

Expanded View Figures

Figure EV1. Smart-seq2 single-cell sequencing data from muscle T cells in patients with idiopathic inflammatory myopathies.

- A Left panel: Violin plots showing the total number of genes captured, the number of transcripts and percentage of mitochondrial genes per patient. Right panel: UMAPs displaying before data integration and after data integration with Harmony package per sequencing batch ($n = 6$ IIM, $n = 1$ undefined myopathy).
- B Violin plots showing the expression levels of selected differentially expressed genes per cluster in muscle T cells. Each color represents one T-cell cluster in the muscle tissue as indicated ($n = 6$ IIM, $n = 1$ undefined myopathy).
- C Violin plot showing the expression level of *ITGA1* per patient in the four T_{RM} clusters. Each color represents one T_{RM} cluster as indicated ($n = 6$ IIM, $n = 1$ undefined myopathy).
- D Violin plot showing the expression level of *KLRG1* in muscle T cells per patient.

Data information: CM: central memory; EM: effector memory, T_{RM} : tissue resident memory. IMNM: Immune-Mediated Necrotizing Myopathy; DM: DermatoMyositis; ASyS: AntiSYnthesase Syndrome; IBM: Inclusion Body Myositis; IIM: Idiopathic Inflammatory Myopathies ($n = 6$ IIM, $n = 1$ undefined myopathy).

