SUPPLEMENTAL INFORMATION ITEMS

Supplemental information includes five figures and one table.

Figure S1. Related to Figure 2

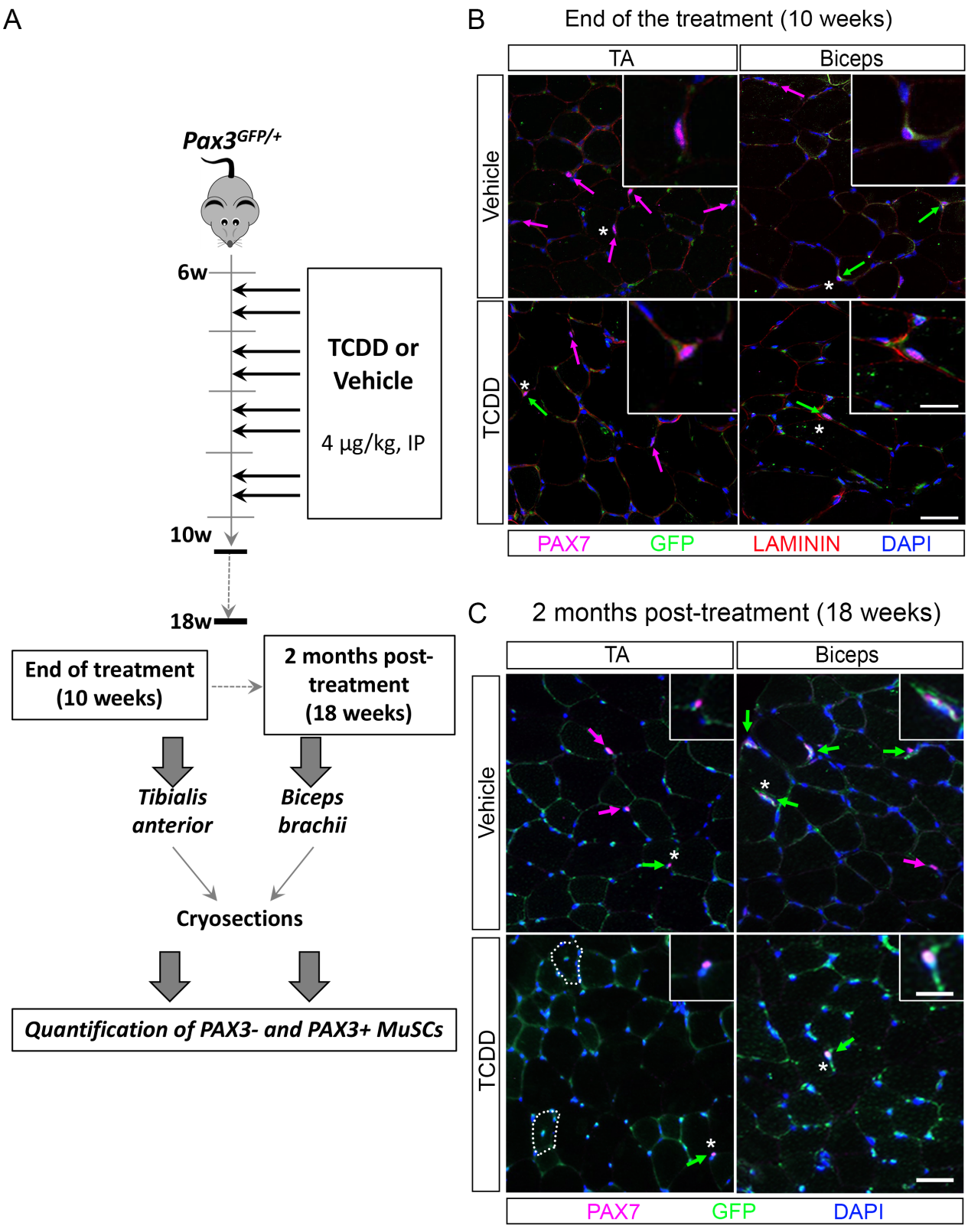

Figure S1. Related to Figure 2

(A) Experimental design: *Pax3*$^{GFP/+}$ mice received intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks before analysis at the end of the treatment (10 weeks) or 2 months (18 weeks) post-treatment.
(B, C) Representative co-immunofluorescence staining of PAX7 (pink), GFP (PAX3 reporter, green), LAMININ (red) and nuclei (DAPI, blue) performed on *Tibialis Anterior* (TA) or *Biceps brachii* (Biceps) muscle sections from *Pax3*$^{GFP/+}$ mice receiving vehicle (nonane, top) or TCDD (4µg/kg, bottom) twice a week during four weeks and analyzed at the end of the treatment (10 weeks) **(B)** or 2 months (18 weeks) post-treatment **(C)**. Pink and green arrows represent respectively PAX3- and PAX3+ MuSCs. Asterisks represent MuSCs shown in the inset. Scale bar, 40µm (overview) or 20µm (inset).

