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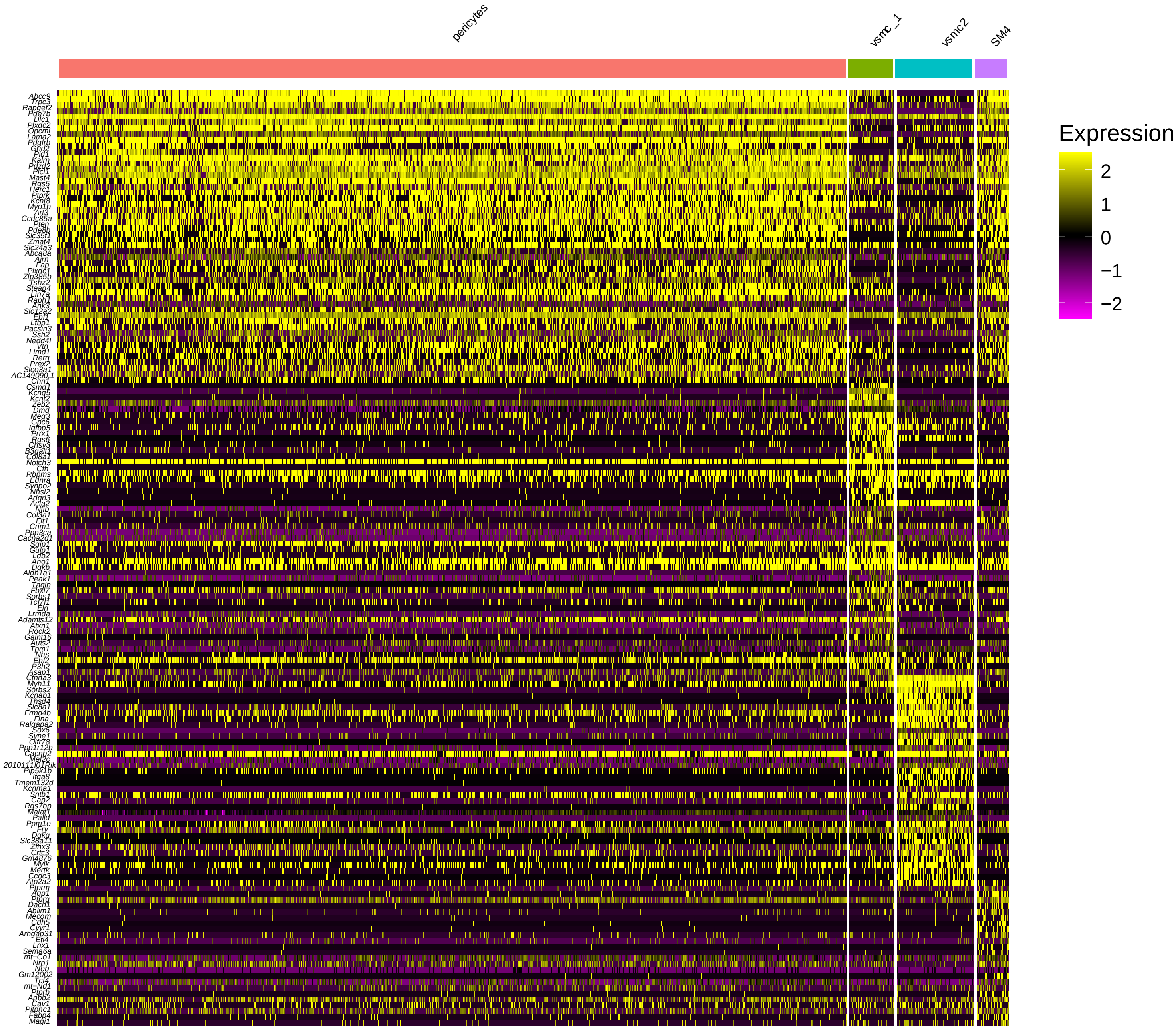
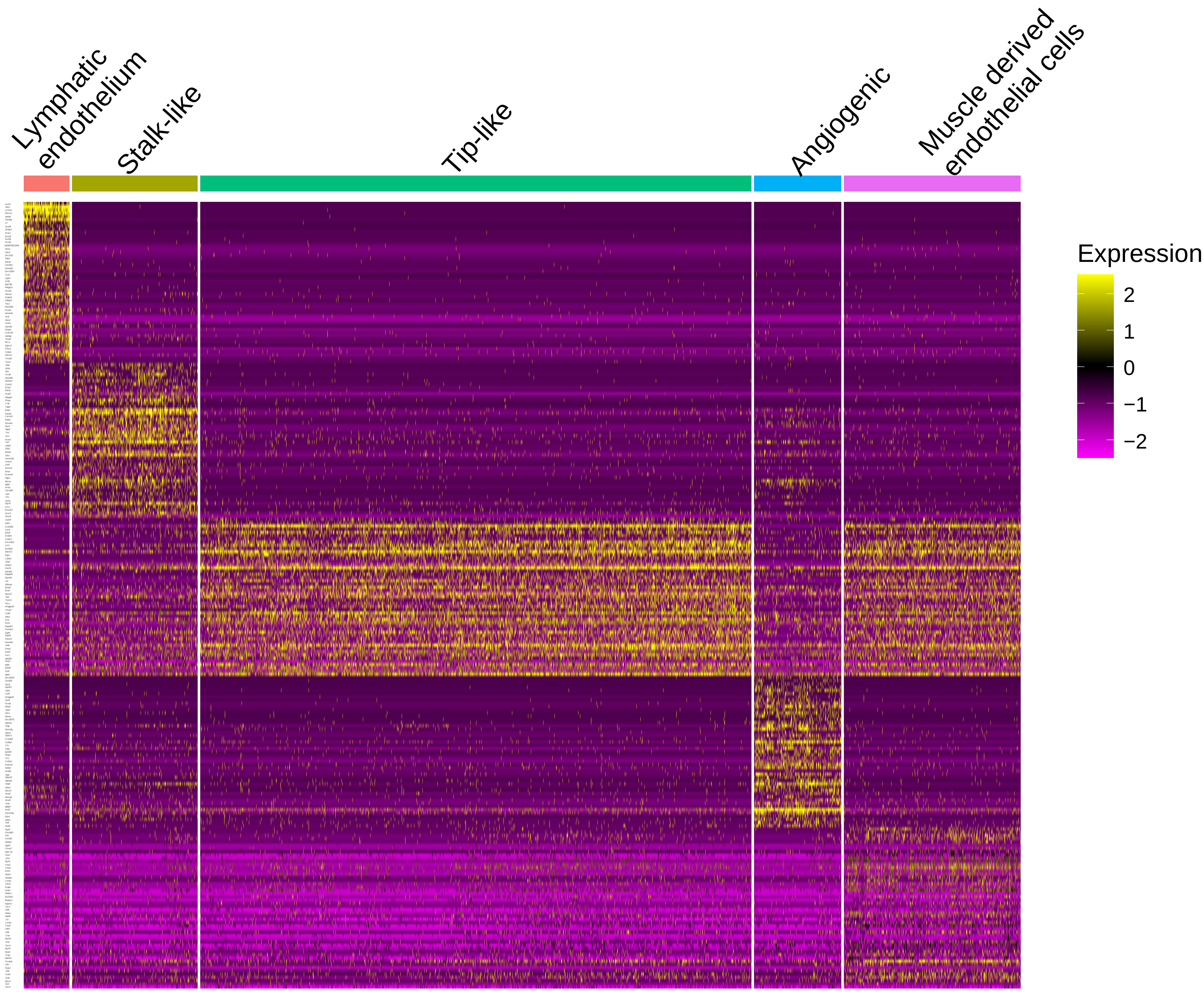


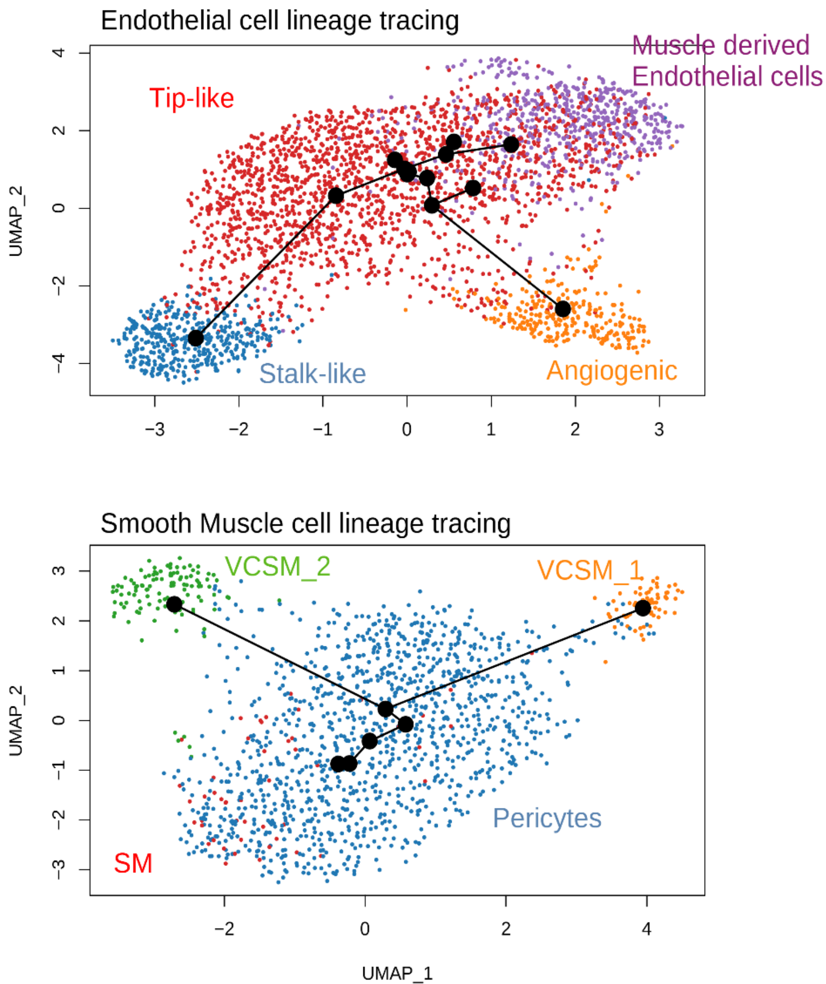
Supplementary Fig. 1: Heat maps mouse: Smooth muscle subclusters
Heatmap of significant marker genes among mouse Smooth muscle cell types. All significant marker genes (Supplementary Data 2) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).



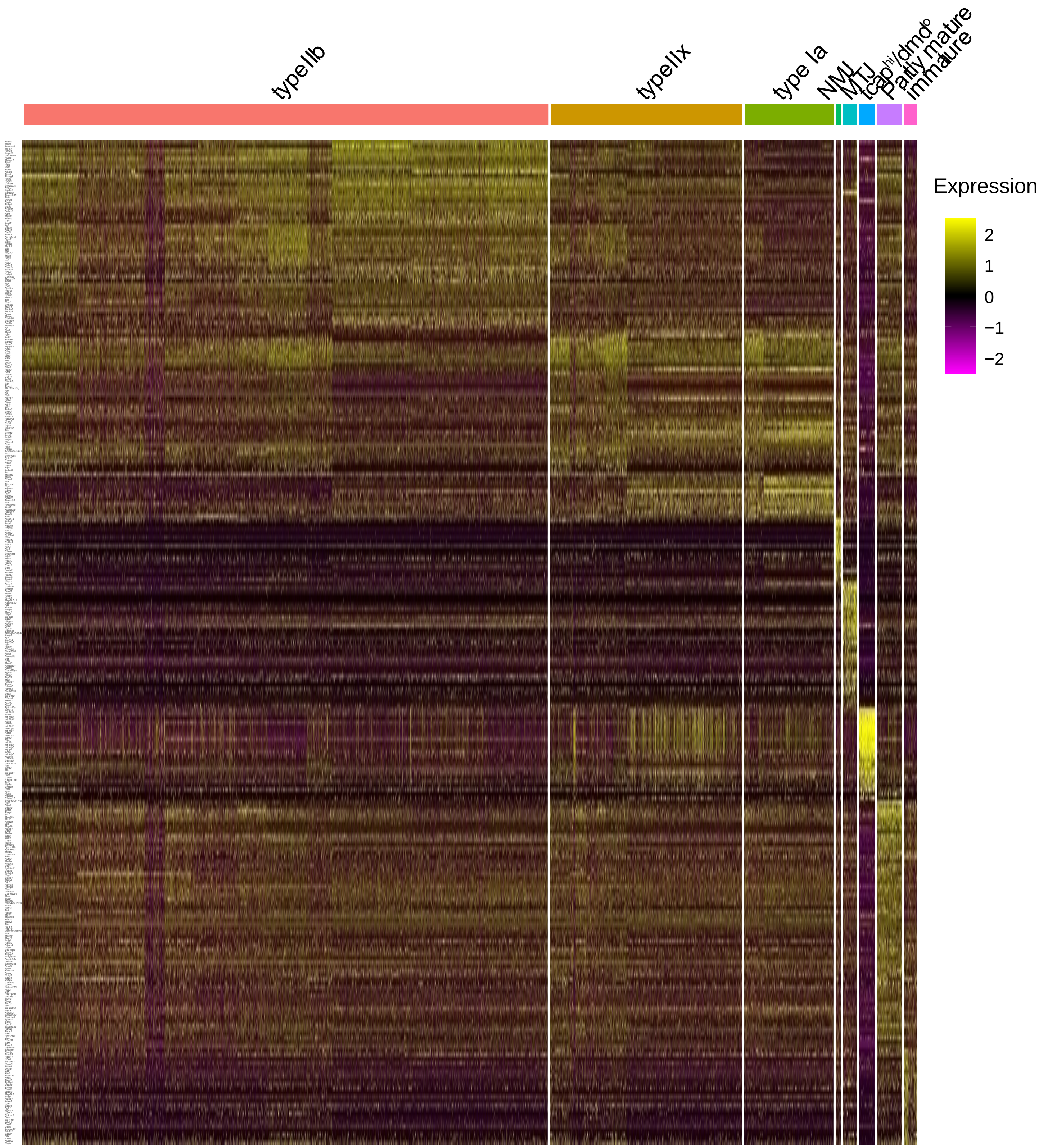
Supplementary Fig. 2: Heat maps mouse: Endothelial subclusters
Heatmap of significant marker genes among mouse Endothelial cell types. All significant marker genes (Supplementary Data 2) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).

a.

