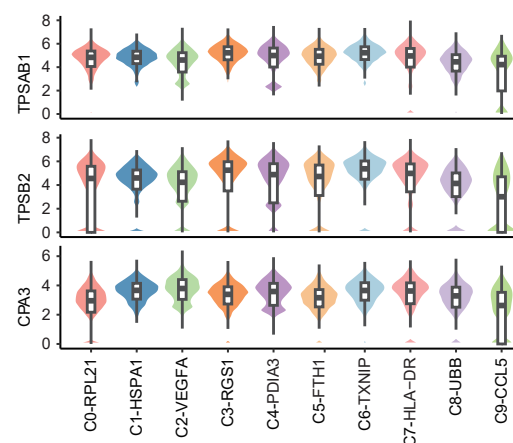
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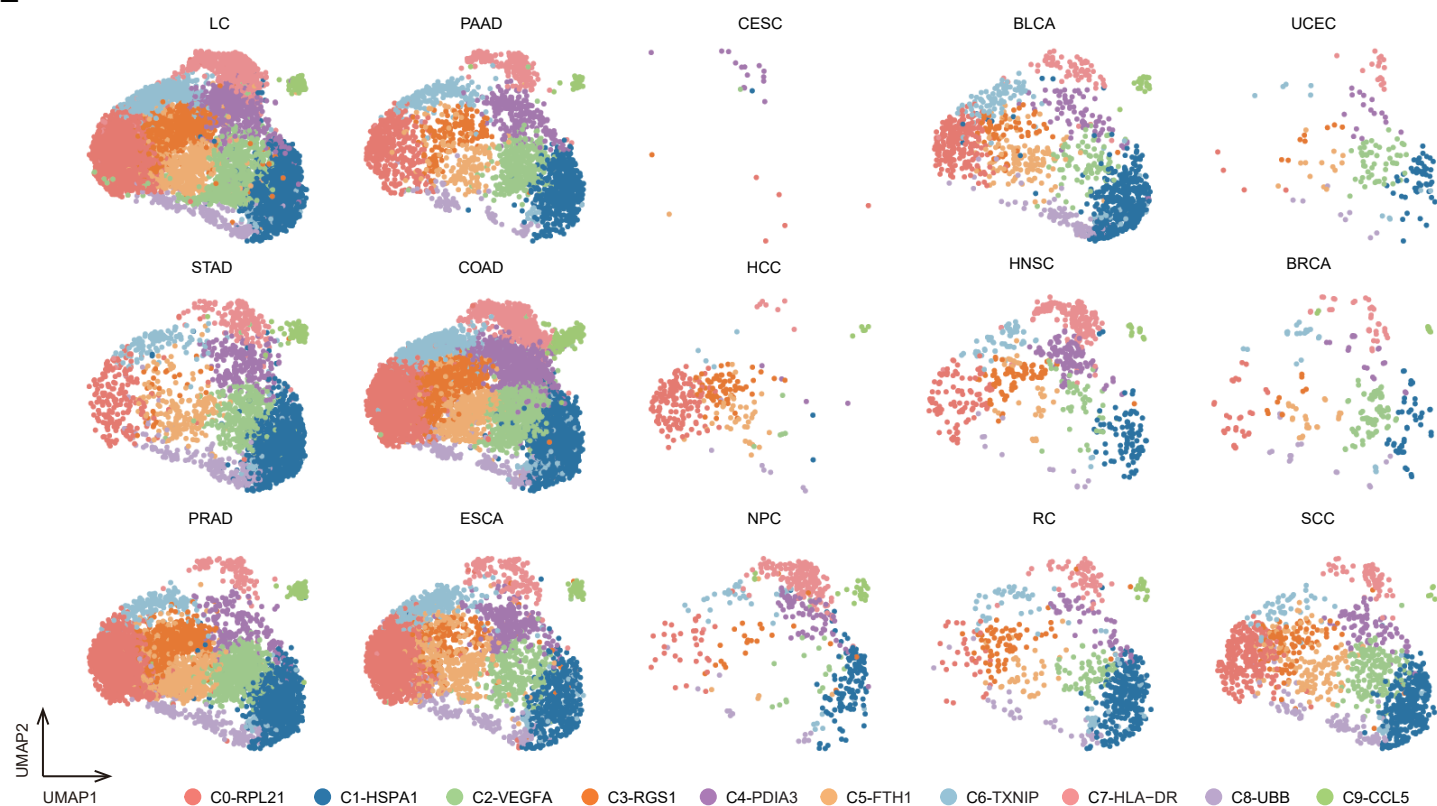
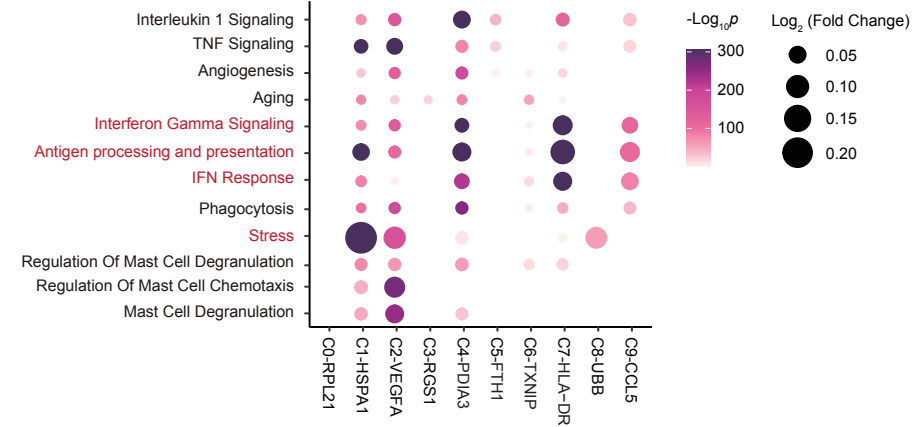