Figure S2. Related to Figure 3

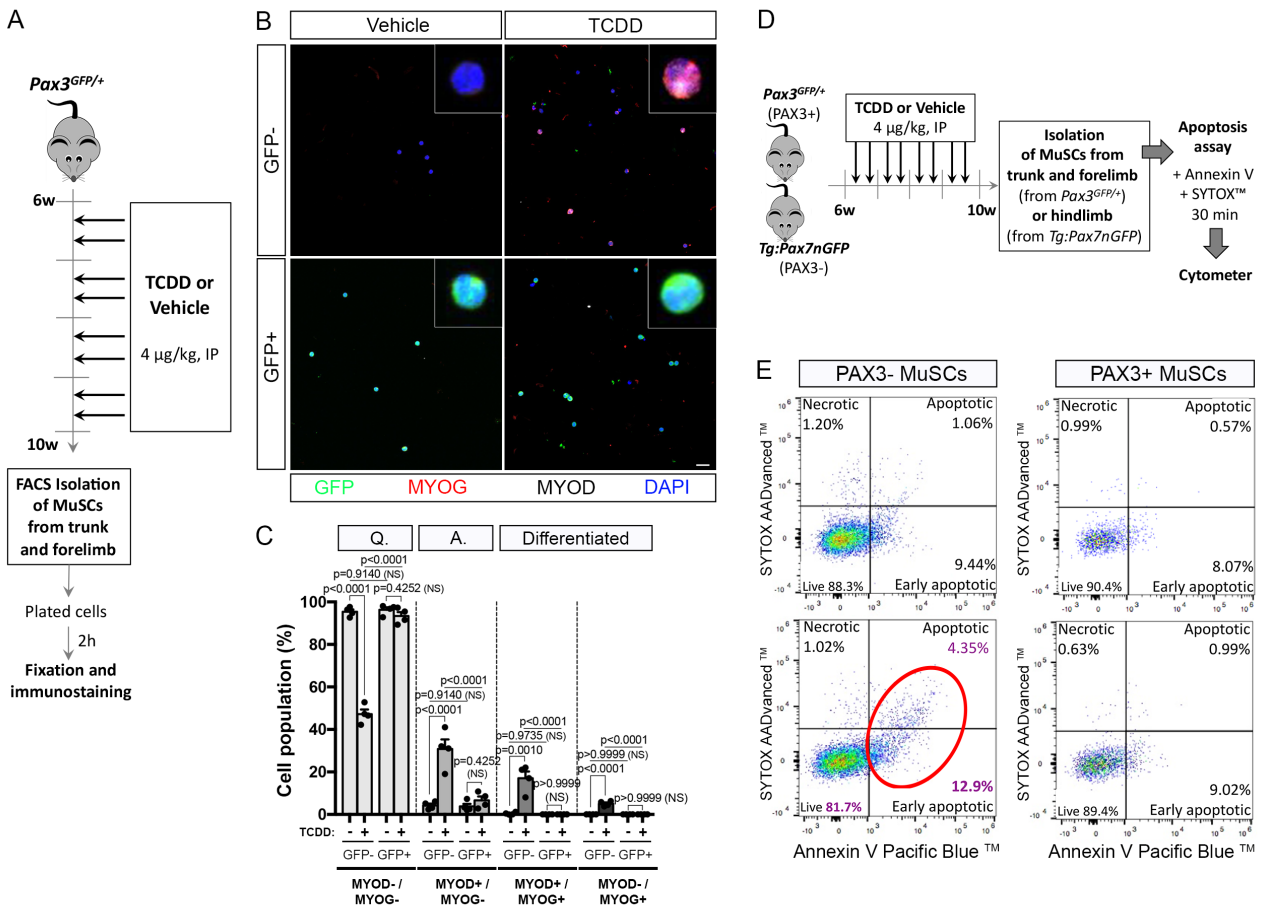

Figure S2. Related to Figure 3

(A) Experimental design: *Pax3*$^{GFP/+}$ mice received intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks. PAX3+ (GFP+) and PAX3- (GFP-) MuSCs were isolated by flow cytometry from trunk and forelimb muscles**,** plated for 2h before fixation and analysis by co-immunostaining.
(B) Representative co-immunofluorescence staining of GFP (PAX3 reporter, green), MYOG (red), MYOD (white) and nuclei (DAPI, blue) from isolated PAX3+ (GFP+) and PAX3- (GFP-) MuSCs from *Pax3*$^{GFP/+}$ mice receiving vehicle (nonane) or TCDD (4µg/kg).
(C) Quantification of **(B)** showing quiescent (MYOD-/MYOG-), activated (MYOD+/MYOG-) and differentiated (MYOG+) MuSCs within isolated PAX3-negative (GFP-) and PAX3-positive (GFP+) MuSCs from *Pax3*$^{GFP/+}$ mice receiving vehicle (nonane) or TCDD (4µg/kg). Means ± SEM (n=4), two-way ANOVA. *P* values calculated by Sidak's post-test. N.S., not significant.
(D) Experimental design: *Pax3*$^{GFP/+}$ or *Tg:Pax7nGFP* mice received intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks before isolation of MuSCs from trunk and forelimb (*Pax3*$^{GFP/+}$, PAX3+ MuSCs) or hindlimb (*Tg:Pax7nGFP*, PAX3- MuSCs) muscles and cell death analysis by Flow Cytometry using Annexin V and SYTOX™ labeling.
(E) Representative dot blots showing living cells (Annexin V-; Sytox-), early apoptotic (Annexin V+; Sytox-), apoptotic (Annexin V+; Sytox+) and necrotic cells (Annexin V-; Sytox+) in PAX3- MuSCs (isolated from *Tg:Pax7nGFP* hindlimb muscles, left) or PAX3+ MuSCs (isolated from *Pax3*$^{GFP/+}$ trunk and forelimb muscles, right). Red circle highlights atypical apoptosis in PAX3- MuSCs.

