

Figure S1: Single-cell primary processing: feature plots showing marker genes or QC metrics on the UMAP projection. Marker genes include *MYH2* (slow/intermediate), *MYH7* (fast/intermediate), *VWF* (endothelial cells), *RGS5* (pericytes), *FBN1* (FBN1+ FAP cells), *LUM* (LUM+ FAP cells), *MAF* (macrophages), *HLA-DRA* (dendritic cells), *PAX7* (satellite cells), *CD3D* (T cells), *NKG7* (NK cells), *MS4A1* (B cells), *KIT* (mast cells). QC metrics include *nCount_RNA* (the number of RNA UMIs per cell), *nCount_ATAC* (the number of ATAC UMIs per cell), and *percent.mt* (percentage of mitochondrial reads per cell).

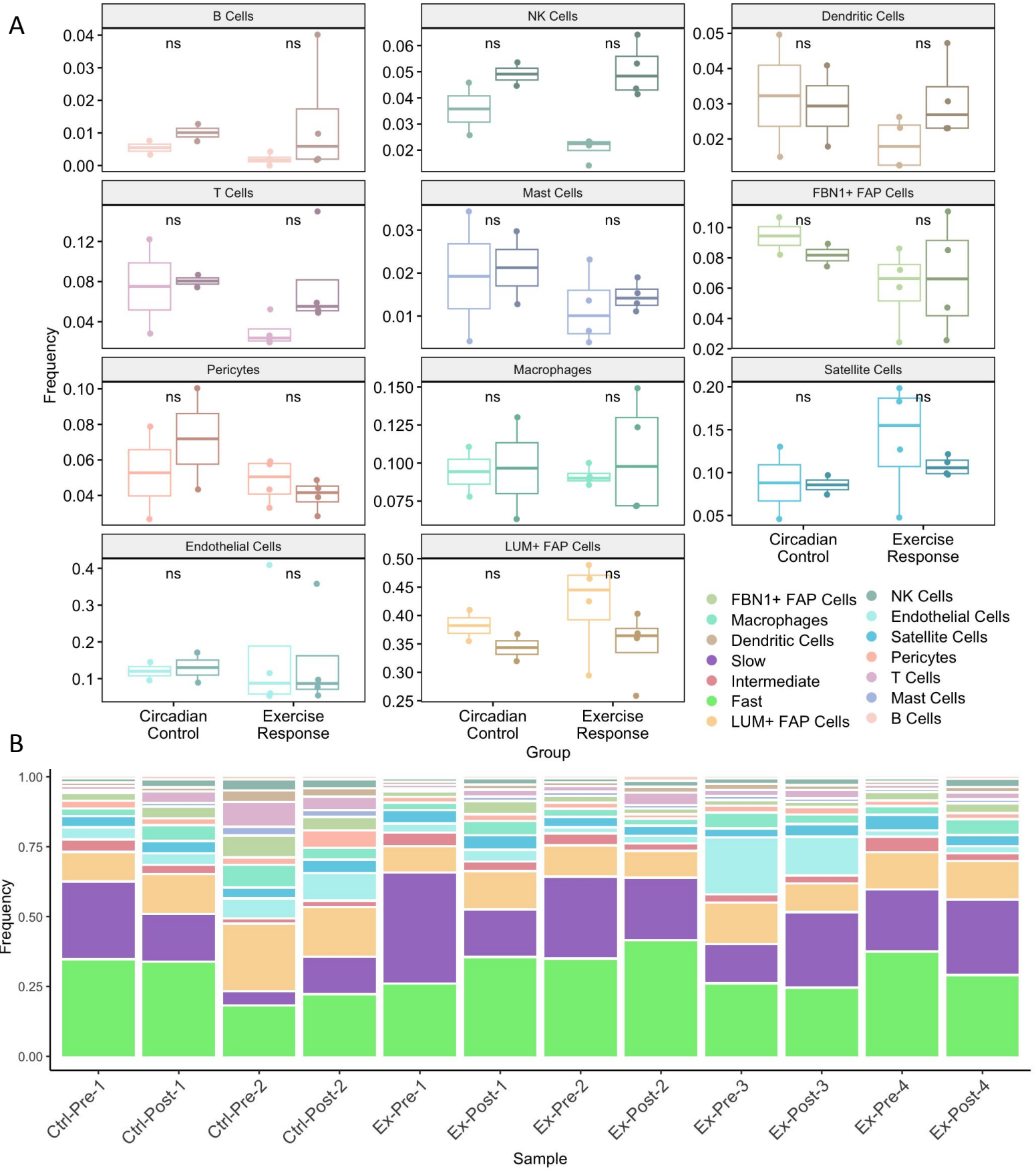


Figure S2: Cell-type proportions are roughly comparable between pre and post time-points. (A) Boxplots reveal frequency of each cell-type within each sample and are split by time-point and group ($n = 2$ control samples per time-point and $n = 4$ exercise samples per time-point). Colors denote cell-type with a darker tint indicating the post time-point. To enable more consistent comparison, fibers are excluded during computation of cell-type frequency. Change between pre and post cell-type proportions is assessed via Holm-Bonferroni adjusted paired t-test with ns: $p > 0.05$, *: $p \leq 0.05$, **: $p \leq 0.01$, ***: $p \leq 0.001$, ****: $p \leq 0.0001$ (B) Barplot indicates frequency of each cell-type, including fibers, for each sample. Subjects Ctrl-1, Ex-1, and Ex-2 are female; subjects Ctrl-2, Ex-3, and Ex-4 are male.

