

Disease exacerbation in human DMD MYOrganoids enables gene therapy evaluation and unveils persistence of fibrotic activity

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Supplementary Figure 1

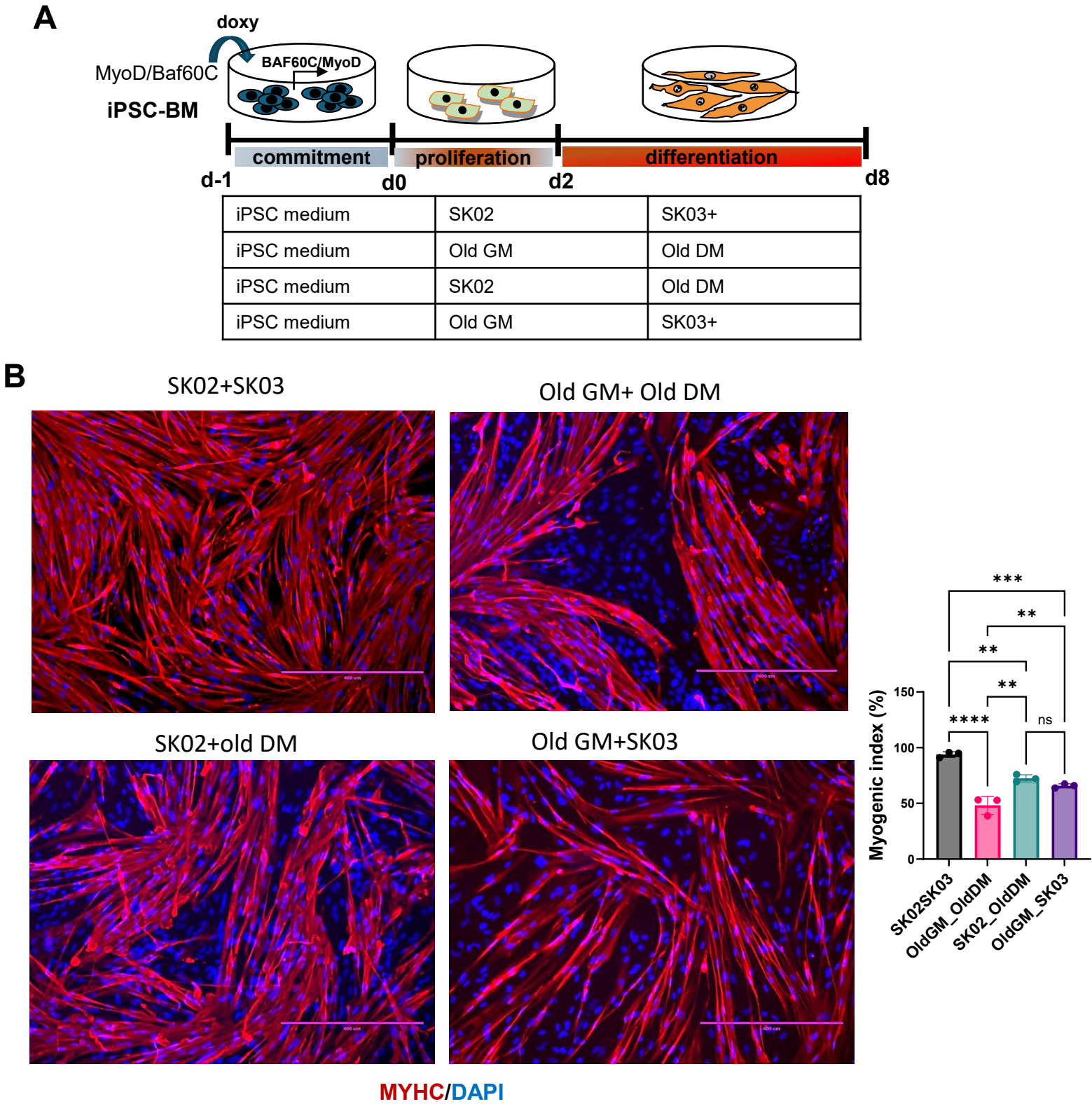


Fig S1. Optimization of direct myogenic differentiation of iPSC (A) Scheme of the protocol for 2D direct muscle differentiation from iPSC (CTR1), adapted from *Caputo et al. 2020*. old GM: homemade growth medium; old DM: homemade differentiation medium in *Albini et al., 2013* and *Caputo et al, 2020*. Commercial proliferation (SK02) and differentiation (SK03+) media were used to achieve optimal differentiation. **(B)** Myogenic index evaluated by the number of nuclei contained in MyHC+ myotubes, as a percentage of the total number of nuclei. Data are presented as means +/- SEM. Statistical analysis was performed with an ordinary one-way ANOVA test (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, ns = not significant) with multiple comparisons corrected with Tukey's test ($n=3$).

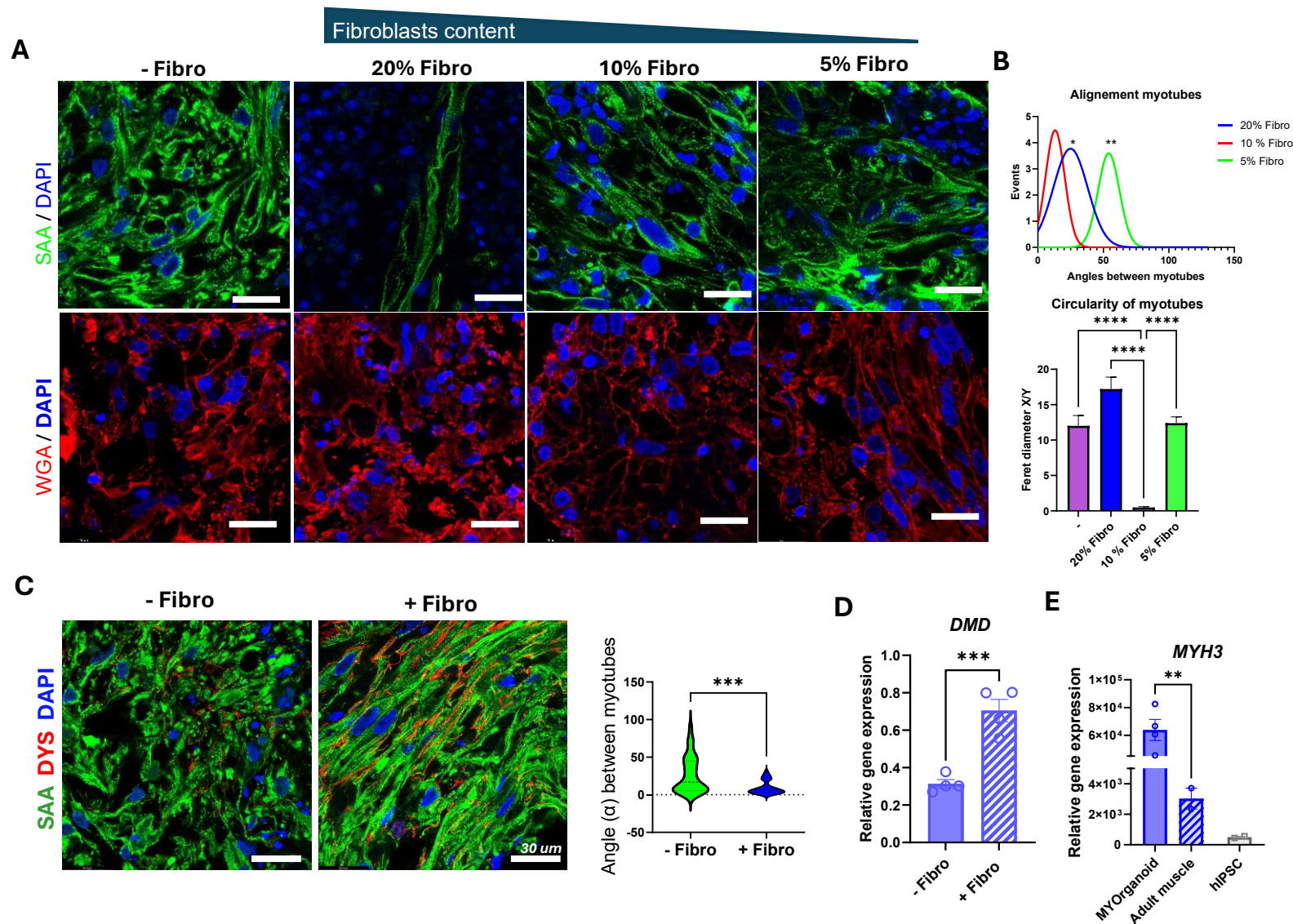


Figure S2. Identification of optimal fibroblasts concentration during MYOrganoid preparation and maturation of organoid including fibroblasts. (A) Representative pictures of iPSC CTR1-derived organoids composed of 0% fibroblasts (-Fibro), 20% fibroblasts, 10% fibroblasts and 5% fibroblasts. Longitudinal sections were immunostained for SAA to measure alignment, while transversal sections were stained for WGA to measure circularity of fibers. Scale bar: 25 μ m (B) Quantification of alignment, based on angle measurements formed by of SAA+ myotubes and circularity quantification based on X/Y diameters ratio. N=3, biological replicates. (C) Representative images of CTR2-derived MYOrganoids +/- fibroblasts longitudinal sections stained for sarcomeric alpha actinin (SAA, green), dystrophin (DYS, red) and nuclei stained with DAPI, and relative quantification of angles between each myotubes. Scale bar = 30 μ m. (D) Relative gene expression of dystrophin gene (DMD) in CTR MYOrganoids with and without fibroblasts normalized for MYOD/GAPDH expression. (E) Myosin 3 (MYH3) relative gene expression in MYOrganoids containing fibroblasts and in adult muscle normalized for RPLP0 gene. hiPSC cells are included as negative control. Results are represented as mean and standard error mean (SEM) is shown. Statistical analysis was performed by one-way analysis of variance with multiple comparisons corrected with Tukey's test. For statistical purposes in panels C-E, unpaired one-tail t-test was performed (* $p < 0.05$, ** $p < 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, ns = not significant)

Supplementary Figure 3

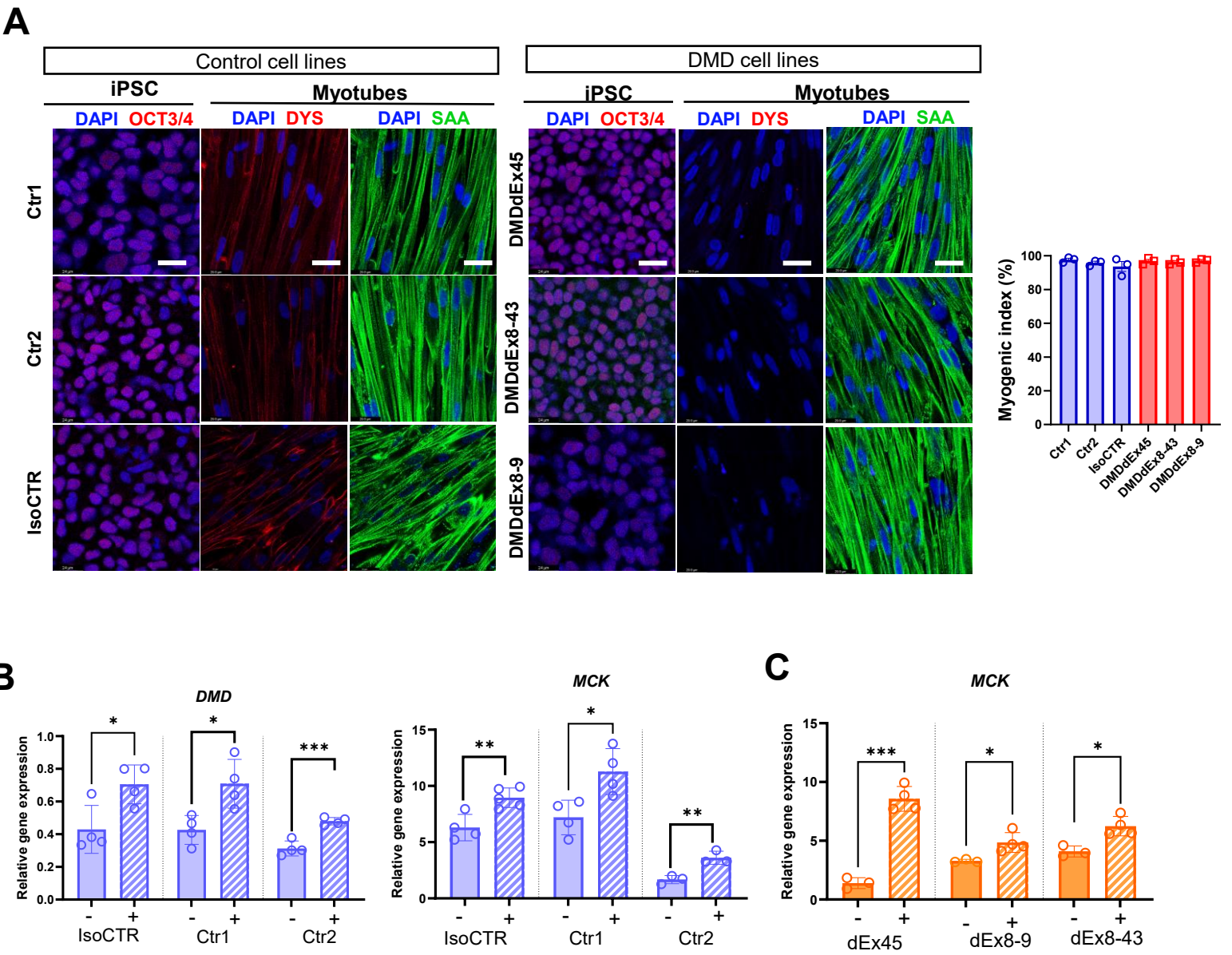


Fig S3. Myotubes differentiation assessment in monolayer culture and characterization of MYOrganoids including and not including fibroblasts (A) Left panel: Oct3/4, Dystrophin (DYS) and sarcomeric alpha-actinin (SAA) staining in hiPSC (OCT3/4) and in myotubes (DYS and SAA) in Ctrl1, Ctrl2, DMDdEx45, DMDdEx8-43 and the isogenic iPSC DMDdEx8-9 with their corrected control (IsoCTR). Scale bar: 25 μ m (OCT3/4) and 30 μ m (DYS and SAA staining) . Right graph: myogenic index calculated as a percentage of the number of nuclei inside SAA-positive myotubes divided by the total number of nuclei present in a field. **(B)** Relative gene expression of Dystrophin (DMD) and muscle creatine kinase (MCK) in IsoCTR, Ctrl1 and Ctrl2 MYOrganoids (blue bars) and in **(C)** DMD dEx45, dEx8-9 and dEx8-43 organoids (orange bars) with and without fibroblasts. Expression was normalized for GAPDH gene expression. Data are presented as means $\pm$ SEM. Statistical analysis was performed with an ordinary one-way ANOVA test (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, ns = not significant) with multiple comparisons corrected with Tukey's test.