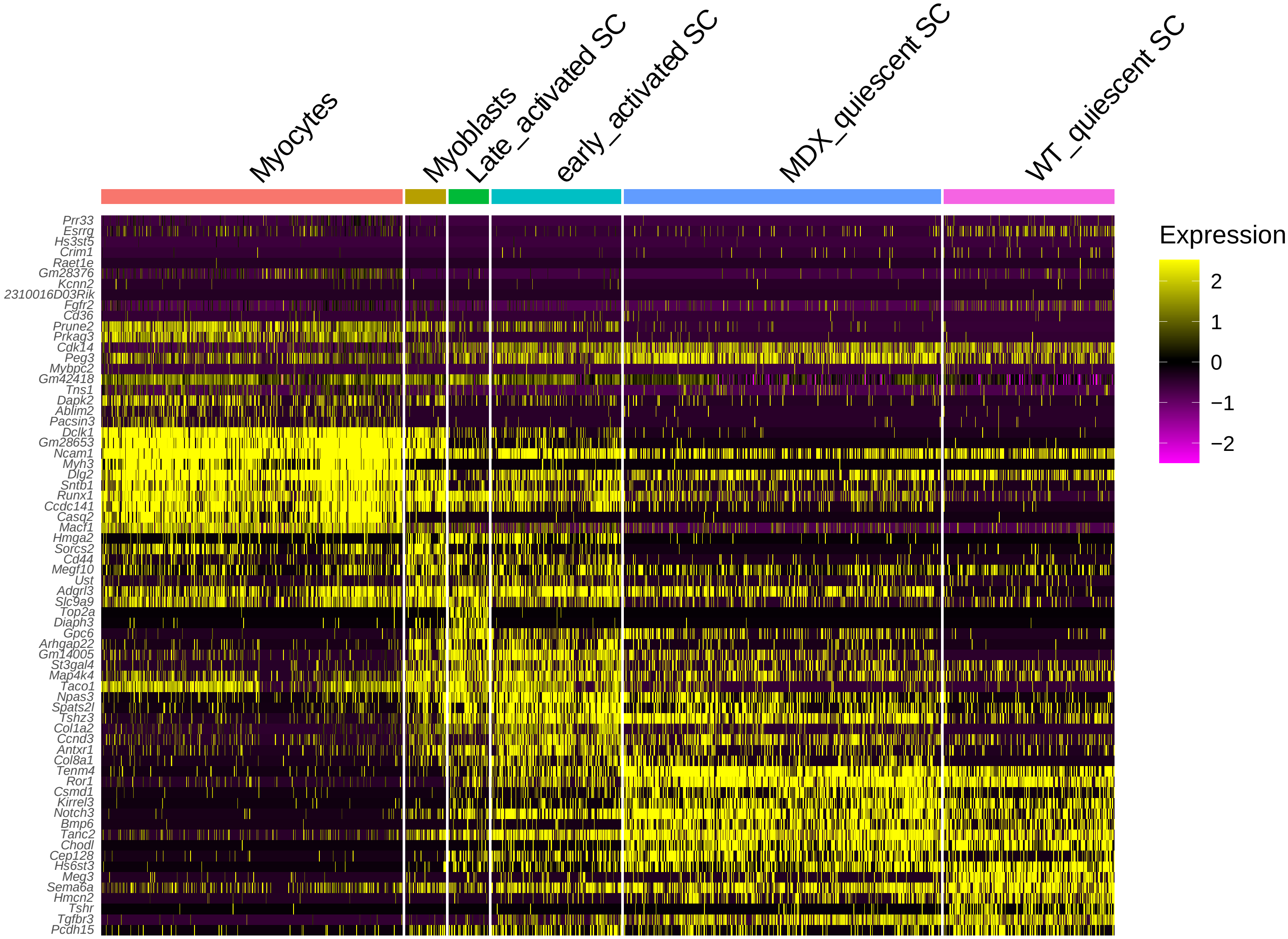
b.



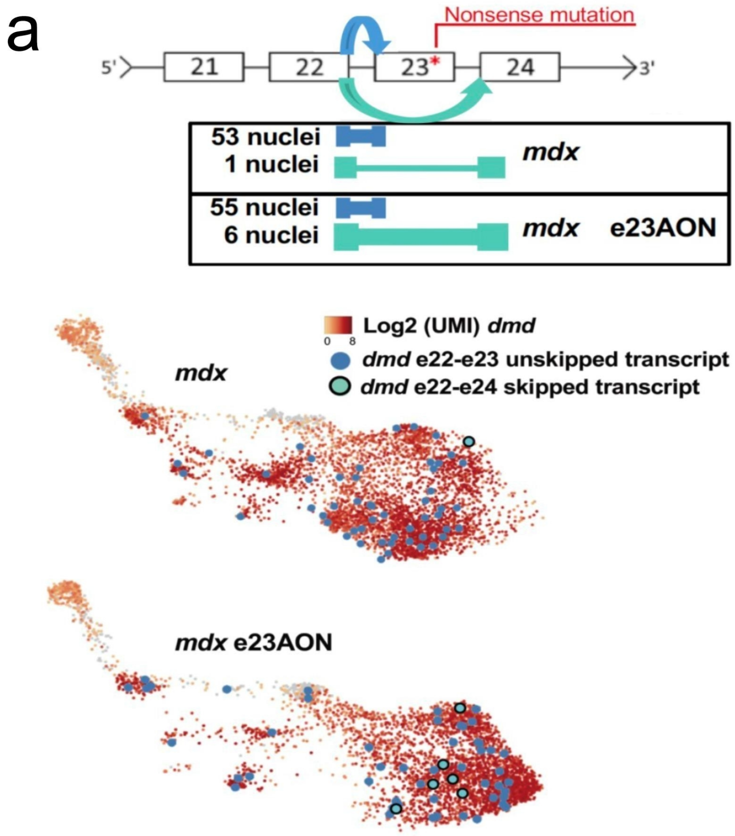
Supplementary Fig. 3. Lineage tracing analysis of subpopulations identifies functional relatedness of endothelial and smooth muscle sub populations.
Lineage tracing analysis of (**a**) Endothelial subpopulations, (**b**) Smooth muscle subpopulations. Subcluster populations are labeled with adjacent, color matched text.



Supplementary Fig. 4: Heat maps mouse: Myofiber subclusters
Heatmap of significant marker genes among mouse myofiber cell types. All significant marker genes (Supplementary Data 2) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).

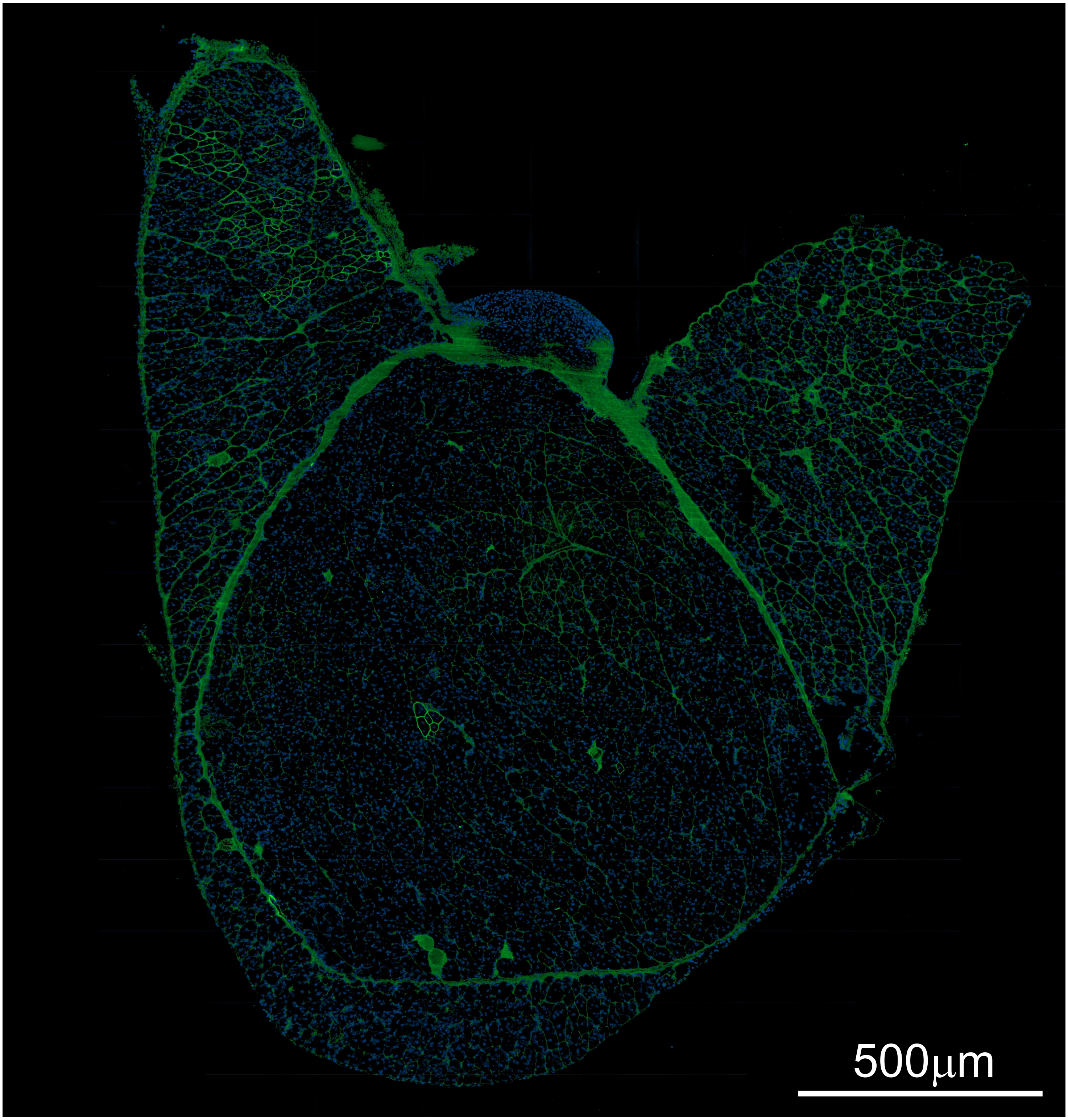


Supplementary Fig. 5: Heat maps mouse: Myoprogenitor subclusters
Heatmap of significant marker genes among mouse Myoprogenitor cell types. All significant marker genes (Supplementary Data 2) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).

