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Targeted therapy guided by single-cell transcriptomic analysis in drug-induced hypersensitivity syndrome: a case report

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Supplementary Information

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Supplementary Figure 2. Histograms and scatter plots showing criteria for filtering out peripheral mononuclear cells with low quality. a, histograms showing the distribution of the proportion of mitochondrial gene in each PBMC. Red line represents the upper limit and the percentages of cells filtered out were labeled. b. Scatter plots showing the number of unique molecular index (nUMI, x axis) and the number of genes (nGene, y axis) in each cell. Red lines represent the upper limit of each value and blue lines show lower limit of nGene. DiHS/DRESS, n=7,660 cells; HV, n=8,688 cells)

Supplementary Table 3. Summary of information on samples and utilized platforms.

Sample name	description	Source	Gender	10x Genomics kit chemistry	Sequencing platform
Skin_Dress1	skin biopsy from the DRESS patient	skin_flank	male	Single Cell 5'	Hiseq3000
PBMC_DRESS1	PBMC from the DRESS patient before treatment	fresh PBMC	male	Single Cell 5'	Hiseq3000
PBMC_HV	PBMC from a sex- and age-matched healthy volunteer (HV)	fresh PBMC	male	Single Cell 5'	Hiseq3000
PBMC_T4_CTRL	Cultured PBMC without SMX/TMP	cultured PBMC	male	Single Cell 5'	Hiseq3000
PBMC_T4_BACT	Cultured PBMC with SMX/TMP	cultured PBMC	male	Single Cell 5'	Hiseq3000
DRESS_Day4_BACT	Cultured PBMC with SMX/TMP alone	cultured PBMC	male	Single Cell 5'	Hiseq3000
DRESS_Day4_TOFA	Cultured PBMC with SMX/TMP and tofacitinib	cultured PBMC	male	Single Cell 5'	Hiseq3000
PBMC_POST2W	PBMC from the DRESS patient 2 weeks after treatment	fresh PBMC	male	Single Cell 5'	Hiseq3000
SKIN_HV1_F1	skin biopsy from HV1 (duplicate 1)	skin_flank	male	Single Cell 3' v2	Hiseq3000
SKIN_HV1_F2	skin biopsy from HV1 (duplicate 2)	skin_flank	male	Single Cell 3' v2	Hiseq3000
SKIN_HV2	skin biopsy from HV2	skin_flank	female	Single Cell 3' v2	Hiseq3000
SKIN_HV3	skin biopsy from HV3	skin_flank	female	Single Cell 3' v2	Hiseq3000
SKIN_HV4	skin biopsy from HV4	skin_flank	male	Single Cell 5'	Hiseq3000
SKIN_HV5	skin biopsy from HV5	skin_flank	male	Single Cell 5'	Hiseq3000

Supplementary Table 4. Summary of information on sequencing output and matrices processed.

Sample name	Cell Ranger version	Estimated Number of Cells	Mean Reads per Cell	Median Genes per Cell	Number of Cell Reads	Sequencing Saturation	Total Genes Detected	Median UMI Counts per Cell
Skin_Dress1	2.1.0	5,653	53,191	2,904	300,693,226	42.30%	23,527	11,660
PBMC_DRESS1	2.1.0	7,660	42,173	1,899	323,050,545	65.50%	20,391	5,917
PBMC_HV	2.1.0	8,779	40,409	1,557	354,755,561	76.40%	20,659	4,576
PBMC_T4_CTRL	2.1.0	4,957	68,190	1,562	338,020,151	86.60%	19,778	4,379
PBMC_T4_BACT	2.1.0	1,999	136,435	1,988	272,734,735	80.20%	19,548	5,924
DRESS_Day4_BACT	2.1.1	1,190	317,505	2,778	377,831,431	84.40%	19,468	9,486
DRESS_Day4_TOFA	2.1.1	2,891	122,250	1,733	353,424,926	88.60%	19,443	5,210
PBMC_POST2W	2.1.1	6,575	47,682	1,302	313,514,003	88.30%	19,681	3,565
SKIN_HV1_F1	2.0.2	1,158	288,629	2,332	334,232,689	64.00%	21,313	9,020
SKIN_HV1_F2	2.0.2	1,921	187,934	2,413	361,021,601	65.20%	22,267	9,580
SKIN_HV2	2.0.2	4,016	90,634	1,959	363,987,282	64.70%	22,755	6,544
SKIN_HV3	2.0.2	4,923	71,046	1,919	349,762,138	66.50%	22,891	6,742
SKIN_HV4	2.1.0	1,589	247,273	2,803	392,918,295	89.70%	22,397	10,001
SKIN_HV5	2.1.0	1,165	224,016	2,788	260,978,774	86.90%	21,368	10,278

Supplementary Table 5. Seurat filtration criteria for the exclusion of cells with low qualities.