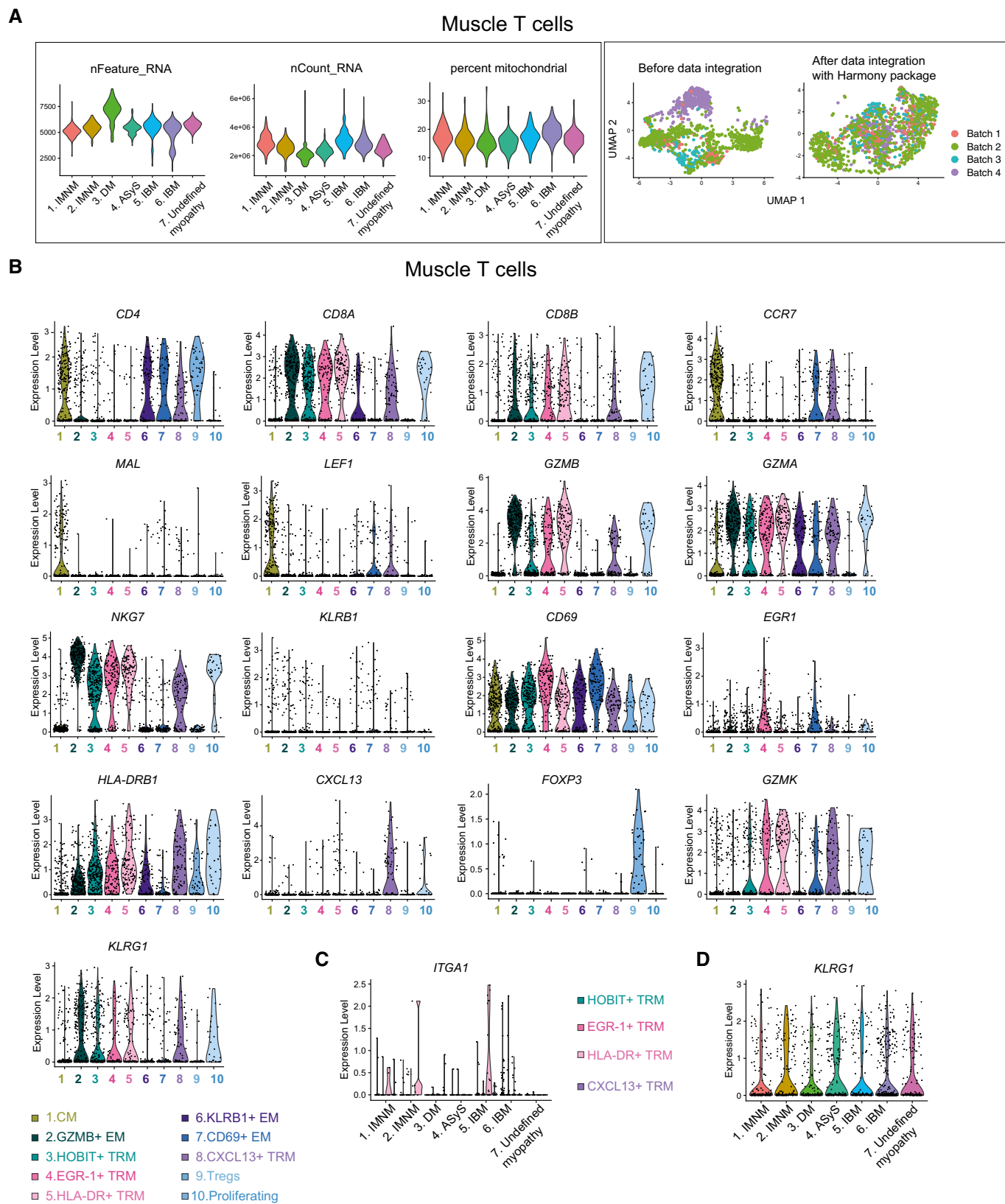


Figure EV1.

Figure EV2. Smart-seq2 single-cell sequencing data from peripheral blood memory T cells in patients with idiopathic inflammatory myopathies.

- A Left panel: Violin plots showing the total number of genes captured, the number of transcripts and percentage of mitochondrial genes per patient. Right panel: UMAPs displaying before data integration and after data integration with Harmony package per sequencing batch ($n = 6$ IIM, $n = 1$ undefined myopathy).
- B Violin plots showing the expression level of selected genes in peripheral blood memory T cells from patients with IIM ($n = 6$ IIM, $n = 1$ undefined myopathy).
- C UMAP feature plots displaying the normalized expression of *KLRC1*, *KLRC2*, *FCGR3A* and *IKZF2* genes.
- D UMAP feature plot showing cells using *TRAV1-2* and *TRAV10* genes.
- E Flow cytometry dot plots showing the frequency of CD3⁺CD8⁺ T cells in peripheral blood (PB) of patients with DM (left) and IMNM (right) patients.
- F Frequency of CD3⁺CD8⁺ T cells in PB of patients with IIM.

Data information: CM: central memory; EM: effector memory. IMNM: Immune-Mediated Necrotizing Myopathy; DM: DermatoMyositis; ASyS: AntiSYnthesase Syndrome; IBM: Inclusion Body Myositis; IIM: Idiopathic Inflammatory Myopathies.