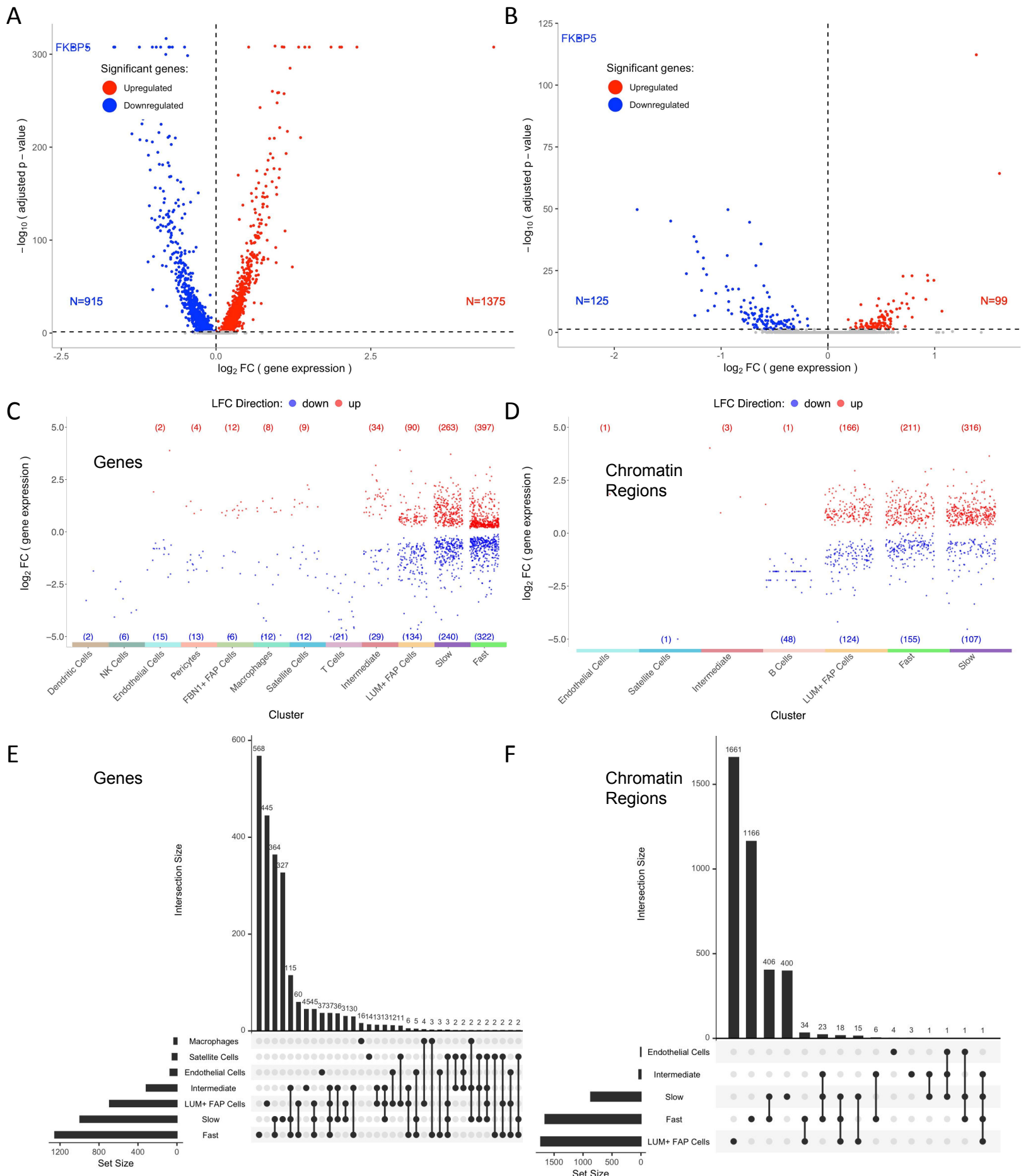


Figure S3: Differential analysis of circadian controls and overlaps of cell-type differential features. (A-B) Volcano plot showing differentially expressed genes pre vs. post (computed at single-cell resolution) for slow fibers in the exercise group (A) and control group (B). *FKBP5* is labeled in both panels and is highly significant with a \log_2 fold change < -2 . (C-D) Volcano plots show the distributions of upregulated and downregulated genes (C) and chromatin regions (D) for each cell-type in circadian controls. These are the features that were excluded from the set of exercise-response features prior to downstream analysis. (E-F) UpSet plots of DEG (E) and DAR (F). Cell-types with fewer than 10 differential features and intersections with 1 differential feature are not shown.

