

Supplementary Materials

Supplementary Note 1

Inferring cell types, states, and stages

Differentially expressed genes for each cell cluster were calculated separately for C1 and 10X datasets using Seurat's FindMarkers (https://satijalab.org/seurat/seurat_clustering_tutorial_part2.html) with `min.pct = 0.25`, applying its Wilcoxon rank sum test, and setting `min.diff.pct` to be 0.2 or 0.4.

The differential gene lists are provided in full in Supplementary Table 4, and representative top markers for each cluster are given in Tables SN1-1 and SN1-2. The top marker genes for each cell cluster are shown in Fig. 3c where each cell cluster was down-sampled to at most 100 cells for 10x data and at most 50 cells for C1 data.

To associate cell clusters with likely cell types/stages, the differential marker expression lists with `min.diff.pct = 0.2` for each cluster were entered into FuncAssociate 3.0 (<http://llama.mshri.on.ca/funcassociate/>)¹, which returned GO attributes that were evaluated by LOD score and p values, requiring that all terms used be $p_{adj} \leq 0.05$, corrected for multiple testing by empirical resampling. Attributes emphasizing terms that are explicitly or implicitly pertinent to developmental processes and cell types were selected by inspection and the appropriate attribute/entity tables were downloaded. The gene symbols from the attribute/entity tables were then used to search the literature to assemble curated marker genes and references (Tables SN1-1 and SN1-2). Key confirmatory literature markers for a candidate cell type were evaluated for significantly differential marker status (Supplementary Data 4) and included as literature markers. In cases where the literature provided a clear naming convention for a cell type association, we adopted that name in the tables. In other cases, the name is assigned from this work (e.g. *Ihh*+chondrocyte). When marker ambiguity prevented an unequivocal cell type assignment, we chose a designation based on the weight of the available evidence that is consistent with known fate mapping, tracing and cell sorting studies.

Our cell type identification was performed independently for data from the two platforms. We then evaluated correlations between the clusters, labeled by their cell type assignments, by logistic regression using all the detected genes (Fig SN1). The core set of 11 major cell types and stages, displayed identity broadly across their entire transcriptomes (Fig 3). Cell types with multiple developmental stages or subdivisions show splitting of C1 state-specific genes across 2 or more 10x clusters (e.g. *mus1*, *mus2*, *mus3* and *mus4*), as would be expected from differences in cell sampling depth and transcriptome-depth.

Cell type sensitivity. The greater cell sampling depth of the 10x Genomics data (~90,000 cells) detected 14 addi-

tional clusters with their own provisional cell-type assignments. Three of the 10x-only cell types were expected to be absent from C1 data due to platform-specific details of cell-size filtration (early and late erythrocytes) and sample preparation (prior removal of sticky epidermal cells). The remaining 10x only clusters include rarer cell types/states with no C1 equivalent, presumably due mainly to sparse cell sampling with C1 plus some additional subdivision of C1 types into multiple 10x types.

Marker gene sensitivity. For several of the best-studied cell types we found that the C1 data identified key known markers from the literature that were not in the corresponding 10x differential lists. Examples that are functionally important include *Pthlh*, a regulator of the proliferation/differentiation choice in early chondrocytes^{2,3}; *Spry1*, which regulates quiescence in *Pax7* muscle precursor cells⁴ that comprise the Mus2 cluster; and *Dmrt2*, which is directly regulated by Pax3 in muscle precursors (Mus1), and in turn directly regulates *Myf5*⁵, which marks *mus1* and *mus2* in C1 data. None of these were significant markers in the corresponding 10x cell types, and all three were expressed at low levels in the corresponding C1 clusters (*Pthl*: 6 copies per cell (cpc)); *Spry1*, 1 cpc; and *Dmrt2*, 3 cpc).

Marker gene context. Defining a marker gene or a multigene cell-type signature also depends heavily on the tissue sample context. This is a pertinent caution for future uses of the marker gene sets derived here, if they are applied to other studies in different biological settings. Conversely, this issue also informed our use of markers from the literature, where we favored the closest context available, although a strong match was often unavailable. Overall, our cell type identity assignments did prove consistent with classical and modern tracing studies and genetic knockouts for the better-studied cell types. We further observed that cell-type marker signatures increased in complexity as several lineages progressed (Fig. 3c and Extended Data Fig. 9 j), making the more mature types (e.g. Muscle 3 or Macrophage) easier to define with high confidence. By contrast, their progenitors (Muscle1, EMP and Mesenchyme1) displayed lower salience signatures, with few progenitor-unique genes compared with their more differentiated counterparts.

Cluster structure sensitivity. It is important to recognize that the relationship of a cell cluster with a dominant cell identity does not (and is not expected to) preclude the presence of additional cell types within the cluster. At this early level of single cell resolution, it is expected that much additional cell type structure is unresolved. For example, in the cell clusters identified here as predominantly EMP, close examination of candidate marker gene sets from the literature found some evidence for the presence of related cells (mast cells), as noted in Tables SN1-1 and SN1-2.