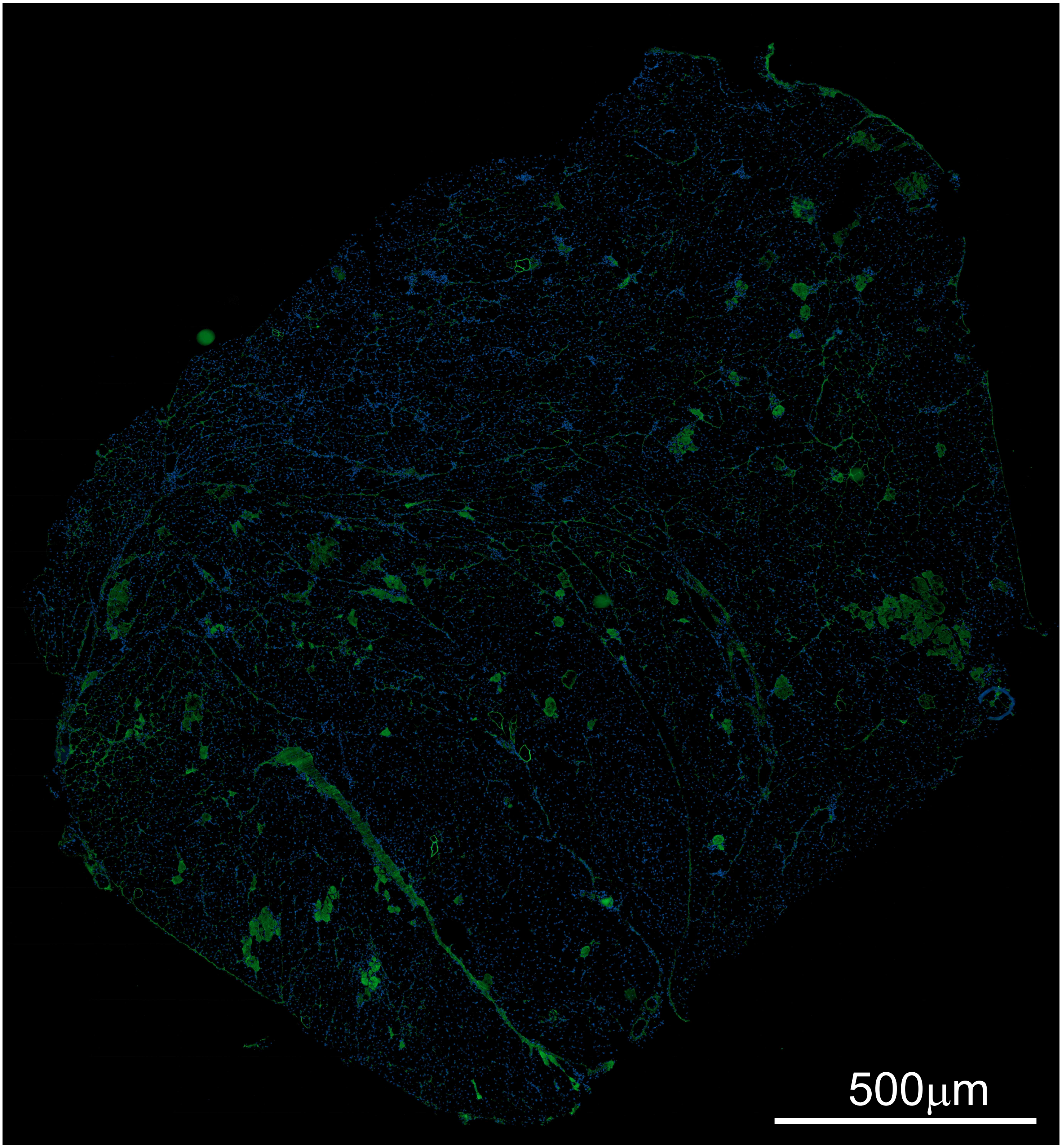


Supplementary Fig. 6 Exon skipping events are mapped to specific nuclei in e23AON-treated *mdx*

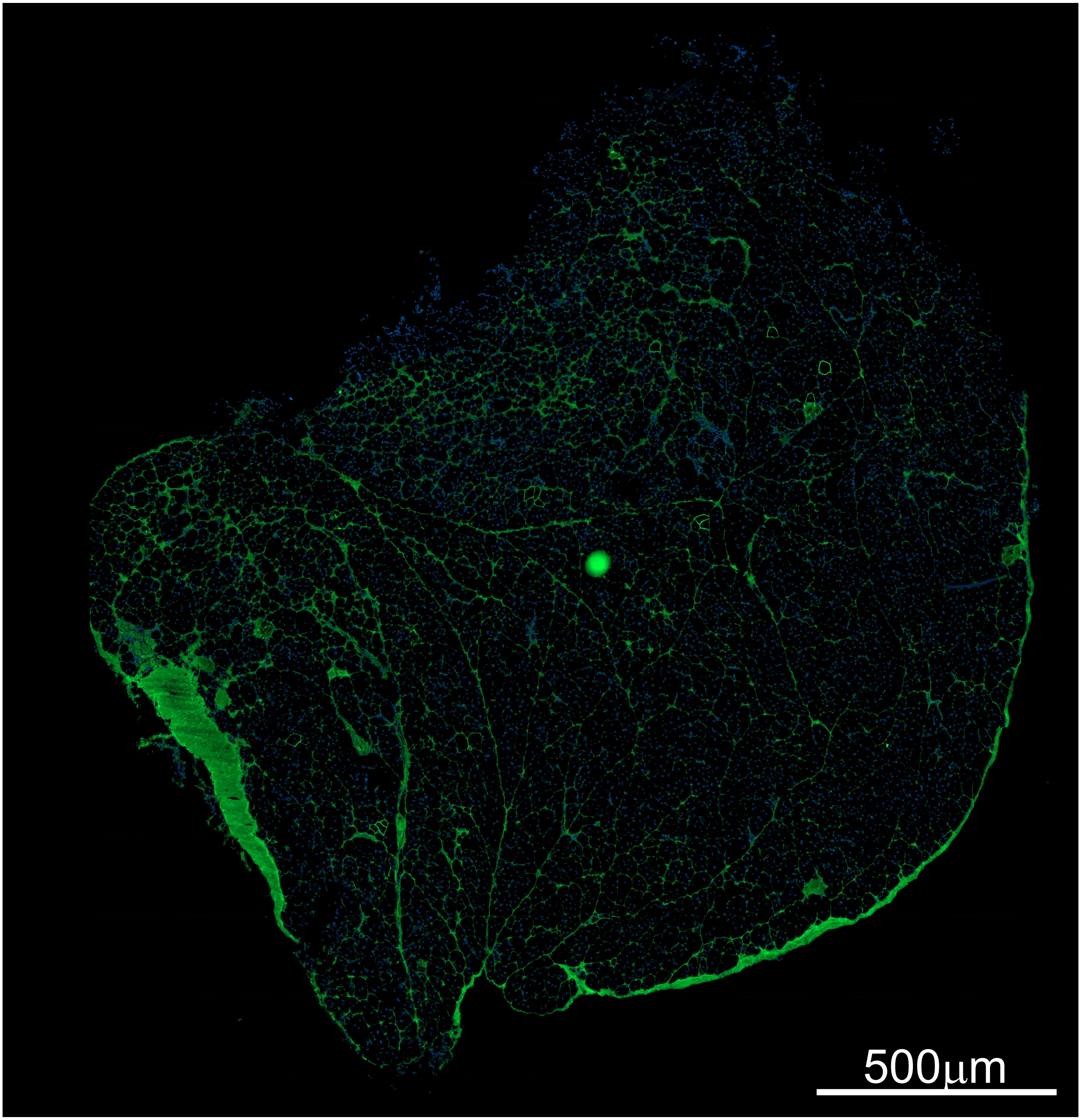
Diagram of *Dmd* expression and e22-e24 *Dmd* exon skipping. Number of nuclei containing *Dmd* e22-e24 (skipped light blue) and e22-e23 (unskipped dark blue) junction reads are shown to the left of the splicing events for each treatment condition. Nuclei where e22-e24 was observed are color coded on the UMAP of myolineage nuclei (from Fig. 3a) with overall *Dmd* abundance shown (Yellow-Red color scale).



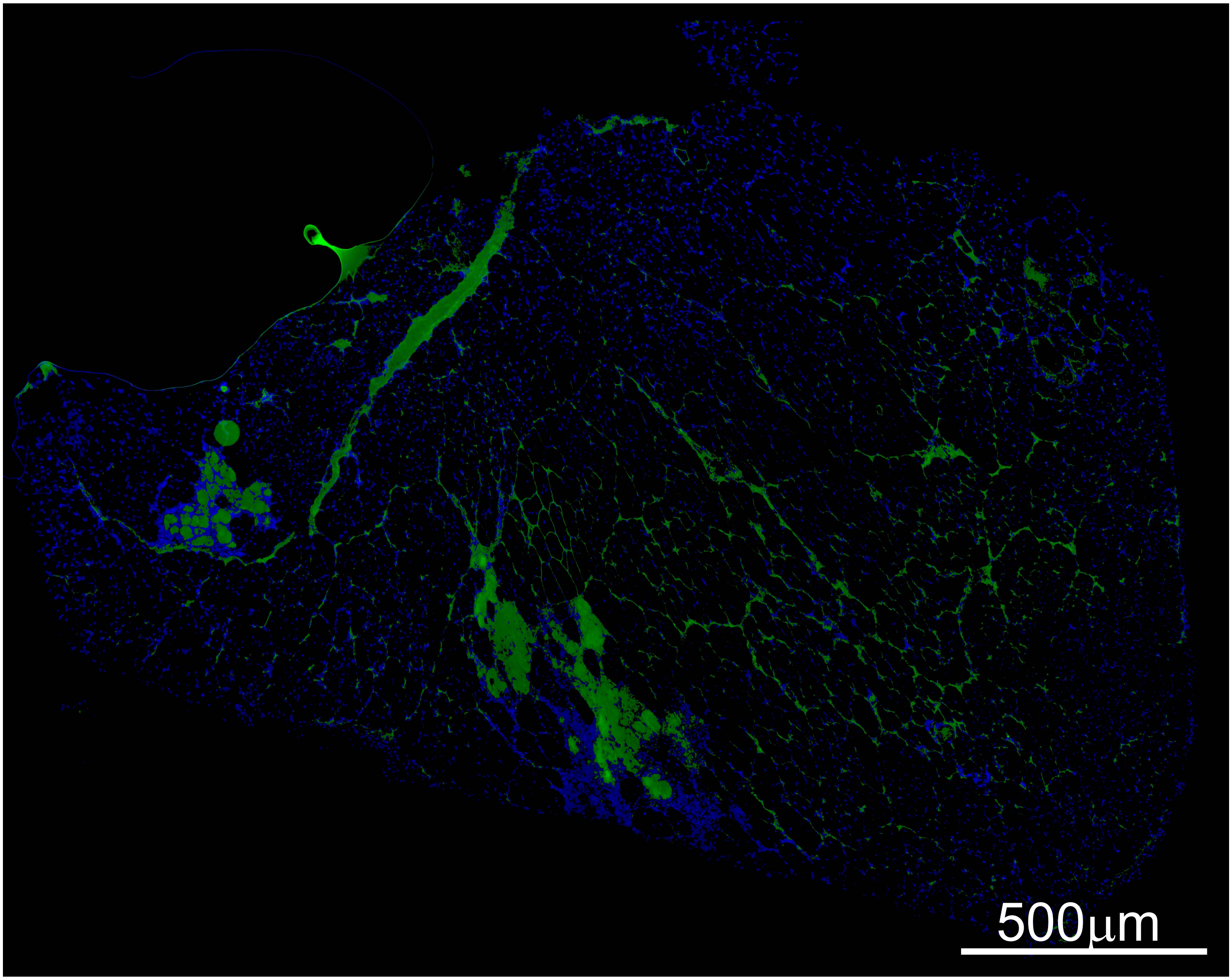
Supplementary Fig. 7. Dystrophin staining MOUSE 25 – *mdx*
Whole quadricep muscles from untreated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500μm



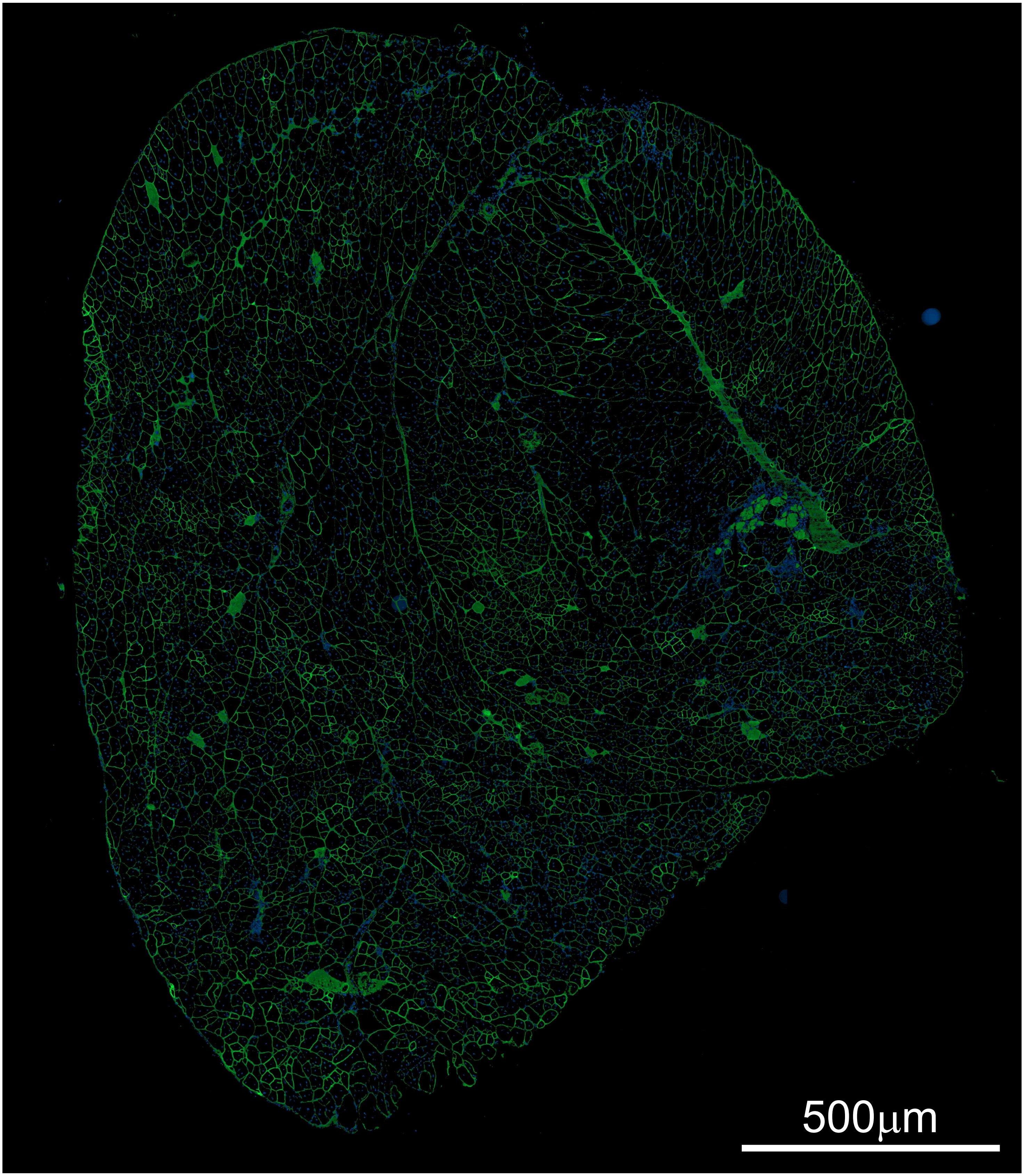
Supplementary Fig. 8. Dystrophin staining MOUSE 73 - *mdx*:
Whole quadricep muscles from untreated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500μm