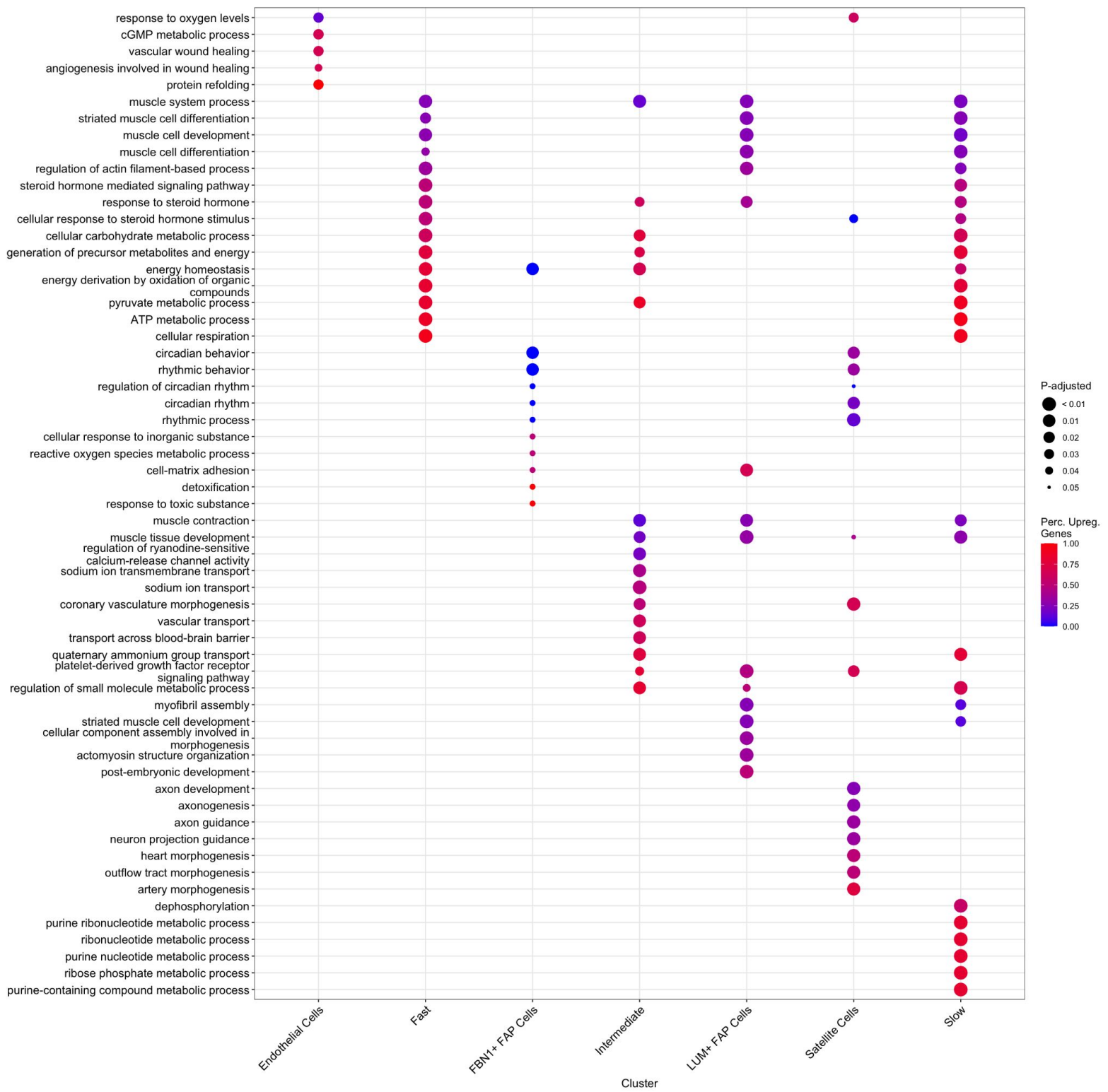


Figure S4: Enrichment analysis for all cell-types. Enrichment analysis of biological processes in each cell-type shows functionally different transcriptome profiles for each cell-type. Color represents the percentage of upregulated genes in a given pathway and larger dot radius denotes more significant biological function.