Supplementary Figures

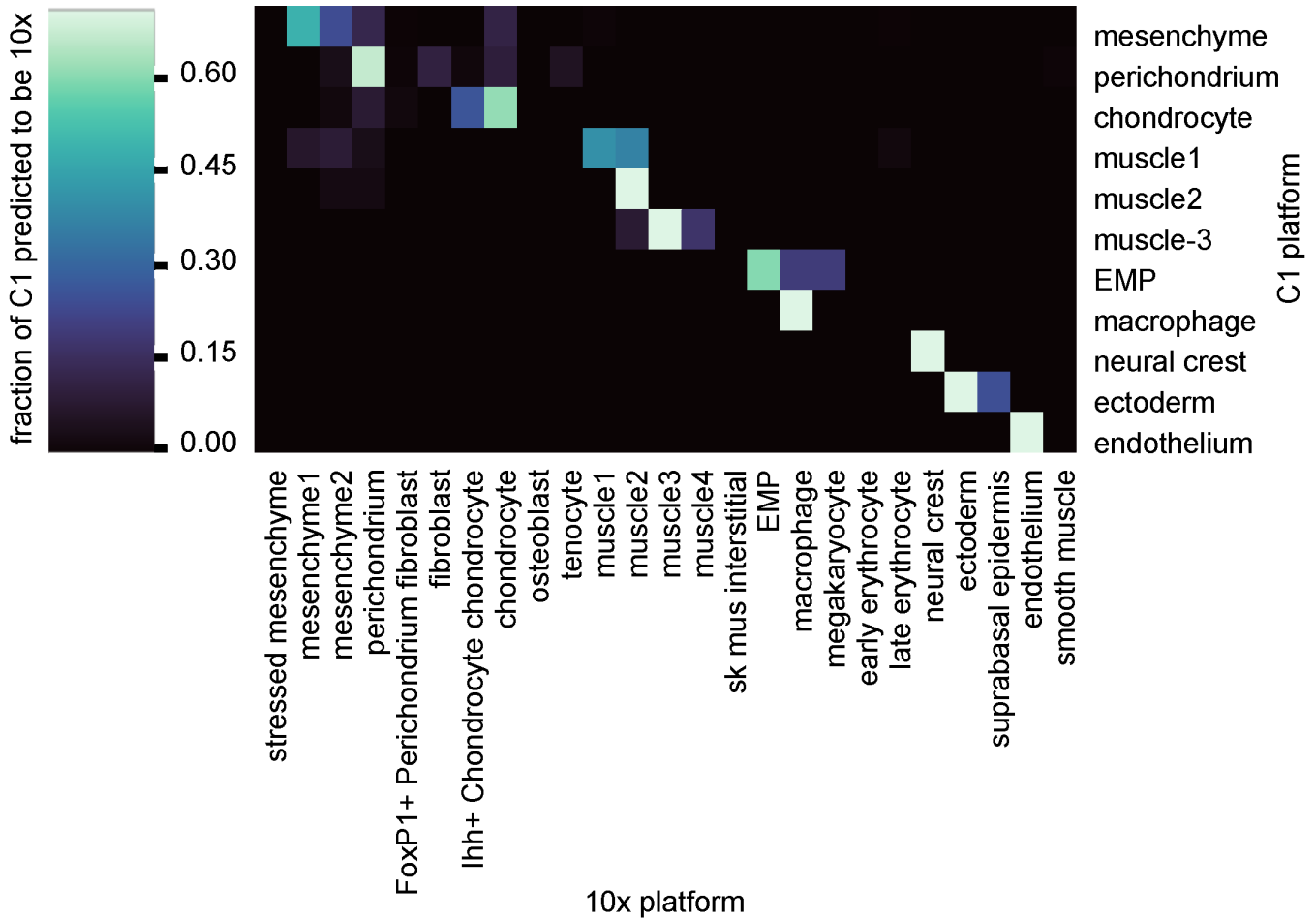


Figure SN 1: Cross-comparison of cell type assignments across the two scRNA-seq platforms.. Logistic regression results are plotted for all pairwise comparisons of cell type assignments across both scRNA-Seq platforms. Scale bar represents the fractional proportion of a C1 cell type predicted to be each 10x cell type. For cell types found in the 10x Genomics data that were not found in the C1 Fluidigm data, the scores are set at 0. Both 10x and C1 data were normalized, *log*-transformed and scaled before regression. To train a multinomial logistic regression model using the scikit-learn python package, the categorical information of the 25 cell types from 10x were used as the dependent variable. The trained model was then used to predict the C1 data. This model assigned each C1 single-cell into one of the 25 cell type categories defined by 10x data. The distribution (fraction) of the assignment per each C1 cell type into 10x categories was visualized as a row in the heatmap.

Supplementary Tables

Table SN1 1: Fluidigm C1 marker genes and inferred cell identities, states and stages. The statistical test for Gene Ontology analysis is a single-hypothesis p -value of the association between attribute and query (based on Fisher's Exact Test). p_{adj} : fraction (as a %) of 1000 null-hypothesis simulations having attributes with this single-hypothesis p value or smaller. Sample sizes for C1 clusters are: mesenchyme, 1242 genes; perichondrium, 3108 genes; chondrocytes, 3756 genes, muscle 3, 2090 genes, muscle 1, 962 genes; neural crest, 2933 genes; EMP, 3463 genes; endothelial, 3145 genes; muscle 2, 2114; macrophage, 3022 genes; epithelial, 2625 genes. Sample sizes for 10x clusters are: Cluster 0, 398 genes; Cluster 1, 248 genes; Cluster 2, 70 genes; Cluster 3, 164 genes; Cluster 4, 146 genes; Cluster 5, 217 genes; Cluster 6, 262 genes; Cluster 7, 265 genes; Cluster 8, 734 genes; Cluster 9, 622 genes; Cluster 10, 160 genes; Cluster 11, 349 genes; Cluster 12, 556 genes; Cluster 13, 156 genes; Cluster 14, 334 genes; Cluster 15, 623 genes; Cluster 16, 542 genes; Cluster 17, 322 genes; Cluster 18, 431 genes; Cluster 19, 397 genes; Cluster 20, 592 genes; Cluster 21, 881 genes; Cluster 22, 117 genes; cluster 23, 42 genes; Cluster 24, 336 genes. p -values for GO term association are single-hypothesis p -values of the association between attribute and query (based on Fisher's Exact Test), and were adjusted by the fraction (as a %) of 1000 null-hypothesis simulations having attributes with this single-hypothesis P value or smaller. GO search sample sizes for C1 clusters are: mesenchymal, 90 genes; perichondrial, 369 genes; chondrocyte, 279 genes; muscle 3, 365 genes; muscle 1, 117 genes; neural crest, 165 genes; EMP, 393 genes; endothelial, 314 genes; muscle 2, 236 genes; macrophage, 632 genes; epithelial, 169 genes. GO search sample sizes for 10x clusters are: cluster 0, 177 genes; cluster 1, 116 genes; cluster 2, 16 genes; cluster 3, 30 genes, cluster 4, 100 genes, cluster 5, 158 genes, cluster 6, 173 genes, cluster 7, 153 genes, cluster 8, 679 genes; cluster 9, 561 genes; cluster 10, 50 genes; cluster 11, 170 genes; cluster 12, 516 genes; cluster 13, 149 genes; cluster 14, 305 genes; cluster 15, 2 genes; cluster 16, 450 genes, cluster 17, 263 genes, cluster 18, 380 genes, cluster 19, 323 genes; cluster 20, 520 genes; cluster 21, 833 genes; cluster 22, 60 genes; cluster 23, 38 genes; cluster 24, 205 genes.

Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from Fluidigm data	LOD score	p_{unadj}	p_{adj}	top 5 genes from C1 clusters	selected literature marker genes
0	mesenchyme (mes)	mesenchyme	GO:0035115	embryonic forelimb morphogenesis	1.67	2.71E-07	≤0.001	[<i>Mecom</i> , <i>Hsd11b2</i> , <i>Lix1</i> , <i>Car14</i> , <i>Hoxd10</i>]	[<i>Hoxd10</i> ⁶ , <i>Hoxd11</i> ⁶ , <i>Hoxd12</i> ⁶ , <i>Msx1</i> ⁷ , <i>Twil</i> ^{8,9}]
			GO:0009954	proximal/distal pattern formation	1.67	4.69E-06	0.006		
			GO:0042733	embryonic digit morphogenesis	1.66	4.75E-12	≤0.001		
			GO:0009952	anterior/posterior pattern specification	1.15	3.95E-07	≤0.001		
1	perichondrium (pchon)	perichondrium	GO:0060351	cartilage development involved in endochondral bone morphogenesis	1.41	7.20E-06	0.032	[<i>Col6a1</i> , <i>Egfl6</i> , <i>Creb3l1</i> , <i>Ogn</i> , <i>Col1a1</i>]	[<i>Col1a1</i> ¹⁰ , <i>Dcn1</i> ¹ , <i>Dkk3</i> ¹² , <i>Ogn</i> ¹¹ , <i>Thbs2</i> ¹²]
			GO:0030199	collagen fibril organization	1.27	1.33E-08	≤0.001		
			GO:0001649	osteoblast differentiation	0.98	7.79E-06	0.039		

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Table SN1 1 – *Continued from previous page*

Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from Fluidigm data	LOD score	<i>P_{unadj}</i>	<i>P_{adj}</i>	top 5 genes from C1 clusters	selected literature marker genes
			GO:0001503	ossification	0.94	7.67E-09	≤0.001		
2	chondrocytes (chon)	immature chondrocytes	GO:0060351	cartilage development involved in endochondral bone morphogenesis	1.64	4.74E-08	≤0.001	[<i>Susd5</i> , <i>Matn1</i> , <i>Foxa3</i> , <i>Ncmap</i> , <i>Acan</i>]	[<i>Acan</i> ³ , <i>Col2a1</i> ³ , <i>Dlx5</i> ¹³ , <i>Ihh3</i> , <i>Pthlh</i> ³ , <i>Runx2</i> ¹³ , <i>Runx3</i> ¹⁴ , <i>Sox5</i> ³ , <i>Sox6</i> ³ , <i>Sox9</i> ³ , <i>Sp7</i> ¹³]
			GO:0032331	negative regulation of chondrocyte differentiation	1.55	1.35E-07	≤0.001		
			GO:0001958	endochondral ossification	1.54	1.01E-09	≤0.001		
			GO:0001502	cartilage condensation	1.50	2.47E-06	0.006		
			GO:0030279	negative regulation of ossification	1.16	8.08E-11	≤0.001		
			GO:0001649	osteoblast differentiation	1.16	7.21E-08	≤0.001		
3	muscle3 (mus3)	myocyte	GO:0003009	skeletal muscle contraction	1.96	1.29E-18	≤0.001	[<i>Gm7325</i> , <i>Ablim3</i> , <i>Kcnk13</i> , <i>Smyd1</i> , <i>Klhl41</i>]	[<i>Actc1</i> ¹⁵ , <i>Act3</i> ¹⁵ , <i>Fgfr4</i> ¹⁶ , <i>Myod1</i> ¹⁶ , <i>Myog</i> ¹⁶ , <i>Myot</i> ¹⁵ , <i>Ryr1</i> ¹⁵ , <i>Tead4</i> ¹⁵]
			GO:0048741	skeletal muscle fiber development	1.54	1.33E-10	≤0.001		
			GO:0007520	myoblast fusion	1.42	6.50E-07	≤0.001		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from Flu-idigm data	LOD score	<i>P_{unadj}</i>	<i>P_{adj}</i>	top 5 genes from C1 clusters	selected literature marker genes
4	muscle1 (mus1)	migratory limb muscle precursor cell	GO:0007517	muscle organ development	1.45	2.67E-10	≤0.001	[<i>Pax3</i> , <i>Lbx1</i> , <i>Pitx2</i> , <i>Myod1</i> , <i>Eya1</i>]	[<i>Dmrt2</i> ⁵ , <i>Eya1</i> ¹⁶ , <i>Eya2</i> ¹⁶ , <i>Lbx1</i> ¹⁶ , <i>Met</i> ¹⁷ , <i>Msc</i> ¹⁶ , <i>Myf5</i> ¹⁶ , <i>Myod1</i> ¹⁶ , <i>Pax3</i> ^{18–20} , <i>Pitx2</i> ¹⁶ , <i>Pitx3</i> ¹⁶]
			GO:0007519	skeletal muscle tissue development	1.50	1.32E-08	≤0.001		
			GO:0001756	somitogenesis	1.35	8.55E-06	0.018		
5	neural crest (neur)	neural crest	GO:0007422	peripheral nervous system development	1.62	8.84E-06	0.015	[<i>Gpr17</i> , <i>Foxd3</i> , <i>St8sia5</i> , <i>Lgi4</i> , <i>Insc</i>]	[<i>Dlx1</i> ²¹ , <i>Dlx2</i> ²¹ , <i>Foxd3</i> ²² , <i>Sox2</i> ²² , <i>Sox10</i> ²² , <i>Zeb2</i> ²²]
			GO:0042552	myelination	1.17	1.68E-06	0.003		
			GO:0045666	positive regulation of neuron differentiation	0.76	3.46E-07	≤0.001		
6	erythro-myeloid precursor (EMP)*	erythro-myeloid precursor	GO:0006909	phagocytosis	1.05	1.36E-07	0.001	[<i>Slc22a3</i> , <i>1110028F10Rik</i> , <i>Ubash3a</i> , <i>Rab44</i> , <i>Gata1</i>]	[<i>Fcgr3</i> ²³ , <i>Gata1</i> ²³ , <i>Gata2</i> ²³ , <i>Gfi1b</i> ²⁴ , <i>Spi1</i> ²³]
			GO:0051707	response to other organism antigen processing and presentation	0.53	3.08E-07	0.001		
			GO:0002478	presentation of exogenous peptide antigen	1.39	9.96E-07	0.003		
7	endothelium (endo)	endothelium	GO:0001945	lymph vessel development	1.81	9.26E-09	≤0.001	[<i>Ccm2l</i> , <i>Myct1</i> , <i>Pcdh12</i> , <i>Sox17</i> , <i>Robo4</i>]	[<i>Aplnr</i> ²⁵ , <i>Flt4</i> ²⁶ , <i>Kdr</i> ²⁶ , <i>Lmo2</i> ²⁷ , <i>Sox17</i> ²⁷]
			GO:0002040	sprouting angiogenesis	1.43	5.46E-08	≤0.001		
			GO:0061028	establishment of endothelial barrier	1.39	8.34E-07	≤0.001		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from Flu-idigm data	LOD score	p_{unadj}	p_{adj}	top 5 genes from C1 clusters	selected literature marker genes
			GO:0001525	angiogenesis	1.17	1.67E-28	≤ 0.001		
8	muscle2 (mus2)	myoblast	GO:0007517	muscle organ development	1.31	1.57E-12	≤ 0.001	[<i>Pax7</i> , <i>Ntrk1</i> , <i>Scn3b</i> , <i>Gm9947</i> , <i>Myf5</i>]	[<i>Dmrt2</i> ⁵ , <i>En1</i> ²⁸ , <i>Eya1</i> ¹⁶ , <i>Eya2</i> ¹⁶ , <i>Hes6</i> ²⁹ , <i>Lbx1</i> ¹⁶ , <i>Met</i> ¹⁷ , <i>Msc</i> ¹⁶ , <i>Myf5</i> ¹⁶ , <i>Myod1</i> ¹⁶ , <i>Notch3</i> ³⁰ , <i>Pax7</i> ³¹ , <i>Pitx2</i> ¹⁶ , <i>Pitx3</i> ¹⁶ , <i>Six1</i> ¹⁶ , <i>Six2</i> ¹⁶ , <i>Sox8</i> ³² , <i>Spry1</i> ⁴ , <i>Vgll2</i> ³³ , <i>Vgll3</i> ^{34,35}]
			GO:0061061	muscle structure development	1.27	4.10E-12	≤ 0.001		
			GO:0051147	regulation of muscle cell differentiation	1.05	4.95E-12	≤ 0.001		
9	macrophage (mac)	tissue resident macrophage	GO:0098542	defense response to other organism	1.01	5.56E-44	≤ 0.001	[<i>Lrrc25</i> , <i>Clec4a3</i> , <i>Cybb</i> , <i>Fcgr1</i> , <i>AI607873</i>]	[<i>Csf1r</i> ²³ , <i>Cx3cr1</i> ²³ , <i>Emr1</i> ²³ , <i>Fcer1g</i> ²³ , <i>Irf8</i> ²³ , <i>Runx1</i> ³⁶ , <i>Spi1</i> ²³]
			GO:0045087	innate immune response	1.03	1.00E-41	≤ 0.001		
			GO:0001819	positive regulation of cytokine production	0.95	2.31E-37	≤ 0.001		
			GO:0006935	chemotaxis	0.98	9.62E-28	≤ 0.001		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from Flu-idigm data	LOD score	<i>P_{unadj}</i>	<i>P_{adj}</i>	top 5 genes from C1 clusters	selected literature marker genes
10	ectoderm (ecto)	ectoderm	GO:0005109	frizzled binding	1.55	1.13E-06	0.001	[4631405K081403, Ap1m2, Fermt1, Krt5, Krt14]	[Fzd6 ³⁷ , Grhl2 ³⁸ , Grhl3 ³⁸ , Klf5 ³⁹ , Krt17 ³⁹ , Krt11 ³⁹ , Krt17 ³⁹ , Wnt3 ³⁷ , Wnt4 ³⁷ , Wnt6 ³⁷ , Wnt7a ³⁷ , Wnt7b ³⁷ , Wnt10a ³⁷]
			GO:0035567	non-canonical Wnt signaling pathway	1.53	1.38E-06	0.002		
			GO:0030216	keratinocyte differentiation	1.41	5.53E-08	≤0.001		
			GO:0035136	forelimb morphogenesis	1.28	1.87E-05	0.038		
			GO:0016055	Wnt signaling pathway	0.89	2.29E-07	≤0.001		
			GO:0001228	transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding	0.80	4.68E-08	≤0.001		
			GO:0007389	pattern specification process	0.68	1.45E-05	0.031		
			GO:0048646	anatomical structure formation involved in morphogenesis	0.61	9.81E-07	0.001		

* 2 cells in this cluster expressed mast cell genes.