Supplementary Figure 4

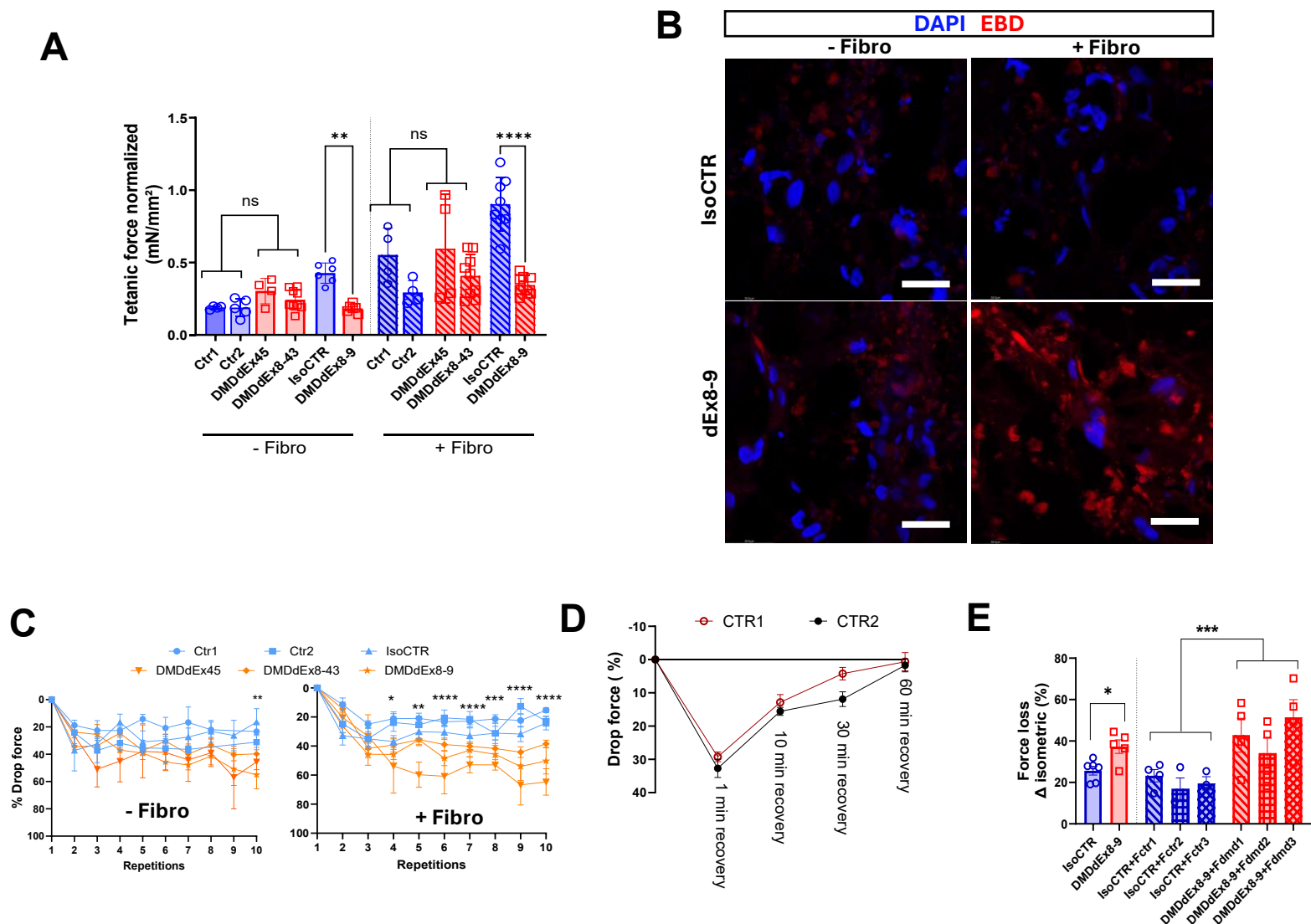


Fig S4. Functional characterization of MYOrganoids including and not including fibroblasts (A) Isometric tetanic force of Ctr and DMD MYOrganoids with and without fibroblasts upon a single isometric pulse. Results are normalized for cross-section area. (B) Evans blue dye (EBD) staining (in red) in IsoCTR and DMD dEx8-9 MYOrganoids including or not fibroblasts. Organoids were subjected to 1X Eccentric contraction (1X ECC) and then incubated with EBD. Scale bar= 30 µm (C) Drop force over 10 eccentric contraction repeated every minutes in Ctr and DMD MYOrganoids, without (left) or with (right) fibroblasts (D) Percentage of drop force of CTR1 and CTR2 MYOrganoids calculated considering the isometric 1 minute, 10 minutes, 30 minutes and 60 minutes after ECC (E) Fatigue index, in organoids generated from IsoCTR and DMDdEx8-9-derived muscle cells with immortalized fibroblasts and with 3 Ctr and 3 DMD fibroblasts obtained from different genetic sources (F1+F2+F3). N=3-6. Data are presented as means +/- SEM. Statistical analysis was evaluated by an ordinary one-way analysis of variance (*p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001, ****p ≤ 0.0001, ns = not significant) with multiple comparisons corrected with Tukey's test.

Supplementary Figure 5

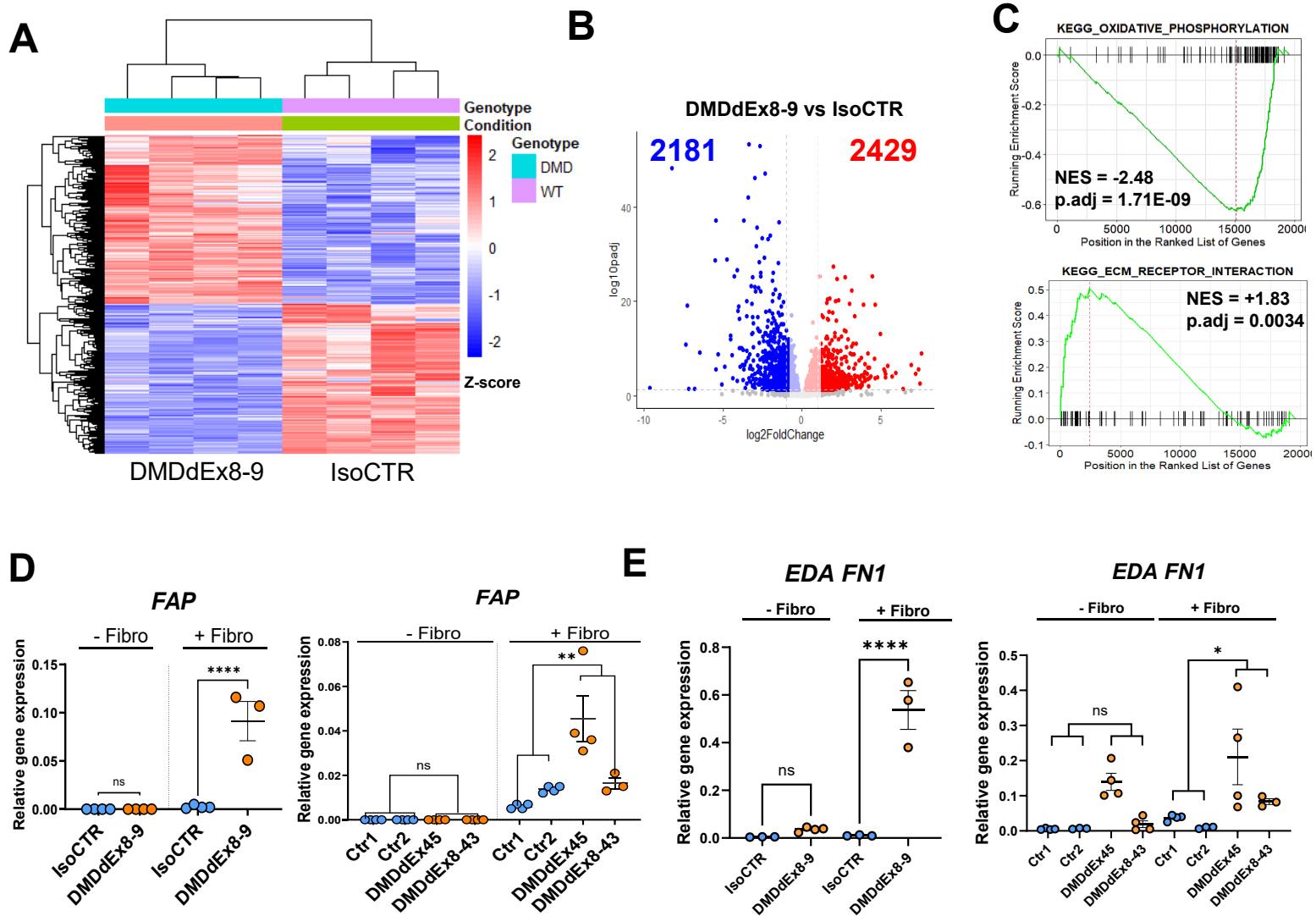


Fig S5. Transcriptomic characterization of DMD MYOrganoids (A) Clustered heatmap of significant differentially expressed genes (DEGs) between DMDdEx8-9 and isogenic control (IsoCTR) MYOrganoid (B) Volcano plot representing DEGs between DMDdEx8-9 and IsoCTR MYOrganoids (C) Kyoto encyclopedia of genes and genome (KEGG) enrichment analysis of DEGs between DMDdEx8-9 and IsoCTR MYOrganoids. X-axis indicates the running enrichment score, while the y-axis the position in the ranked gene list. (D) Relative gene expression of Fibroblast activating protein (FAP) and (E) alternative splicing Extra domain A of Fibronectin1 (EDA FN1) in Ctr and DMD MYOrganoids, including or not fibroblasts. Gene expression was normalized for GAPDH housekeeping gene expression. In panel D-E Data are presented as means $\pm$ SEM. Statistical analysis was performed with an ordinary one-way ANOVA test (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, ns = not significant) with multiple comparisons corrected with Tukey's test.

Supplementary Figure 6

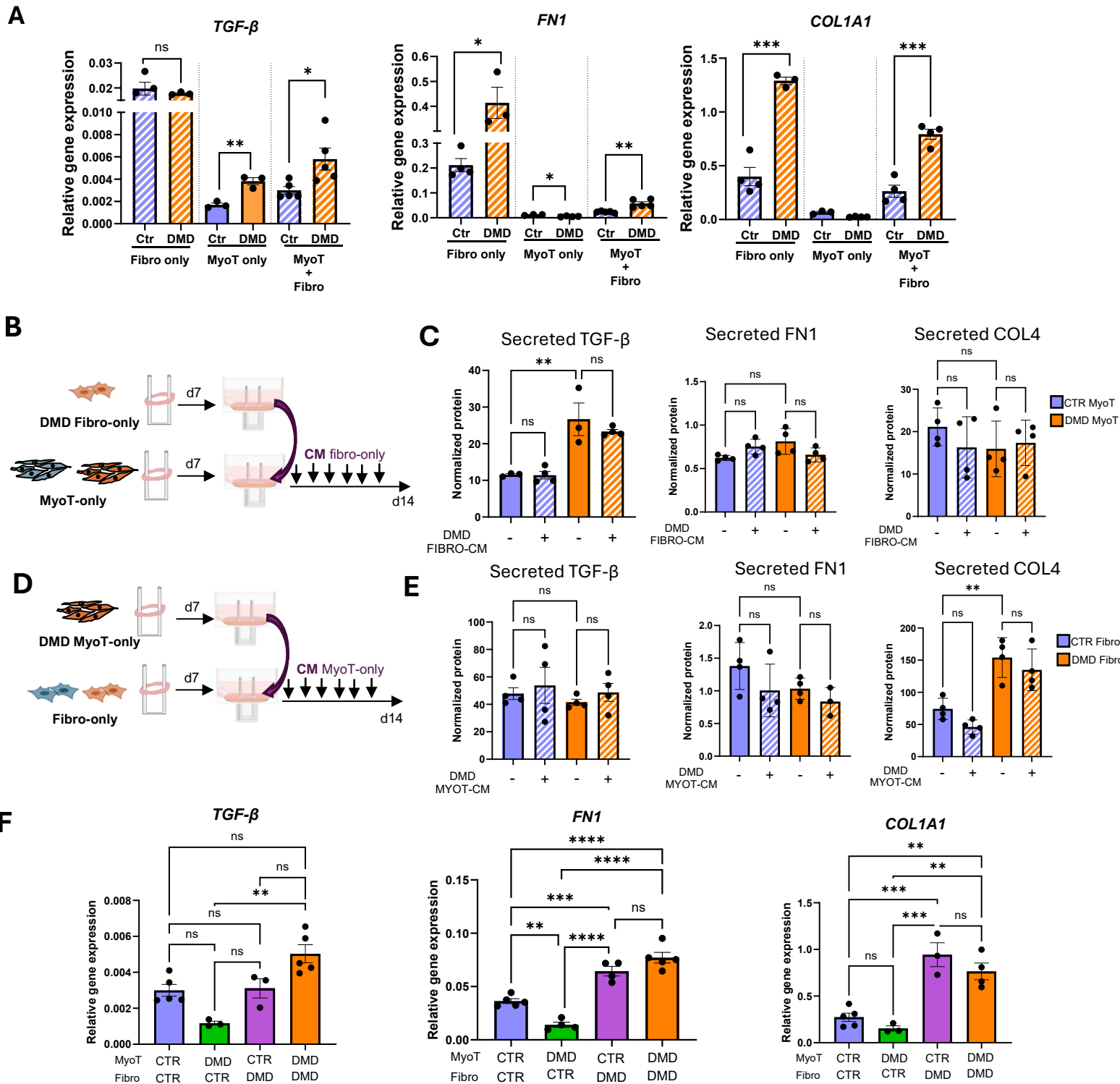


Fig S6. Fibroblast role in the modeling of DMD phenotype (A) Gene expression analysis of Transforming Growth Factor-beta (TGF- β), Fibronectin 1 (FN1) and Collagen 1A1 (Col1A1) in fibroblasts only (Fibro-only), myotubes-only (MyoT-only) 3D cell cultures and MYOrganoids containing myotubes with fibroblasts (MyoT+Fibro) in control (Ctr) and DMD conditions (B) Schematic illustration of the conditioned medium (CM) experiment. Conditioned medium was collected from DMD Fibro-only cultures and applied every other day to MyoT-only 3D cultures (both Ctr and DMD) from day 7 to day 14 in vitro (C) TGF- β , FN1 and Collagen 4 (COL4) secreted protein level in CTR (blue) and DMD (orange) MyoT only 3D cultures, treated or not with DMD Fibro CM. (D) Schematic representation of DMD MyoT only CM experiment on Ctr and DMD Fibro-only tissues. (E) Secreted TGF- β , FN1 and COL4 protein in the cell culture media of CTR and DMD Fibro-only 3D cultures, treated or not with DMD MyoT CM, normalized for total protein (F) FN1, COL1A1 and TGF- β secreted protein in CTR organoids (CTR MyoT + CTR Fibro), CTR mixed organoids (CTR MyoT + DMD Fibro), DMD organoids (DMD MyoT + DMD Fibro) and DMD mixed organoids (DMD MyoT + CTR Fibro). Data are presented as means $\pm$ SEM. Statistical analysis was performed with an ordinary one-way ANOVA test (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, ns = not significant) with multiple comparisons corrected with Tukey's test.

Supplementary Figure 7

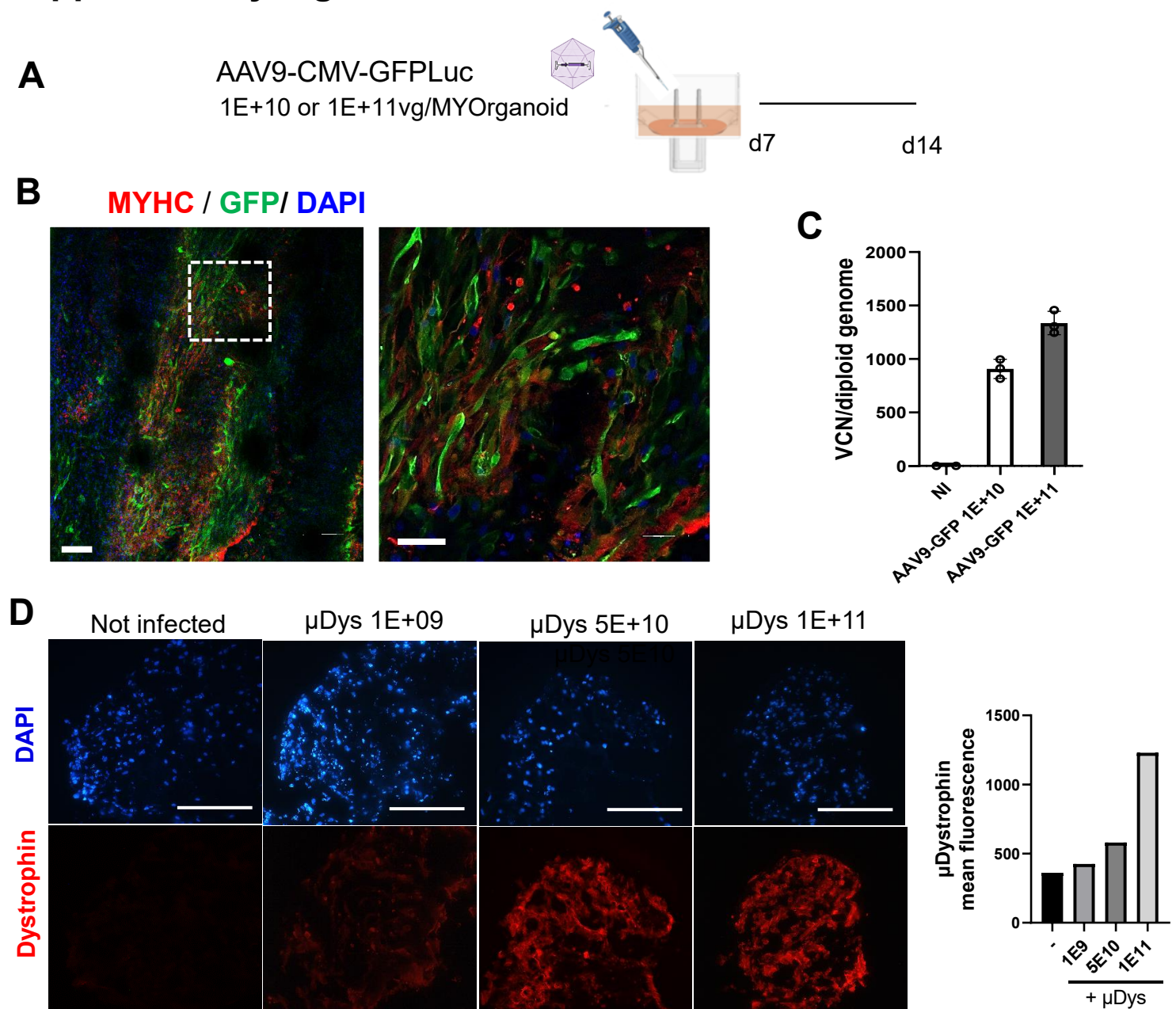


Fig S7. Optimization of AAV infection in MYOrganoids (A) Infection method using AAV9-CMV-GFP_{Luc}. (B) Representative images showing infection efficiency using whole-mount staining with GFP antibody. (C) VCN quantification from MYOrganoids infected with AAV9-CMV-GFP-Luc at two different doses: 1E+10 and 1E+11 viral genome per organoid. (D) Myofiber transduction, evaluated by dystrophin staining, following increasing dosing of AAV9-Sp512- μ Dys vector. DAPI stains nuclei. Scale bar: 100 μ m.

