**Supplementary Figure S1: Characterization of M1/M2 and MDSC nature of macrophage profile.**

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**Figure S1: Characterization of M1/M2 and MDSC nature of macrophage profile. a** Pearson correlations between gene expression profiles from the four representative ImmGen immune cell subsets and 29 different macrophage conditions from a previous study. Orange text refers to M1-like macrophages while green text refers to M2-like macrophages. **b** Boxplots comparing the Pearson correlation coefficients measuring the gene expression profile similarity between the ImmGen macrophage cell used to calculate macrophage infiltration scores (MF.LU) and the M1 and M2-like macrophages depicted in **a**. Each box spans quartiles with the lines representing the median correlation coefficient for each group. Whiskers represent absolute range excluding outliers. All outliers were included in the plot. P-value was calculated using a Wilcoxon-sum-rank test. **c** Heatmap depicting Spearman correlation coefficients quantifying the relationship between macrophage infiltration scores and myeloid derived suppressor cell-specific gene expression for 23 different cancer types and pan-cancer.

**Supplementary Figure S2: Mutation burden and infiltration from B cells, NK cells, and macrophages.**

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**Figure S2. Mutation burden and infiltration from B cells, NK cells, and macrophages.** Scatterplot of median somatic mutation number per tumor sample across 23 cancer types (log10 scale) compared to each tumor’s corresponding median B cell (B.FRE.BM), NK cell (NK.DAP12neg.SP), and macrophage (MF.LU) infiltration scores. Pearson correlation coefficient and least-squares regression line presented include the five outlier tumor types identified in the CD8+ T cell analysis (Fig. 3A).

**Supplementary Figure S3: Conservation of correlation structure between TCGA and PRECOG datasets.**

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**Figure S3. Conservation of correlation structure between TCGA and PRECOG datasets.** Scatterplot of the median pairwise CD8+ T cell co-infiltration scores from both TCGA and solid tumor PRECOG datasets. Each point represents a median CD8+ T cell co-infiltration score for each of the ImmGen cell types that were negatively correlated with tumor purity (R < -0.1). Pearson correlation is presented. Co-infiltration scores for this analysis were not adjusted for tumor purity due to the lack of purity data available for the PRECOG datasets.

**Supplementary Figure S4: Stratification thresholds for CD8+ T cell Kaplan-Meier analysis.**

**../../../../Documents/PanCancer/Figures/SuppFig3-CD8_densitiesF5.pdf**

**Figure S4. Stratification thresholds for CD8+ T cell Kaplan-Meier analysis.** Density plots of the CD8+ T cell (T.8MEM.SP.OT1.D45.LISOVA) infiltration scores across each dataset. The four datasets presented are GSE16011 (glioma), GSE8401 (melanoma), GSE13213 (lung adenocarcinoma), and GSE5479 (bladder). Red lines indicate the threshold at which patients were stratified into CD8+ T cell high and CD8+ T cell low groups. These thresholds were designed based on the infiltration score distribution, with cutoffs at local minima for bimodal distributions and global maxima for unimodal and trimodal distributions. Kaplan-Meier analyses of these two groups are shown Figure 4B.

**Supplementary Figure S5: Survival meta-analysis for infiltration from B cells, NK cells, and macrophages.**

**../../../../Documents/PanCancer/Figures/SuppFig4-other_cell_surv_waterfall.pdf**

**Figure S5. Survival meta-analysis for infiltration from B cells, NK cells, and macrophages.** Meta-z-score absolute values indicating prognostic associations of infiltration from B cells (B.FRE.BM; left), NK cells (NK.DAP12neg.SP; middle), and macrophages (MF.LU; right) in 23 different tumor types comprising 18,190 samples from the PRECOG dataset. Cancers were ranked by weighted meta-z-score. Green bars indicate a weighted absolute meta-z-score >1.96 while grey bars indicate a weighted meta-z-score whose absolute value is < 1.96.