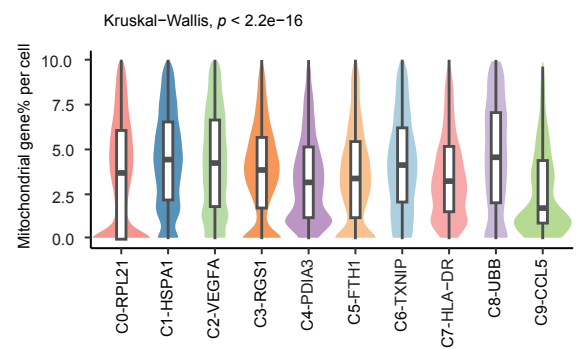
Figure S1. Overview of data and integration for mast cells, related to Figure 1. A.

Bar plots showing the distribution of cancer types across consensus mast cell infiltration levels. B. Consensus infiltration levels of mast cells across different immune subtypes (TCGA dataset). ANOVA test was used to assess significant differences among groups. C. Proportion of mast cells among all CD45⁺ cells across tissues. D. Violin plots showing the expression levels of mast cell markers across all mast cell clusters. E. UMAP plots of mast cell clusters from different cancer types.

A



C



B

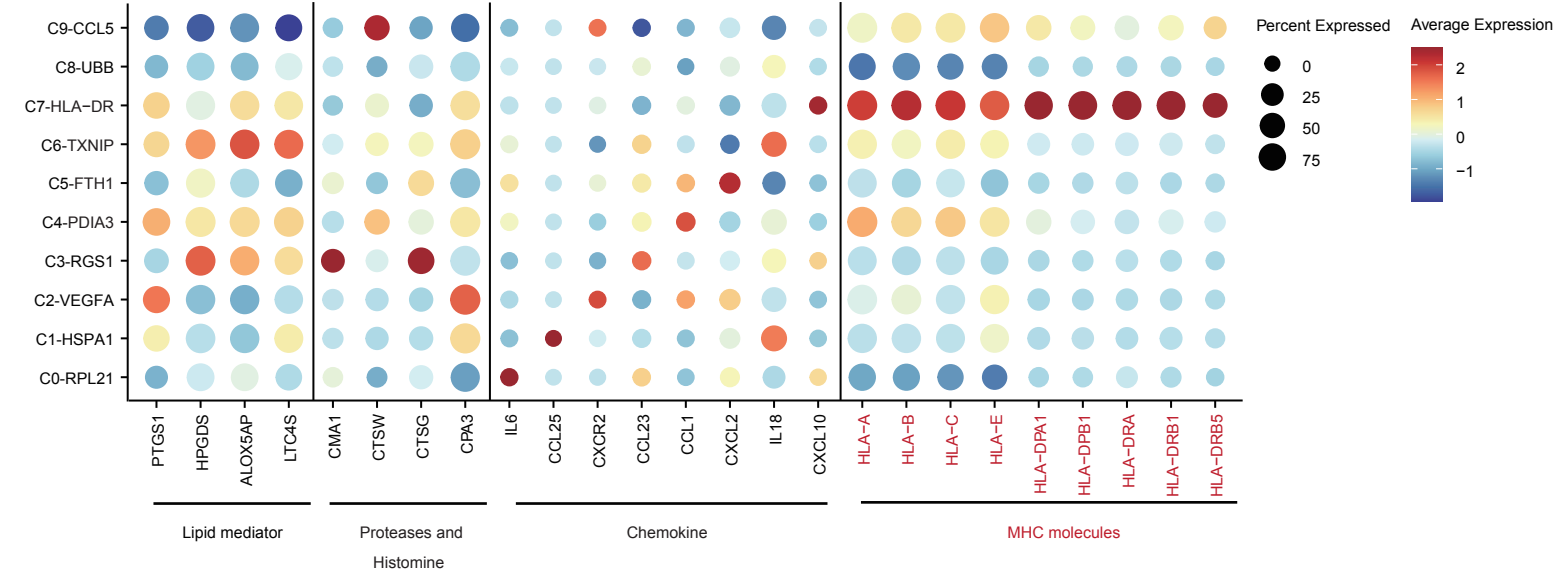
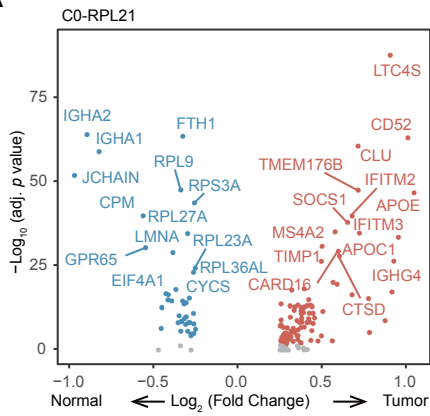


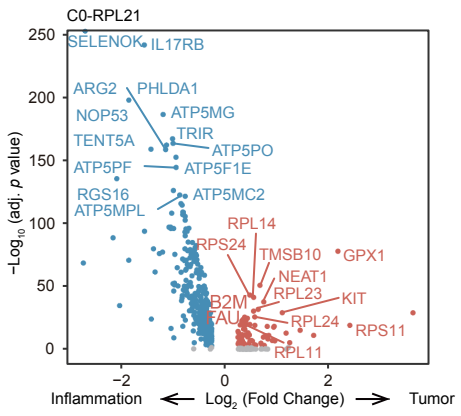
Figure S2. Characteristics of mast cell major lineages, related to Figure 2. A.

Expression of 12 curated gene signatures across mast cell clusters. Significance was determined using the Wilcoxon Rank Sum test. B. Dot plots of gene expression related to lipid mediators, proteases, histamines, chemokines, and MHC molecules in mast cell clusters. C. Violin plots showing the percentage of counts in mitochondrial genes across different mast cell clusters, Kruskal-wallis test.