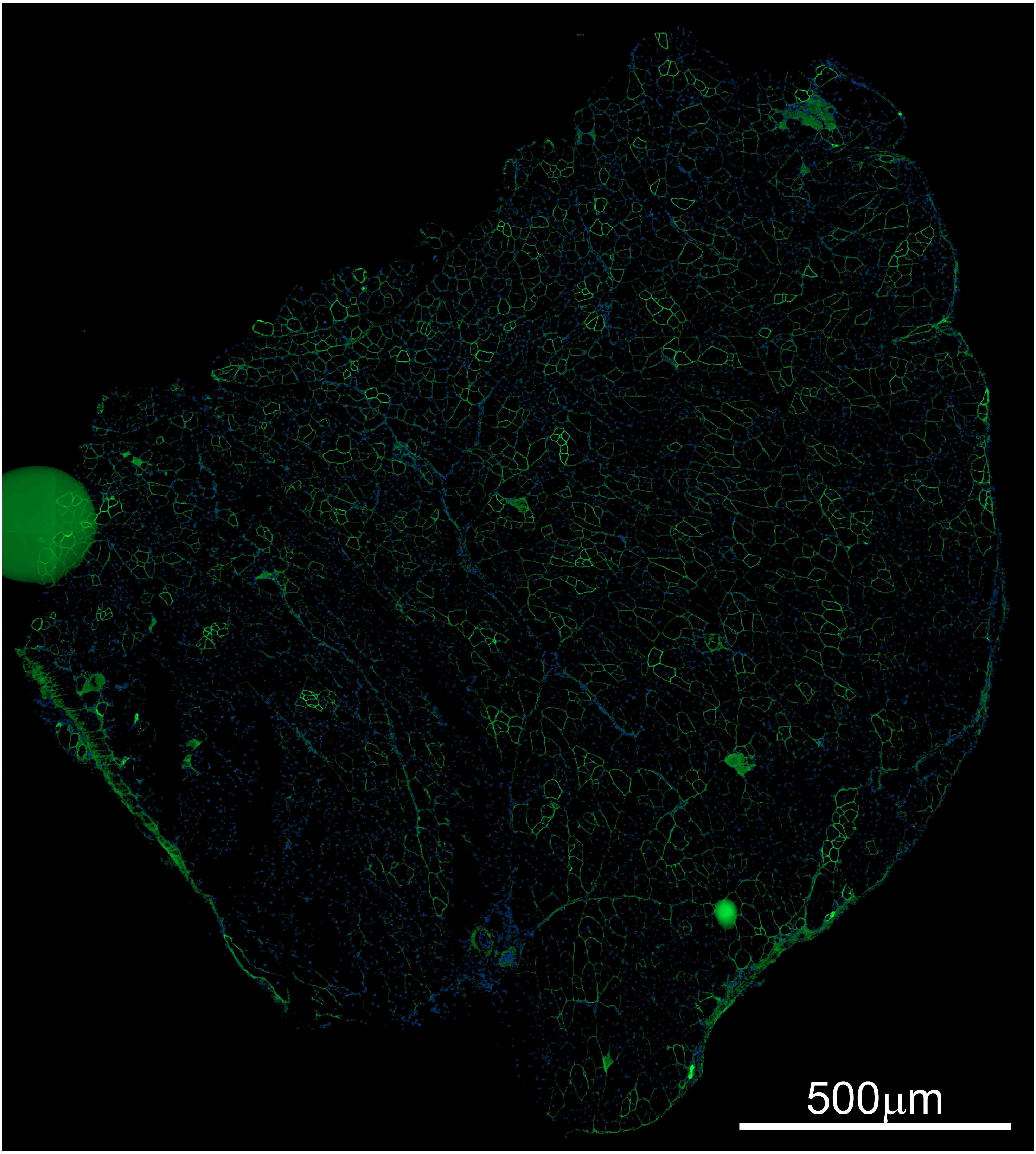
Supplementary Fig. 9. Dystrophin staining MOUSE 128 - *mdx*:
Whole quadricep muscles from untreated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500µm



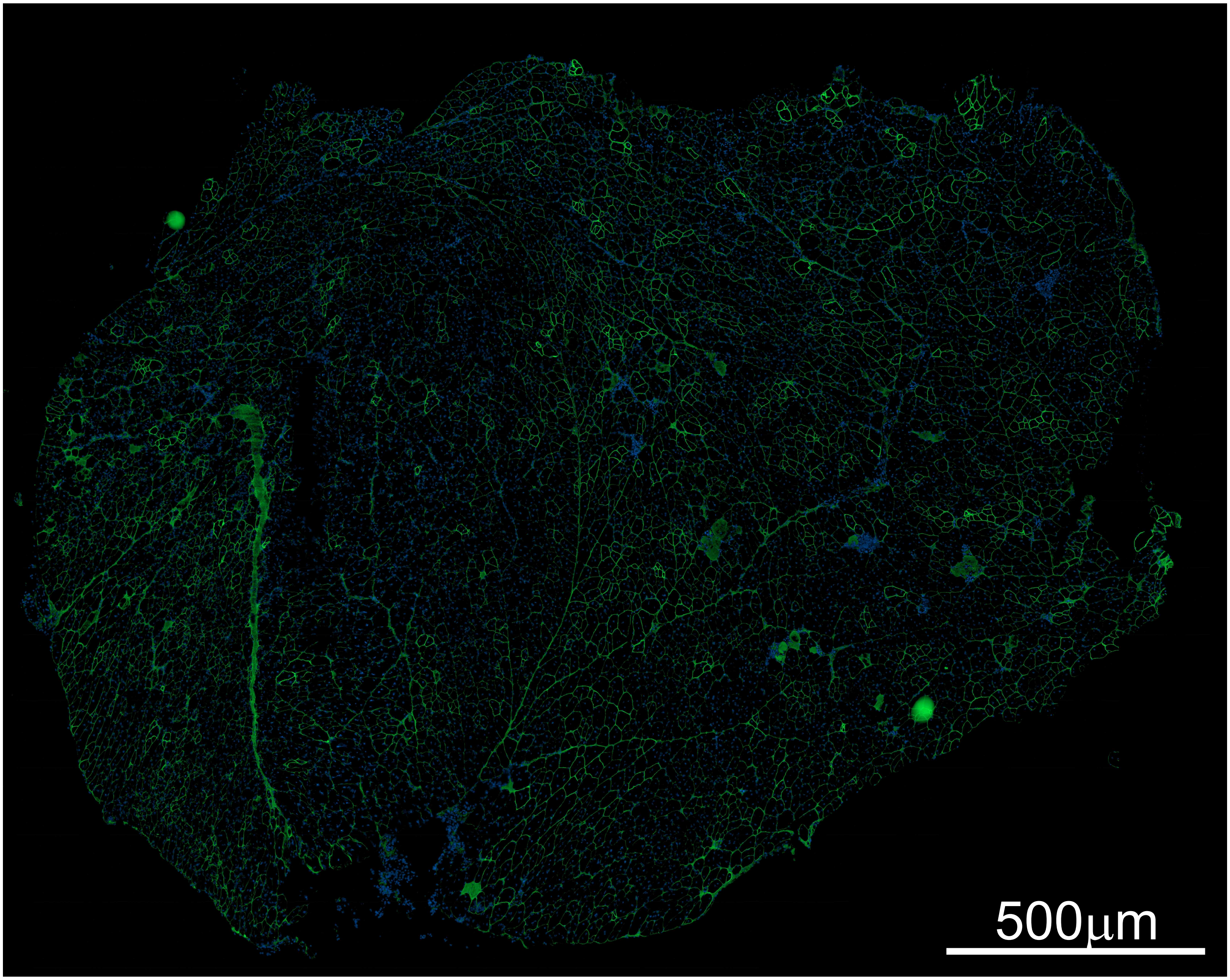
Supplementary Fig. 10. Dystrophin staining MOUSE 155 - *mdx*:
Whole quadricep muscles from untreated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500μm



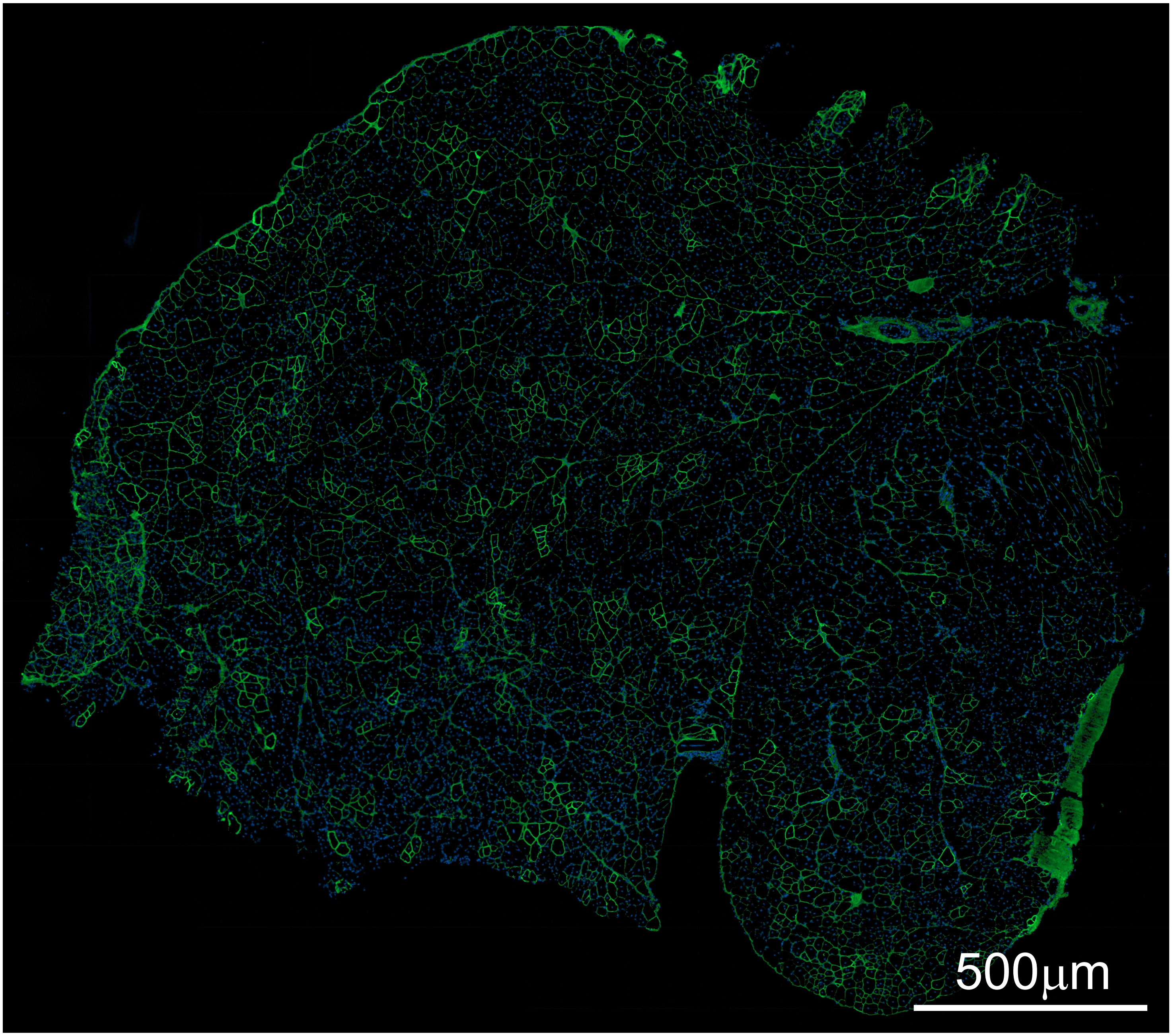
Supplementary Fig. 11. Dystrophin staining MOUSE 43 - *mdx* e23AON:
Whole quadricep muscles from e23AON treated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500μm