Supplementary Figure 8

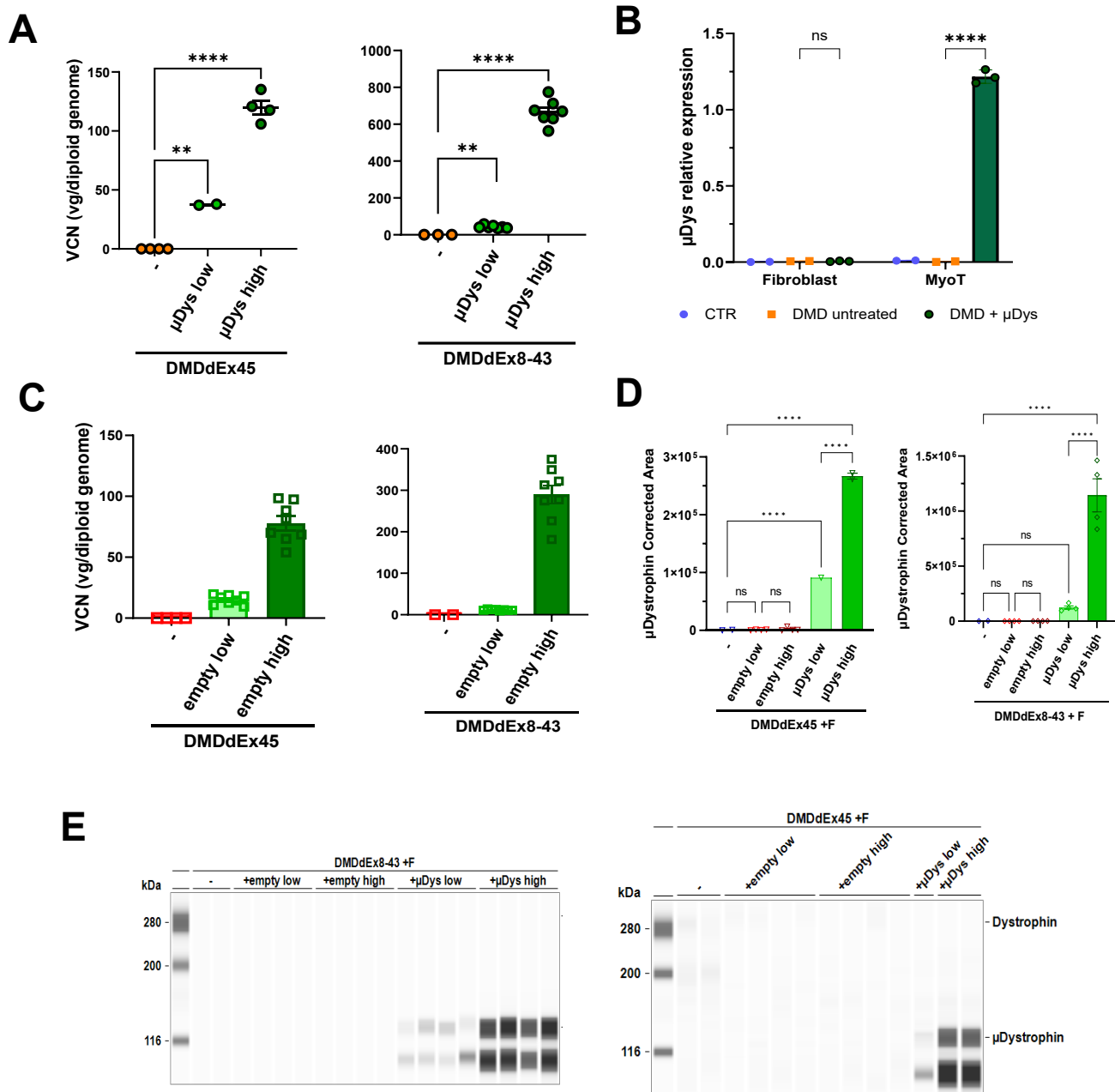


Fig S8. Efficacy of μDystrophin and AAV empty vector gene transfer in MYOrganoids functionality (A) Viral copy number (VCN) of μDys in DMDdEx8-43 and DMDdEx45 MYOrganoids (B) μDystrophin protein expression evaluated by Capillary western blot in fibroblasts or iPSC-derived muscle cells, infected or not with AAV9-μDys (C) VCN analysis of empty vector genome in DMDdEx45 and DMDdEx8-43 MYOrganoids infected with AAV9-empty vector (D) Capillary western blot quantification of μDys in DMDdEx45 MYOrganoids infected or not with AAV9-μDys and AAV9 empty vector at 2 doses (E) Run pictures of capillary western blot of DMDdEx45 MYOrganoids or DMDdEx8-43 MYOrganoids infected at two doses with AAV9-μDys and AAV9-empty vector. For all panels, data are presented as means $\pm$ SEM. Statistical analysis was performed with an ordinary one-way ANOVA test (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, ns = not significant).

Supplementary Figure 9

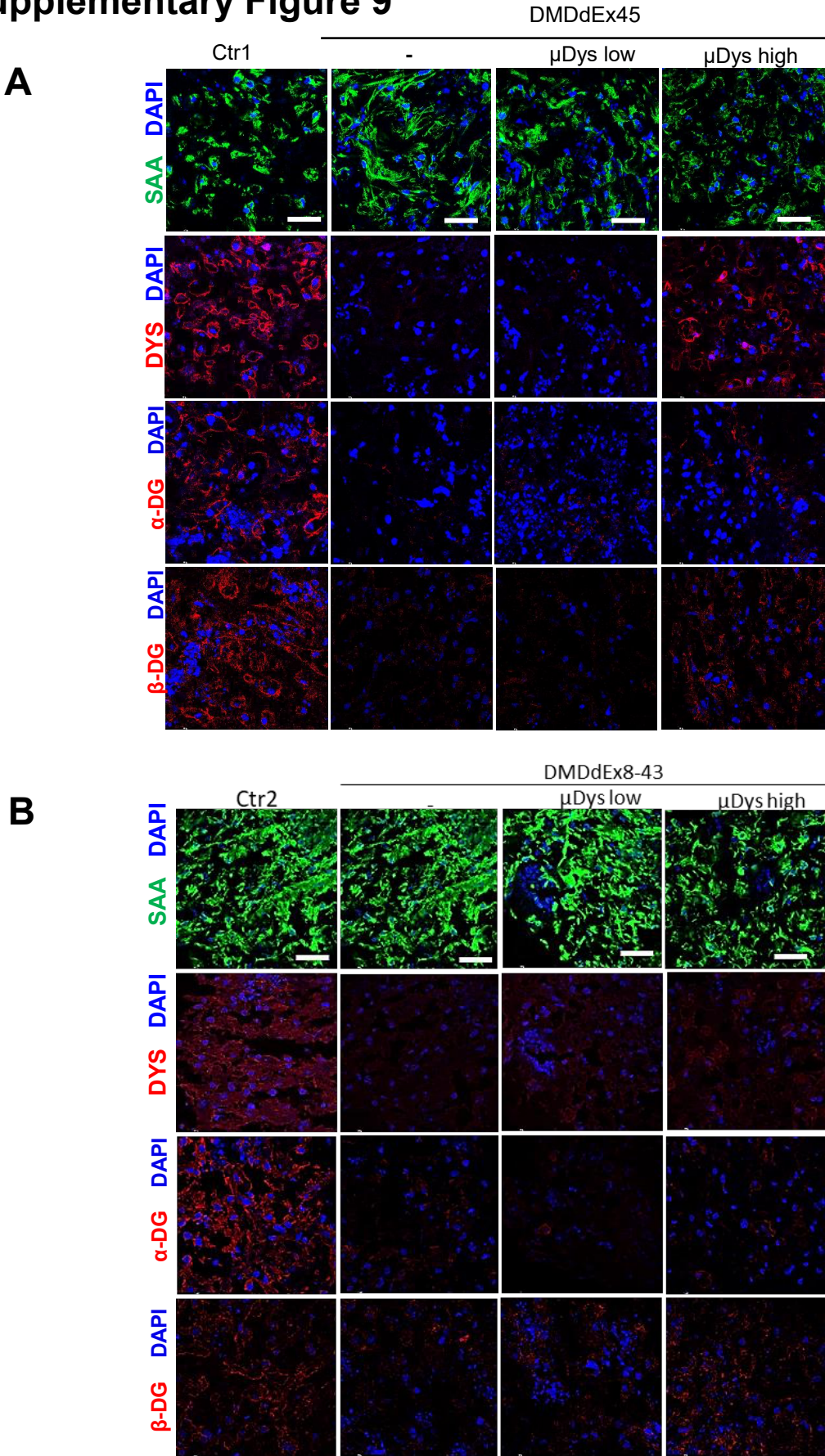


Fig S9. Efficacy of μ Dystrophin infection and restoration of dystrophin Glycoprotein complex in additional iPSC derived-MYOrganoids (A) Sarcomeric alpha-actinin (SAA), dystrophin (dys), α -dystroglycan (α -DG) and β -dystroglycan (β -DG) immunostaining in Ctr1, DMDdEx45 untreated and infected at two doses (low and high) of μ Dystrophin (μ Dys) transversal sections. Scale bar: 50 μ m. Relative quantifications have been performed by calculating the percentage of DYS/ α -DG/ β -DG and SAA positive myotubes **(B)** Sarcomeric alpha-actinin (SAA), dystrophin (dys), α -dystroglycan (α -DG) and β -dystroglycan (β -DG) immunostaining in Ctr2, and DMDdEx8-43 untreated and infected at low and high doses of μ Dys longitudinal sections. Scale bar: 50 μ m.

Supplementary Figure 10

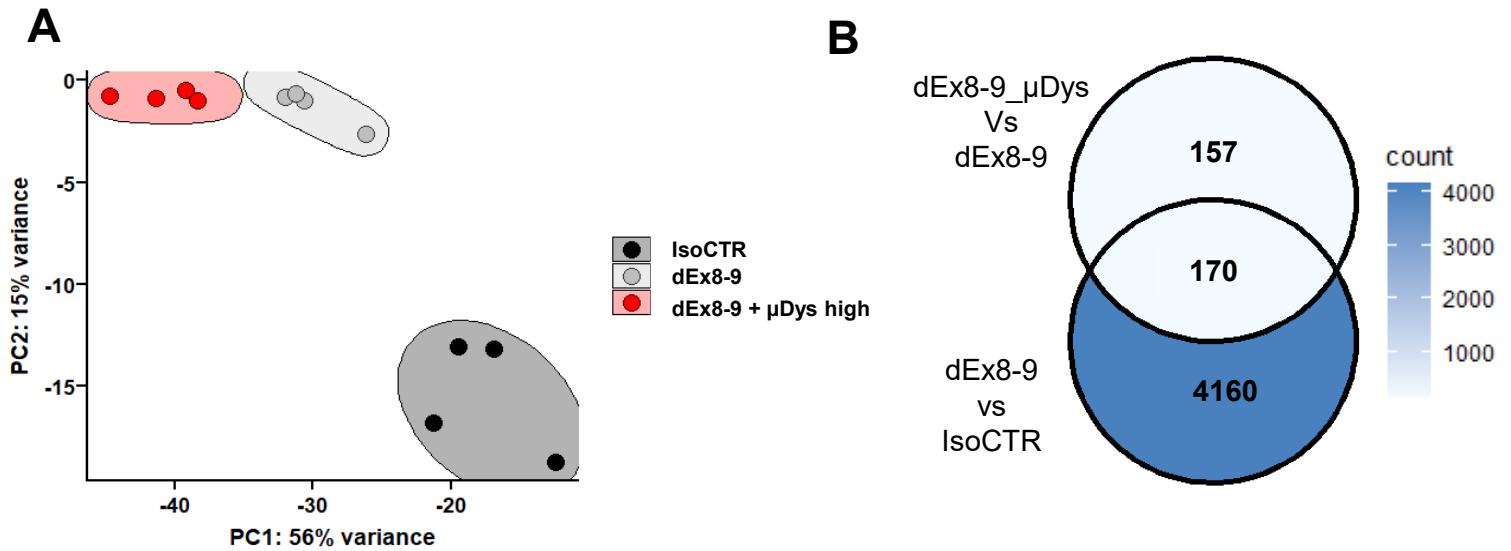


Fig S10. Transcriptomic analysis in DMDdEx8-9 treated with μ Dys and comparison with untreated and isogenic control (A) Principal component analysis (PCA) of DMDdEx8-9 MYOrganoids (dEx8-9) treated with μ Dys (dEx8-9 + μ Dys high) compared with isogenic control (IsoCTR) **(B)** Venn diagram of differentially expressed genes (DEGs) between dEx8-9 MYOrganoids treated with μ Dys and untreated (dEx8-9_ μ Dys vs dEx8-9) and dEx8-9 MYOrganoids vs isogenic control (dEx8-9 vs IsoCTR).