A LV-defined expression patterns across RNA and ATAC Samples

B LVs with associated enriched pathways

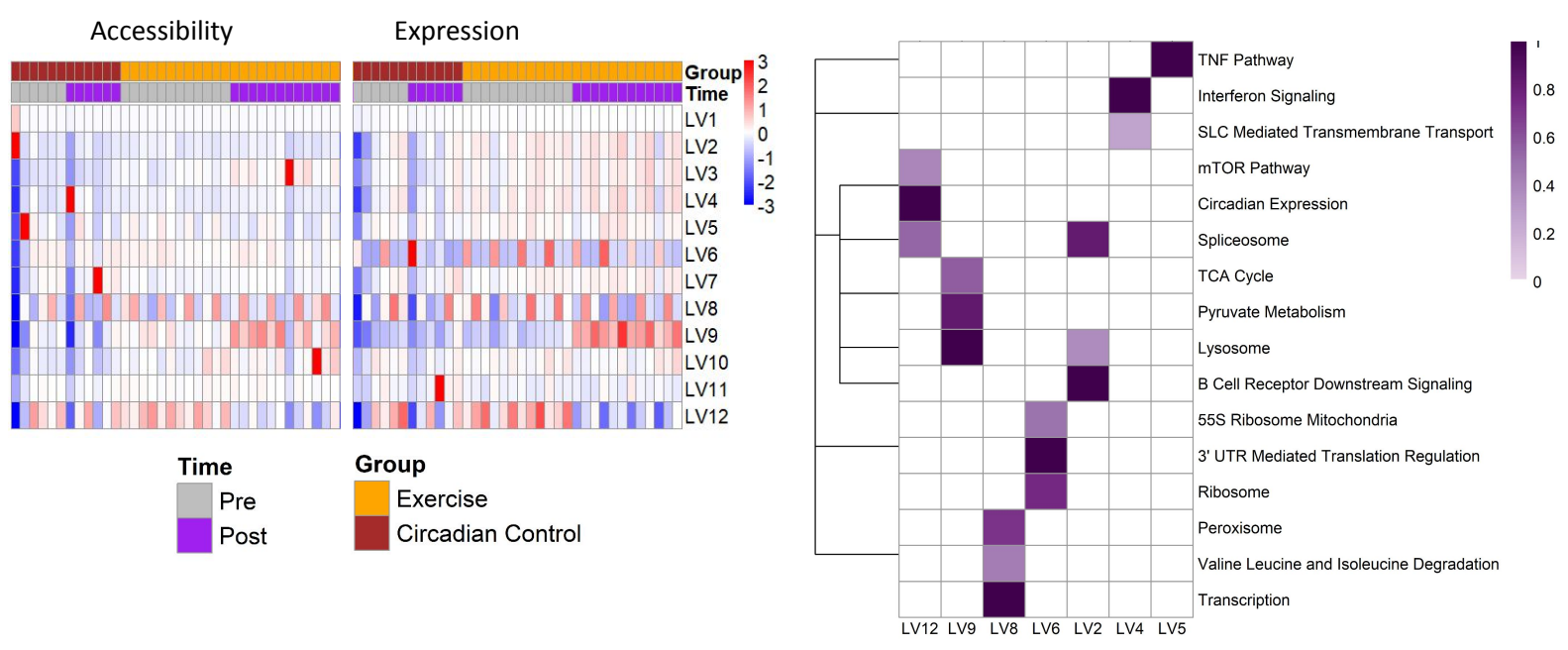


Figure S5: PLIER Supplementary Panels. (A) Heatmap represents summary values for all PLIER-identified LVs. Each column represents one fiber-type sample; columns are ordered by ome type, exercise group, and time-point. Each row represents one LV. (B) Heatmap of enriched pathways associated with select latent variables. Box color reflects AUC for association of pathway to LV.

Supplementary Table S1: Subject Characteristics

Subject	Sex	Group	Age	Height (cm)	Weight (kg)	BMI (kg·m²)	Body Fat %	Absolute VO₂max(L/min)	Relative VO₂max(ml/kg/min)
E	F	Exercise	23	173	72.90	24.4	34.6	2.86	39.24
G	M	Exercise	23	175	88.24	28.8	24.4	3.49	39.57
I	F	Exercise	26	164.2	68.9	25.6	30.8	2.78	40.37
J	M	Exercise	26	175	91.3	29.8	33.1	4.31	47.24
L	M	Control	23	184	82.7	24.4	19.4	3.89	47.02
N	F	Control	24	151	59.63	26.2	34.6	3.03	50.76

BMI, body mass index; F, female; M, male; VO₂max, maximal oxygen consumption.

Supplementary Table S2: QC RNA-seq Metrics

Subj	Time	Estimated number of nuclei	Mean reads/cell	Median UMI/cell	Median genes/cell	Reads mapped to transcriptome	Reads mapped to genome	Fraction of transcriptomic reads in cells