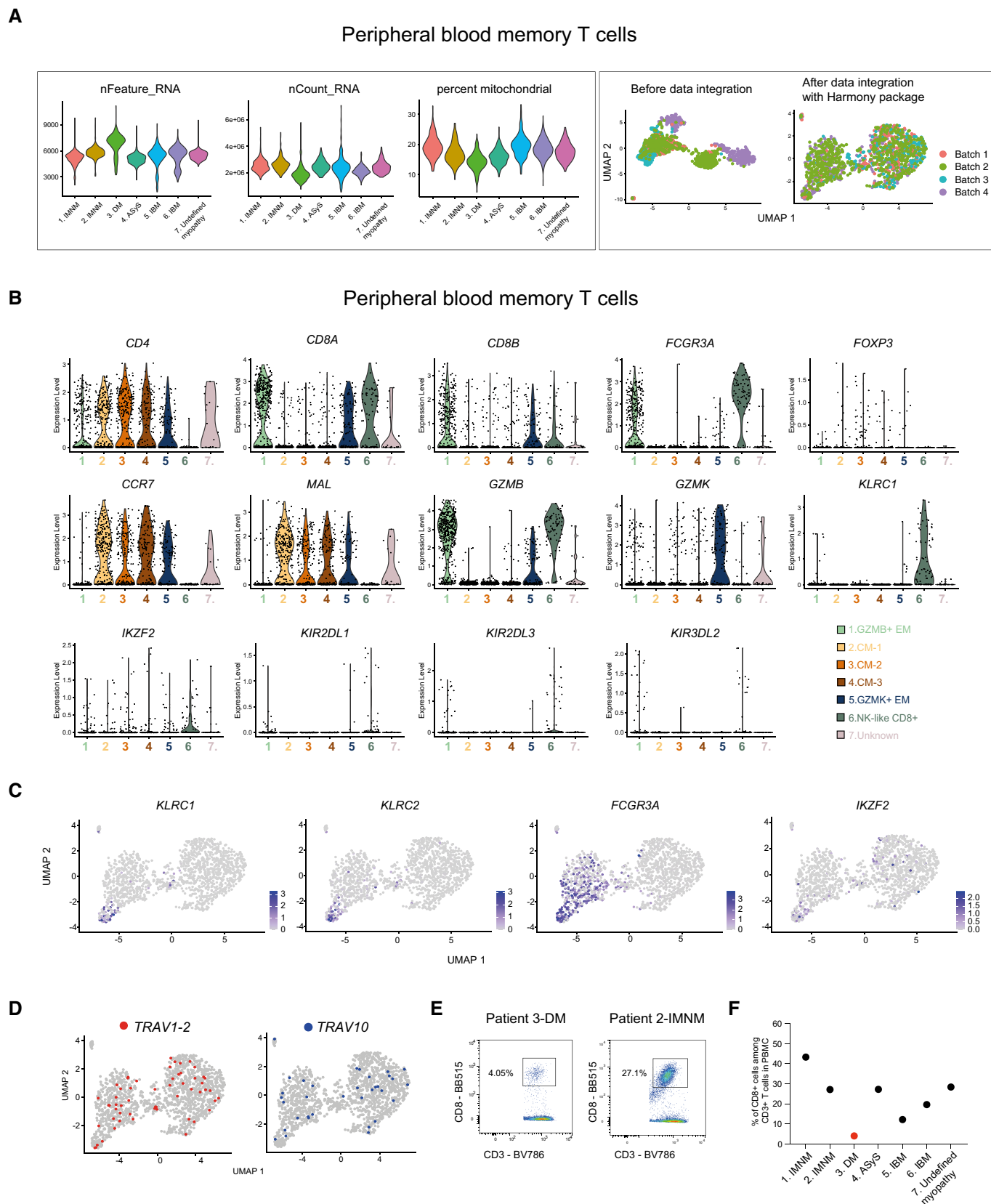


Figure EV2.

Figure EV3. Single-cell sequencing data from healthy donors and patients with idiopathic inflammatory myopathies.

- A Workflow for Smart-seq3 sequencing.
- B UMAP displaying eight memory T-cell clusters identified in peripheral blood (PB) of healthy donors ($n = 439$ cells, $n = 3$ donors).
- C UMAP feature plots displaying the normalized expression of *CD4*, *CD8A*, *CD8B*, *IKZF2*, *KLRC1* and *KLRC2*.
- D Heatmap showing the normalized and scaled expression of the top 10 differentially expressed genes per cluster (Wilcoxon Rank Sum, P value < 0.009 ; \log_2 fold change > 0.25).
- E Violin plots showing the expression level of *TRAV1-2* and *TRAV10* genes per cluster in PB memory T cells from healthy donors ($n = 3$).
- F Heatmap showing the normalized and scaled expression of the top 25 upregulated and top 25 downregulated genes sorted by average \log_2 FC values (Wilcoxon Rank Sum, P value $< 10^{-15}$, $-2.6 < \log_2$ fold change < 4.2).
- G Heatmap showing the normalized and scaled expression of the top 25 upregulated and top 25 downregulated genes in muscle T cells versus PB memory T cells from patients with IIM after filtering out genes identified in Dataset EV5 (Wilcoxon Rank Sum, P value $< 8 \times 10^{-5}$, $-0.25 < \log_2$ fold change < 2.3).
- H Dotplots showing selected genes in PB of patients with IIM ($n = 7$).
- I Dotplots showing selected genes in PB of healthy donors ($n = 3$).

