Supplementary Material
**Fig. S1. Major PBMC subsets fail to identify Long-Stay/Died patients (Initial Cohort).**

UMAP projection of ungated CyTOF-derived data from the Initial cohort (n=14) (A). Proportion of immune cell subsets in Healthy Controls (HC), Short-Stay (SS) and Long-Stay/Died (LS/D) patient outcome groups (B). Mean marker expression heatmap of clusters shown in a (C). Absolute counts of adaptive PBMC subsets (CD4 T, CD8 T, B) (D). Innate and unconventional subsets (NK, MAIT, γδ T, pDC, DC2/3) (E). Monocytes and stem cells (F). *, p < 0.05; **, p < 0.01; ***, p < 0.001; ns, p ≥ 0.05 by two-tailed, two-sample unequal variance Student’s t-test.
Fig. S2. T cell subsets fail to identify Long-Stay/Died patients. Representative gating of CD3⁺ cells (A). Initial Cohort UMAP projections of CD3⁺ gated cells (all samples combined; limited clustering channels) and mean marker expression heatmap (B). Same as in B but for the Replication Cohort (C). Initial Cohort absolute counts of T cell subsets identified based on gated clustering (D). Same as in D but for the Replication Cohort (E).

*, p < 0.05; **, p < 0.01; ***, p < 0.001; ns, p ≥ 0.05 by two-tailed, two-sample unequal variance Student’s t-test.
A) IL-10 (pg/ml) vs. Length of ICU stay (days)
B) Max IL-10 (pg/ml) vs. Length of ICU stay (days)
C) TNF-α (pg/ml) vs. Length of ICU stay (days)
D) CD11c<sup>low</sup> Classical Mono (x10<sup>7</sup>/L) vs. Length of ICU stay (days)

Legend:
- SS
- LS/D
**Fig. S3. Cytokine and length of ICU stay correlations.** Correlations of length of ICU stay with ICU admission serum IL-10 levels (A), maximum serum IL-10 during ICU stay (B) serum TNFα ICU admission levels (C) and CD11c<sub>low</sub> Classical Monocytes (D). *, p < 0.05; **, p < 0.01; ***, p < 0.001; ns, p ≥ 0.05 by two-tailed, two-sample unequal variance Student’s t-test and R² by two-tailed Pearson correlation with 95% confidence interval.
| Antibody/Tetramer | Metal/Fluorophore* | Clone | Company | Used in Cohort |
|-------------------|-------------------|-------|---------|---------------|
| **CD1c**          | 151Eu             | L161  | Biolegend | Replication   |
| **CD3ε**          | 143Nd             | OKT3  | Biolegend | both          |
| **CD4**           | 174Yb             | SK3   | Biolegend | both          |
| **CD8α**          | 168Er             | SK1   | Biolegend | both          |
| **CD8β**          | 141Pr             | SIDI8BEE | eBioscience | both          |
| **CD11c**         | 147Sm             | Bu15  | Biolegend | both          |
| **CD14**          | 153Eu             | M5E2  | Biolegend | both          |
| **CD16**          | 158Gd             | 3G8   | Biolegend | both          |
| **CD19**          | 142Nd             | HIB19 | Biolegend | both          |
| **CD25**          | 169Tm             | BC96  | Biolegend | both          |
| **CD27**          | 175Lu             | O323  | Biolegend | Replication   |
| **CD31**          | 145Nd             | WM59  | Biolegend | both          |
| **CD32**          | 160Gd             | IV.3  | Stemcell Technologies | both |
| **CD34**          | 156Gd             | 581   | Biolegend | both          |
| **CD38**          | 106Cd             | HIT2  | Biolegend | both          |
| **CD45**          | 89Y               | HI30  | Biolegend | both          |
| **CD45RA**        | 110Cd             | HI100 | Biolegend | both          |
| **CD45RO**        | 112Cd             | UCHL1 | Biolegend | both          |
| **CD56**          | 148Nd             | NCAM16.2 | BD Bioscience | both |
| **CD94 (NKG2C)**  | 161Dy             | DX22  | Biolegend | both          |
| **CD116**         | 150Nd             | 4H1   | Biolegend | both          |
| **CD117**         | 171Yb             | 104D2 | Biolegend | Initial       |
| **CD123**         | 164Dy             | 6H6   | Biolegend | both          |
| **CD127**         | 165Ho             | A019D5 | Biolegend | both          |
| **CD161**         | 159Tb             | HP-3G10 | Biolegend | both          |
| **CD197/CCR7**    | 171Dy             | G043H7| Biolegend | Replication   |
| **CD200R**        | 173Yb             | 0X-108| BD Bioscience | both |
| **CD294 (CRTH2)** | 163Dy             | BM16  | Biolegend | both          |
| **CD301 (CLEC10A)** | 154Sm         | H037G3 | Biolegend | Replication   |
| **CD304 (NRP1)**  | 172Yb             | 12C2  | Biolegend | Replication   |
| **FceRIα**        | 176Yb             | AER-37| Biolegend | both          |
| **HLA-DR**        | 170Er             | L243  | Biolegend | both          |
| **IgD**           | 116Cd             | IA6-2 | Biolegend | both          |
| **IL-18Rα**       | 162Dy             | H44   | Biolegend | both          |
| **KLRG1**         | 144Nd             | SA231A2 | Biolegend | both          |
| **LAG3**          | 175Lu             | 11C3C65 | Biolegend | Initial       |
| **TCRαβ**         | 155Gd             | T10B9.1A-31 | BD Bioscience | both |
| **TCRγδ**         | 152Sm             | B1    | Biolegend | both          |
| **TRAV1-2**       | 115Ln             | 3C10  | Biolegend | both          |
| Anti-APC (Secondary) | 149Sm | APC003 | Biolegend | both |
| **MR1-5-OP-RU (Primary)** | APC  | NA   | NIH Tetramer Facility | both |
Table S2. Mean absolute counts and p-values (ungated cluster analyses)