Supplementary Figure 11

Figure 3I

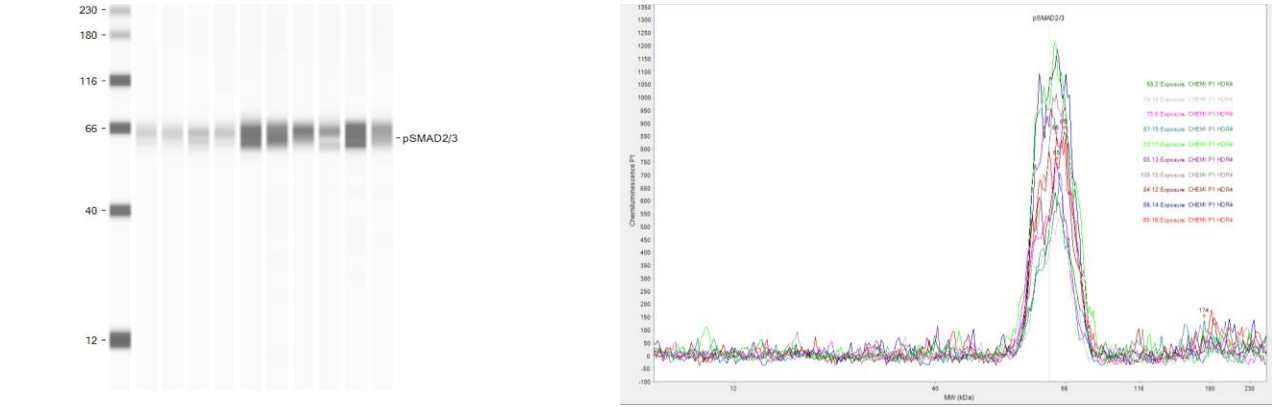


Figure 5D

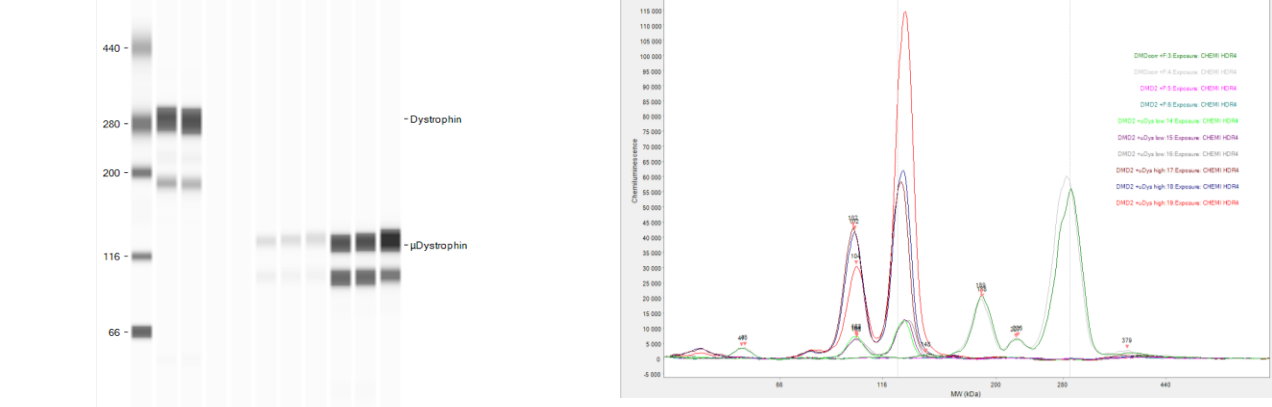


Figure S8E

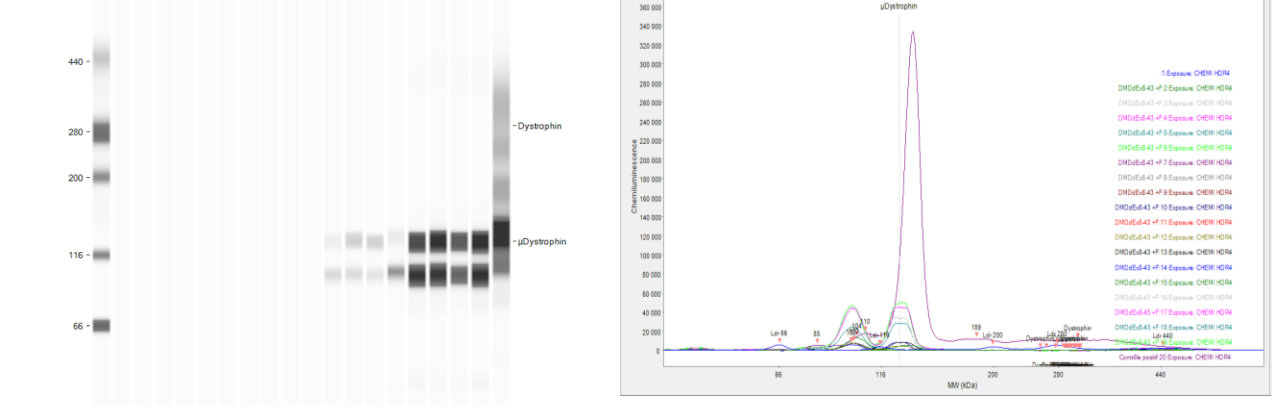


Figure S8E

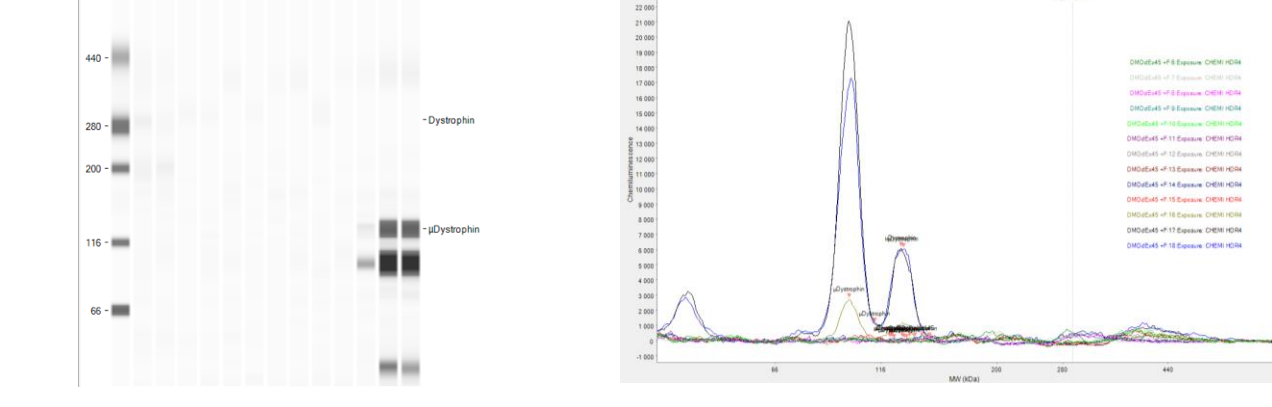


Fig S11. Unprocessed capillary western blot lanes and respective chemiluminescence peaks

Supplementary table 1: List of GO biological processes differentially expressed between DMD organoids (DMDdEx8-9) and isogenic control (IsoCTR)

Description	setSize	NES	p.adjust	qvalue
GOBP_MUSCLE_SYSTEM_PROCESS	390	-2,103	1,31E-09	1,22E-09
GOBP_MUSCLE_CONTRACTION	308	-2,170	2,18E-09	2,03E-09
GOBP_NEGATIVE_REGULATION_OF_MEGAKARYOCYTE_DIFFERENTIATION	17	2,429	1,92E-08	1,79E-08
GOBP_CYTOPLASMIC_TRANSLATION	146	-2,375	3,62E-08	3,38E-08
GOBP_MITOCHONDRIAL_RESPIRATORY_CHAIN_COMPLEX_ASSEMBLY	89	-2,454	2,86E-07	2,66E-07
GOBP_AEROBIC_RESPIRATION	166	-2,247	2,86E-07	2,66E-07
GOBP_DNA_REPLICATION_DEPENDENT_CHROMATIN_ORGANIZATION	32	2,473	8,37E-07	7,81E-07
GOBP_CELLULAR_RESPIRATION	208	-2,085	3,31E-06	3,09E-06
GOBP_STRIATED_MUSCLE_CONTRACTION	161	-2,132	5,59E-06	5,21E-06
GOBP_OXIDATIVE_PHOSPHORYLATION	119	-2,216	6,40E-06	5,97E-06
GOBP_DNA_CONFORMATION_CHANGE	307	1,867	1,28E-05	1,19E-05
GOBP_NADH_DEHYDROGENASE_COMPLEX_ASSEMBLY	53	-2,451	1,33E-05	1,24E-05
GOBP_ENERGY_DERIVATION_BY_OXIDATION_OF_ORGANIC_COMPOUNDS	281	-1,946	1,33E-05	1,24E-05
GOBP_SKELETAL_MUSCLE_CONTRACTION	41	-2,383	3,21E-05	2,99E-05
GOBP_STRIATED_MUSCLE_CELL_DEVELOPMENT	64	-2,305	1,05E-04	9,82E-05
GOBP_REGULATION_OF_MUSCLE_CONTRACTION	143	-2,058	1,16E-04	1,08E-04
GOBP_REGULATION_OF_MUSCLE_SYSTEM_PROCESS	209	-1,926	1,38E-04	1,29E-04
GOBP_REGULATION_OF_SYSTEM_PROCESS	482	-1,671	1,38E-04	1,29E-04
GOBP_ATP_METABOLIC_PROCESS	240	-1,868	1,76E-04	1,64E-04
GOBP_MITOCHONDRIAL_ELECTRON_TRANSPORT_NADH_TO_UBIQUINONE	43	-2,292	2,94E-04	2,74E-04
GOBP_DNA_REPLICATION_INDEPENDENT_CHROMATIN_ORGANIZATION	34	2,221	2,94E-04	2,74E-04

GOBP_DETECTION_OF_STIMULUS_INVOLVED_IN_SENSORY_PERCEPTION	118	2,017	2,94E-04	2,74E-04
GOBP_MITOTIC_NUCLEAR_DIVISION	282	1,814	2,94E-04	2,74E-04
GOBP_MULTICELLULAR_ORGANISMAL_MOVEMENT	53	- 2,297	3,32E-04	3,10E-04
GOBP_CHROMOSOME_SEGREGATION	315	1,731	3,65E-04	3,41E-04
GOBP_SARCOMERE_ORGANIZATION	40	- 2,259	6,36E-04	5,94E-04
GOBP_ATP_SYNTHESIS_COUPLED_ELECTRON_TRANSPORT	77	- 2,149	6,36E-04	5,94E-04
GOBP_HEART_PROCESS	224	- 1,807	6,36E-04	5,94E-04
GOBP_NUCLEAR_CHROMOSOME_SEGREGATION	257	1,767	6,36E-04	5,94E-04
GOBP_DNA_DEPENDENT_DNA_REPLICATION	156	1,843	6,98E-04	6,51E-04
GOBP_RESPIRATORY_ELECTRON_TRANSPORT_CHAIN	98	- 2,053	7,47E-04	6,97E-04
GOBP_SISTER_CHROMATID_SEGREGATION	191	1,862	9,30E-04	8,67E-04
GOBP_ACTIVATION_OF_GTPASE_ACTIVITY	107	1,980	1,18E-03	1,10E-03
GOBP_REGULATION_OF_MEGAKARYOCYTE_DIFFERENTIATION	35	2,169	1,21E-03	1,13E-03
GOBP_REGULATION_OF_HEART_CONTRACTION	181	- 1,814	1,30E-03	1,21E-03
GOBP_SARCOPLASMIC_RETICULUM_CALCIIUM_ION_TRANSPORT	36	- 2,192	1,38E-03	1,29E-03
GOBP_MITOTIC_SISTER_CHROMATID_SEGREGATION	166	1,857	1,39E-03	1,30E-03
GOBP_REGULATION_OF_BLOOD_CIRCULATION	219	- 1,775	1,61E-03	1,50E-03
GOBP_RIBOSOME_BIOGENESIS	298	- 1,676	1,82E-03	1,70E-03
GOBP_REGULATION_OF_STRIATED_MUSCLE_CONTRACTION	83	- 2,048	1,89E-03	1,76E-03
GOBP_MITOCHONDRIAL_TRANSLATION	72	- 2,074	2,04E-03	1,90E-03
GOBP_SPINDLE_ORGANIZATION	199	1,772	2,06E-03	1,92E-03
GOBP_DNA_PACKAGING	212	1,765	2,06E-03	1,92E-03
GOBP_ORGANELLE_FISSION	447	1,568	2,50E-03	2,33E-03
GOBP_COLLAGEN_FIBRIL_ORGANIZATION	60	2,023	2,67E-03	2,49E-03

GOBP_MITOCHONDRION_ORGANIZATION	492	- 1,519	4,90E- 03	4,57E- 03
GOBP_STRIATED_MUSCLE_CELL_DIFFERENTIATION	251	- 1,659	5,62E- 03	5,24E- 03
GOBP_EXTERNAL_ENCAPSULATING_STRUCTURE_ORGANIZATION	281	1,665	5,69E- 03	5,31E- 03
GOBP_GENERATION_OF_PRECURSOR_METABOLITES_AND_ENERGY	436	- 1,524	5,69E- 03	5,31E- 03
GOBP_CELLULAR_COMPONENT_ASSEMBLY_INVOLVED_IN_MORPHOGENESIS	99	- 1,941	6,78E- 03	6,33E- 03
GOBP_ACTIN_MYOSIN_FILAMENT_SLIDING	14	- 2,098	7,64E- 03	7,13E- 03
GOBP_MUSCLE_CELL_DEVELOPMENT	168	- 1,754	1,07E- 02	9,94E- 03
GOBP_DNA_GEOMETRIC_CHANGE	94	1,853	1,15E- 02	1,08E- 02
GOBP_REGULATION_OF_CATION_TRANSMEMBRANE_TRANSPORT	298	- 1,571	1,20E- 02	1,12E- 02
GOBP_VENTRICULAR_CARDIAC_MUSCLE_TISSUE_DEVELOPMENT	52	- 1,998	1,23E- 02	1,15E- 02
GOBP_SPINDLE_ASSEMBLY	134	1,760	1,23E- 02	1,15E- 02
GOBP_INTERLEUKIN_1_MEDIATED_SIGNALING_PATHWAY	26	- 2,113	1,31E- 02	1,22E- 02
GOBP_THYROID_HORMONE_METABOLIC_PROCESS	21	2,007	1,41E- 02	1,31E- 02
GOBP_NEUROMUSCULAR_PROCESS	138	- 1,755	1,46E- 02	1,36E- 02
GOBP_DNA_REPLICATION	275	1,618	1,65E- 02	1,54E- 02
GOBP_REGULATION_OF_CALCIIUM_ION_IMPORT	36	- 1,988	1,66E- 02	1,55E- 02
GOBP_DETECTION_OF_STIMULUS	213	1,629	1,66E- 02	1,55E- 02
GOBP_CELL_FATE_COMMITMENT	215	1,628	1,80E- 02	1,68E- 02
GOBP_RIBOSOME_ASSEMBLY	59	- 1,943	1,87E- 02	1,74E- 02
GOBP_CARDIAC_VENTRICLE_MORPHOGENESIS	63	- 1,935	1,87E- 02	1,75E- 02
GOBP_CATECHOLAMINE_SECRETION	47	- 1,934	1,87E- 02	1,75E- 02
GOBP_MITOCHONDRIAL_GENE_EXPRESSION	104	- 1,795	1,92E- 02	1,79E- 02
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE_PROCESS	211	1,637	1,92E- 02	1,79E- 02
GOBP_RIBONUCLEOPROTEIN_COMPLEX_BIOGENESIS	422	- 1,472	1,92E- 02	1,79E- 02

GOBP_SISTER_CHROMATID_COHESION	53	1,919	1,96E-02	1,83E-02
GOBP_ATP_BIOSYNTHETIC_PROCESS	48	-1,903	2,27E-02	2,12E-02
GOBP_BIOMINERALIZATION	143	1,724	2,27E-02	2,12E-02
GOBP_RECOMBINATIONAL_REPAIR	156	1,630	2,27E-02	2,12E-02
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE	285	1,543	2,27E-02	2,12E-02
GOBP_SENSORY_PERCEPTION_OF_SMELL	68	1,868	2,43E-02	2,26E-02
GOBP_REGULATION_OF_PROTEIN_DEPOLYMERIZATION	85	-1,844	2,44E-02	2,28E-02
GOBP_MEGAKARYOCYTE_DIFFERENTIATION	55	1,891	2,47E-02	2,30E-02
GOBP_MUSCLE_ADAPTATION	98	-1,795	2,47E-02	2,30E-02
GOBP_MORPHOGENESIS_OF_AN_EPITHELIAL_FOLD	20	1,953	2,47E-02	2,30E-02
GOBP_REGULATION_OF_SKELETAL_MUSCLE_CONTRACTION	16	-2,009	2,64E-02	2,46E-02
GOBP_ATP_SYNTHESIS_COUPLED_PROTON_TRANSPORT	22	-2,005	2,77E-02	2,58E-02
GOBP_ACUTE_INFLAMMATORY_RESPONSE	78	-1,847	2,77E-02	2,58E-02
GOBP_ACTIN_MEDIATED_CELL_CONTRACTION	94	-1,774	2,85E-02	2,66E-02
GOBP_REGULATION_OF_ATP_DEPENDENT_ACTIVITY	70	-1,855	2,89E-02	2,69E-02
GOBP_CARDIAC_MUSCLE_CONTRACTION	123	-1,751	2,89E-02	2,69E-02
GOBP_RIBOSOMAL_LARGE_SUBUNIT_BIOGENESIS	71	-1,905	2,95E-02	2,75E-02
GOBP_AMINE_TRANSPORT	80	-1,825	2,95E-02	2,75E-02
GOBP_NEGATIVE_REGULATION_OF_PROTEIN_CONTAINING_COMPLEX_DISASSEMBLY	79	-1,799	2,95E-02	2,75E-02
GOBP_CARDIAC_VENTRICLE_DEVELOPMENT	115	-1,698	2,95E-02	2,75E-02
GOBP_MICROTUBULE_CYTOSKELETON_ORGANIZATION_INVOLVED_IN_MITOSIS	150	1,691	3,09E-02	2,88E-02
GOBP_PROTEIN_DNA_COMPLEX_ASSEMBLY	172	1,643	3,14E-02	2,93E-02
GOBP_MUSCLE_CELL_DIFFERENTIATION	345	-1,497	3,14E-02	2,93E-02
GOBP_REGULATION_OF_EMBRYONIC_DEVELOPMENT	60	1,818	3,37E-02	3,15E-02