Data information: CM: central memory; EM: effector memory. IMNM: Immune-Mediated Necrotizing Myopathy; DM: DermatoMyositis; ASyS: AntiSYnthesase Syndrome; IBM: Inclusion Body Myositis; IIM: Idiopathic Inflammatory Myopathies; HD: healthy donors.

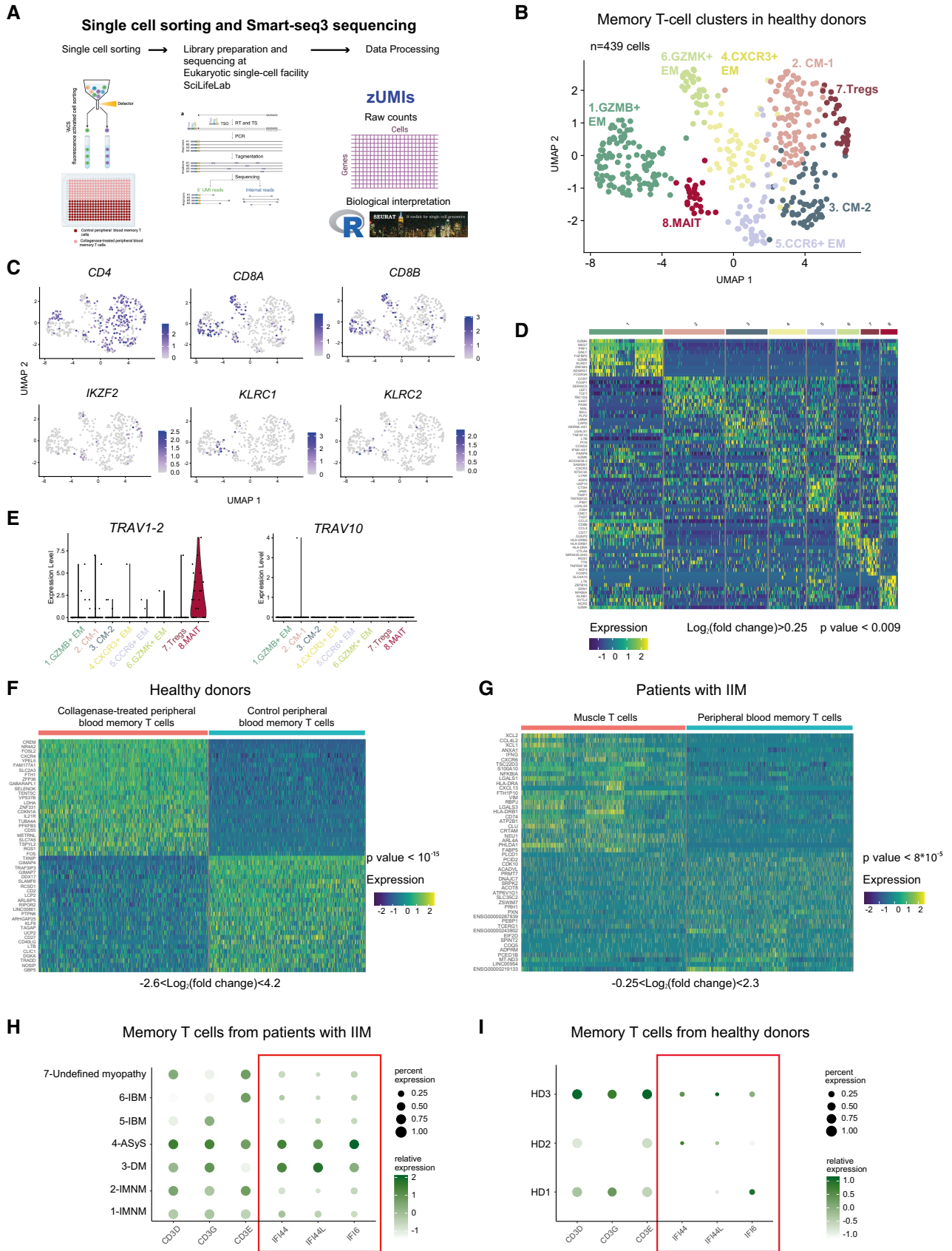


Figure EV3.