E	1.0	7960	52666	3906	1727	0.30	0.93	0.80
E	2.0	5391	67791	3865	1841	0.32	0.93	0.77
G	1.0	3003	131480	4386	1950	0.28	0.92	0.80
G	2.0	4335	91301	3328	1660	0.33	0.92	0.78
I	1.0	5854	48101	3660	1652	0.31	0.94	0.84
I	2.0	4608	57218	3356	1678	0.31	0.94	0.80
J	1.0	8772	32451	3797	1780	0.31	0.94	0.85
J	2.0	2524	109593	3944	1874	0.35	0.94	0.81
L	1.0	632	667124	4788	2115	0.41	0.91	0.61
L	2.0	961	502041	4531	2035	0.49	0.91	0.49
N	1.0	6499	67568	4064	1805	0.34	0.93	0.72
N	2.0	1372	557108	5070	2194	0.29	0.92	0.71

Supplementary Table S3: QC ATAC-seq Metrics

Subj	Time	Median high-quality fragments/cell	Fraction of transposition events in peaks in cells	Number of peaks	Fraction of genome in peaks	TSS enrichment score	Confidently mapped read pairs	Fraction of high quality fragments overlapping peaks
E	1	18055	0.332	84518	0.023	5.47	0.93	0.33
E	2	20117	0.320	78916	0.022	5.02	0.93	0.32
G	1	25973	0.378	97398	0.027	6.09	0.92	0.38
G	2	18539	0.314	75830	0.021	4.74	0.92	0.31
I	1	10428.5	0.347	92023	0.026	6.27	0.94	0.38
I	2	8209	0.188	54498	0.015	4.24	0.93	0.21
J	1	10601	0.348	100678	0.028	6.05	0.94	0.38
J	2	25056	0.314	83645	0.023	5.16	0.93	0.34
L	1	26888.5	0.208	35652	0.010	3.77	0.91	0.21
L	2	21707	0.156	29919	0.008	3.28	0.91	0.16
N	1	10489	0.378	92724	0.026	6.50	0.93	0.38
N	2	23827	0.344	66074	0.018	5.09	0.92	0.34