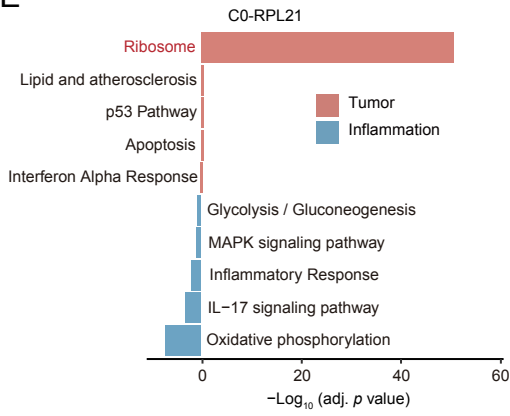
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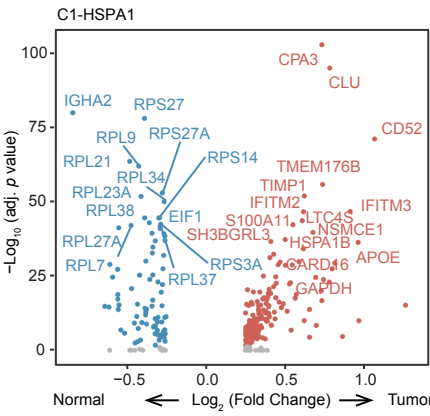
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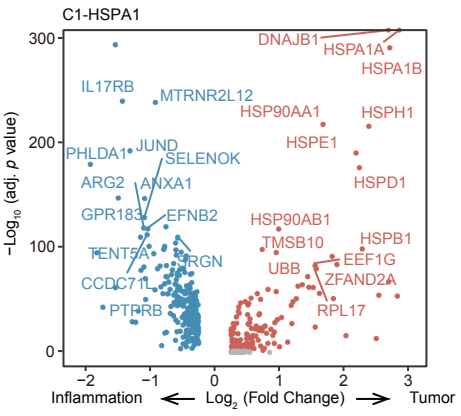
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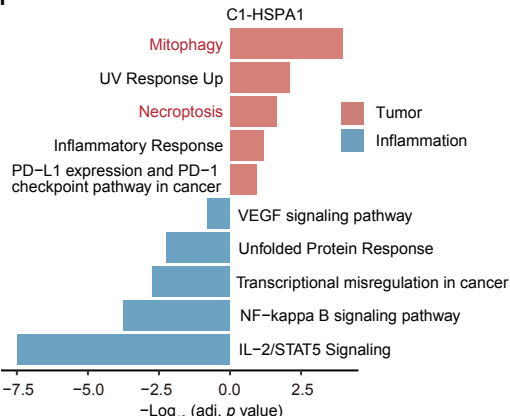