| Cohort     | Total cell subset | H    | SS   | LS/D | p-values |
|------------|-------------------|------|------|------|----------|
|            |                   | Mean absolute counts (x10^6/L) | H vs SS | H vs LS/D | SS vs LS/D |
| Initial    |                   |                  |        |        |          |
| CD4 T cells|                   | 0.936            | 0.330  | 0.244 | 0.067    |
| CD8 T cells|                   | 0.428            | 0.304  | 0.198 | 0.383    |
| B cells    |                   | 0.267            | 0.143  | 0.184 | 0.176    |
| Monocytes  |                   | 0.392            | 0.392  | 0.589 | 0.997    |
| Stem cells |                   | 0.002            | 0.001  | 0.003 | 0.247    |
| Initial    | NK cells          | 0.230            | 0.234  | 0.109 | 0.961    |
| Initial    | MAIT cells        | 0.057            | 0.008  | 0.012 | 0.122    |
| Initial    | γδ T cells        | 0.058            | 0.018  | 0.014 | 0.077    |
| Initial    | pDC               | 0.012            | 0.000  | 0.001 | 0.029    |
| Initial    | DC2/3             | 0.028            | 0.002  | 0.006 | 0.026    |
| Replication| CD4 T cells       | 0.911            | 0.511  | 0.309 | 0.008    |
| Replication| CD8 T cells       | 0.386            | 0.374  | 0.184 | 0.914    |
| Replication| B cells           | 0.247            | 0.285  | 0.237 | 0.584    |
| Replication| Monocytes         | 0.403            | 0.657  | 0.740 | 0.041    |
| Replication| Stem cells        | 0.002            | 0.004  | 0.003 | 0.223    |
| Replication| NK cells          | 0.259            | 0.179  | 0.199 | 0.108    |
| Replication| MAIT cells        | 0.047            | 0.007  | 0.003 | 0.001    |
| Replication| γδ T cells        | 0.058            | 0.022  | 0.028 | 0.003    |
| Replication| pDC               | 0.009            | 0.001  | 0.001 | <0.001   |
| Replication| DC2/3             | 0.037            | 0.014  | 0.012 | 0.003    |

p-values calculated using a two-tailed, two-sample unequal variance Student’s t-test. 
H = Healthy; SS = Short-Stay; LS/D = Long-Stay/Died
Table S3. Mean absolute counts and p-values (gated monocyte and T cell cluster analyses)