GOBP_PROTON_TRANSMEMBRANE_TRANSPORT	123	- 1,728	3,37E- 02	3,15E- 02
GOBP_TELOMERE_ORGANIZATION	160	1,649	3,37E- 02	3,15E- 02
GOBP_NEGATIVE_REGULATION_OF_ACTIN_FILAMENT_DEPOLYMERIZATION	43	- 1,852	3,40E- 02	3,17E- 02
GOBP_CELLULAR_RESPONSE_TO_INTERLEUKIN_1	86	- 1,763	3,40E- 02	3,17E- 02
GOBP_HOMOPHILIC_CELL_ADHESION_VIA_PLASMA_MEMBRANE_ADHESION_MOLECULES	157	1,654	3,45E- 02	3,22E- 02
GOBP_POSITIVE_REGULATION_OF_CALCIIUM_ION_IMPORT	18	- 1,939	3,65E- 02	3,40E- 02
GOBP_VENTRICULAR_CARDIAC_MUSCLE_TISSUE_MORPHOGENESIS	44	- 1,916	4,04E- 02	3,77E- 02
GOBP_MITOCHONDRIAL_ATP_SYNTHESIS_COUPLED_PROTON_TRANSPORT	16	- 1,961	4,21E- 02	3,92E- 02
GOBP_REGULATION_OF_TRANSMEMBRANE_TRANSPORT	479	- 1,369	4,21E- 02	3,92E- 02
GOBP_ACUTE_PHASE_RESPONSE	32	- 1,941	4,47E- 02	4,17E- 02
GOBP_WNT_SIGNALING_PATHWAY_INVOLVED_IN_MIDBRAIN_DOPAMINERGIC_NEURON_DIFFERENTIATION	12	1,926	4,47E- 02	4,17E- 02
GOBP_RIBOSOMAL_SMALL_SUBUNIT_BIOGENESIS	72	- 1,780	4,63E- 02	4,32E- 02
GOBP_RELEASE_OF_SEQUESTERED_CALCIIUM_ION_INTO_CYTOSOL_BY_ENDOPLASMIC_RETICULUM	29	- 1,978	4,79E- 02	4,47E- 02
GOBP_RESPONSE_TO_INTERLEUKIN_1	111	- 1,699	4,79E- 02	4,47E- 02
GOBP_REGULATION_OF_SIGNALING_RECEPTOR_ACTIVITY	131	- 1,651	4,95E- 02	4,62E- 02

Supplementary table 2: List of differentially expressed fibrotic genes (DEG) between DMD organoids (DMDdEx8-9) and isogenic control (IsoCTR)

SYMBOL	log2FoldChange	lfcSE	stat	padj	ENTREZID
LTBP2	1.46482	0.35696	4.10356	0.00059	4054
TGFB2-AS1	-1.27189	0.39203	-3.24435	0.00882	728463
COL26A1	1.07146	0.16936	6.3266	0	136227
COL11A1	1.69747	0.27921	6.0796	0	1301
COLEC11	3.7397	0.79652	4.69502	0.00006	78989
FN1	1.87416	0.5581	3.35811	0.00641	2335
LAMA1	0.54774	0.13076	4.18889	0.00043	284217
LAMA3	2.04302	0.54692	3.73553	0.00204	3910
ADAMTS16	2.41955	0.34774	6.95784	0	170690
ADAMTS3	1.35807	0.3278	4.14294	0.00051	9508
ADAMTS16-DT	0.79431	0.19251	4.12602	0.00054	101929176
ITGB8	0.9818	0.19317	5.08253	0.00001	3696
ITGA10	1.62742	0.35784	4.54791	0.00011	8515
ITGA11	2.72462	0.68871	3.95611	0.00099	22801
ITGA1	1.03706	0.26424	3.9247	0.00111	3672
ITGB3	1.06219	0.34528	3.07631	0.01369	3690
MMP11	2.49726	0.42584	5.86435	0	4320
MMP8	2.47365	0.61807	4.0022	0.00084	4317
POSTN	1.62385	0.74374	2.18336	0.02901	10631

Supplementary table 3: List of significant (p.adj < 0.05) differentially expressed genes (DEGs) between DMD organoids treated with μ Dystrophin (dEx8-9- μ Dys) and untreated (dEx8-9)

SYMBOL	baseMean	log2FoldChange	padj	SYMBOL	baseMean	log2FoldChange	padj
LIG1	1000,5392	0,6531	5,83E-06	GOLGA7B	48,5240	-1,3446	6,54E-03
MIR22HG	1063,4607	-0,6968	5,83E-06	C11orf96	180,9138	-0,9547	6,97E-03
SOHLH2	576,2194	-0,9356	8,75E-06	CHAMP1	560,1796	0,5941	7,04E-03
NUP160	1050,8418	0,7835	3,34E-05	JUN-DT	70,4570	-1,2729	7,04E-03
PRKG1	1450,4331	-0,7294	8,66E-05	ATG4C	134,2072	0,8595	7,24E-03
CAVIN1	5254,7199	-0,6814	9,77E-05	CLN6	827,2692	0,4361	7,44E-03
SLC37A4	626,1722	0,5484	1,15E-04	DGKB	64,23627942	-1,1852905	7,71E-03
ZMAT3	3171,2789	0,6578	1,56E-04	MPP4	27,2614601	-1,6941284	7,84E-03
OAS2	77,1247	-1,9659	3,33E-04	OAS3	196,4213086	-1,8024204	7,92E-03
LIPG	290,8780	1,0119	4,36E-04	YPEL5	1201,664733	-0,4021043	9,36E-03
RHAG	19,2703	-2,8476	4,66E-04	RRM2B	2060,696768	0,6613807	9,62E-03
SELPLG	193,8823	-0,8892	4,66E-04	LINC02897	76,44035369	-1,3247572	1,02E-02
PTCHD4	657,6944	0,7178	6,61E-04	CEBPD	587,5727939	-1,0087498	1,06E-02
GLIPR2	659,5379	-0,5602	6,93E-04	CDKN1A	29145,72183	0,6142807	1,07E-02
KIFC3	1212,9565	-0,5268	6,93E-04	EPSTI1	126,7282082	-1,3570121	1,07E-02
XRCC6	6453,6493	0,3962	6,93E-04	MCM8	440,9408017	0,5645331	1,07E-02
ZNF197	559,6452	0,4867	6,93E-04	F13A1	1256,824034	-1,4600273	1,11E-02
GBP4	42,3899	-1,5463	9,35E-04	NPPC	28,13761912	1,259235	1,11E-02
RBMX	4139,7228	0,4207	9,35E-04	SKA2	550,1168461	0,4656071	1,11E-02
NASP	3361,1595	0,5295	9,69E-04	LINC00943	29,83861433	-1,4574996	1,12E-02
POU3F4	67,5933	0,8698	9,83E-04	MAP1LC3C	295,4775752	-0,7460999	1,12E-02
POU3F3	126,0967	1,1402	1,03E-03	PDIK1L	134,48107	0,7817684	1,12E-02
CDC7	345,0627	0,7043	1,06E-03	TBXA2R	103,523345	-1,0657371	1,12E-02
PLEKHD1	52,1518	-1,0157	1,31E-03	WIPI1	2004,456144	-0,4469893	1,12E-02
CCNF	382,9842	0,5132	1,32E-03	PRR32	419,7438019	-0,75543	1,13E-02
TGFB2-OT1	66,1781	-8,1647	1,86E-03	SHFL	338,9832493	-1,111155	1,13E-02
ZNF736	136,6268	-1,9833	1,90E-03	TLX3	51,04172393	-1,0277524	1,13E-02
IFIT3	174,8642	-2,0282	2,09E-03	TRIM24	1156,273009	0,5795963	1,13E-02
IRS3P	69,3159	-1,7759	2,23E-03	UGP2	2436,639538	-0,3658706	1,13E-02
IGF2BP1	4514,1792	0,6571	3,57E-03	AIF1L	905,0844211	0,4839651	1,15E-02
SPATA18	588,7327	1,1042	3,57E-03	CDC5L	1134,788738	0,2518117	1,15E-02
ZMYND8	1088,0392	0,5686	3,57E-03	FBLIM1	1709,336299	-0,5761398	1,15E-02
EDA2R	725,5891	0,8696	3,73E-03	FZD3	1130,016024	0,6218632	1,15E-02
CCDC69	161,8949	-0,6429	3,73E-03	LINC-PINT	139,4969872	-1,0267185	1,15E-02
NOS1	31,1763	-2,9205	3,73E-03	MYADM	3372,638902	-0,4688729	1,15E-02
DYSF	7420,6525	-0,5755	4,05E-03	MTTP	45,88954342	0,7756902	1,26E-02
ASS1	3601,5646	-0,9537	4,31E-03	CCNA2	292,8950383	0,6175241	1,28E-02
POU5F1	109,6639	-1,2288	4,65E-03	FANCB	35,22102936	1,0979167	1,35E-02
FADS2	2164,0381	0,5955	4,82E-03	SRPK1	828,0131426	0,6477474	1,35E-02
EPHA7	690,0865	0,8938	5,18E-03	HBA1	13,06940795	-2,9004757	1,39E-02
GNRHR2	116,1791	-1,4601	5,18E-03	MIR503HG	1765,733501	-0,7430187	1,44E-02
LOXL1-AS1	141,8355	-1,2244	5,18E-03	RN7SL525P	17,87251773	-1,5683208	1,46E-02

SYMBOL	baseMean	log2FoldChang		padj	SYMBOL	baseMean	log2FoldChang		padj
		e					e		
RN7SL811P	59,6374	-1,5225		5,18E-03	XRCC2	211,865771	0,57941254		1,46E-02
STON2	565,8415	0,4972		5,18E-03	IFIT1	175,35659	-1,24446444		1,52E-02
AOPEP	459,9833	-0,7111		5,31E-03	CIDEC1	12,2418102	-21,4703528		1,60E-02
CSRP3	2424,9814	-1,0191		5,31E-03	PITX3	471,136095	-0,62737975		1,61E-02
FRMPD1	522,2480	-1,0549		5,31E-03	LRRC43	20,8386894	-1,24784732		1,63E-02
MX1	152,4593	-2,0200		5,31E-03	PIP5K1B	82,916257	0,68764793		1,65E-02
PPIC	926,5184	-0,5455		5,31E-03	CEP78	641,15656	0,53812082		1,68E-02
USP44	129,2749	0,9939		5,31E-03	TRIM7	228,962678	-0,7467415		1,68E-02
ZNF454	42,4108	-1,2562		5,31E-03	EDNRB	296,254773	0,78888298		1,69E-02
ALDH1L1	82,8467	-1,9848		5,33E-03	ESYT3	60,8344838	-1,32147179		1,69E-02
ISG15	248,3680	-1,5269		5,35E-03	OAS1	253,934837	-1,27461209		1,69E-02
PCDHGA6	111,0031	-1,0891		5,35E-03	PYHIN1	24,0456204	-1,45646901		1,71E-02
PPP1CC	2943,4065	0,3492		5,35E-03	SRSF10	2139,36676	0,36109586		1,71E-02
NRIP3	168,0446	-0,8902		5,36E-03	UCA1-AS1	26,3118752	-1,4921939		1,78E-02
ZNF37BP	294,6567	0,7470		5,54E-03	CPNE5	447,907943	-0,67578407		1,79E-02
PCDHGC3	5251,3722	-0,7528		5,89E-03	POLE	970,061897	0,74801259		1,79E-02
INMT	70,1100	-1,6625		6,51E-03	SESN1	1215,68951	0,48138682		1,79E-02
ZNF283	167,480938	-1,41189398		1,87E-02	STING1	503,645733	-0,7414322		2,56E-02
ERMN	27,0675747	-1,57384389		1,90E-02	ANP32A	3389,51705	0,36538935		2,56E-02
LYNX1	112,282142	2,96788048		1,90E-02	CDC6	261,235223	0,86998067		2,56E-02
ODAD1	45,0083839	-0,90639136		1,90E-02	CDH4	235,957339	0,63232976		2,56E-02
OR2A1-AS1	46,3106148	-1,54670901		1,90E-02	CERS6-AS1	209,0198	-1,3998158		2,56E-02
PSRC1	327,314093	0,60184032		1,90E-02	CMBL	965,850471	0,45022932		2,56E-02
BUB3	1547,54929	0,42872707		1,96E-02	HNRNPD	5628,93922	0,36578071		2,56E-02
KIF21A	709,972158	0,55028805		1,97E-02	NLRP10	16,1606333	-1,60647097		2,56E-02
KLK10	25,9419403	-1,5144194		1,97E-02	SSRP1	3879,38071	0,25296334		2,56E-02
RFC3	220,422361	0,56179904		1,97E-02	TMEM176A	24,1690012	-1,5468932		2,56E-02
ZCCHC24	2516,2161	-0,39718062		1,98E-02	PRXL2C	345,925678	-0,62565625		2,57E-02
DDX31	382,894563	0,38043155		2,01E-02	RARB	46,947835	-0,91977848		2,57E-02
HOXD8	116,94034	-1,09757201		2,01E-02	SOX18	28,9697216	-1,68544517		2,57E-02
LIPC	28,7927267	-1,58787362		2,01E-02	BRI3BP	264,834378	0,61473963		2,58E-02
LIPH	23,6618941	-1,51538455		2,01E-02	CCDC50	955,782014	0,36509167		2,58E-02
LINC00499	35,9908253	-1,07008293		2,03E-02	CHI3L1	154,763257	-1,01927984		2,58E-02
ARL6IP5	3119,8625	-0,39684186		2,04E-02	GPR83	17,7632471	-1,48932172		2,58E-02
CTNNA2	164,344797	0,56661585		2,04E-02	NUDT11	349,844894	0,36813909		2,58E-02
CSDE1	14212,3104	0,31028189		2,05E-02	SF3A3	2187,91601	0,38811093		2,58E-02
ILDR2	868,050967	1,08078504		2,05E-02	SOX11	2998,83523	0,38974097		2,58E-02
LINC01091	31,4637231	-1,34031157		2,05E-02	USP1	544,092255	0,46036528		2,58E-02
MIR3945HG	40,5285933	-1,58092647		2,05E-02	PMP22	1018,85507	-0,48992965		2,64E-02
ATAD5	145,036264	0,55778651		2,06E-02	MYBPHL	51,8185948	-1,32327766		2,70E-02
KLC4	531,504412	-0,49319453		2,07E-02	TMEM97	1182,11045	0,5197425		2,70E-02
FOXO6	101,783136	-0,82350763		2,09E-02	EEPD1	489,703333	-0,55720839		2,70E-02