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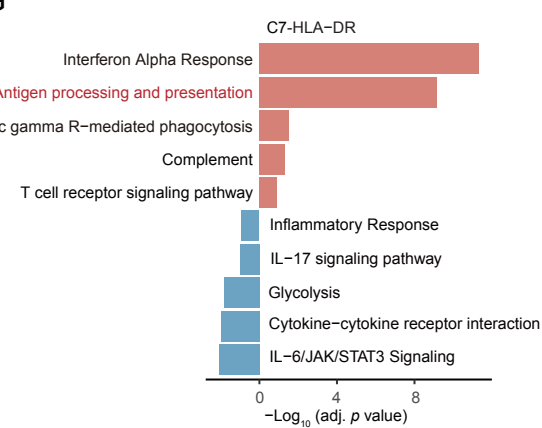
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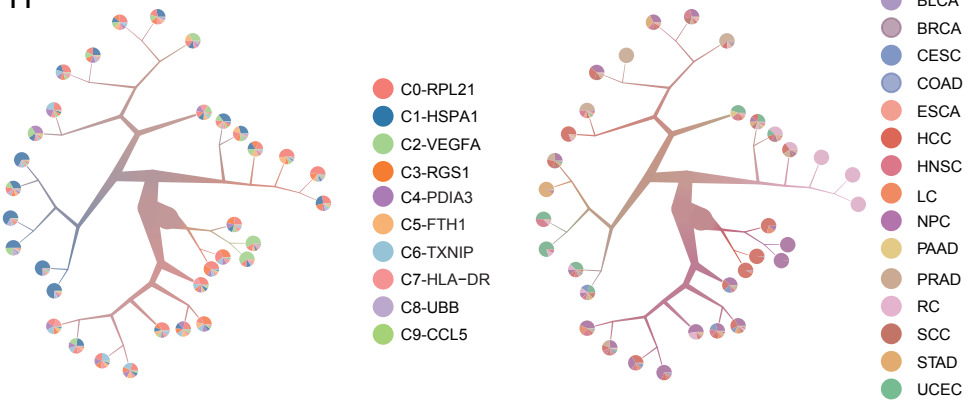
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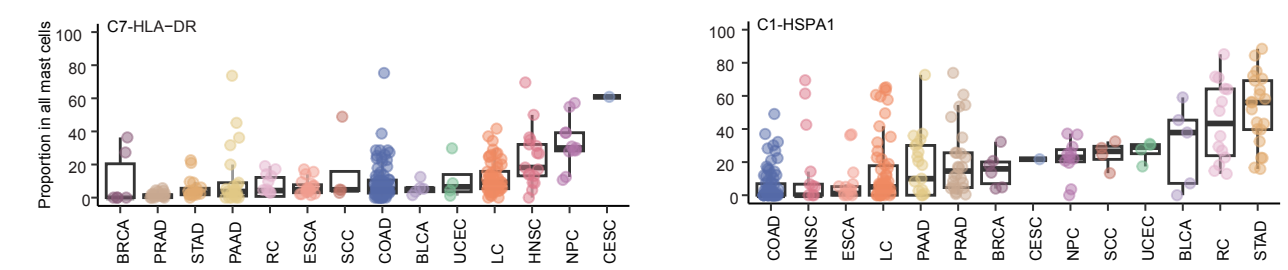