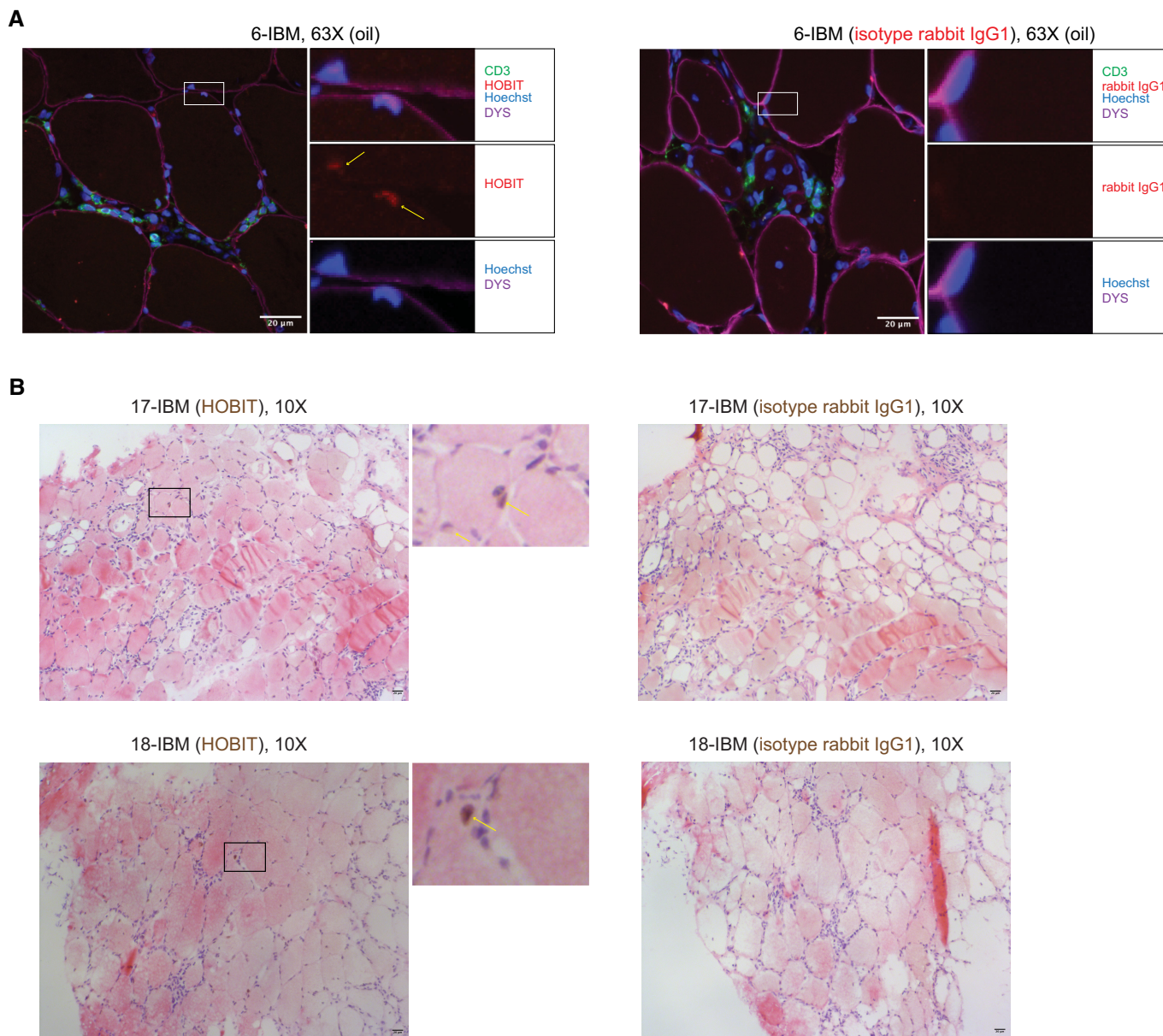


Figure EV4. Immunofluorescence and immunohistochemistry stainings showing HOBIT expression in muscle fibers of biopsies from patients with inclusion body myositis.

A Representative immunofluorescence stainings of HOBIT (red), CD3 (green), dystrophin (purple) and Hoechst 33342 (blue) performed on muscle tissue from patient 6 (IBM) (left panel) and isotype rabbit IgG1 staining (red) (right panel). Images were acquired using a LSM 880 confocal without Airyscan microscope (63× oil objective). Scale bar = 20 µm. The yellow arrows show HOBIT expression in muscle nuclei.

B Representative immunohistochemistry stainings of HOBIT (brown, left panels), and isotype rabbit IgG (right panels) with hematoxylin (purple) and eosin (red) stainings performed on muscle tissue of two patients with IBM. Images were acquired using a Leica Reichert Polyvar 2 light microscope (10× objective). Scale bar = 20 µm. The yellow arrows show HOBIT expression in muscle nuclei. IBM: Inclusion Body Myositis.