SYMBOL	baseMean	log2FoldChange	p
POLH	1274,15352	0,56373593	2,09E-02
GRM6	42,721619	-0,89174221	2,10E-02
ANKRD1	799,655446	-0,84401649	2,13E-02
FUT9	36,0394186	1,09392342	2,13E-02
MTUS1	71,1237166	1,04469475	2,13E-02
AQP6	13,7031049	-1,40147273	2,17E-02
EPB41	763,48974	0,52991359	2,17E-02
FLACC1	15,4497271	-1,55499984	2,17E-02
LINC01291	18,2214416	-2,75554674	2,17E-02
MGP	103,207147	-1,70136348	2,17E-02
QNG1	154,114192	-0,86773983	2,17E-02
FANCI	599,901227	0,87069573	2,20E-02
SPATA1	30,4436869	-1,08899809	2,20E-02
CXXC5	2991,76552	-0,42588254	2,22E-02
DHX58	37,664992	-1,47538424	2,25E-02
CBX5	3737,72288	0,46506731	2,26E-02
HRK	100,919519	-0,85201675	2,27E-02
LMNA	17158,2938	-0,41465111	2,27E-02
NXPE3	540,530988	0,50815849	2,27E-02
PDZRN3	1773,33403	-0,4491143	2,27E-02
STOX2	347,124414	0,72791639	2,27E-02
METTL8	646,706111	0,64501018	2,31E-02
RACGAP1	436,920539	0,73999513	2,31E-02
TBC1D10A	473,123966	-0,42414148	2,31E-02
ERCC6L	66,2139124	0,70019767	2,32E-02
SERBP1	8510,23578	0,24569264	2,32E-02
DRAXIN	740,673379	0,69388962	2,34E-02
ODAD4	71,2214476	0,84997115	2,38E-02
SHOX	91,2163305	-1,22492757	2,38E-02
CHCHD2	1853,40946	-0,82703332	2,41E-02
SLC9A1	1105,79822	-0,48602902	2,42E-02
ADRA1A	15,9256137	-1,3991845	2,45E-02
EZH2	806,462882	0,4990288	2,55E-02
MAP3K7CL	334,705811	-0,73086497	2,55E-02
SLC35F1	257,698992	0,51923616	2,55E-02
TMPO	1284,66103	0,62025084	2,55E-02
USP18	53,3874799	-1,2072564	2,74E-02
WNK3	200,657631	0,66973085	2,76E-02
PCDH19	235,086853	1,06829187	2,76E-02
DSTN	3204,74446	-0,32961377	2,86E-02
GMPS	1381,26199	0,4438754	2,88E-02
ACOT2	522,121924	-0,82616567	2,88E-02

SYMBOL	baseMean	log2FoldChange	p
PELI1	252,217803	0,66295131	2,89E-02
IFI44L	78,2668217	-2,10589865	2,96E-02
KCTD1	382,201993	0,62304446	2,96E-02
LINC00906	169,214111	-1,41499517	2,96E-02
P2RY6	145,023623	-0,97115538	2,96E-02
TRIM71	763,801797	0,74168532	2,96E-02
MEX3A	2635,24951	0,29546221	2,99E-02
OR7A17	80,1726944	-1,38364805	2,99E-02
STEAP2	228,462796	-1,06938105	2,99E-02
TLCD2	414,25935	-0,76385411	2,99E-02
TGFBR1	1362,7939	0,58355195	3,03E-02
ZNF676	47,0298453	-1,40574889	3,27E-02
LINC01284	43,4770399	-1,26138533	3,33E-02
TCF23	82,9552366	-1,34111258	3,33E-02
DBET	10,5430892	-2,04311204	3,36E-02
DHX33	816,130284	0,57843117	3,36E-02
NCAPG	360,12047	0,74945051	3,36E-02
PLK2	1649,53785	0,57936085	3,36E-02
SALL2	1399,7216	0,52761439	3,36E-02
SLITRK6	23,5975929	1,04935378	3,45E-02
LGMN	1188,1994	-0,36114093	3,47E-02
RN7SL693P	9,10095369	-1,80541088	3,48E-02
KCNJ15	140,149492	-1,28581717	3,49E-02
HSPB6	551,668317	-1,04794127	3,50E-02
FUT2	47,6456569	-1,3059679	3,55E-02
MGLL	1191,75611	-0,54239522	3,55E-02
KIF14	205,192034	0,74416251	3,57E-02
MYT1L	202,820634	-0,9024693	3,57E-02
KLHL23	489,315657	0,57867241	3,57E-02
ACTL6A	720,932895	0,49356944	3,58E-02
CTSF	184,30954	-0,79632765	0,03579871
LMCD1	602,458709	-0,69652737	0,03579871
NPNT	1412,59973	-0,66726875	0,03579871
PA2G4	4159,10279	0,28081156	0,03579871
TMEM74B	93,9888354	-0,6223597	0,03579871
TRIM7-AS1	16,5424639	-1,85560793	0,03579871
IFIT2	64,9669999	-1,84914502	0,03580412
TRAC	28,8670893	-1,13382726	0,03596447
MIOS	416,698574	0,464336	0,03622571
USH1C	52,1065915	-2,04301545	0,0363394
ACTA1	16756,0636	-0,7011716	0,03635759
ZNF195	886,866103	0,48126523	0,03635759

SYMBOL	baseMean	log2FoldChange	padj
PLP2	1317,47877	-0,70731028	0,03683504
PANTR1	27,8375799	1,41253013	3,72E-02
USP3	715,6791	0,44532947	3,75E-02
DNMT1	2786,88978	0,58887636	3,77E-02
SH3BGRL2	188,445927	0,46191252	3,82E-02
HMGB3	1505,11334	0,44760613	3,91E-02
LINC01836	52,1355315	-1,03278381	3,94E-02
P3H2-AS1	32,4041892	-1,19073158	3,97E-02
ANGPT1	73,982223	0,77455461	4,02E-02
ANXA2	10633,3481	-0,59065215	4,02E-02
TRPV3	118,117847	0,42670428	4,02E-02
TSC22D2	943,745267	0,3835247	4,02E-02
EXPH5	119,343359	-0,84959224	4,03E-02
HMGA2	885,551762	0,6920233	4,03E-02
IPO9	2920,94477	0,4773307	4,03E-02
RBL1	148,810088	0,58467359	4,03E-02
RNF40	2671,4555	0,33783875	4,03E-02
TNFRSF12A	2365,62997	-0,5009047	4,03E-02
RAVER2	313,441009	0,5035075	4,05E-02
TRPA1	14,8684788	-3,69231915	4,05E-02
ZNF561	1007,07414	0,51170599	4,05E-02
DKC1	1213,93811	0,36284362	4,13E-02
AGBL4	30,5218083	-1,57919569	4,23E-02
CA7	35,5226054	-1,54103649	4,23E-02
CDH8	272,014685	0,67907635	4,23E-02
CYFIP2	2608,97205	0,40895033	4,23E-02
GJC1	661,257461	0,55201593	4,23E-02
MEIS1	349,994528	0,94374198	4,23E-02
SLC30A3	101,989839	-1,00801858	4,23E-02
KRT80	75,5458366	-0,8713149	4,23E-02
TG	35,7901253	-2,09691612	4,32E-02
SFPQ	5378,37143	0,29981342	4,33E-02
MCM7	2377,60618	0,47589273	4,34E-02
POLD3	293,73598	0,57773064	4,34E-02
CBS	1440,41818	0,55047575	4,36E-02
RN7SL274P	23,1475721	-1,26472716	4,36E-02
SLC14A2	47,9952905	-1,32891763	4,39E-02
FBXO45	396,588789	0,33333201	4,40E-02

Supplementary table 4: List of GO biological processes differentially expressed between DMD organoids treated with μ Dystrophin (dEx8-9- μ Dys) and isogenic control (IsoCTR)

Description	setSize	NES	p.adjust	qvalue
GOBP_CHROMOSOME_SEGREGATION	315	2,441	2,438E-15	2,123E-15
GOBP_DNA_CONFORMATION_CHANGE	307	2,393	2,687E-14	2,340E-14
GOBP_NUCLEAR_CHROMOSOME_SEGREGATION	257	2,415	8,634E-14	7,519E-14
GOBP_MITOTIC_NUCLEAR_DIVISION	282	2,405	8,634E-14	7,519E-14
GOBP_MUSCLE_CONTRACTION	308	-2,389	8,634E-14	7,519E-14
GOBP_MUSCLE_SYSTEM_PROCESS	390	-2,271	9,797E-14	8,531E-14
GOBP_SISTER_CHROMATID_SEGREGATION	191	2,555	1,137E-13	9,904E-14
GOBP_ORGANELLE_FISSION	447	2,144	2,189E-13	1,907E-13
GOBP_MITOTIC_SISTER_CHROMATID_SEGREGATION	166	2,560	6,143E-13	5,349E-13
GOBP_DNA_REPLICATION	275	2,340	9,545E-13	8,312E-13
GOBP_DNA_DEPENDENT_DNA_REPLICATION	156	2,503	8,007E-12	6,972E-12
GOBP_SPINDLE_ORGANIZATION	199	2,294	8,586E-10	7,477E-10
GOBP_DNA_REPLICATION_DEPENDENT_CHROMATIN_ORGANIZATION	32	2,676	5,077E-09	4,421E-09
GOBP_DNA_PACKAGING	212	2,237	5,519E-09	4,806E-09
GOBP_CELL_CYCLE_PHASE_TRANSITION	487	1,883	6,046E-09	5,265E-09
GOBP_RECOMBINATIONAL_REPAIR	156	2,316	6,395E-09	5,569E-09
GOBP_DOUBLE_STRAND_BREAK_REPAIR	261	2,105	4,960E-08	4,319E-08
GOBP_NEGATIVE_REGULATION_OF_MEGAKARYOCYTE_DIFFERENTIATION	17	2,531	1,318E-07	1,147E-07
GOBP_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	399	1,901	1,807E-07	1,573E-07
GOBP_STRIATED_MUSCLE_CONTRACTION	161	-2,289	2,013E-07	1,753E-07
GOBP_DNA_RECOMBINATION	290	2,029	2,013E-07	1,753E-07
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE	285	1,993	2,667E-07	2,323E-07
GOBP_SPINDLE_ASSEMBLY	134	2,237	4,124E-07	3,591E-07
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE_PROCESS	211	2,086	4,124E-07	3,591E-07
GOBP_REGULATION_OF_MITOTIC_CELL_CYCLE	430	1,849	4,124E-07	3,591E-07
GOBP_REGULATION_OF_SYSTEM_PROCESS	482	-1,866	5,351E-07	4,659E-07
GOBP_AEROBIC_RESPIRATION	166	-2,210	6,655E-07	5,795E-07
GOBP_DNA_REPLICATION_INDEPENDENT_CHROMATIN_ORGANIZATION	34	2,490	7,647E-07	6,659E-07
GOBP_MICROTUBULE_CYTOSKELETON_ORGANIZATION_INVOLVED_IN_MITOSIS	150	2,167	9,443E-07	8,223E-07

GOBP_REGULATION_OF_MUSCLE_SYSTEM_PROCESS	209	-2,111	9,443E-07	8,223 E-07
GOBP_OXIDATIVE_PHOSPHORYLATION	119	-2,294	1,544E-06	1,345 E-06
GOBP_ENERGY_DERIVATION_BY_OXIDATION_OF_ORGANIC_C OMPOUNDS	281	-2,004	1,544E-06	1,345 E-06
GOBP_CELLULAR_RESPIRATION	208	-2,124	2,099E-06	1,828 E-06
GOBP_REGULATION_OF_MUSCLE_CONTRACTION	143	-2,244	2,512E-06	2,187 E-06
GOBP_REGULATION_OF_CELL_CYCLE_PHASE_TRANSITION	368	1,857	2,512E-06	2,187 E-06
GOBP_ACTIVATION_OF_GTPASE_ACTIVITY	107	2,221	3,770E-06	3,283 E-06
GOBP_CHROMATIN_ASSEMBLY_OR_DISASSEMBLY	200	2,012	3,873E-06	3,373 E-06
GOBP_CYTOPLASMIC_TRANSLATION	146	-2,104	7,567E-06	6,590 E-06
GOBP_PROTEIN_DNA_COMPLEX_ASSEMBLY	172	2,044	7,567E-06	6,590 E-06
GOBP_SKELETAL_MUSCLE_CONTRACTION	41	-2,400	9,857E-06	8,583 E-06
GOBP_ATP_SYNTHESIS_COUPLED_ELECTRON_TRANSPORT	77	-2,246	1,091E-05	9,502 E-06
GOBP_PROTEIN_DNA_COMPLEX_SUBUNIT_ORGANIZATION	220	1,930	1,381E-05	1,203 E-05
GOBP_DNA_GEOMETRIC_CHANGE	94	2,232	1,515E-05	1,319 E-05
GOBP_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANS ITION	284	1,866	1,636E-05	1,425 E-05
GOBP_SISTER_CHROMATID_COHESION	53	2,312	2,002E-05	1,743 E-05
GOBP_HEART_PROCESS	224	-1,990	2,002E-05	1,743 E-05
GOBP_ACTIN_MYOSIN_FILAMENT_SLIDING	14	-2,278	2,131E-05	1,856 E-05
GOBP_MITOCHONDRIAL_RESPIRATORY_CHAIN_COMPLEX_ASS SEMBLY	89	-2,290	2,225E-05	1,937 E-05
GOBP_CHROMOSOME_SEPARATION	89	2,163	2,294E-05	1,998 E-05
GOBP_REGULATION_OF_BLOOD_CIRCULATION	219	-2,011	2,350E-05	2,046 E-05
GOBP_MICROTUBULE_ORGANIZING_CENTER_ORGANIZATION	141	2,061	2,536E-05	2,208 E-05
GOBP_TELOMERE_ORGANIZATION	160	2,014	2,931E-05	2,552 E-05
GOBP_REGULATION_OF_DNA_REPLICATION	128	2,049	3,085E-05	2,687 E-05
GOBP_MULTICELLULAR_ORGANISMAL_MOVEMENT	53	-2,319	3,613E-05	3,146 E-05
GOBP_REGULATION_OF_CHROMOSOME_ORGANIZATION	207	1,904	3,613E-05	3,146 E-05
GOBP_HISTONE_MODIFICATION	470	1,656	3,613E-05	3,146 E-05
GOBP_CENTROMERE_COMPLEX_ASSEMBLY	31	2,322	3,801E-05	3,310 E-05
GOBP_REGULATION_OF_STRIATED_MUSCLE_CONTRACTION	83	-2,182	3,801E-05	3,310 E-05
GOBP_CILIUM_ORGANIZATION	384	1,733	3,801E-05	3,310 E-05
GOBP_REGULATION_OF_CHROMOSOME_SEGREGATION	82	2,195	3,914E-05	3,409 E-05
GOBP_REGULATION_OF_HEART_CONTRACTION	181	-2,014	4,084E-05	3,556 E-05