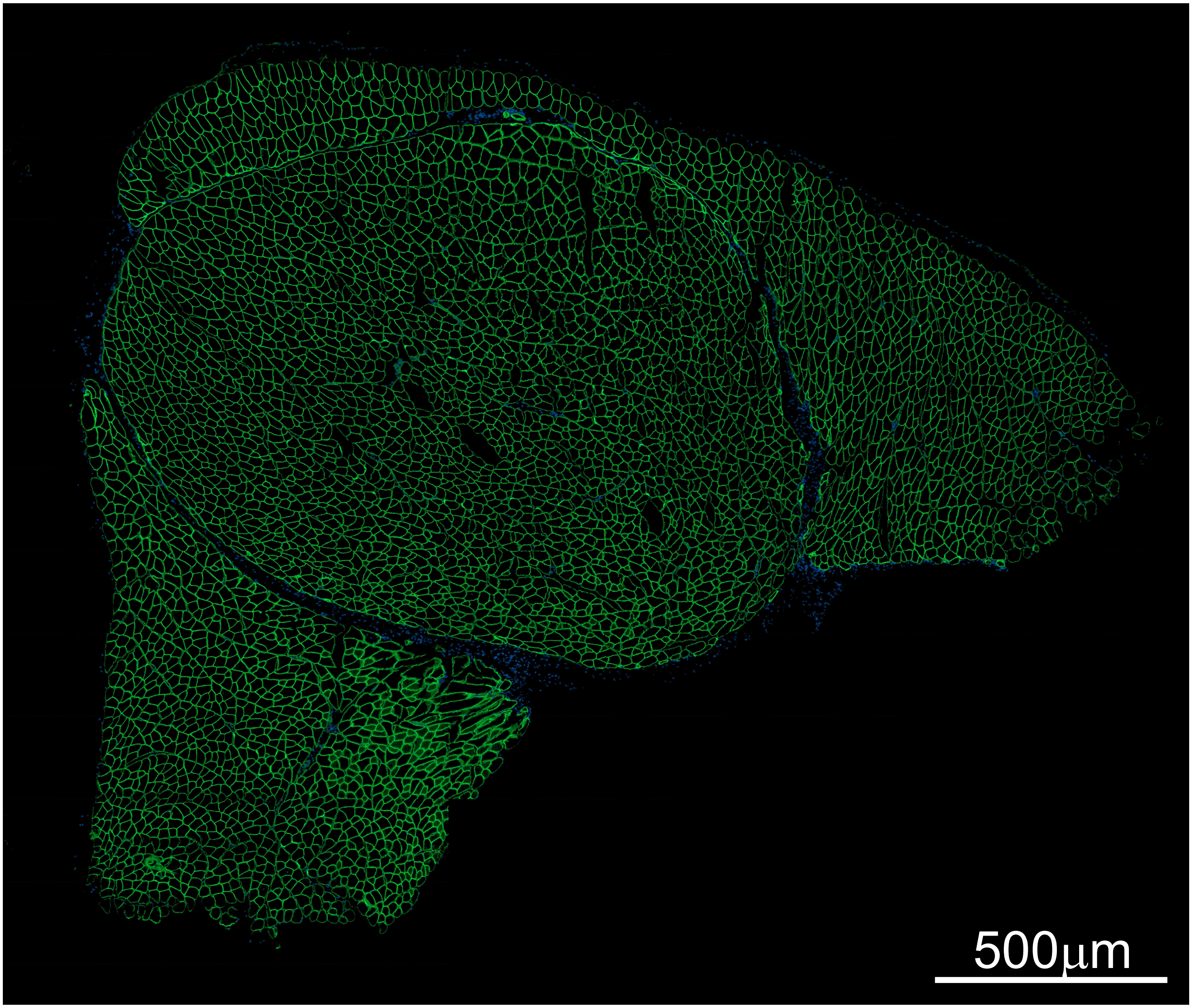
Supplementary Fig. 12. Dystrophin staining MOUSE 45 - *mdx* e23AON:
Whole quadricep muscles from e23AON treated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500µm



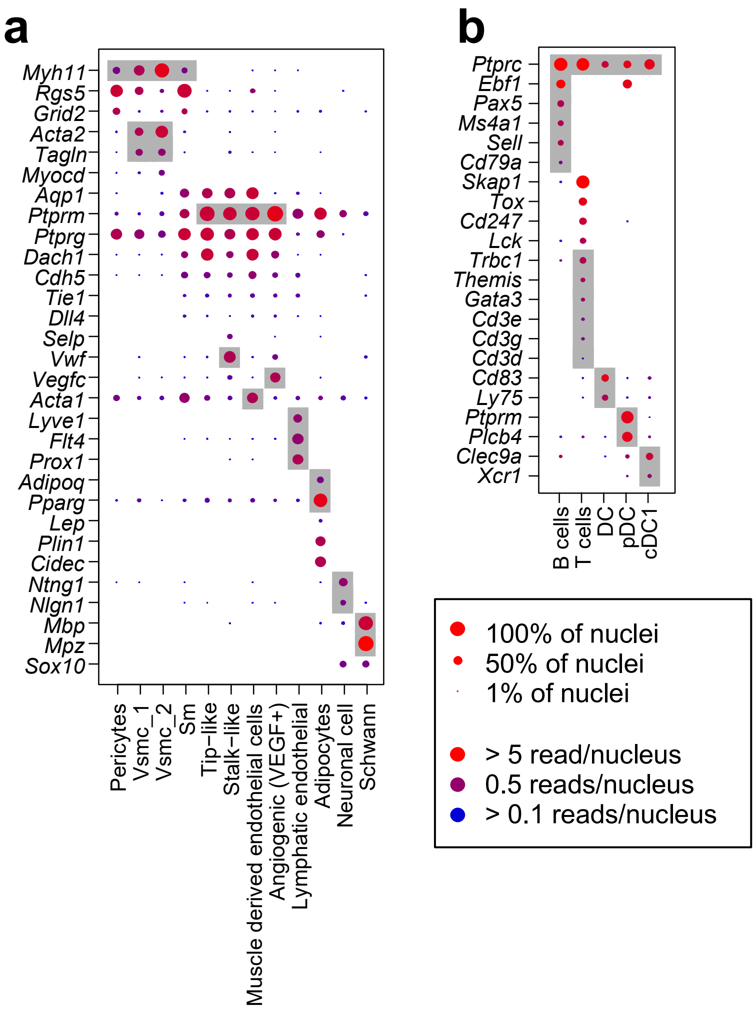
Supplementary Fig. 13. Dystrophin staining MOUSE 152 - *mdx* e23AON:
Whole quadricep muscles from e23AON treated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500μm



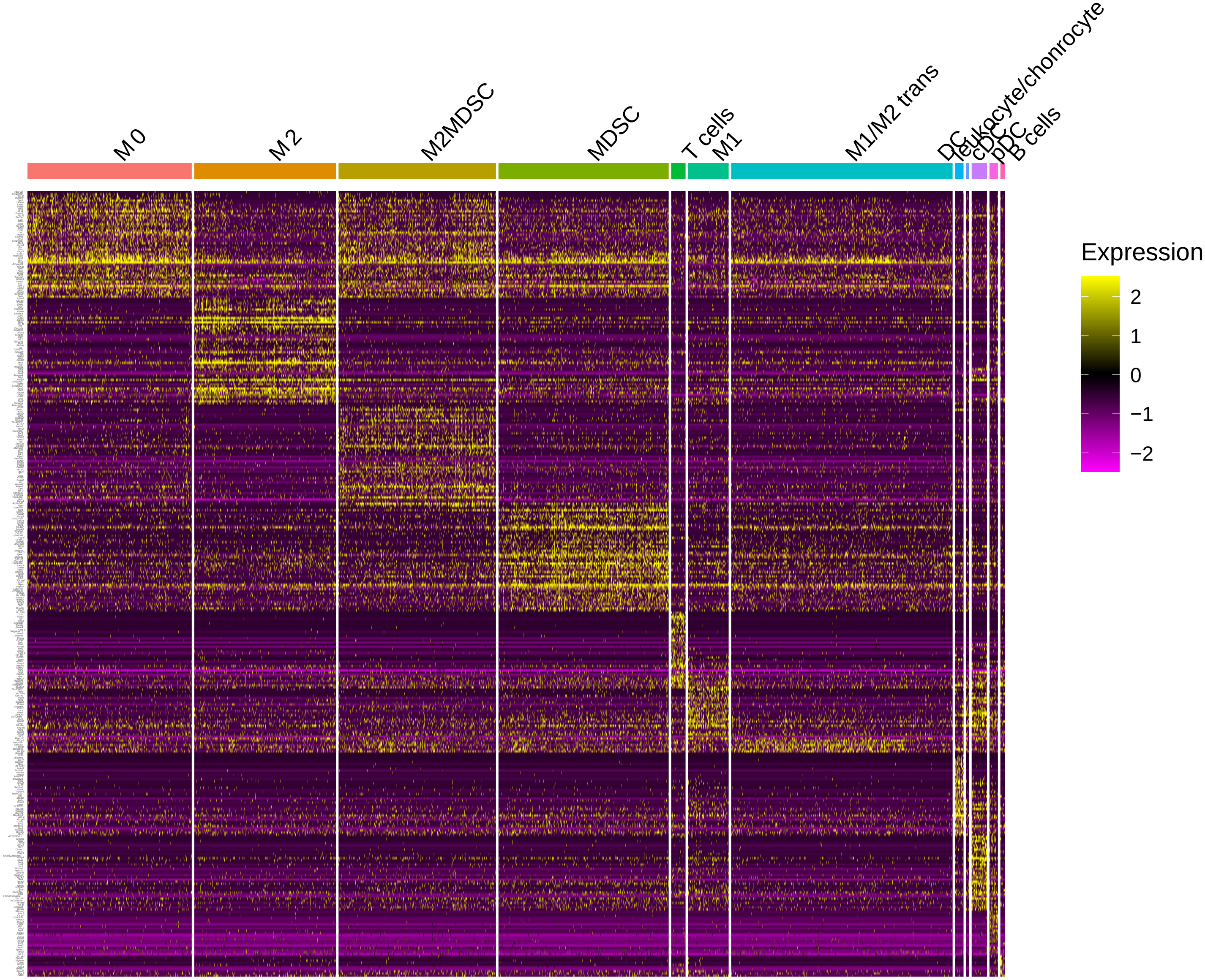
Supplementary Fig. 14. Dystrophin staining MOUSE 169 – *mdx* e23AON:
Whole quadricep muscles from e23AON treated *mdx* was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500μm



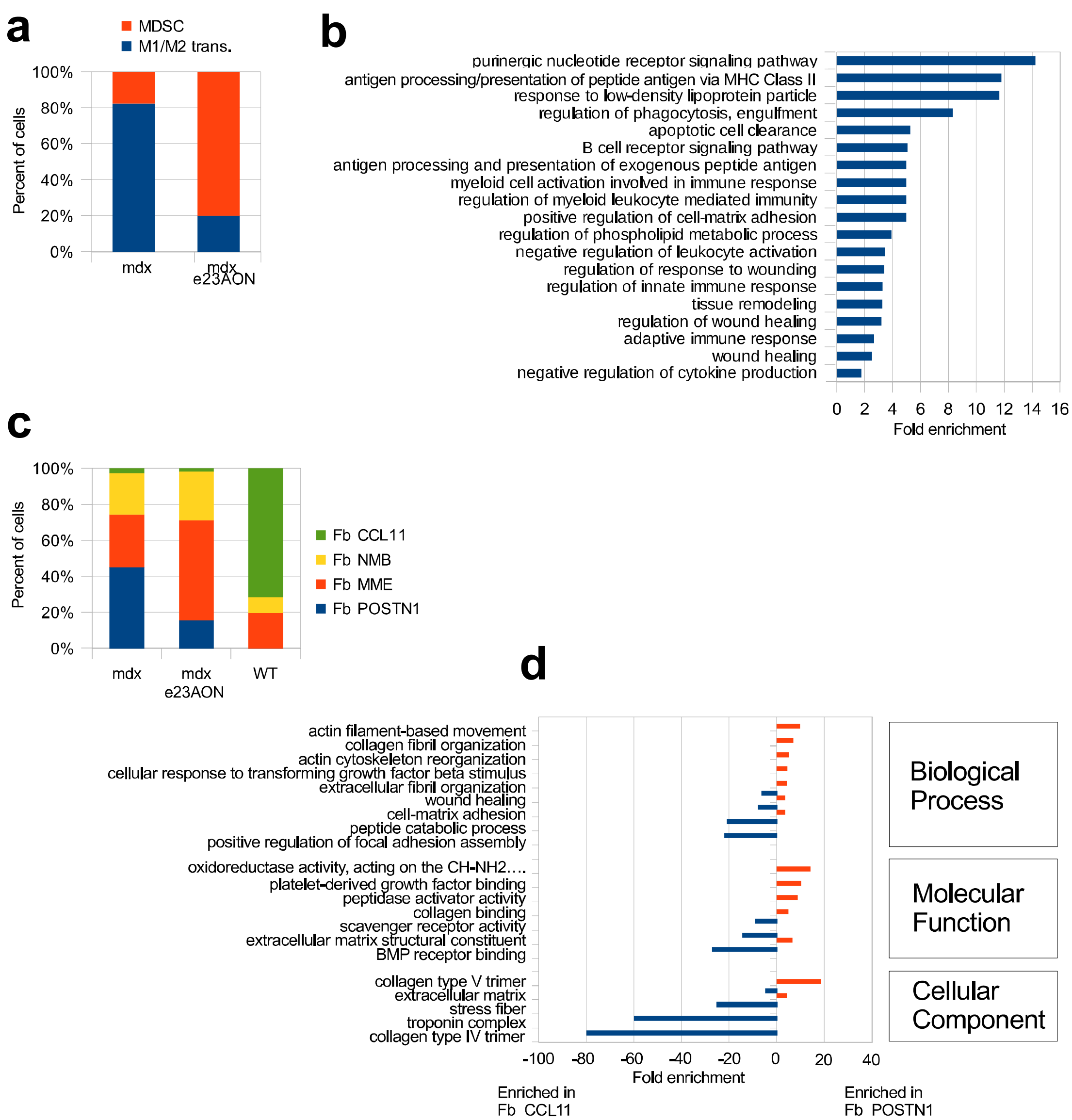
Supplementary Fig. 15. Dystrophin staining MOUSE c57 WT:
Whole quadricep muscles from c57 WT was frozen, cryosectioned and subjected to immunofluorescent staining for dystrophin protein (green). Scale bar = 500µm