Table SN1 2: 10x Genomics marker genes and inferred cell identities, states and stages. The statistical test for Gene Ontology analysis is a single-hypothesis p -value of the association between attribute and query (based on Fisher's Exact Test). p_{adj} : fraction (as a %) of 1000 null-hypothesis simulations having attributes with this single-hypothesis p value or smaller. Sample sizes for C1 clusters are: mesenchyme, 1242 genes; perichondrium, 3108 genes; chondrocytes, 3756 genes, muscle 3, 2090 genes, muscle 1, 962 genes; neural crest, 2933 genes; EMP, 3463 genes; endothelial, 3145 genes; muscle 2, 2114; macrophage, 3022 genes; epithelial, 2625 genes. Sample sizes for 10x clusters are: Cluster 0, 398 genes; Cluster 1, 248 genes; Cluster 2, 70 genes; Cluster 3, 164 genes; Cluster 4, 146 genes; Cluster 5, 217 genes; Cluster 6, 262 genes; Cluster 7, 265 genes; Cluster 8, 734 genes; Cluster 9, 622 genes; Cluster 10, 160 genes; Cluster 11, 349 genes; Cluster 12, 556 genes; Cluster 13, 156 genes; Cluster 14, 334 genes; Cluster 15, 623 genes; Cluster 16, 542 genes; Cluster 17, 322 genes; Cluster 18, 431 genes; Cluster 19, 397 genes; Cluster 20, 592 genes; Cluster 21, 881 genes; Cluster 22, 117 genes; cluster 23, 42 genes; Cluster 24, 336 genes. p -values for GO term association are single-hypothesis p -values of the association between attribute and query (based on Fisher's Exact Test), and were adjusted by the fraction (as a %) of 1000 null-hypothesis simulations having attributes with this single-hypothesis P value or smaller. GO search sample sizes for C1 clusters are: mesenchymal, 90 genes; perichondrial, 369 genes; chondrocyte, 279 genes; muscle 3, 365 genes; muscle 1, 117 genes; neural crest, 165 genes; EMP, 393 genes; endothelial, 314 genes; muscle 2, 236 genes; macrophage, 632 genes; epithelial, 169 genes. GO search sample sizes for 10x clusters are: cluster 0, 177 genes; cluster 1, 116 genes; cluster 2, 16 genes; cluster 3, 30 genes, cluster 4, 100 genes, cluster 5, 158 genes, cluster 6, 173 genes, cluster 7, 153 genes, cluster 8, 679 genes; cluster 9, 561 genes; cluster 10, 50 genes; cluster 11, 170 genes; cluster 12, 516 genes; cluster 13, 149 genes; cluster 14, 305 genes; cluster 15, 2 genes; cluster 16, 450 genes, cluster 17, 263 genes, cluster 18, 380 genes, cluster 19, 323 genes; cluster 20, 520 genes; cluster 21, 833 genes; cluster 22, 60 genes; cluster 23, 38 genes; cluster 24, 205 genes.

Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	p_{unadj}	p_{adj}	top 5 genes from 10x clusters	selected literature marker genes
0	proximal mesenchyme (mesprox)	proximal mesenchyme	GO:0030326	embryonic limb morphogenesis	1.22	3.72E-09	≤0.001	[<i>Lix1</i> , <i>Asb4</i> , <i>Igdcc3</i> , <i>Hmga2</i> , <i>Rrm2</i>]	[<i>Hoxa9</i> ⁶ , <i>Hoxd9</i> ⁶ , <i>Hoxd10</i> ⁶ , <i>Hoxd11</i> ⁶ , <i>Shox2</i> ⁴⁰]
			GO:0048704	embryonic skeletal system morphogenesis	1.06	7.90E-06	0.018		
			GO:0022402	cell cycle process	0.70	1.06E-08	≤0.001		
1	perichondrium (pchon)	perichondrium	GO:0005583	fibrillar collagen trimer	2.48	2.86E-12	≤0.001	[<i>Dlk1</i> , <i>Meg3</i> , <i>Col3a1</i> , <i>Igf1</i> , <i>Col1a1</i>]	[<i>Col1a1</i> ¹⁰ , <i>Col5a1</i> ⁴¹ , <i>Igf1</i> , <i>Shox0</i> ⁴⁰]
			GO:0001649	osteoblast differentiation	1.44	3.22E-08	0.001		
			GO:0009653	anatomical structure morphogenesis	0.59	3.33E-07	0.002		
2	distal mesenchyme (mesdist)	distal mesenchyme	GO:0030326	embryonic limb morphogenesis	2.63	8.06E-21	≤0.001	[<i>Msx1</i> , <i>Hoxd13</i> , <i>Prrx2</i> , <i>Hoxa11os</i> , <i>Hoxd12</i>]	[<i>Hoxa10</i> ⁶ , <i>Hoxd12</i> ⁶ , <i>Hoxd13</i> ⁶ , <i>Hoxa11os</i> , <i>Msx1</i> ⁷ , <i>Hoxd12</i> ⁷ , <i>Msx2</i> ⁷]

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Table SN1 2 – *Continued from previous page*

Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	P_{unadj}	P_{adj}	top 5 genes from 10x clusters	selected literature marker genes
			GO:0042733	embryonic digit morphogenesis	2.48	1.37E-14	≤0.001		
			GO:0007389	pattern specification process	1.74	1.31E-10	≤0.001		
			GO:0009952	anterior/posterior pattern specification	1.93	1.24E-09	≤0.001		
			GO:0051216	cartilage development	2.12	2.98E-09	≤0.001		
3	chondrocytes (chon)	immature chondrocytes	GO:0060174	limb bud formation	2.54	3.21E-07	≤0.001	[<i>Sox9</i> , <i>Col2a1</i> , <i>Wwp2</i> , <i>Col9a1</i> , <i>Gdf5</i>]	[<i>Acan</i> ^{3,14} , <i>Col2a1</i> ^{3,14} , <i>Sox5</i> ^{3,14} , <i>Sox6</i> ^{3,14} , <i>Sox9</i> ^{3,14}]
			GO:0002063	chondrocyte development	2.38	1.09E-08	≤0.001		
			GO:0001503	ossification	1.63	4.41E-07	0.001		
4	muscle2 (mus2)	early myoblast	GO:0007519	skeletal muscle tissue development	1.57	4.40E-09	≤0.001	[<i>Msc</i> , <i>Kcne1l</i> , <i>Itm2a</i> , <i>Pdgfa</i> , <i>Vgll2</i>]	[<i>Msc1</i> ⁶ , <i>Myf5</i> ¹⁶ , <i>Myod1</i> ¹⁶ , <i>Pax7</i> ³¹ , <i>Pitx2</i> ¹⁶ , <i>Six1</i> ¹⁶ , <i>Vgll2</i> ³³]
			GO:0014706	striated muscle tissue development	1.39	7.43E-09	≤0.001		
			GO:0007389	pattern specification process	0.93	3.52E-08	≤0.001		
5	ectoderm (ecto)	ectoderm	GO:0010482	regulation of epidermal cell division	3.02	3.11E-07	≤0.001	[<i>Cxcl14</i> , <i>Pdgfa</i> , <i>Wnt6</i> , <i>Krt14</i> , <i>Gjb2</i>]	[<i>Cxcl14</i> ⁴³ , <i>En1</i> ⁴⁴ , <i>Fzd6</i> ³⁷ , <i>Fzd10</i> ³⁷ , <i>Wnt4</i> ³⁷ , <i>Wnt6</i> ³⁷ , <i>Wnt7b</i> ³⁷ , <i>Wnt10a</i> ³⁷]
			GO:0003334	keratinocyte development	1.85	1.42E-06	0.001		
			GO:0043588	skin development	1.67	1.39E-15	≤0.001		
			GO:0009954	proximal/distal pattern formation	1.53	1.44E-06	0.001		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	P_{unadj}	P_{adj}	top 5 genes from 10x clusters	selected literature marker genes
6	fibroblast (fibro)	fibroblast	GO:0048407	platelet-derived growth factor binding	2.14	1.41E-10	≤0.001	[<i>Crabp1</i> , <i>Crip1</i> , <i>Twist2</i> , <i>Lum</i> , <i>Rspo1</i>]	[<i>Irx1</i> ⁴⁵ , <i>Irx2</i> ⁴⁵ , <i>Irx3</i> ⁴⁵ , <i>Irx5</i> ⁴⁵ , <i>Tbx15</i> ⁴⁶ , <i>Twist2</i> ⁴⁷]
			GO:0045667	regulation of osteoblast differentiation	1.11	5.88E-09	≤0.001		
			GO:0030278	regulation of ossification	0.97	1.06E-08	≤0.001		
			GO:0048705	skeletal system morphogenesis	0.97	7.70E-06	0.011		
7	muscle1 (mus1)	migratory limb muscle precursor cells	GO:0014706	striated muscle tissue development	1.13	3.02E-06	0.007	[<i>Pax3</i> , <i>Lbx1</i> , <i>Tcf15</i> , <i>Ppp1r14b</i> , <i>Slc25a5</i>]	[<i>Lbx1</i> ¹⁶ , <i>Met</i> ¹⁷ , <i>Pax3</i> ^{18–20}]
			GO:0048562	embryonic organ morphogenesis	1.06	3.72E-07	≤0.001		
			GO:0060537	muscle tissue development	1.05	9.13E-06	0.021		
8	macrophage (mac)	macrophage	GO:0048246	macrophage chemotaxis	1.41	1.52E-06	0.002	[<i>ApoE</i> , <i>Fcer1g</i> , <i>Tyrobp</i> , <i>C1qb</i> , <i>C1qc</i>]	[<i>Aif1</i> ²³ , <i>Cx3cr1</i> ²³ , <i>Emr1</i> ²³ , <i>Csf1r</i> ²³ , <i>Fcgr1</i> ²³ , <i>Fcgr3</i> ²³ , <i>Grn</i> ²³ , <i>Irf8</i> ²³ , <i>Maf</i> ²³ , <i>Spi1</i> ²³ , <i>Zeb2</i> ²³]
			GO:0019884	antigen processing and presentation of exogenous antigen	1.40	6.53E-11	≤0.001		
			GO:0006911	phagocytosis, engulfment	1.19	1.57E-08	≤0.001		
9	endothelium (endo)	endothelium	GO:0001945	lymph vessel development	1.55	2.91E-07	≤0.001	[<i>Gng11</i> , <i>S100a16</i> , <i>Egfl7</i> , <i>Cdh5</i> , <i>Crip2</i>]	[<i>Aplnr</i> ²⁵ , <i>Efnb2</i> ⁴⁸ , <i>Ets1</i> ⁴⁹ , <i>Ets2</i> ⁴⁹ , <i>Flt4</i> ²⁶ , <i>Kdr</i> ²⁶ , <i>Sox17</i> ²⁷]