GOBP_CELL_CYCLE_CHECKPOINT_SIGNALING	165	1,968	4,886E-05	4,255 E-05
GOBP_MITOTIC_CELL_CYCLE_CHECKPOINT_SIGNALING	127	2,036	5,866E-05	5,108 E-05
GOBP_ATP_METABOLIC_PROCESS	240	-1,881	6,521E-05	5,678 E-05
GOBP_NADH_DEHYDROGENASE_COMPLEX_ASSEMBLY	53	-2,272	8,750E-05	7,619 E-05
GOBP_NEURAL_PRECURSOR_CELL_PROLIFERATION	136	1,997	9,374E-05	8,163 E-05
GOBP_MEIOTIC_CELL_CYCLE	215	1,842	9,621E-05	8,378 E-05
GOBP_MEIOTIC_CELL_CYCLE_PROCESS	164	1,912	1,334E-04	1,162 E-04
GOBP_MITOTIC_SPINDLE_ORGANIZATION	124	2,015	1,437E-04	1,251 E-04
GOBP_PROTEIN_LOCALIZATION_TO_CHROMOSOME	90	2,068	1,766E-04	1,538 E-04
GOBP_REGULATION_OF_MEGAKARYOCYTE_DIFFERENTIATION	35	2,251	1,879E-04	1,637 E-04
GOBP_NEGATIVE_REGULATION_OF_CELL_CYCLE_PHASE_TRANSITION	224	1,809	1,879E-04	1,637 E-04
GOBP_CELL_CYCLE_DNA_REPLICATION	43	2,218	1,948E-04	1,697 E-04
GOBP_NEGATIVE_REGULATION_OF_CELL_CYCLE	339	1,684	2,000E-04	1,742 E-04
GOBP_MUSCLE_CELL_DEVELOPMENT	168	-1,916	2,240E-04	1,951 E-04
GOBP_REGULATION_OF_CATION_TRANSMEMBRANE_TRANSPORT	298	-1,794	2,263E-04	1,970 E-04
GOBP_RESPIRATORY_ELECTRON_TRANSPORT_CHAIN	98	-2,138	2,353E-04	2,049 E-04
GOBP_CHROMATIN_REMODELING	234	1,810	2,353E-04	2,049 E-04
GOBP_STRIATED_MUSCLE_CELL_DEVELOPMENT	64	-2,244	2,922E-04	2,544 E-04
GOBP_CELL_CELL_ADHESION_VIA_PLASMA_MEMBRANE_ADHESION_MOLECULES	246	1,743	2,922E-04	2,544 E-04
GOBP_CELLULAR_RESPONSE_TO_INTERLEUKIN_1	86	-2,035	3,145E-04	2,738 E-04
GOBP_MITOCHONDRIAL_ELECTRON_TRANSPORT_NADH_TO_UBIQUINONE	43	-2,231	3,763E-04	3,276 E-04
GOBP_REGULATION_OF_DNA_DEPENDENT_DNA_REPLICATION	51	2,164	4,143E-04	3,608 E-04
GOBP_REGULATION_OF_CHROMOSOME_SEPARATION	67	2,100	4,186E-04	3,645 E-04
GOBP_NEGATIVE_REGULATION_OF_MITOTIC_CELL_CYCLE	205	1,826	4,665E-04	4,062 E-04
GOBP_REGULATION_OF_DENDRITIC_CELL_DIFFERENTIATION	11	-2,085	4,756E-04	4,142 E-04
GOBP_NEGATIVE_REGULATION_OF_CELL_CYCLE_PROCESS	266	1,719	4,988E-04	4,343 E-04
GOBP_REGULATION_OF_DNA_METABOLIC_PROCESS	376	1,600	5,115E-04	4,454 E-04
GOBP_REGULATION_OF_MITOTIC_NUCLEAR_DIVISION	104	1,953	5,195E-04	4,524 E-04
GOBP_REGULATION_OF_NUCLEAR_DIVISION	124	1,938	5,478E-04	4,770 E-04
GOBP_NEUROMUSCULAR_PROCESS	138	-1,906	6,132E-04	5,340 E-04
GOBP_NUCLEUS_ORGANIZATION	129	1,886	6,132E-04	5,340 E-04
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE_PHASE_TRANSITION	109	1,926	6,133E-04	5,341 E-04

GOBP_GENERATION_OF_PRECURSOR_METABOLITES_AND_ENERGY	436	-1,642	6,135E-04	5,342E-04
GOBP_NEGATIVE_REGULATION_OF_CHROMOSOME_ORGANIZATION	86	1,985	6,897E-04	6,006E-04
GOBP_SARCOMERE_ORGANIZATION	40	-2,200	7,359E-04	6,408E-04
GOBP_HOMOPHILIC_CELL_ADHESION_VIA_PLASMA_MEMBRANE_ADHESION_MOLECULES	157	1,870	7,359E-04	6,408E-04
GOBP_DIVALENT_INORGANIC_CATION_HOMEOSTASIS	401	-1,656	7,406E-04	6,449E-04
GOBP_PROTON_TRANSMEMBRANE_TRANSPORT	123	-2,009	8,395E-04	7,311E-04
GOBP_SEX_DIFFERENTIATION	234	1,735	8,522E-04	7,421E-04
GOBP_DNA_REPLICATION_INITIATION	36	2,150	8,635E-04	7,519E-04
GOBP_CELL_CYCLE_G2_M_PHASE_TRANSITION	150	1,819	8,660E-04	7,541E-04
GOBP_DNA_INTEGRITY_CHECKPOINT_SIGNALING	119	1,899	8,722E-04	7,595E-04
GOBP_STRIATED_MUSCLE_CELL_DIFFERENTIATION	251	-1,745	8,722E-04	7,595E-04
GOBP_ACTIN_MEDIATED_CELL_CONTRACTION	94	-1,963	8,894E-04	7,745E-04
GOBP_CENTROSOME_DUPLICATION	72	1,964	1,016E-03	8,847E-04
GOBP_REGULATION_OF_DNA_REPAIR	149	1,848	1,035E-03	9,012E-04
GOBP_HETEROCHROMATIN_ORGANIZATION	75	2,009	1,069E-03	9,305E-04
GOBP_METAPHASE_ANAPHASE_TRANSITION_OF_CELL_CYCLE	62	2,083	1,082E-03	9,420E-04
GOBP_DNA_STRAND_ELONGATION_INVOLVED_IN_DNA_REPLICATION	15	2,128	1,174E-03	1,022E-03
GOBP_MITOTIC_SPINDLE_ASSEMBLY	70	1,988	1,215E-03	1,058E-03
GOBP_REGULATION_OF_CELL_CYCLE_G2_M_PHASE_TRANSITION	104	1,890	1,368E-03	1,191E-03
GOBP_REGULATION_OF_ION_TRANSMEMBRANE_TRANSPORT	404	-1,653	1,485E-03	1,293E-03
GOBP_SARCOPLASMIC_RETICULUM_CALCIIUM_ION_TRANSPORT	36	-2,140	1,553E-03	1,353E-03
GOBP_NUCLEOSOME_ORGANIZATION	146	1,828	1,599E-03	1,392E-03
GOBP_DNA_DEPENDENT_DNA_REPLICATION_MAINTENANCE_OF_FIDELITY	47	2,053	1,612E-03	1,404E-03
GOBP_BLASTOCYST_GROWTH	20	2,162	1,646E-03	1,434E-03
GOBP_CARDIAC_MUSCLE_CONTRACTION	123	-1,968	1,650E-03	1,437E-03
GOBP_NEGATIVE_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	160	1,796	1,653E-03	1,439E-03
GOBP_RESPONSE_TO_BACTERIUM	454	-1,607	1,653E-03	1,439E-03
GOBP_MUSCLE_ORGAN_DEVELOPMENT	314	-1,680	1,723E-03	1,500E-03
GOBP_MALE_SEX_DIFFERENTIATION	140	1,796	1,725E-03	1,502E-03
GOBP_HISTONE_METHYLATION	148	1,793	1,725E-03	1,502E-03
GOBP_POSITIVE_REGULATION_OF_MITOTIC_CELL_CYCLE	114	1,889	1,730E-03	1,507E-03
GOBP_NUCLEOSOME_ASSEMBLY	99	1,916	1,804E-03	1,571E-03

GOBP_REGULATION_OF_METAL_ION_TRANSPORT	340	-1,676	1,842E-03	1,604 E-03
GOBP_KINETOCHORE_ORGANIZATION	23	2,143	1,856E-03	1,617 E-03
GOBP_REGULATION_OF_DOUBLE_STRAND_BREAK_REPAIR_VIA_HOMOLOGOUS_RECOMBINATION	68	1,977	1,878E-03	1,636 E-03
GOBP_POSITIVE_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANSITION	87	1,908	1,878E-03	1,636 E-03
GOBP_INNER_CELL_MASS_CELL_PROLIFERATION	13	2,079	1,965E-03	1,711 E-03
GOBP_RESPONSE_TO_INTERLEUKIN_1	111	-2,009	1,986E-03	1,729 E-03
GOBP_DNA_UNWINDING_INVOLVED_IN_DNA_REPLICATION	22	2,129	2,011E-03	1,751 E-03
GOBP_CHROMOSOME_CONDENSATION	37	2,098	2,508E-03	2,184 E-03
GOBP_REGULATION_OF_SKELETAL_MUSCLE_ADAPTATION	12	-2,025	2,508E-03	2,184 E-03
GOBP_POSITIVE_REGULATION_OF_DNA_METABOLIC_PROCESS	221	1,637	2,826E-03	2,461 E-03
GOBP_METAPHASE_PLATE_CONGRESSION	66	1,971	3,015E-03	2,626 E-03
GOBP_NEGATIVE_REGULATION_OF_GENE_EXPRESSION_EPIGENETIC	74	1,920	3,073E-03	2,676 E-03
GOBP_REGULATION_OF_EMBRYONIC_DEVELOPMENT	60	1,952	3,157E-03	2,749 E-03
GOBP_CALCIIUM_ION_TRANSPORT	353	-1,582	3,157E-03	2,749 E-03
GOBP_EOSINOPHIL_CHEMOTAXIS	14	-2,051	3,237E-03	2,818 E-03
GOBP_NEUROBLAST_PROLIFERATION	57	1,965	3,555E-03	3,096 E-03
GOBP_ELECTRON_TRANSPORT_CHAIN	148	-1,775	3,555E-03	3,096 E-03
GOBP_REGULATION_OF_TRANSMEMBRANE_TRANSPORT	479	-1,522	3,555E-03	3,096 E-03
GOBP_MUSCLE_CELL_DIFFERENTIATION	345	-1,584	3,754E-03	3,269 E-03
GOBP_PROTEIN_LOCALIZATION_TO_CHROMOSOME_CENTROMERIC_REGION	25	2,053	3,917E-03	3,411 E-03
GOBP_REPLICATION_FORK_PROCESSING	39	2,019	3,917E-03	3,411 E-03
GOBP_CELL_FATE_COMMITMENT	215	1,653	3,917E-03	3,411 E-03
GOBP_MITOTIC_DNA_INTEGRITY_CHECKPOINT_SIGNALING	82	1,900	4,047E-03	3,524 E-03
GOBP_ACUTE_INFLAMMATORY_RESPONSE	78	-1,982	4,172E-03	3,633 E-03
GOBP_MITOTIC_METAPHASE_PLATE_CONGRESSION	53	1,944	5,156E-03	4,489 E-03
GOBP_REGULATION_OF_MITOTIC_SISTER_CHROMATID_SEGREGATION	43	1,966	5,376E-03	4,681 E-03
GOBP_SIGNAL_TRANSDUCTION_IN_RESPONSE_TO_DNA_DAMAGE	168	1,683	5,739E-03	4,998 E-03
GOBP_FOREBRAIN_DEVELOPMENT	344	1,538	5,739E-03	4,998 E-03
GOBP_DOUBLE_STRAND_BREAK_REPAIR_VIA_BREAK_INDUCED_REPLICATION	12	2,036	5,869E-03	5,111 E-03
GOBP_REGULATION_OF_CALCIIUM_ION_TRANSPORT	211	-1,694	6,003E-03	5,227 E-03
GOBP_SPINDLE_MIDZONE_ASSEMBLY	11	1,991	6,141E-03	5,347 E-03
GOBP_MIDBRAIN_DEVELOPMENT	84	1,795	6,198E-03	5,397 E-03

GOBP_NEGATIVE_REGULATION_OF_LEUKOCYTE_MIGRATION	41	-1,975	6,215E-03	5,412 E-03
GOBP_REGULATION_OF_DNA_DIRECTED_DNA_POLYMERASE_ACTIVITY	13	2,001	6,343E-03	5,524 E-03
GOBP_MEGAKARYOCYTE_DIFFERENTIATION	55	1,918	6,796E-03	5,918 E-03
GOBP_MUSCLE_ADAPTATION	98	-1,893	6,796E-03	5,918 E-03
GOBP_REGULATION_OF_DNA_RECOMBINATION	120	1,734	6,796E-03	5,918 E-03
GOBP_SENSORY_ORGAN_MORPHOGENESIS	231	1,604	6,796E-03	5,918 E-03
GOBP_LEUKOCYTE_MIGRATION	293	-1,603	6,796E-03	5,918 E-03
GOBP_REGULATION_OF_GTPASE_ACTIVITY	336	1,513	6,796E-03	5,918 E-03
GOBP_CELLULAR_COMPONENT_ASSEMBLY_INVOLVED_IN_MORPHOGENESIS	99	-1,908	6,934E-03	6,038 E-03
GOBP_ACUTE_PHASE_RESPONSE	32	-2,016	7,004E-03	6,099 E-03
GOBP_ACTIN_FILAMENT_BASED_MOVEMENT	121	-1,793	7,004E-03	6,099 E-03
GOBP_REGULATION_OF_NEURAL_PRECURSOR_CELL_PROLIFERATION	79	1,803	7,426E-03	6,467 E-03
GOBP_REGULATION_OF_SKELETAL_MUSCLE_CONTRACTION	16	-2,014	7,509E-03	6,539 E-03
GOBP_LYMPHOCYTE_MIGRATION	89	-1,912	7,509E-03	6,539 E-03
GOBP_NEPHRIC_DUCT_MORPHOGENESIS	11	1,963	7,666E-03	6,676 E-03
GOBP_CIRCULATORY_SYSTEM_PROCESS	500	-1,486	7,837E-03	6,824 E-03
GOBP_CELL_CELL_SIGNALING_BY_WNT	416	1,453	7,945E-03	6,918 E-03
GOBP_MICROTUBULE_BUNDLE_FORMATION	109	1,707	8,193E-03	7,134 E-03
GOBP_WNT_SIGNALING_PATHWAY_INVOLVED_IN_MIDBRAIN_DOPAMINERGIC_NEURON_DIFFERENTIATION	12	2,008	8,324E-03	7,248 E-03
GOBP_EOSINOPHIL_MIGRATION	17	-2,024	9,110E-03	7,933 E-03
GOBP_NEUTROPHIL_MIGRATION	90	-1,822	9,150E-03	7,968 E-03
GOBP_INTERLEUKIN_1_MEDIATED_SIGNALING_PATHWAY	26	-1,976	9,216E-03	8,025 E-03
GOBP_REGULATION_OF_TRANSPORTER_ACTIVITY	246	-1,618	9,652E-03	8,405 E-03
GOBP_MITOTIC_SISTER_CHROMATID_COHESION	26	2,015	1,022E-02	8,900 E-03
GOBP_REGULATION_OF_HIPPO_SIGNALING	21	1,998	1,022E-02	8,900 E-03
GOBP_REGULATION_OF_GENE_EXPRESSION_EPIGENETIC	130	1,713	1,048E-02	9,122 E-03
GOBP_ATTACHMENT_OF_SPINDLE_MICROTUBULES_TO_KINETOCHORE	37	1,961	1,089E-02	9,487 E-03
GOBP_POSITIVE_REGULATION_OF_GTPASE_ACTIVITY	250	1,557	1,107E-02	9,639 E-03
GOBP_EMBRYONIC_PATTERN_SPECIFICATION	56	1,849	1,115E-02	9,714 E-03
GOBP_REGULATION_OF_ORGANELLE_ASSEMBLY	220	1,580	1,152E-02	1,003 E-02
GOBP_NEGATIVE_REGULATION_OF_METAPHASE_ANAPHASE_TRANSITION_OF_CELL_CYCLE	40	1,941	1,163E-02	1,012 E-02