| Cohort | Monocyte subset | H     | SS    | LS/D  | H vs SS | H vs LS/D | SS vs LS/D |
|--------|-----------------|-------|-------|-------|---------|-----------|------------|
|        |                 | Mean absolute counts (x10⁹/L) | p-values |       |         |           |            |
| Initial CD11c<sup>low</sup> Classical | 0.004 | 0.019 | 0.082 | 0.536* | 0.133* | 0.388*     |
|        | Total Classical | 0.108 | 0.110 | 0.181 | 0.620   | 0.136    | 0.212      |
|        | Total Intermediate | 0.218 | 0.247 | 0.377 | 0.939   | 0.234    | 0.338      |
|        | Total Non-Classical | 0.019 | 0.020 | 0.011 | 0.844   | 0.080    | 0.462      |
| CD4 T cells | 0.888 | 0.312 | 0.219 | 0.010  | 0.004   | 0.506     |
| CD8 T cells | 0.403 | 0.277 | 0.182 | 0.309  | 0.005   | 0.415     |
| MAIT cells | 0.052 | 0.008 | 0.011 | 0.014  | 0.018   | 0.724     |
| γδ T cells | 0.057 | 0.016 | 0.015 | 0.009  | 0.006   | 0.868     |
| Replication CD11c<sup>low</sup> classical | 0.001 | 0.015 | 0.058 | <0.001* | 0.010* | 0.076*     |
|        | Total Classical | 0.117 | 0.193 | 0.271 | 0.035   | 0.010    | 0.167      |
|        | Total Intermediate | 0.196 | 0.412 | 0.422 | 0.025   | 0.021    | 0.925      |
|        | Total Non-Classical | 0.022 | 0.026 | 0.015 | 0.890   | 0.061    | 0.404      |
| CD4 T cells | 0.899 | 0.477 | 0.292 | 0.004  | 0.061   | 0.098     |
| CD8 T cells | 0.412 | 0.341 | 0.171 | 0.489  | <0.001  | 0.083     |
| MAIT cells | 0.035 | 0.005 | 0.002 | 0.001  | <0.001  | 0.093     |
| γδ T cells | 0.055 | 0.022 | 0.028 | 0.003  | 0.140   | 0.769     |

p-values calculated using a two-tailed, two-sample unequal variance Student’s t-test. H = Healthy; SS = Short-Stay; LS/D = Long-Stay/Died

*p-values that have been Bonferroni-adjusted for multiple comparisons
| Analyses | Cell type          | Cell surface protein signatures for cluster assignment |
|----------|--------------------|--------------------------------------------------------|
| CD4 T cells | CD3+ TCRαβ+ CD4+ CD8- |
| CD8 T cells | CD3+ TCRαβ+ CD4− CD8+ |
| B cells    | HLA-DR+ IgD+ CD19+  |
| Monocytes  | CD116+ CD3- CD19- CD11c+ HLA-DR+ CD32+ |
| Ungated Stem cells | CD34+ |
| NK cells   | CD94+ CD3- CD116-  |
| MAIT cells | CD3+ TCRαβ+ IL-18Rα+ MR1-5-OP-RU+ |
| γδ T cells | CD3+ TCRαβ- TCRγδ+  |
| pDC        | CD11c- NRP1+ CD123+ FceRα1+ CD116+ HLA-DR+ |
| DC2/3      | CD11c+ CD1c+ NRP1- CD123+ FceRα1+ HLA-DR+ |
| CD11c<sup>low</sup> classical | CD116+ CD14<sup>high</sup> CD16- CD11c<sup>low</sup> |
| Gated on CD3-CD19- CD116+ (Monocytes) | | |
| Total Classical | CD116+ HLA-DR+ CD14<sup>high</sup> CD16- CD123- |
| Total Intermediate | CD116+ HLA-DR+ CD14<sup>high</sup> int CD16<sup>low</sup> CD123<sup>low</sup> |
| Total Non-Classical | CD116+ HLA-DR+ CD14<sup>low</sup> CD16<sup>high</sup> |
Table S5. Sensitivity and specificity calculations for serum IL-6.

|                       | Sensitivity | Specificity | False Positives | False Negatives | LR+  |
|-----------------------|-------------|-------------|-----------------|-----------------|------|
| IL-6 screen (Cytokine Cohort; n = 90) | 39%         | 76%         | 24%             | 42%             | 1.6  |
|                       | (22/56)     | (22/29)     | (7/29)          | (24/56)         |      |