Supplementary Figure 16: Cell type identity based on expression of significantly expressed genes (additional cell types)
Gene expression differences between subtypes of major cell classes, not shown in other figures within the main text. (**a**) endothelial, smooth muscle, other. (**b**) non-macrophage immune cells, Subtype names indicated on x-axis, gene names indicated on y-axis. Log2 (Average gene expression) for each subtype shown by Blue-Red gradient. Percentage of cells expressing genes from 0% to 100% indicated by dot size. Gray background indicates known markers of the respective cell type on x-axis. Marker genes are listed in Supplementary Data 2, 3a.

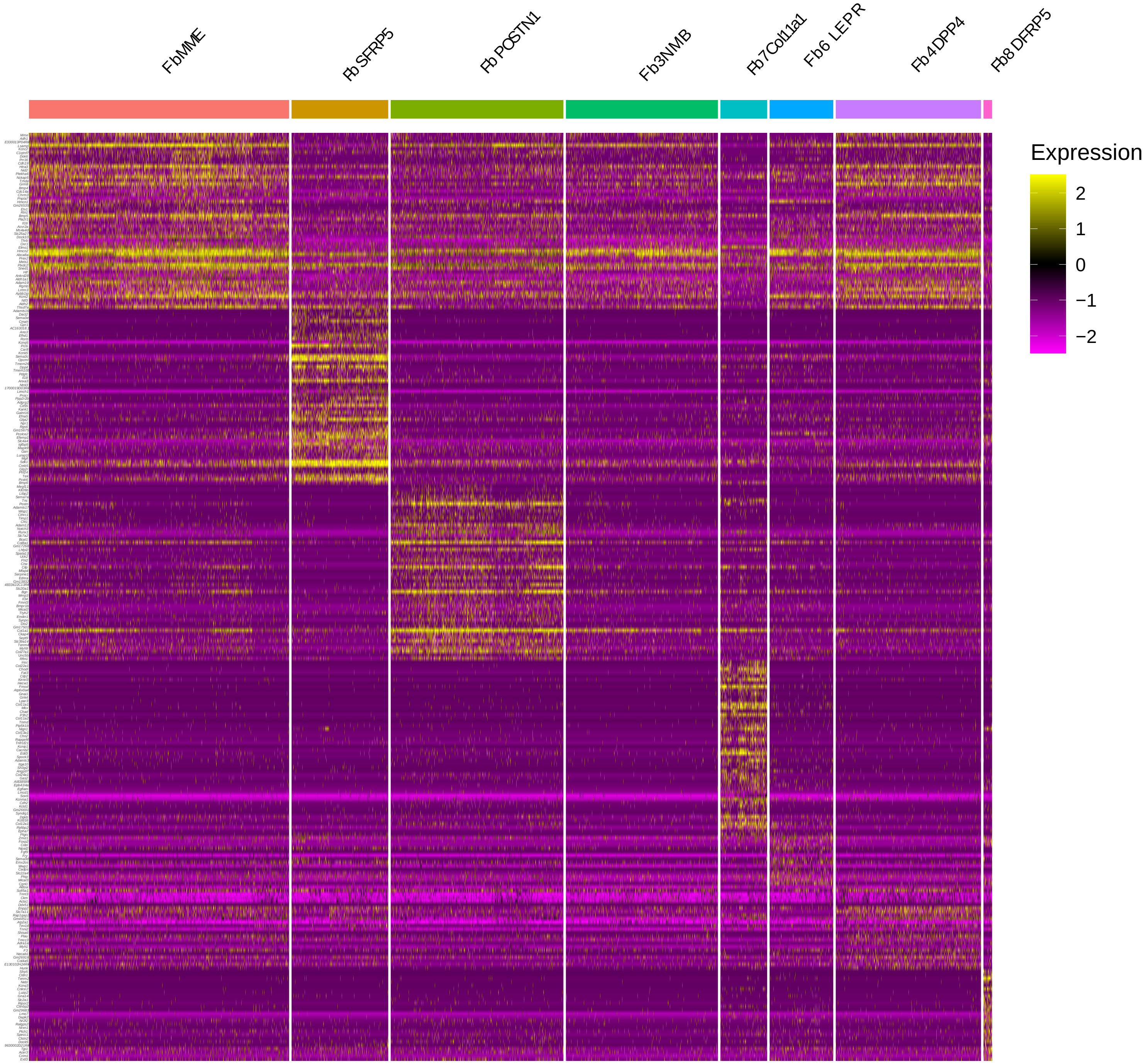


Supplementary Fig. 17: Heat maps mouse: Immune cell subclusters
Heatmap of significant marker genes among mouse Immune cell types. All significant marker genes (Supplementary Data 2) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).

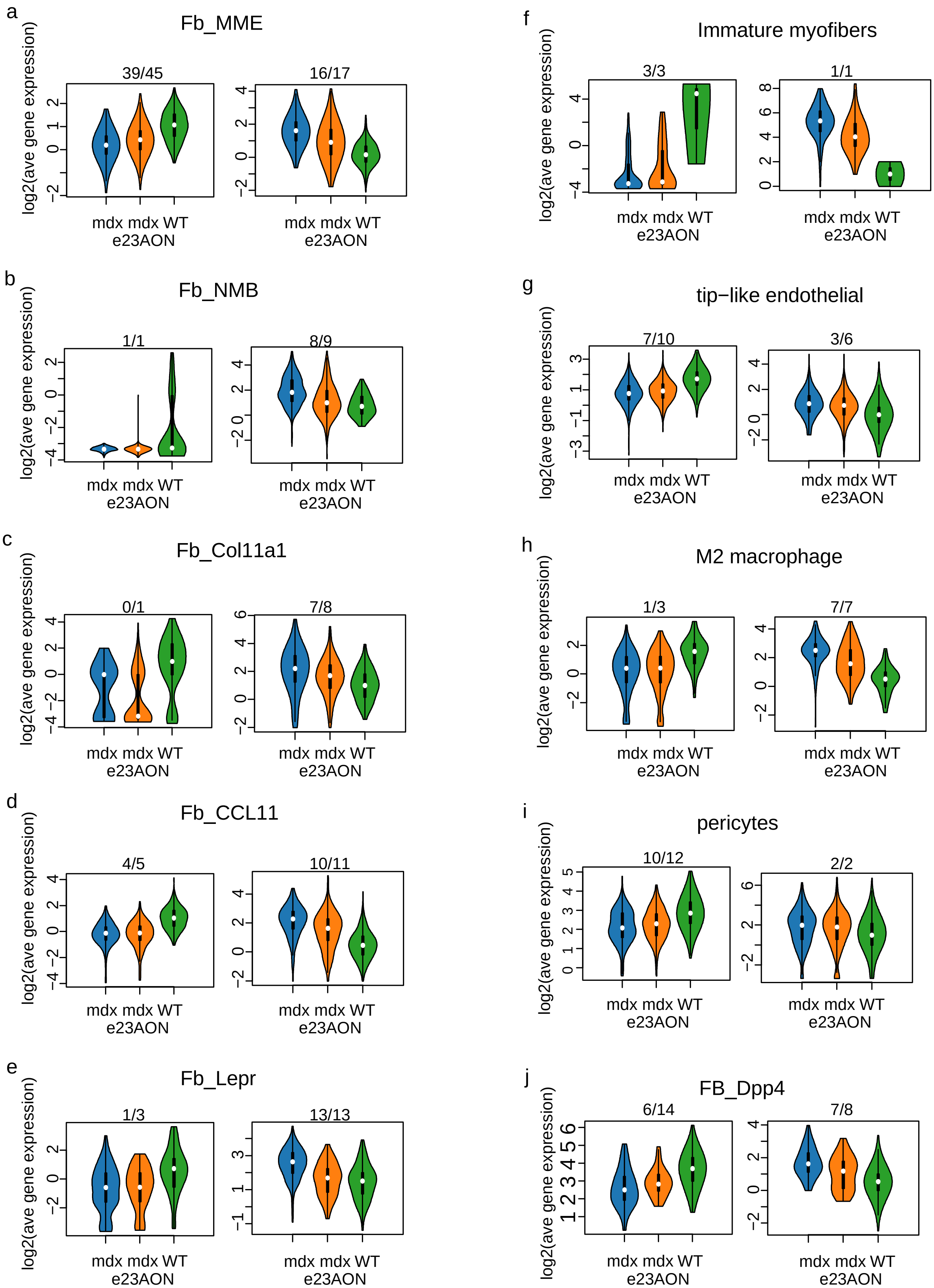


Supplementary Figure 18: Biological processes and proportional shift in immune and fibroblast cell types

(**a**) Depletion of M1/M2 trans and expansion of MDSC with e23AON treatment. Y-axis shows the relative percentage M1/M2 trans and MDSC populations in *mdx* and *mdx* e23AON. (**b**) Representative list of enriched GO terms (Y-axis) based on genes upregulated in MDSC relative to M1/M2 trans. Fold enrichment indicated on x-axis. List of DE Genes between MDSC and M1/M2 transitional cells listed in Supplementary Data 5. (**c**) Relative changes in cell proportions of Fb CCL11 and Fb POSTN1 populations and WT intermediates (Fb MME and Fb NMB) between *mdx*, *mdx* e23AON and WT conditions, Y-axis shows percentages of cell types (**d**) Representative list of enriched GO terms (Y-axis) based on genes differentially expressed between Fb CCL11 and Fb POSTN1. Fold enrichment indicated on x-axis, >0 shows GO terms enriched for genes upregulated in Fb POSTN1, <0 shows GO terms enriched for genes upregulated in Fb CCL11. List of DE Genes between Fb POSTN1 and Fb CCL11 listed in Supplementary Data 6.