**Supplementary Figure S6: Stratification thresholds for CD8+ T cells in CD8+ T cell/macrophage multiclass Kaplan-Meier analysis.**

**../../../../Documents/PanCancer/Figures/SuppFig5-CD8_densitiesF6.pdfFigure S6. Stratification thresholds for CD8+ T cells in CD8+ T cell/macrophage multiclass Kaplan-Meier analysis.** Density plots of the CD8+ T cell (T.8MEM.SP.OT1.D45.LISOVA) infiltration scores across each dataset. The four datasets presented are GSE5479 (bladder), GSE16011 (glioma), van de Vijver et al (breast), and GSE13213 (lung adenocarcinoma). Red lines indicate the threshold at which patients were stratified into CD8+ T cell high and CD8+ T cell low groups. These thresholds were designed based on the infiltration score distribution, with cutoffs at local minima for bimodal distributions and global maxima for unimodal and trimodal distributions. Multiclass Kaplan-Meier analyses using these cutoffs are shown Figure 5C.

**Supplementary Figure S7: Stratification thresholds for macrophages in CD8+ T cell/macrophage multiclass Kaplan-Meier analysis.**

**../../../../Documents/PanCancer/Figures/SuppFig6-Mac_densitiesF6.pdf**

**Figure S7. Stratification thresholds for macrophages in CD8+ T cell/macrophage multiclass Kaplan-Meier analysis.** Density plots of the macrophage (MF.LU) infiltration scores across each dataset. The four datasets presented are GSE5479 (bladder), GSE16011 (glioma), van de Vijver et al (breast), and GSE13213 (lung adenocarcinoma). Red lines indicate the threshold at which patients were stratified into macrophage high and macrophage low groups. These thresholds were designed based on the infiltration score distribution, with cutoffs at local minima for bimodal distributions and global maxima for unimodal and trimodal distributions. Multiclass Kaplan-Meier analyses using these cutoffs are shown Figure 5C.

**Supplemental Figure S8: Effect of CD8+ T cell infiltration and macrophage infiltration on patient survival in three additional datasets.**

**../../../../Documents/PanCancer/Figures/SuppFig7-RepF6.pdf**

**Figure S8. Effect of CD8+ T cell infiltration and macrophage infiltration on patient survival in three additional datasets.** Kaplan-Meier plots depicting the survival distributions of all four classes: CD8+ T low/macrophage low (orange), CD8+ T high/macrophage low (blue), CD8+ T low/macrophage high (green), and CD8+ T high/macrophage high (red). Datasets tested include Nutt et al (glioma), GSE11121 (breast), and GSE31210 (lung adenocarcinoma). For all Kaplan-Meier plots, samples were stratified into high and low groups based on their infiltration score distributions (thresholds available in Figure S8). P-values were calculated using the log-rank test and indicate that at least one curve is significantly different from the rest. Vertical hash marks indicate censored data.

**Supplemental Figure S9: Stratification thresholds for CD8+ T cell/macrophage Kaplan-Meier analysis in three additional datasets.**

**../../../../Documents/PanCancer/Figures/SuppFig8-Imm_densities_thr_F6supp.pdf**

**Figure S9. Stratification thresholds for CD8+ T cell/macrophage Kaplan-Meier analysis in three additional datasets.** Density plots of CD8+ T cell (T.8MEM.SP.OT1.D45.LISOVA; top) and macrophage (MF.LU; bottom) infiltration scores across each dataset. The three datasets presented are Nutt et al (glioma), GSE11121 (breast), and GSE31210 (lung adenocarcinoma). Red lines indicate the threshold at which patients were stratified into high and low groups for the respective cell type. These thresholds were designed based on the infiltration score distribution, with cutoffs at local minima for bimodal distributions and global maxima for unimodal and trimodal distributions. Multiclass Kaplan-Meier analyses using these cutoffs are shown Figure S7.