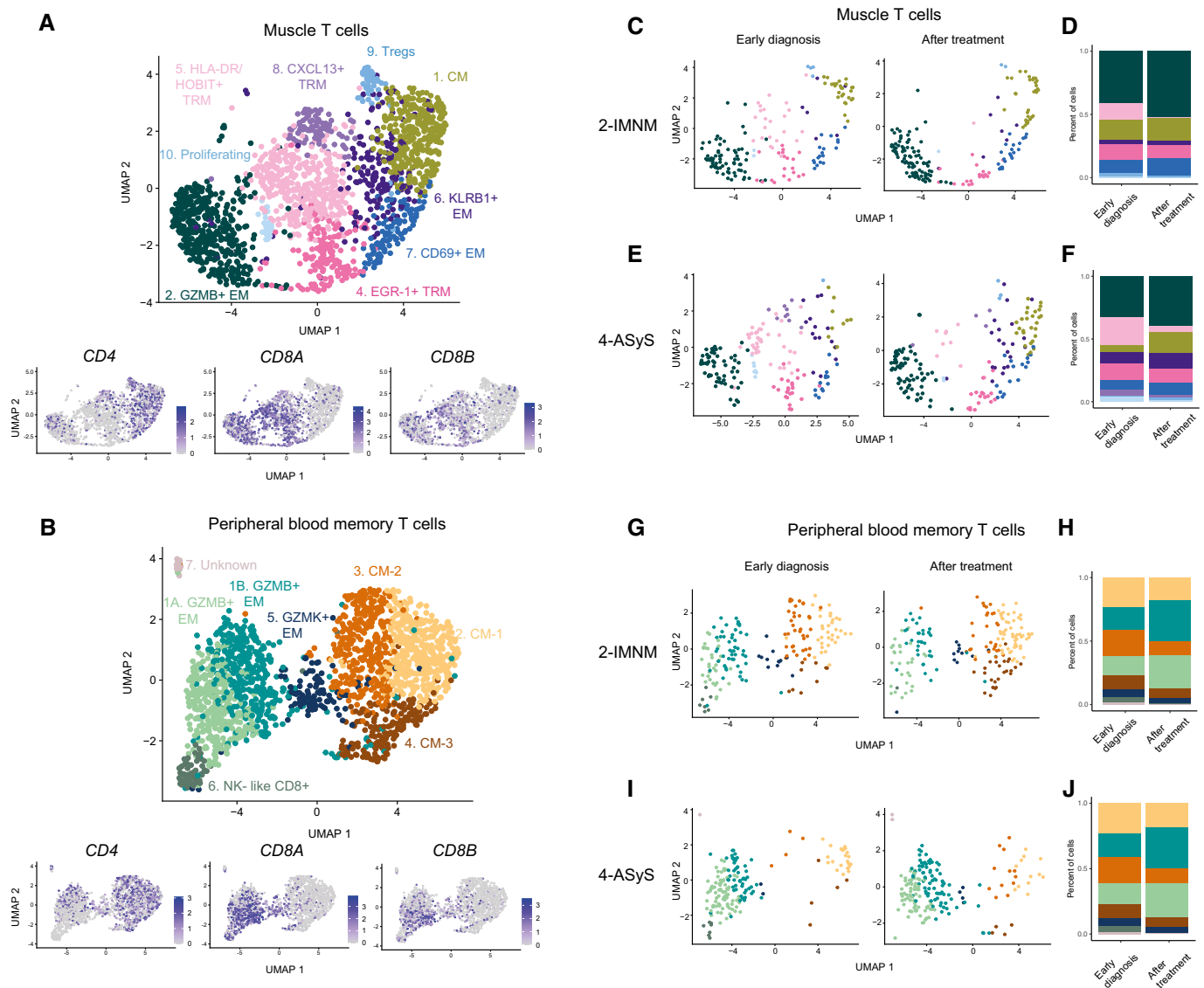


Figure EV5. Smart-seq2 single-cell data from muscle T cell and peripheral blood memory T cells from patients at early diagnosis and after treatment.

- A Upper Panel: UMAP displaying nine T-cell clusters in the muscle of patients with idiopathic inflammatory myopathies (IIM) at early diagnosis ($n = 7$) and after treatment ($n = 2$) ($n = 1747$ cells). Lower panel: UMAP feature plots displaying the normalized expression of *CD4*, *CD8A*, and *CD8B*.
- B Upper panel: UMAP displaying eight T-cell clusters in peripheral blood (PB) memory T cells of patients with IIM at early diagnosis ($n = 7$) and after treatment ($n = 2$) ($n = 1788$ cells). Lower panel: UMAP feature plots displaying the normalized expression of *CD4*, *CD8A* and *CD8B*.
- C UMAP displaying nine T-cell clusters split by treatment status in muscle of patient 2 (IMNM).
- D Stacked bar plots of T-cell cluster composition in early diagnosis and after treatment in muscle of patient 2 (IMNM).
- E UMAP displaying nine T-cell clusters split by treatment status in muscle of patient 4 (ASyS).
- F Stacked bar plots of T-cell cluster composition in early diagnosis and after treatment in muscle of patient 4 (ASyS).
- G UMAP displaying eight T-cell clusters split by treatment status in PB of patient 2 (IMNM).
- H Stacked bar plots of T-cell cluster composition in early diagnosis and after treatment in PB of patient 2 (IMNM).
- I UMAP displaying eight T-cell clusters split by treatment status in PB of patient 4 (ASyS).
- J Stacked bar plots of T-cell cluster composition in early diagnosis and after treatment in PB of patient 4 (ASyS).

Data information: IMNM: Immune-Mediated Necrotizing Myopathy; ASyS: AntiSynthetase Syndrome; IIM: Idiopathic Inflammatory Myopathies.