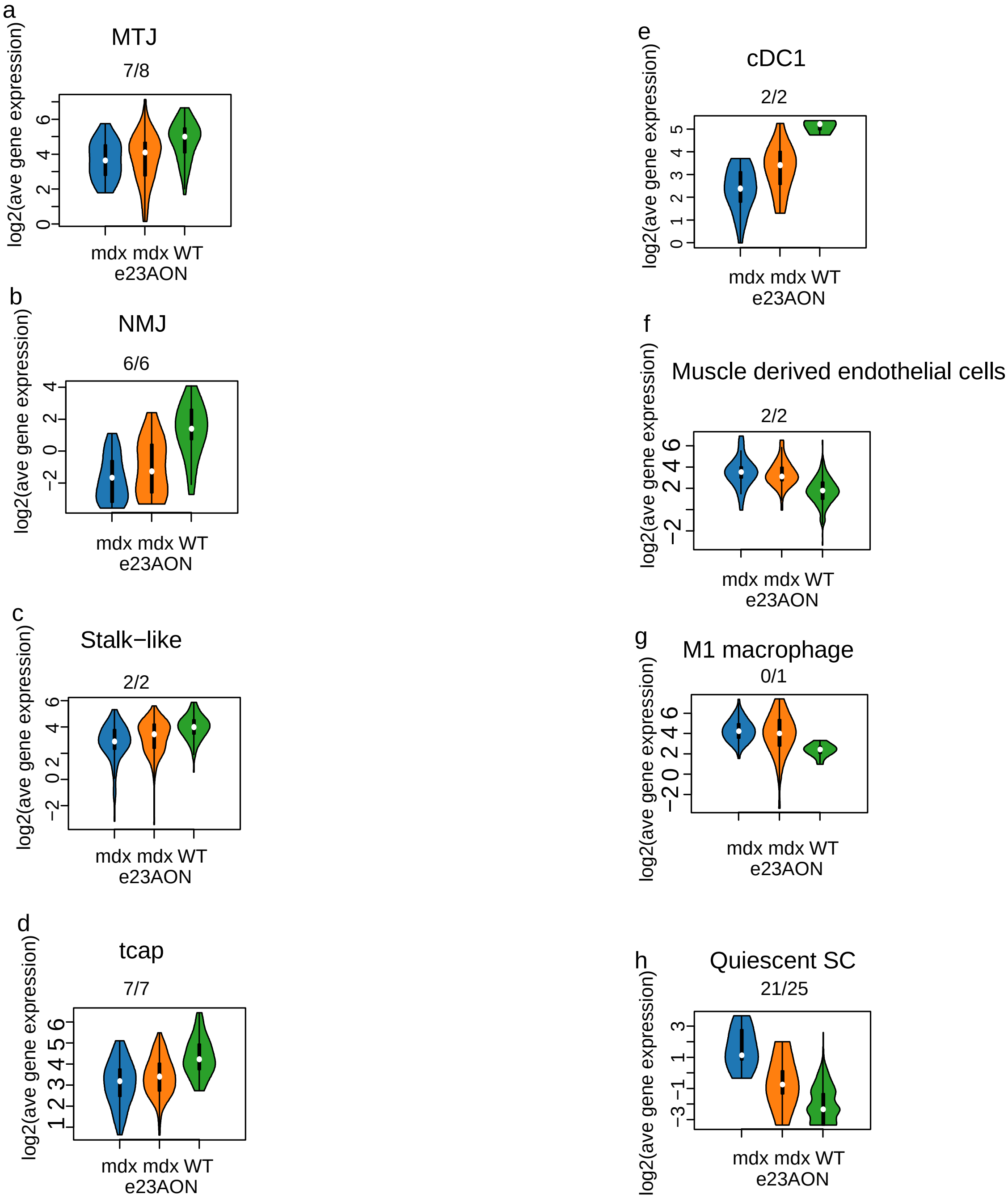


Supplementary Fig. 19: Heat maps mouse: Fibroblast subclusters
Heatmap of significant marker genes among mouse Fibroblast cell types. All significant marker genes (Supplementary Data 2) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).


a
Fb_MME
39/45
16/17
b
Fb_NMB
1/1
8/9
c
Fb_Col11a1
0/1
7/8
d
Fb_CCL11
4/5
10/11
e
Fb_Lepr
1/3
13/13
f
Immature myofibers
3/3
1/1
g
tip−like endothelial
7/10
3/6
h
M2 macrophage
1/3
7/7
i
pericytes
10/12
2/2
j
FB_Dpp4
6/14
7/8
log2(ave gene expression)
mdx mdx WT
e23AON

Supplementary Fig. 20. e23AON treatment in *mdx* shifts multiple distinct cell types towards more WT behavior (additional cell types) part 1

Average expression of genes upregulated or downregulated in WT relative to untreated *mdx*. Cell type names are listed above plot. Y axes = log2average UMI for differentially expressed genes. White dot represents mean, box = q1 to q3, thin line represents min and max values. List of Genes between WT and *mdx* are listed in Supplementary Data 1.



Supplementary Fig. 21. e23AON treatment in *mdx* shifts multiple distinct cell types towards more WT behavior (additional cell types) part 2

Average expression of genes upregulated or downregulated in WT relative to untreated *mdx*. Cell type names are listed above plot. Y axes = log2average UMI for differentially expressed genes. (**a** - **d**) no significant genes were detected to be down regulated in WT. (**e** – **h**) no significant genes were detected to be up regulated in WT. White dot represents mean, box = q1 to q3, thin line represents min and max values. List of Genes between WT and *mdx* are listed in Supplementary Data 1.

Major cell types	Healthy	*DMD*
Adipocytes	0.12	1.66
Myoblasts	0.44	4.55
Satellite cells	2.19	12.83
Immunne - Macrophages	0.96	5.35
Fibroblasts	6.26	17.35
Immune - Tcells and B cells	0.76	1.86
Endothelial cells	5.90	13.11
Myofibers	79.86	45.16
Smooth muscle cells	3.83	2.77
Immune - Mast cells	0.12	0.24

Myofibers	Healthy	*DMD*
Type I fibers	12.68	15.76
Type II-Tcap myonuclei	11.25	2.78
Type IIa fibers	26.71	11.74
Type IIx fibers	20.01	6.54
Type I-Tcap myonuclei	6.18	3.13

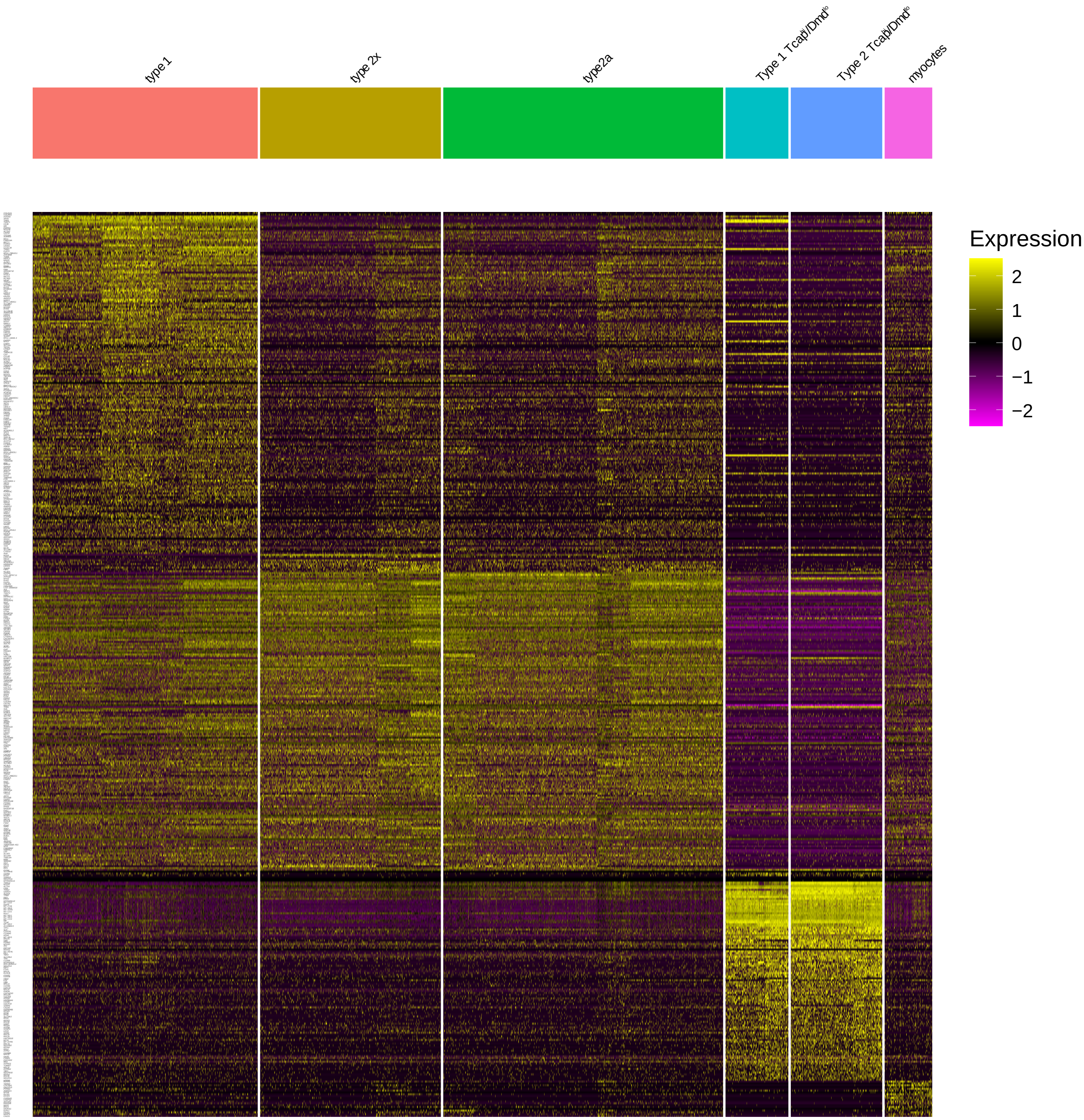
Smooth muscle cells	Healthy	*DMD*
Vsmc 1	0.12	0.70
Pericytes 1	1.04	1.29
Pericytes 2	2.03	0.26
Vsmc 2	0.60	0.52

Macrophages	Healthy	*DMD*
Mac 4	0.08	0.87
Mac 1	0.24	2.51
Mac 2	0.28	1.07
Mac 3	0.36	0.81

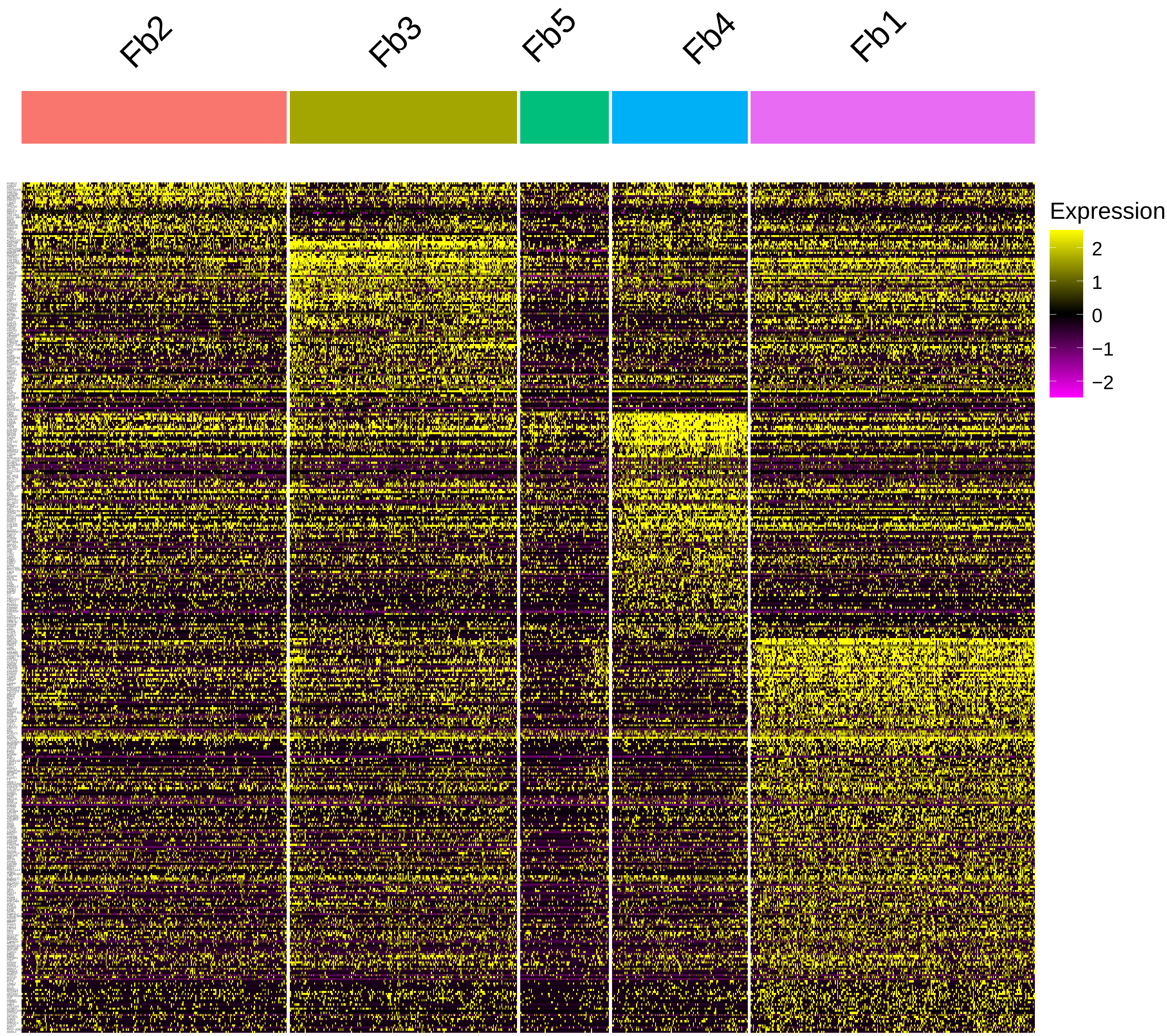
Fibroblasts/ FAPS	Healthy	*DMD*
Fb 1	0.00	5.90
Fb 2	0.36	5.31
Fb 4	0.44	2.58
Fb 5	1.72	0.90
Fb 3	3.75	2.67

Endothelial cells	Healthy	*DMD*
Stalk-like	1.24	5.22
Angiogenic	1.00	1.90
Tip-like	3.67	5.25