Sample name	Filtration criteria						Filtration result	
	% mitochondrial gene_max	nUMI_min	nUMI_max	nGene_min	nGene_max	nCell_min expressing a gene	nCell_before	nCell _postfilter
Skin_Dress1	10	2000	40000	1000	5500	3	5,653	4,676
PBMC_DRESS1	10	2000	25000	500	5000	3	7,660	6,956
PBMC_HV	10	2000	20000	500	4000	3	8,688	7,976
PBMC_T4_CTRL	7	2000	15000	NA	NA	2	4,957	4,253
PBMC_T4_BACT	7	2000	20000	NA	NA	2	1,999	1,628
DRESS_Day4_BACT	10	2000	50000	1000	5000	2	1,190	941
DRESS_Day4_TOFA	10	2000	50000	1000	5000	2	2,891	1,128
PBMC_POST2W	10	2000	15000	800	3500	3	6,579	5,294
SKIN_HV1 (merged)	10	2000	25000	1000	4200	3	3,069	2,685
SKIN_HV2	10	2000	22500	1200	4000	3	4,016	3,698
SKIN_HV3	10	2000	25000	1000	4200	3	4,923	4,790
SKIN_HV4	10	2000	30000	1250	5000	3	1,589	1,361
SKIN_HV5	10	2000	30000	1300	5000	3	1,165	1,008

*NA, not applied

Supplementary Table 6. Parameters used for canonical correlation analysis and clustering.

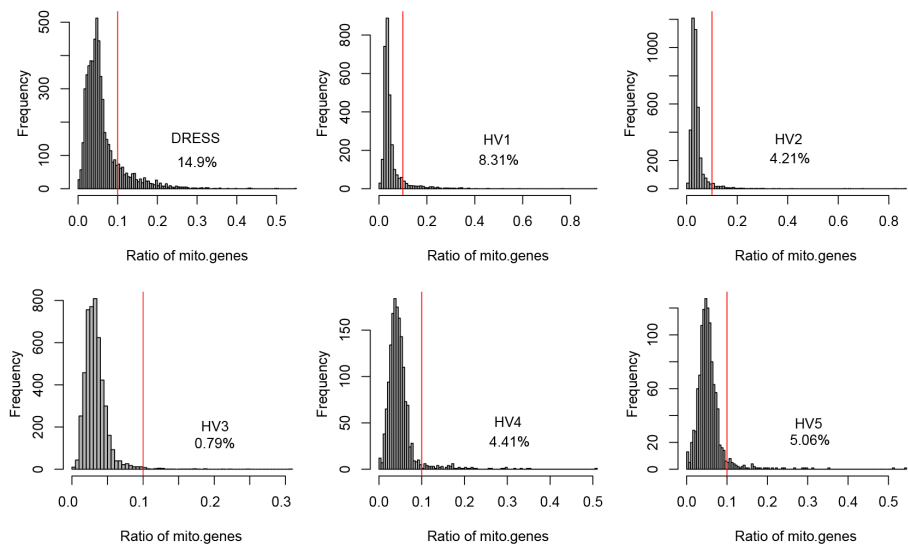
Merged dataset	Datasets used	# variable genes for CCA	# selected CC dimensions	resolution
skin	Skin_Dress1 + 5 HVs (HV1~HV5)	2,465	18	0.7
skin_lymphocyte_subclustering	Cluster 4 of the merged skin dataset	699	12	0.7
PBMC	PBMC_DRESS1 + 1 HV	2,437	18	0.8
PBMC_posttreatment	PBMC_DRESS1 + PBMC_Post_2wk	2,598	18	1
LTT with/without SMX/TMP	Culture PBMC with SMX/TMP + culture PBMC with media alone	2,639	8	0.5
LTT with/without tofacitinib	Culture PBMC with tofacitinib + culture PBMC with SMX/TMP alone	2,800	8	1

Supplementary Table 7. Clustering of the merged skin dataset based on different number of variable genes.