Figure S3. Features of mast cell major lineages, related to Figure 3. (A and B).

Volcano plot showing differentially expressed genes for C0-RPL21(A) and C1-HSPA1 (B) clusters between tumor and normal tissues. Two-sided unpaired Wilcoxon test. (C and D). Volcano plot showing differentially expressed genes between tumor and inflammation derived C0-RPL21(C) and C1-HSPA1 (D) clusters. Two-sided unpaired Wilcoxon test. (E, F and G). Differential pathways enriched between tumor and inflammation derived C0-RPL21 (E), C1-HSPA1 (F) and C7-HLA-DR (G) clusters. H. Mast cell tree structure according to cell clusters (left) and cancer types (right) using TooManyCells. I. Proportion of C7-HLA-DR (left) and C1-HSPA1 (right) clusters for each sample across cancer types.

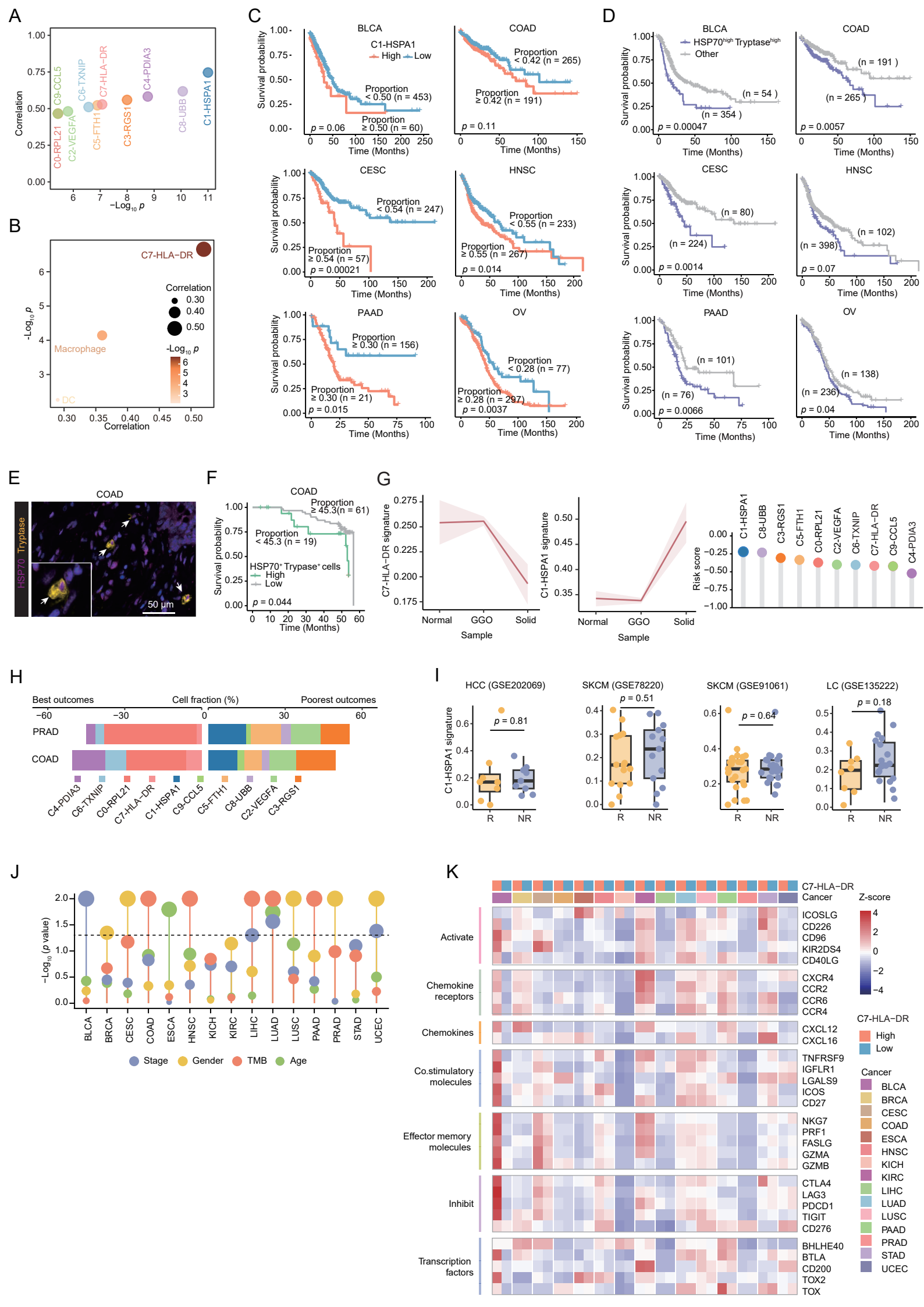
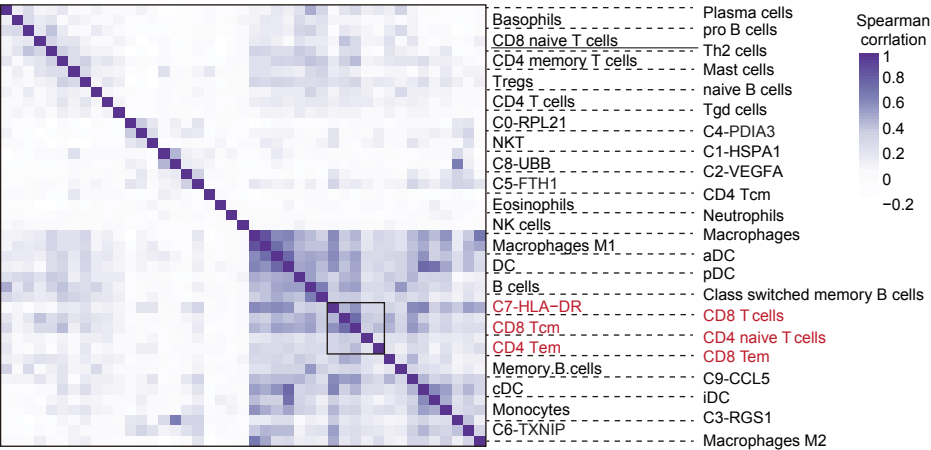


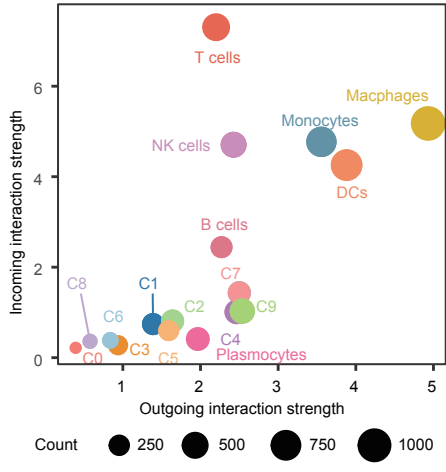
Figure S4. C1-HSPA1 cluster was linked to patient prognosis, related to Figure 4.