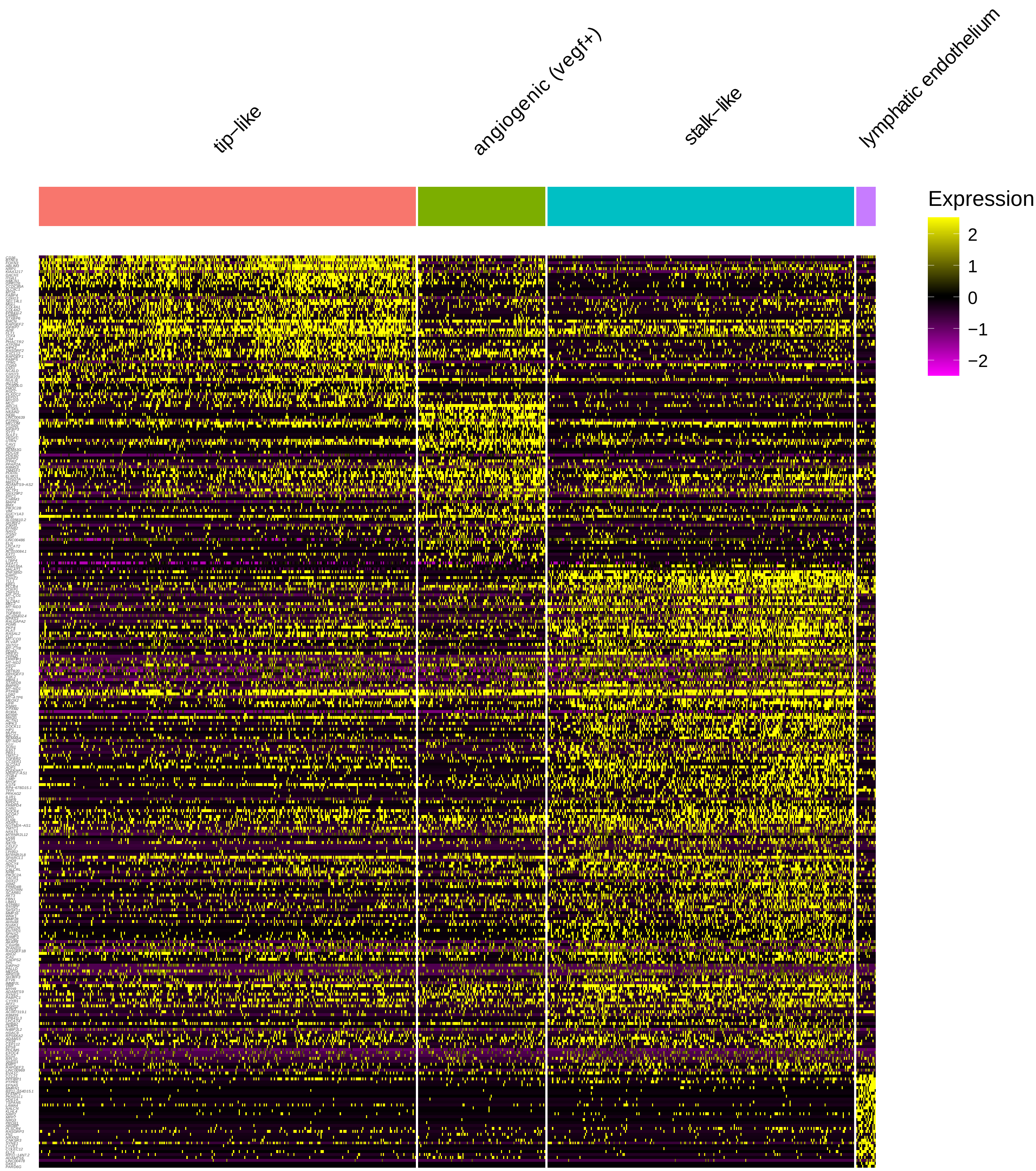
Supplementary Figure 22: Frequencies of cell subsets in human muscle tissue
Frequencies of cell populations identified in human healthy and DMD muscle. Percentages for each cell population named in the 1st column for healthy individuals and in the 2nd column for DMD affected individuals. Following the major cell types, cell types are further broken down to their respective subclusters. Yellow = increase and Blue = decrease in DMD percentage relative to healthy. Subsets within categories are listed in order of decreasing magnitude of difference between DMD and healthy.



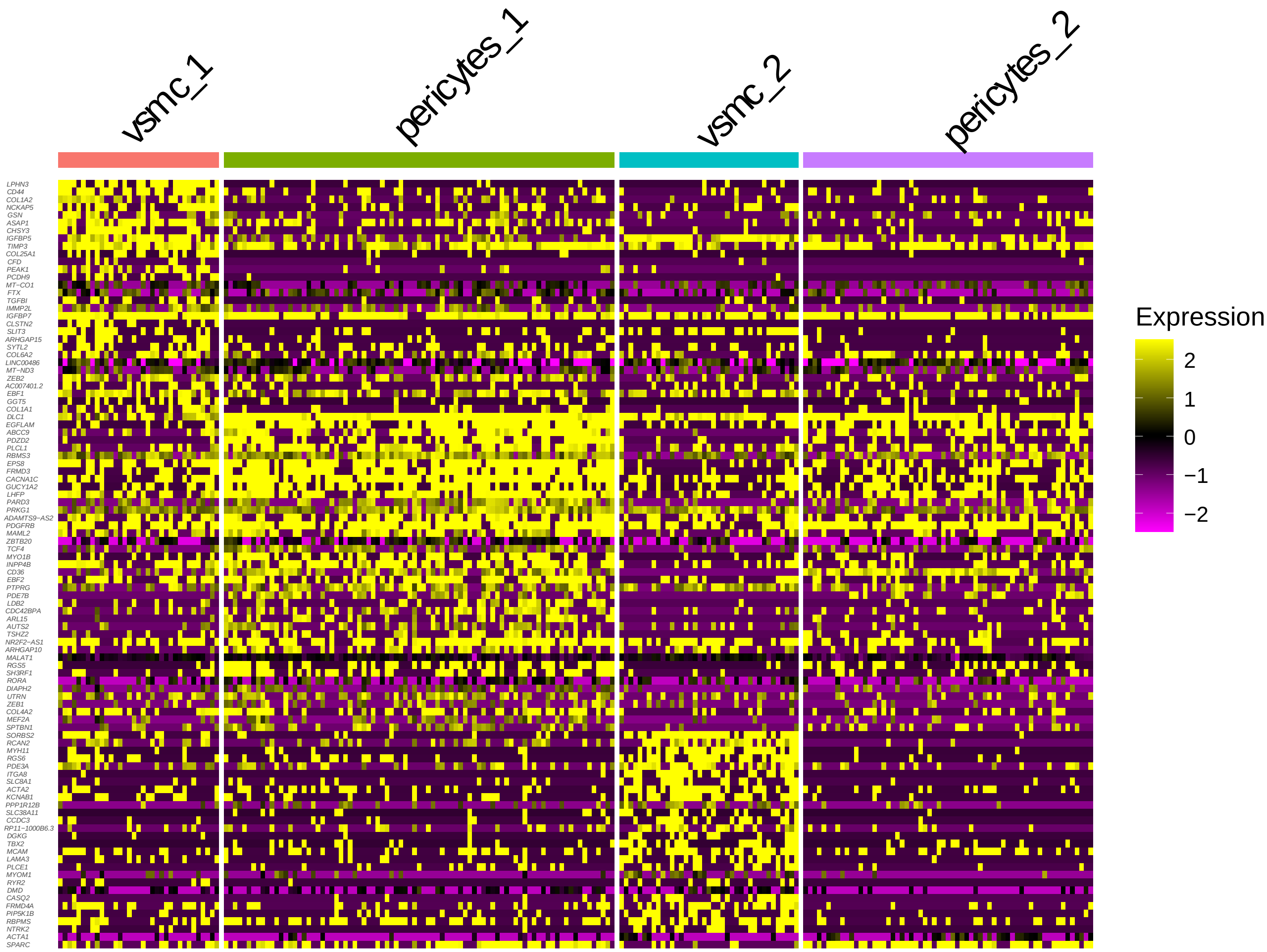
Supplementary Fig. 23: Heat maps human: Myofiber subclusters
Heatmap of significant marker genes among human myofiber cell types. All significant marker genes (Supplementary Data 9) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).



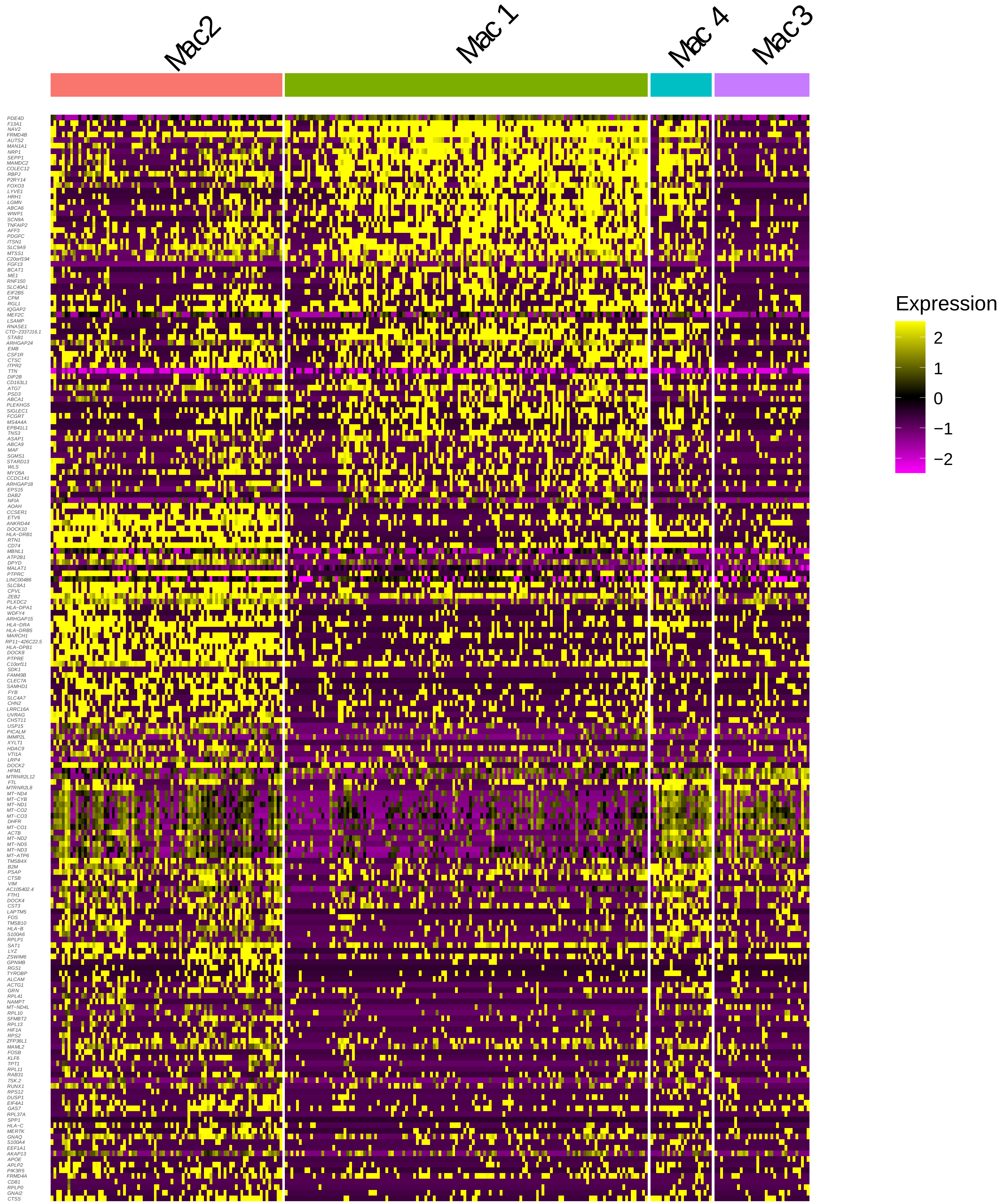
Supplementary Fig. 24: Heat maps human: Fibroblast subclusters
Heatmap of significant marker genes among human Fibroblast cell types. All significant marker genes (Supplementary Data 9) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).



Supplementary Fig. 25: Heat maps human: Endothelial cell subclusters
Heatmap of significant marker genes among human Endothelial cell types. All significant marker genes (Supplementary Data 9) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).



Supplementary Fig. 26: Heat maps human: Smooth muscle subclusters
Heatmap of significant marker genes among human Smooth muscle cell types. All significant marker genes (Supplementary Data 9) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).



Supplementary Fig. 27: Heat maps human: Macrophage subclusters
Heatmap of significant marker genes among human myofiber cell types. All significant marker genes (Supplementary Data 9) were used to generate these heatmaps, gene names listed on the beginning of each row. Each column represents an individual cell (grouped together by cell type identification). Color indicates normalized expression level as shown in legend).

Supplementary References:

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