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	p_{unadj}	p_{adj}	top 5 genes from 10x clusters	selected literature marker genes
			GO:0045446	endothelial cell differentiation	1.35	2.77E-07	≤0.001		
			GO:1903672	positive regulation of sprouting angiogenesis	1.24	1.14E-06	≤0.001		
10	FoxP + perichondrium (pchon-FoxP+)	perichondrial cells expressing FoxP1	GO:0030199	collagen fibril organization	1.98	3.15E-10	≤0.001	[<i>Foxp1</i> , <i>Foxf2</i> , <i>Foxq1</i> , <i>Rprm</i> , <i>Pid1</i>]	[<i>Col1a1</i> ¹⁰ , <i>Emx2</i> ⁵⁰ , <i>FoxP1</i> ⁵¹ , <i>Lmx1b</i> ^{50,52}]
			GO:0001501	skeletal system development	1.32	1.15E-05	0.021		
			GO:0009653	anatomical structure morphogenesis	0.84	5.30E-08	≤0.001		
11	tenocytes (teno)	tenocytes	GO:0035989	tendon development	2.98	3.88E-07	0.002	[<i>Col1a1</i> , <i>Tnmd</i> , <i>Col1a2</i> , <i>Scx</i> , <i>Ogn</i>]	[<i>Col5a1</i> ⁵³ , <i>Col5a2</i> ⁵³ , <i>Col11a1</i> ⁵³ , <i>Mkx</i> ⁵⁴ , <i>Scx</i> ⁵⁵ , <i>Selm</i> ⁵⁶ , <i>Thbs4</i> ⁵⁵ , <i>Tnmd</i> ⁵⁵]
			GO:0005583	fibrillar collagen trimer	2.31	2.93E-11	≤0.001		
			GO:0061448	connective tissue development	1.24	4.21E-06	0.007		
12	muscle4 (mus4)	myocyte	GO:0035995	detection of muscle stretch	2.60	2.43E-07	0.001	[<i>Mylpf</i> , <i>Myl1</i> , <i>Actc1</i> , <i>Tnnc1</i> , <i>Myl4</i>]	[<i>Actc1</i> ¹⁵ , <i>Chrng</i> ¹⁵ , <i>Jsrp1</i> ¹⁵ , <i>Myl1</i> ¹⁵ , <i>Mylpf</i> ¹⁵ , <i>Ryr1</i> ¹⁵ , <i>Sln</i> ¹⁵ , <i>Tnnc1</i> ¹⁵ , <i>Tnnt1</i> ¹⁵]
			GO:0070296	sarcoplasmic reticulum calcium ion transport	1.98	2.95E-10	≤0.001		
			GO:0003009	skeletal muscle contraction	1.81	1.18E-16	≤0.001		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	P_{unadj}	P_{adj}	top 5 genes from 10x clusters	selected literature marker genes
13	early erythrocyte (eryth1)	early erythrocyte	GO:0005833	hemoglobin complex	3.38	3.95E-16	≤0.001	[<i>Hba-x</i> , <i>Hbb-bh1</i> , <i>Hba-a1</i> , <i>Hba-a2</i> , <i>Hbb-bt</i>]	[<i>Gata1</i> ⁵⁷ , <i>Hbb-y</i> ⁵⁷ , <i>Klf1</i> ⁵⁷ , <i>Lyl1</i> ⁵⁷ , <i>Spta1</i> ⁵⁷ , <i>Sptb</i> ⁵⁷ , <i>Tal1</i> ⁵⁷ , <i>Zfpml1</i> ⁵⁷]
			GO:0048821	erythrocyte development	1.98	7.18E-13	≤0.001		
			GO:0030097	hemopoiesis	1.13	5.32E-07	0.002		
14	neural crest (neur)	neural crest	GO:0014044	Schwann cell development	1.72	5.81E-06	0.017	[<i>Ednrb</i> , <i>Arpc1b</i> , <i>Plp1</i> , <i>Fabp7</i> , <i>Phactr1</i>]	[<i>Ets1</i> ²² , <i>Foxd3</i> ²² , <i>Lmo4</i> ⁵⁸ , <i>Metrn</i> ⁵⁹ , <i>Pax3</i> ²² , <i>Sox5</i> ²² , <i>Sox10</i> ²² , <i>Zeb2</i> ²²]
			GO:0001755	neural crest cell migration	1.25	6.86E-07	0.002		
			GO:0010001	glial cell differentiation	1.19	4.66E-11	≤0.001		
15	(mesX) stressed mesenchyme	mesenchymal cells expressing cell stress genes	GO:0034663	endoplasmic reticulum chaperone complex	1.84	1.17E-10	≤0.001		[<i>Dnajc10</i> ⁶⁰ , <i>Hspa5</i> ⁶¹ , <i>Hsp90</i> ⁶²]
			GO:0098803	respiratory chain complex	1.19	6.90E-13	≤0.001		
			GO:0045454	cell redox homeostasis	1.10	1.82E-10	≤0.001		
16	osteoblast (ost)	osteoblast	GO:0001958	endochondral ossification	1.40	1.80E-09	≤0.001	[<i>Ibsp</i> , <i>Ifitm5</i> , <i>Smpd3</i> , <i>Sgms2</i> , <i>Sp7</i>]	[<i>Col1a1</i> ¹⁰ , <i>Dlx5</i> ¹³ , <i>Mef2c</i> ⁶³ , <i>Pth1r</i> ⁶⁴ , <i>Runx2</i> ¹³ , <i>Sp7</i> ¹³]
			GO:0002062	chondrocyte differentiation	1.21	7.45E-09	≤0.001		
			GO:0001649	osteoblast differentiation	1.04	3.86E-08	0.001		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	P_{unadj}	P_{adj}	top 5 genes from 10x clusters	selected literature marker genes
17	muscle3 (mus3)	late myoblast	GO:0003009	skeletal muscle contraction	1.88	1.71E-14	≤0.001	[<i>Myog</i> , <i>Actc1</i> , <i>Tnnt1</i> , <i>Acta2</i> , <i>Vgll2</i>]	[<i>Dll1</i> ⁶⁵ , <i>Mef2c</i> ¹⁶ , <i>Myod1</i> ¹⁶ , <i>Myog</i> ¹⁶ , <i>Pitx2</i> ¹⁶ , <i>Six1</i> ¹⁶ , <i>Sox8</i> ³² , <i>Tnnc1</i> ¹⁵ , <i>Tnnt1</i> ¹⁵ , <i>Vgll2</i> ³³ , <i>Zbtb18</i> ⁶⁶]
			GO:0007519	skeletal muscle tissue development	1.36	3.09E-11	≤0.001		
			GO:0045661	regulation of myoblast differentiation	1.24	1.78E-08	≤0.001		
18	suprabasal epithelium (sup epi)	suprabasal epithelium	GO:0061436	establishment of skin barrier	1.75	3.75E-13	≤0.001	[<i>Krt14</i> , <i>Perp</i> , <i>Hspb1</i> , <i>Sfn</i> , <i>Krt5</i>]	[<i>Krt1</i> ³⁹ , <i>Krt10</i> ³⁹ , <i>Krt14</i> ³⁹ , <i>Krt-dap</i> ³⁹ , <i>Notch1</i> ³⁹ , <i>Sbsn</i> ³⁹ , <i>Trp63</i> ³⁹]
			GO:0003334	keratinocyte development	1.72	2.91E-08	≤0.001		
			GO:0008544	epidermis development	1.31	2.35E-12	≤0.001		
19	smooth muscle (smm)	smooth muscle	GO:0014910	regulation of smooth muscle cell migration	1.04	1.49E-07	≤0.001	[<i>Acta2</i> , <i>Rgs5</i> , <i>Tagln</i> , <i>Ndufa4l2</i> , <i>Rasgrp2</i>]	[<i>Acta2</i> ⁶⁷ , <i>Cav1</i> ⁶⁸ , <i>Coro1b</i> ⁶⁹ , <i>Cspg4</i> ⁶⁸ , <i>Cyr61</i> ⁶⁸ , <i>Egr1</i> ⁶⁸ , <i>Jag1</i> ⁶⁸ , <i>Pten</i> ⁶⁷ , <i>Tagln</i> ⁶⁷ , <i>Tagln2</i> ⁶⁷]
			GO:0001525	angiogenesis	0.93	2.08E-14	≤0.001		
			GO:0048514	blood vessel morphogenesis	0.91	1.98E-06	0.006		
			GO:0060537	muscle tissue development	0.88	3.59E-06	0.012		

