#### **Description of Additional Supplementary Files**

## **Supplementary Data 1**

Clinical information for all subjects in our study including 60 patients with Crohn's disease and 27 non-IBD control subjects.

## **Supplementary Data 2**

Lipidomics information.

## **Supplementary Data 3**

Table of differences in lipid metabolites between H-MAT and CF. Descriptive statistics are provided. The variable importance in projection (VIP) was calculated based on the orthogonal partial least squares discriminant analysis (OPLS-DA), and the P-value and fold change (FC) of the nonparametric test were used in combination to screen the differential lipid metabolites. Then, the cut offs of VIP  $\geq$  1, FC  $\geq$  2 or FC  $\leq$  0.5 and P <0.05 were used as standards to screen differential lipid metabolites. The p value were analysed using hypergeometric test.

## **Supplementary Data 4**

Characterization for 8 subjects used in scRNA survey.

## **Supplementary Data 5**

Table of the cluster marker genes for each cell type identified. Descriptive statistics are provided. Data were analysed using two-sided Wilcoxon rank sum test.

### **Supplementary Data 6**

Table of general characteristics of patients used to generate flow cytometry validation experiments. Descriptive statistics are provided for each population.

## **Supplementary Data 7**

Table of the markers' GO enrichment analysis results for each cell type identified. Descriptive statistics are provided. Data were analysed using two-sided Wilcoxon rank sum test.

## **Supplementary Data 8**

Table of the differentially expressed genes between CF and H-MAT. Descriptive statistics are provided. DEG analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments. Data were analysed using two-sided Wilcoxon rank sum test.

## **Supplementary Data 9**

Table of the differentially expressed genes' GO enrichment analysis results for each cell type identified. Descriptive statistics are provided. Data were analysed using two-sided Wilcoxon rank sum test.

#### **Supplementary Data 10**

Table of genes in disease and their associated pathways.

## **Supplementary Data 11**

Table of the differentially expressed genes between CD-MAT and H-MAT for each cell type identified. Descriptive statistics are provided. DEG analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

#### **Supplementary Data 12**

Table of the differentially expressed genes between CF and CD-MAT for each cell type identified. Descriptive statistics are provided. DEG analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

## **Supplementary Data 13**

Table of genome-wide association signals for candidate risk genes with CD. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test.

## **Supplementary Data 14**

Table of the cluster marker genes for each MSC subpopulation identified. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

### **Supplementary Data 15**

Table of the lineage marker genes and primers.

## **Supplementary Data 16**

Table of the differentially expressed genes for each MSC1 subset identified. Descriptive statistics are provided. DEG analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

## **Supplementary Data 17**

List of genes over transition from MSC1 to MSC2 and then MSC3 and the markers' GO enrichment analysis results for the main Module. Data were analysed using two-sided Wilcoxon rank sum test.

## **Supplementary Data 18**

Table of the cluster marker genes for each myeloid cell subpopulation identified. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

## **Supplementary Data 19**

Table of the cluster marker genes for each cMo subset identified. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

## **Supplementary Data 20**

Table of the interaction of ligand-receptor pairs between cMos and MSCs. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test.

# **Supplementary Data 21**

Table of the cluster marker genes for each EC subpopulation identified. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.

## **Supplementary Data 22**

Table of the cluster marker genes for each PC subpopulation identified. Descriptive statistics are provided. Data analysis was performed using a two-sided Wilcoxon rank sum test. The Benjamini-Hochberg Procedure was used for adjustments.