A. Correlation between mast cell subset infiltration levels estimated from bulk RNA-seq and their proportions in scRNA-seq data. B. Correlation between the C7-HLA-DR signature score from simulated bulk RNA-seq data and the proportions of macrophages, dendritic cells, and C7-HLA-DR⁺ mast cells in scRNA-seq data. C. Kaplan-Meier plots illustrate the prognostic significance of C1-HSPA1 cluster score in tumors using the TCGA dataset, assessed by log-rank test. D. Kaplan-Meier plots illustrate the prognostic significance of HSP70^{high} Tryptase^{high} and other expression groups using the TCGA dataset, assessed by log-rank test. E. Representative mIHC images showing HSP70 and Tryptase expression in COAD. F. Survival analysis of HSP70⁺ Tryptase⁺ mast cells in the COAD TMA cohort by mIHC. Proportion of HSP70⁺ Tryptase⁺ to all cells was analyzed. G. C7-HLA-DR and C1-HSPA1 signature scores across different mast cell subgroups, with shaded areas representing the upper and lower quartiles (left). Distribution of risk scores among mast cell subgroups is shown on the right. H. Histogram showing mast cell subgroup proportions in PRAD and COAD. Left: associated with better prognosis; right: associated with poorer prognosis. I. Boxplots showing that C1-HSPA1 cluster score of R and NR class in immunotherapy bulk RNA-seq datasets, Student's t test. J. Lollipop plot demonstrates the distribution of clinicopathologic features in patients from the TCGA dataset stratified by high and low C7-HLA-DR cluster score, analyzed using Chi-square test. K. Heatmap showing immune modulators in pan-cancer patients (TCGA dataset) with high and low C7-HLA-DR cluster score.

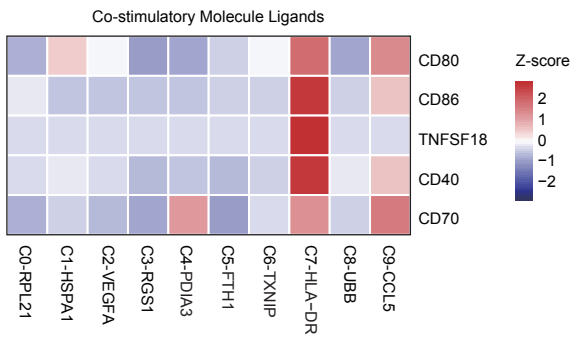
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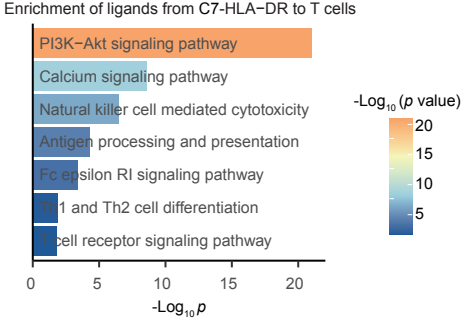
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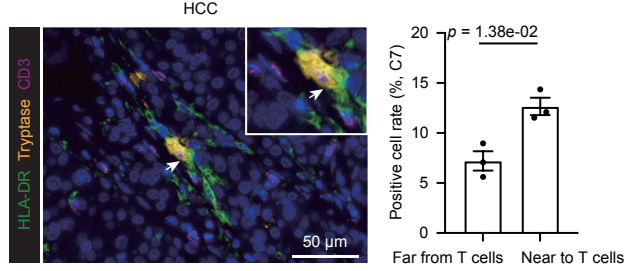


Figure S5. C7-HLA-DR cluster link with T cell activation, related to Figure 5. A.

Heatmap showing the correlation between immune cell types and mast cell clusters (TCGA dataset). Spearman correlation test. B. Scatter plots illustrating the incoming and outgoing interaction strength of the 27 annotated cell types. C. Heatmap showing the gene expression levels of co-stimulatory molecule ligands in mast cell clusters. D. Enriched pathways of ligands from C7-HLA-DR cluster to T cells, based on signatures from KEGG and Hallmark databases. E. Representative mIHC images (left) and quantification of fluorescence intensity (right; Student t test) of HLA-DR⁺ mast cells (HLA-DR and Tryptase) adjacent to and distant from T cells (CD3) in HCC. White arrows represent HLA-DR⁺ mast cells adjacent to T cells.