Supplementary Table S4: PPAR δ Targets

Cell type	PPAR δ targets
Fast fiber	<p>ADORA2A-AS1, P4HA2-AS1, DPP6, C16orf46, TBC1D1, PTTG2, FABP3, PTPRG, CCDC197, RELL1, SERPINB9, ACKR3, SLC25A18, SLC26A9, VEGFA, CASTOR2, SPIRE1, IQCC, RNF144B, TFEB, SERINC2, ANGPTL2, MBP, CDHR3, SLC41A1, SLC38A4, RFTN1, RAB29, ITIH6, RAB7B, RHBDF1, MOCS1, MIA2, PHKG1, STC2, PTPRJ, SLC30A2, FAM83E, PDE11A, CDS2, ADM, OLFM1, RTN4RL1, LANCL1-AS1, NDRG1, GCOM1, CDKN1A, SLC22A23, SLC22A5, TMEM52, HADHB, LARGE-AS1, CES3, SPTBN4, RSPH9, C3orf35, CREB3L2, MID1IP1, SH3BP2, EML1, ZNF366, PSMG4, CPEB4, C4orf19, FAM43A, VGLL2, TMEM164, MIR3936HG, UQCRFS1, LIMD1-AS1, RIPOR1, DAAM2, LARGE1, RRS1, HHATL, POR, ZBTB43, ABCC1, ANKRD9, ERAP1, TSPAN9, PARVA, KLHL40, PSMD8, RANBP10, IGF2R, TMEM140, SCARF1, TRAF5, TECPR2, PPTC7, SLC25A5, DHDDS, KCNC1, LINC01968, SLC16A1-AS1, CALML6, IAH1, SOCS7, FARP1, RAB11FIP3, GANC, SAMD4A, HIVEP2, SLC22A4, ASAP3, DNAJA4, DLGAP4-AS1, IBTK, ZCCHC17, EIF4EBP2, ZMIZ1, NAGLU, SFMBT1, TNS3, CCDC13, CLIP4, KIF13A, MPC1, NCR3LG1, COLQ, RHOBTB2, DLGAP4, RAD9B, C19orf12, EPS15L1, TKT, UBE2O, ABHD3, PTC3, GOLGA4, RBMS3-AS3, CRK, AFG3L2, LINC01909, RGS3, OSBPL2, MIR1-1HG, NODAL, RBM38, ZNF385C, PRKCD, LGALS1, PDCD11, SLC22A1, DEK, GBF1, ADHFE1, ABCC8, PIM1, PRAG1, ARMH3, TOGARAM2, IDI2-AS1, SPECC1L, FKBP9, SEPTIN11, CD79A, ZBED6, SH3KBP1, GPR179, LCA5L, PARM1, LINC01754, PALMD, RETSAT, WDR60, CHD2, STAT3, SETD3, ITGB1BP1, SLC37A1, PITPNM2, ACSBG1, BCL2L14, PREB, PAFAH2, PARVB, SLC11A2, SGSM1, C16orf70, PTPN3, MTHFD1, ACACB, SLC4A4, MAN1C1, FNBP1L, ATP5MG, RILPL1, DUS2, NCOA3, GREB1L, JMJD6, UBAC1, ZNF609, FAM181A, ETV6, SLC31A1, LRIG2-DT, PHF20, DPEP2, CES2, PLAGL1, CLIC5, SLC29A1, BCAT2, ATP5MD, MTCH2, CEP68, GLCC1, SNHG1, LACTB, ABHD2, CIAO2A, CFL2, CAMSAP1, RHBDF2, MIOS, CCDC28B, ZCWPW2, ANKRD28, HSPB1, DHRS7C, SELENON, PLEKHA4, SLC66A2, WDR37, PFKFB1, CGREF1, ABHD1, ARHGEF10L, GEM, MIPEP, ANP32A, STK24, GPR157, RDH5, SH2B3, TBC1D22A, PDCD10, GREB1, PPP4C</p>
Slow fiber	<p>CGREF1, KLF13, CNNM1, TKT, GCOM1, JUNB, LINC00598, AMOTL1, IDH3A, ACSBG1, PREB, TRIM63, GDAP1L1, NRP1, STAT3, CCM2, ZMIZ1, ACOT11, MAP4K3-DT, SLC41A1, UBAC1, FAM151A, NOP16, PKIG, ZNF44, ATP5MG, EPDR1, GOT1, HOOK2</p>