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	<i>P_{unadj}</i>	<i>P_{adj}</i>	top 5 genes from 10x clusters	selected literature marker genes
20	erythro-myeloid precursor (EMP) *	erythro-myeloid precursor	GO:0030099	myeloid cell differentiation	0.90	9.59E-14	≤0.001	[<i>Cma1</i> , <i>Srgn</i> , <i>Cpa3</i> , <i>Rac2</i> , <i>Tyrobp</i>]	[<i>Cd34</i> ⁷⁰ , <i>Fcgr3</i> ²³ , <i>Gata1</i> ²³ , <i>Gata2</i> ²³ , <i>Kit</i> ²³ , <i>Spi1</i> ²³]
			GO:0050764	regulation of phagocytosis	0.85	2.17E-06	0.009		
			GO:0002821	regulation of adaptive immune response	0.79	2.80E-06	0.011		
			GO:0002819	regulation of adaptive immune response	0.79	9.95E-09	≤0.001		
21	megakaryocyte (meg)	megakaryocyte	GO:0030220	platelet formation	1.57	7.03E-12	≤0.001	[<i>Pf4</i> , <i>Ppbp</i> , <i>Ctla2a</i> , <i>Gp1bb</i> , <i>Gp9</i>]	[<i>Fli1</i> ⁷¹ , <i>Gata1</i> ⁷¹ , <i>Nfe2</i> ⁷¹ , <i>Mef2c</i> ⁷¹ , <i>Meis1</i> ⁷² , <i>Runx1</i> ⁷¹]
			GO:0070527	platelet aggregation	1.29	4.23E-09	≤0.001		
			GO:0035855	megakaryocyte development	1.25	1.70E-06	0.006		
22	interstitial fibroblast (int/mus)	interstitial fibroblast	GO:0005861	troponin complex	3.33	4.35E-18	≤0.001	[<i>Mylpf</i> , <i>Acta1</i> , <i>Myh1</i> , <i>Myh4</i> , <i>Sln</i>]	[<i>Col3a1</i> ⁷³ , <i>Col6a1</i> ⁷³ , <i>Col6a3</i> ⁷³ , <i>Cxcl12</i> ⁷³ , <i>Lum</i> ⁷³ , <i>Osr1</i> ⁷³ , <i>Vim</i> ⁷³]
			GO:0005583	fibrillar collagen trimer	2.45	8.44E-09	≤0.001		
			GO:0003009	skeletal muscle contraction	2.12	2.50E-09	≤0.001		
23	late erythrocyte (eryth2)	late erythrocyte	GO:0031722	hemoglobin beta binding	3.50	2.62E-06	0.008	[<i>Snca</i> , <i>Alas2</i> , <i>Car2</i> , <i>Gypa</i> , <i>Ube2l6</i>]	[<i>Bpgm</i> ⁵⁷ , <i>Hbb-bt</i> ⁵⁷ , <i>Hbb-bs</i> ⁵⁷ , <i>Hbb-bh1</i> ⁵⁷ , <i>Hba-a2</i> ⁵⁷ , <i>Hba-a1</i> ⁵⁷]

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Cell Cluster #	cell cluster name	provisional cell type/state	GO ID	GO terms from 10x Genomics data	LOD score	p_{unadj}	p_{adj}	top 5 genes from 10x clusters	selected literature marker genes
			GO:0031721	hemoglobin alpha binding	3.18	1.63E-08	≤0.001		
			GO:0048821	erythrocyte development	2.07	6.14E-06	0.01		
24	Ihh + chondrocyte (chonIhh+)	chondrocyte expressing Ihh	GO:0005594	collagen type IX trimer	2.90	6.82E-07	0.003	[<i>Col2a1</i> , <i>Col11a1</i> , <i>Hapln1</i> , <i>Col9a3</i> , <i>Col9a1</i>]	[<i>Acan</i> ³ , <i>Col2a1</i> ³ , <i>Ihh</i> ³ , <i>Mef2c</i> ³ , <i>Pth1r</i> ⁷⁴ , <i>Runx2</i> ⁷⁴ , <i>Sox9</i> ¹⁴]
			GO:0002063	chondrocyte development cartilage development	1.81	2.69E-10	≤0.001		
			GO:0060351	involved in endochondral bone morphogenesis	1.78	7.57E-09	≤0.001		
			GO:0045667	regulation of osteoblast differentiation	1.08	2.97E-09	≤0.001		

* Two markers of mast cells that are not expressed in macrophages are seen in this cluster.

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