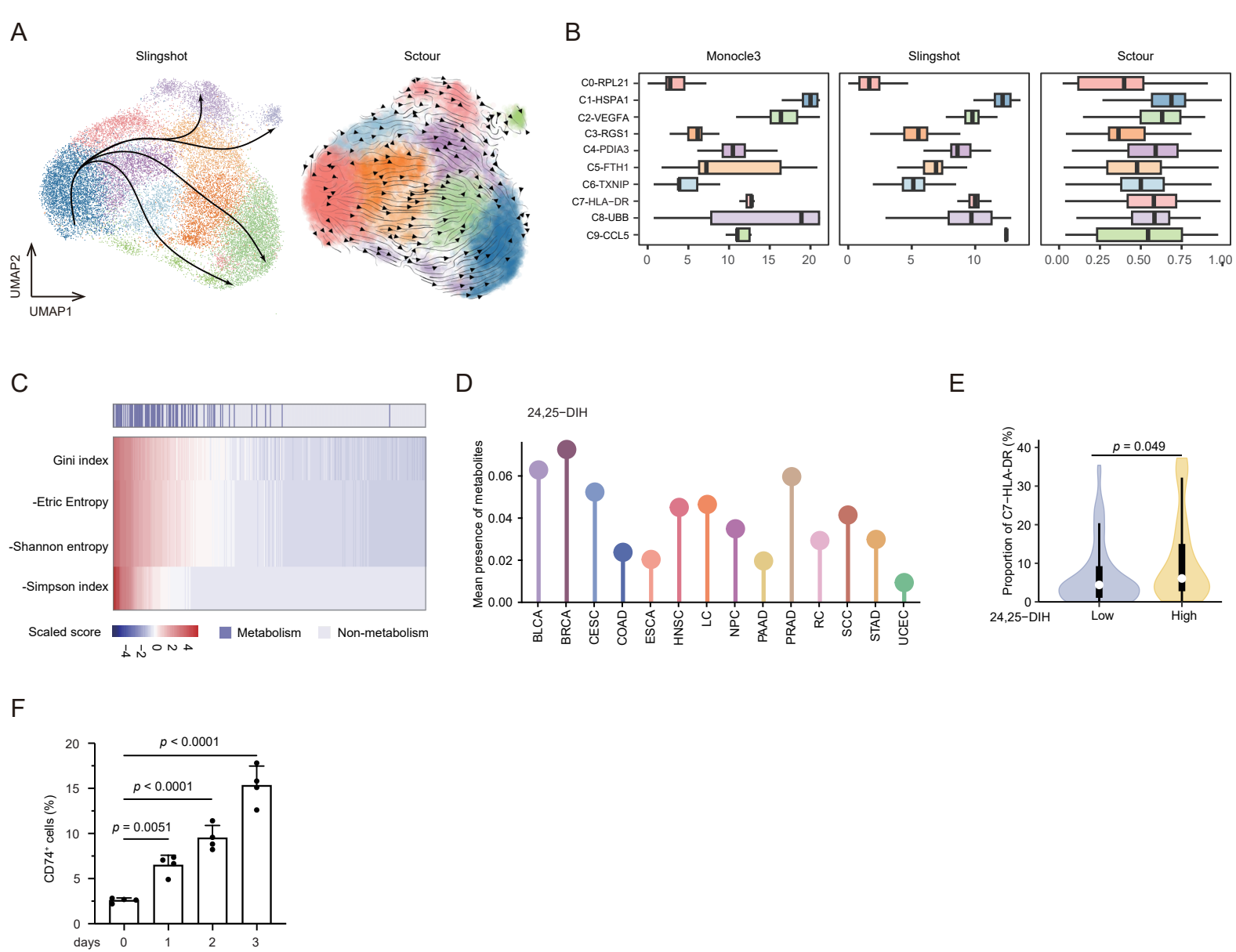


Figure S6. The developmental trajectories of mast cells, related to Figure 6. A. Estimation of differentiation state using Slingshot and sctour algorithms. B. Boxplots comparing pseudotime estimates by Monocle 3, Slingshot, and SCTour algorithms for single cells across mast cell clusters. C. Heatmap showing metabolic pathway exhibited a higher pathway activity than other pathway in mast cells. D. 24,25-Dihydrolanosterol metabolite presence levels in all mast cells across different cancer types. E. Violin plots showing the proportion of C7-HLA-DR⁺ cells between the high and low 24,25-Dihydrolanosterol groups. Student's t test. F. HMC-1 cells exhibited an increased percentage of CD74⁺ cells following incubation with 24,25-Dihydrolanosterol (100 μ M) in a time-dependent manner. one-way ANOVA with multiple comparisons.