GOBP_REGULATION_OF_SMOOTHENED_SIGNALING_PATHWAY	78	1,829	1,163E-02	1,012 E-02
GOBP_REPRODUCTIVE_SYSTEM_DEVELOPMENT	374	1,450	1,163E-02	1,012 E-02
GOBP_DNA_REPLICATION_CHECKPOINT_SIGNALING	16	1,999	1,177E-02	1,025 E-02
GOBP_REGULATION_OF_CALCIIUM_ION_TRANSMEMBRANE_TRANSPORT	131	-1,738	1,177E-02	1,025 E-02
GOBP_PROTEIN_AUTOPHOSPHORYLATION	214	1,576	1,201E-02	1,046 E-02
GOBP_POSITIVE_REGULATION_OF_CYTOKINE_PRODUCTION	373	-1,521	1,201E-02	1,046 E-02
GOBP_DNA_STRAND_ELONGATION	37	1,949	1,216E-02	1,059 E-02
GOBP_UROGENITAL_SYSTEM_DEVELOPMENT	327	1,464	1,216E-02	1,059 E-02
GOBP_REGULATION_OF_SISTER_CHROMATID_COHESION	21	1,963	1,330E-02	1,158 E-02
GOBP_PROTEIN_LOCALIZATION_TO_CHROMATIN	30	1,958	1,330E-02	1,158 E-02
GOBP_REGULATION_OF_ATPASE_COUPLED_CALCIIUM_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	12	-1,905	1,330E-02	1,158 E-02
GOBP_SPINAL_CORD_DEVELOPMENT	87	1,737	1,330E-02	1,158 E-02
GOBP_OSSIFICATION	371	1,425	1,330E-02	1,158 E-02
GOBP_REGULATION_OF_CHROMOSOME_CONDENSATION	11	1,929	1,335E-02	1,163 E-02
GOBP_REGULATION_OF_ATP_DEPENDENT_ACTIVITY	70	-1,794	1,336E-02	1,164 E-02
GOBP_CARDIAC_MUSCLE_TISSUE_MORPHOGENESIS	55	-1,866	1,349E-02	1,175 E-02
GOBP_REGULATION_OF_CALCIIUM_ION_TRANSMEMBRANE_TRANSPORTER_ACTIVITY	81	-1,801	1,349E-02	1,175 E-02
GOBP_CHROMOSOME_LOCALIZATION	80	1,782	1,408E-02	1,226 E-02
GOBP_MEIOTIC_CHROMOSOME_SEGREGATION	74	1,778	1,421E-02	1,237 E-02
GOBP_DNA_TEMPLATED_TRANSCRIPTION_INITIATION	126	1,636	1,465E-02	1,276 E-02
GOBP_INTERLEUKIN_6_PRODUCTION	125	-1,731	1,468E-02	1,278 E-02
GOBP_NEGATIVE_REGULATION_OF_INNATE_IMMUNE_RESPONSE	62	-1,890	1,519E-02	1,323 E-02
GOBP_CYTOCHROME_COMPLEX_ASSEMBLY	35	-1,943	1,567E-02	1,365 E-02
GOBP_RESPONSE_TO_INORGANIC_SUBSTANCE	470	-1,453	1,581E-02	1,377 E-02
GOBP_CHROMOSOME_ORGANIZATION_INVOLVED_IN_MEIOTIC_CELL_CYCLE	54	1,825	1,681E-02	1,464 E-02
GOBP_DEVELOPMENT_OF_PRIMARY_SEXUAL_CHARACTERISTICS	192	1,588	1,681E-02	1,464 E-02
GOBP_HIPPO_SIGNALING	40	1,899	1,711E-02	1,490 E-02
GOBP_STRIATED_MUSCLE_ADAPTATION	42	-1,961	1,762E-02	1,535 E-02
GOBP_NEGATIVE_REGULATION_OF_NUCLEAR_DIVISION	52	1,883	1,772E-02	1,543 E-02
GOBP_MAINTENANCE_OF_CELL_NUMBER	132	1,671	1,901E-02	1,655 E-02
GOBP_CELL_DIFFERENTIATION_IN_SPINAL_CORD	41	1,882	1,915E-02	1,668 E-02
GOBP_MEIOSIS_I_CELL_CYCLE_PROCESS	106	1,703	1,936E-02	1,686 E-02

GOBP_MORPHOGENESIS_OF_AN_EPITHELIAL_FOLD	20	1,961	1,974E-02	1,719 E-02
GOBP_INTERSTRAND_CROSS_LINK_REPAIR	31	1,848	2,026E-02	1,764 E-02
GOBP_ATP_BIOSYNTHETIC_PROCESS	48	-1,885	2,028E-02	1,766 E-02
GOBP_MITOTIC_G2_M_TRANSITION_CHECKPOINT	47	1,824	2,028E-02	1,766 E-02
GOBP_MONONUCLEAR_CELL_MIGRATION	148	-1,640	2,132E-02	1,857 E-02
GOBP_CALCIIUM_ION_TRANSMEMBRANE_TRANSPORT	264	-1,530	2,180E-02	1,898 E-02
GOBP_LYMPHOCYTE_CHEMOTAXIS	40	-1,874	2,197E-02	1,913 E-02
GOBP_SKELETAL_MUSCLE_ADAPTATION	21	-1,927	2,246E-02	1,955 E-02
GOBP_POSITIVE_REGULATION_OF_TRANSFERASE_ACTIVITY	499	1,359	2,246E-02	1,955 E-02
GOBP_CATECHOLAMINE_SECRETION	47	-1,860	2,255E-02	1,963 E-02
GOBP_RESPONSE_TO_STIMULUS_INVOLVED_IN_REGULATION_OF_MUSCLE_ADAPTATION	13	-1,915	2,276E-02	1,982 E-02
GOBP_PROTEIN_LOCALIZATION_TO_CONDENSED_CHROMOSOME	19	2,013	2,297E-02	2,000 E-02
GOBP_PATTERN_SPECIFICATION_PROCESS	398	1,427	2,386E-02	2,078 E-02
GOBP_CELL_CHEMOTAXIS	233	-1,573	2,440E-02	2,125 E-02
GOBP_REGULATION_OF_ATTACHMENT_OF_SPINDLE_MICROTUBULES_TO_KINETOCHORE	13	1,888	2,445E-02	2,129 E-02
GOBP_POSITIVE_REGULATION_OF_INTERLEUKIN_1_PRODUCTION	60	-1,876	2,445E-02	2,129 E-02
GOBP_POSITIVE_REGULATION_OF_NERVOUS_SYSTEM_DEVELOPMENT	250	1,494	2,445E-02	2,129 E-02
GOBP_FAT_SOLUBLE_VITAMIN_METABOLIC_PROCESS	30	1,889	2,458E-02	2,140 E-02
GOBP_HISTONE_H3_K4_METHYLATION	67	1,756	2,458E-02	2,140 E-02
GOBP_CELL_CYCLE_G1_S_PHASE_TRANSITION	217	1,517	2,491E-02	2,170 E-02
GOBP_POSITIVE_REGULATION_OF_HISTONE_METHYLATION	45	1,845	2,555E-02	2,225 E-02
GOBP_REGULATION_OF_CYTOSOLIC_CALCIIUM_ION_CONCENTRATION	264	-1,517	2,556E-02	2,226 E-02
GOBP_POSITIVE_REGULATION_OF_INTERLEUKIN_1_BETA_PRODUCTION	51	-1,841	2,556E-02	2,226 E-02
GOBP_VENTRICULAR_CARDIAC_MUSCLE_TISSUE_MORPHOGENESIS	44	-1,864	2,562E-02	2,231 E-02
GOBP_REGULATION_OF_DOUBLE_STRAND_BREAK_REPAIR	107	1,683	2,575E-02	2,242 E-02
GOBP_SKIN_DEVELOPMENT	194	1,515	2,575E-02	2,242 E-02
GOBP_CHROMATIN_REMODELING_AT_CENTROMERE	11	1,886	2,653E-02	2,310 E-02
GOBP_PEPTIDYL_LYSINE_METHYLATION	134	1,650	2,685E-02	2,338 E-02
GOBP_PROTEIN_METHYLATION	185	1,511	2,685E-02	2,338 E-02
GOBP_DEFENSE_RESPONSE_TO_BACTERIUM	159	-1,652	2,814E-02	2,451 E-02
GOBP_RESPONSE_TO_PEPTIDOGLYCAN	10	-1,844	2,864E-02	2,494 E-02

GOBP_POSITIVE_REGULATION_OF_DOUBLE_STRAND_BREAK_REPAIR_VIA_HOMOLOGOUS_RECOMBINATION	35	1,849	2,872E-02	2,501E-02
GOBP_VENTRICULAR_CARDIAC_MUSCLE_TISSUE_DEVELOPMENT	52	-1,882	2,893E-02	2,519E-02
GOBP_SENSORY_ORGAN_DEVELOPMENT	490	1,340	2,904E-02	2,529E-02
GOBP_MITOTIC_CHROMOSOME_CONDENSATION	19	1,983	2,933E-02	2,554E-02
GOBP_KINETOCHORE_ASSEMBLY	18	1,933	3,074E-02	2,676E-02
GOBP_REGULATION_OF_LEUKOCYTE_MIGRATION	171	-1,593	3,096E-02	2,696E-02
GOBP_RESPONSE_TO_VITAMIN_A	12	1,898	3,101E-02	2,701E-02
GOBP_NEPHRON_DEVELOPMENT	137	1,540	3,130E-02	2,726E-02
GOBP_POSITIVE_REGULATION_OF_SMOOTHENED_SIGNALING_PATHWAY	34	1,862	3,217E-02	2,801E-02
GOBP_NEGATIVE_REGULATION_OF_CALCIIUM_ION_TRANSPORT	48	-1,813	3,251E-02	2,831E-02
GOBP_SMOOTHENED_SIGNALING_PATHWAY	134	1,626	3,456E-02	3,009E-02
GOBP_REGULATION_OF_MEIOTIC_CELL_CYCLE	40	1,805	3,470E-02	3,022E-02
GOBP_T_CELL_MIGRATION	52	-1,845	3,685E-02	3,209E-02
GOBP_REGULATION_OF_HISTONE_METHYLATION	73	1,707	3,767E-02	3,281E-02
GOBP_STEM_CELL_PROLIFERATION	59	1,720	3,958E-02	3,446E-02
GOBP_PROTEIN_ACETYLATION	202	1,520	3,958E-02	3,446E-02
GOBP_LONG_CHAIN_FATTY_ACID_BIOSYNTHETIC_PROCESS	22	1,885	4,020E-02	3,501E-02
GOBP_KIDNEY_EPITHELIUM_DEVELOPMENT	132	1,611	4,023E-02	3,503E-02
GOBP_POSITIVE_REGULATION_OF_NEUROGENESIS	206	1,521	4,033E-02	3,512E-02
GOBP_HOMOLOGOUS_RECOMBINATION	49	1,709	4,087E-02	3,559E-02
GOBP_FEMALE_SEX_DIFFERENTIATION	107	1,635	4,105E-02	3,574E-02
GOBP_SPINAL_CORD_ASSOCIATION_NEURON_DIFFERENTIATION	10	1,836	4,246E-02	3,698E-02
GOBP_MORPHOGENESIS_OF_AN_EPITHELIAL_BUD	15	1,843	4,461E-02	3,884E-02
GOBP_EPIDERMIS_MORPHOGENESIS	29	1,794	4,859E-02	4,231E-02
GOBP_PEPTIDYL_LYSINE_ACETYLATION	179	1,509	4,859E-02	4,231E-02
GOBP_REGULATION_OF_NEUROGENESIS	334	1,395	4,859E-02	4,231E-02

Supplementary table 5: Cell lines list

	Current name	Reference	Healthy individuals and patients
Human induced pluripotent stem cells (hiPSCs)	Ctr1	AG08C5 Coriell	Skin fibroblast, 1-year-old healthy male
	Ctr2	M180 CECS	Skeletal myoblasts, healthy male
	isoCTR	<i>Kyrychenko et al 2017</i>	Peripheral blood mononuclear cells healthy male
	DMDdEx45	GM25313 Coriell	Skin fibroblast, 13-year-old DMD male patient, deletion ex45
	DMDdEx8-9	<i>Kyrychenko et al 2017</i>	Peripheral blood mononuclear cells healthy male
	DMDdEx8-43	M202	Skeletal myoblasts, DMD male patient, out-of-frame deletion exon 8-43
Immortalized skin fibroblasts (hTERT/CDK4)	Ctr fibroblasts	AB1191C16PV	Skin, 16-year-old healthy male
	DMD fibroblasts	AB1024DMD11Q	Skin, 11-year-old DMD male, stop-codon exon 59
Primary skin fibroblasts	Fibroblasts control 1	5-8898 DNA Bank Genethon	Skin fibroblasts healthy patient
	Fibroblasts control 2	11-1610 DNA Bank Genethon	Skin fibroblasts healthy patient
	Fibroblasts control 3	11-1973 DNA Bank Genethon	Skin fibroblasts healthy patient
	Fibroblasts DMD 1	5-11618 DNA Bank Genethon	Skin fibroblasts DMD patient (stop mut.c.10141C>T, p.Arg3381X).
	Fibroblasts DMD 2	5-12608 DNA Bank Genethon	Skin fibroblasts DMD patient (delEx3-20)

	Fibroblasts DMD 3	5-11613 DNA Bank Genethon	Skin fibroblasts DMD patient (delEx45)
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Supplementary table 6: Antibodies used for immunofluorescence and capillary western blot

Antibodies	Supplier	Reference
Mouse monoclonal Myosin Heavy Chain (used at 1:10)	DSHB	Cat# MF20, RRID:AB_2147781
Rabbit polyclonal Vimentin (used at 1:100)	Proteintech	Cat#10366-1-AP, RRID:AB_2273020
Mouse monoclonal Dystrophin (used at 1:20)	Leica Biosystem	Cat# NCL-DYSB, RRID:AB_563691
Mouse monoclonal Myosin heavy chain, Type I (used at 1:100)	DSHB	Cat# BA-D5, RRID: AB_2235587
Mouse monoclonal Myosin heavy chain, Type IIA (used at 1:100)	DSHB	Cat# SC-71, RRID: AB_2147165
Mouse monoclonal Myosin heavy chain, Type IIB (used at 1:100)	DSHB	Cat# BF-F3, RRID: AB_2266724
Rabbit polyclonal pSMAD-3 (used at 1:100)	Abcam	Cat# ab52903, RRID:AB_882596
Mouse monoclonal α -Dystroglycan (used at 1:100)	Millipore	Cat# 05-298, RRID:AB_309674
Mouse monoclonal β -Dystroglycan (used at 1:100)	Leica Biosystems	Cat# NCL-b-DG, RRID:AB_442043
Rabbit polyclonal alpha-actinin 2 (used at 1:100)	Thermo Fisher Scientific	Cat# 701914, RRID:AB_2688290
Mouse monoclonal Oct3/4 (used at 1:200)	Santa Cruz Biotechnology	Cat# sc-5279, RRID: AB_628051
Rabbit polyclonal GFP (used at 1:500)	Invitrogen	Cat# A-21311, RRID:AB_221477
Goat anti-Mouse IgG1 Cross-Adsorbed Secondary Antibody, Alexa Fluor 594	Thermo Fisher Scientific	Cat# A-21125, RRID:AB_2535767
Goat anti-Rabbit IgG (Heavy chain), Supercloonal™ Recombinant Secondary Antibody, Alexa Fluor 488	Thermo Fisher Scientific	Cat# A27034, RRID:AB_2536097

Goat anti-Mouse IgG2a Cross-Adsorbed Secondary Antibody, Alexa Fluor 594	Thermo Fisher Scientific	Cat# A-21135, RRID:AB_2535774
Goat anti-Mouse IgG2b Cross-Adsorbed Secondary Antibody, Alexa Fluor 647	Thermo Fisher Scientific	Cat# A-21242, RRID:AB_2535811

Supplementary table 7: List of primers used for viral copy number analysis and gene expression

Primers for gene expression analysis		
Gene	Forward	Reverse
GAPDH	ACAAC TTTGGTATCGTGGAAGG	GCCATCACGCCACAGTTTC
MYOD	TGCTCCGACGGCATGATGGACT A	TTGTAGTAGGGCGCCTTCGTAGCA
MCK	TGGAGAAGCTCTCTGTGGAAG CT	TCCGTCATGCTCTTCAGAGGGTA
MYH2	AGAAACTTCGCATGGACCTAG A	CCAAGTGCCTGTTTCATCTTCA
MYH7	ACTGCCGAGACCGAGTATG	GCGATCCTTGAGGTTGTAGAGC
COL1A 1	AAGAGGAAGGCCAAGTCGAG	GTTTCCACACGTCTCGGTCA
FN1	AGCCGAGGTTTTAACTGCGA	CCCACTCGGTAAGTGTTCCC
FAP	ATGAGCTTCCTCGTCCAATTCA	AGACCACCAGAGAGCATATTTTG
DMD	GTAACAGAAAGAAAGCAACAG TTGG	CTTTCCCCAGGCAACTTCAGAATC CAAA
POSTN	CTCATAGTCGTATCAGGGGTCG	ACACAGTCGTTTTCTGTCCAC
EDA FN1	GGAGAGAGTCAGCCTCTGGTT CAG	TCTGCAGTGTCTTCTTCACC
TGF- β 1	GCCTGAGGCCGACTACTA	CTGTGTGTACTCTGCTTGAAC
ITGA10	ATCTGTGAGGTCGAAACAGGA	TGGAGCATACTCAACAGTCTTTG
μ DYS	GCACCACCAGATGCACTAT	GTGTAGGCGTAGCTCTTGAAT
Primers for VCN analysis		
Gene	Forward	Reverse
P0	CTCCAAGCAGATGCAGCAGA	ATAGCCTTGCGCATCATGGT
μ Dys	GCACCACCAGATGCACTAT	GTGTAGGCGTAGCTCTTGAAT

Supplementary table 8: ELISA kit used for secreted protein analysis

Protein target	Supplier	Reference
Fibronectin 1	Abcam	ab219046
TGF- β 1	Abcam	ab100647
Collagen IV	Bio-technie	NBP2-75864