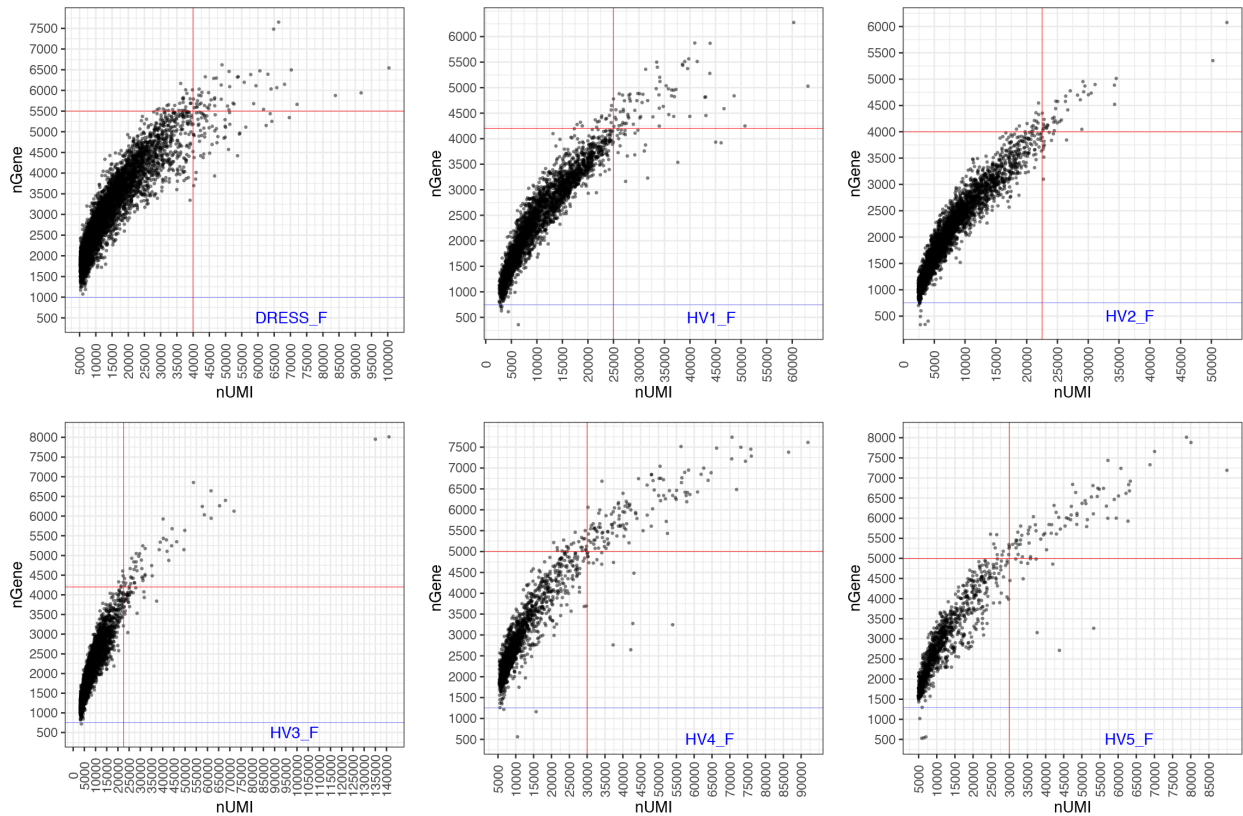
Selection of variable genes per each dataset	Combined gene list for CCA	Number of selected CCs	Cell numbers per cell type	Keratinocytes	Pericytes/smooth muscles	Fibroblast	Endothelium	Lymphoid cells	Myeloid cells	Melanocytes	Total cell count
Top 2,000 genes	2,465	18		5,676	4,276	3,306	1,889	1,737	978	356	18,218
Top 1,000 genes	1,239	18		5,664	4,269	3,372	1,852	1,742	983	336	18,218

Supplementary Figure 1. Histograms and scatter plots showing criteria for filtering out skin cells with low quality.

a

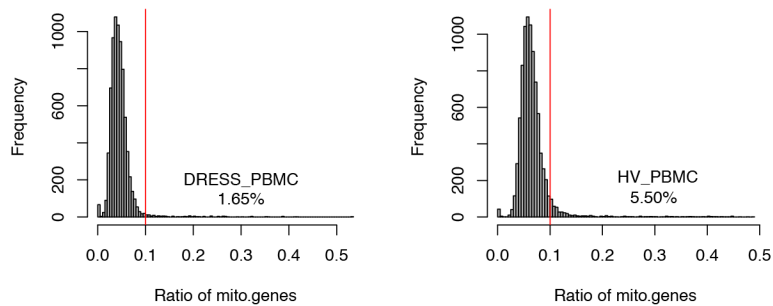


b



Supplementary Figure 2. Histograms and scatter plots showing criteria for filtering out peripheral mononuclear cells with low quality.

a



b