Figure S3. Related to Figure 5

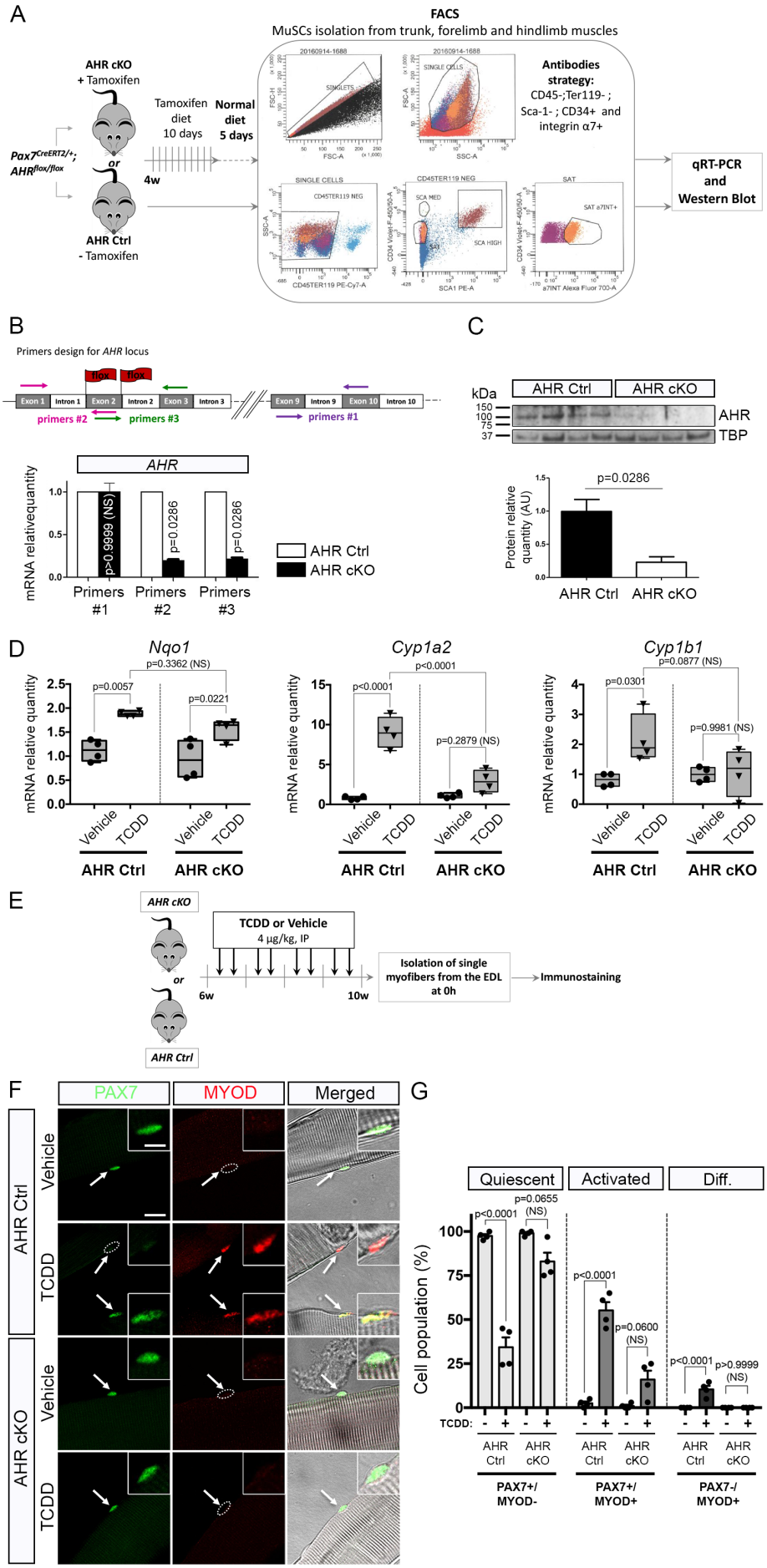

Figure S3. Related to Figure 5

(A): Experimental design: *Pax7*$^{creERT2/+}$*; AHR*$^{flox/flox}$ mice fed with tamoxifen or control diet (AHR cKO and AHR Ctrl mice, respectively) before flow-cytometry isolation of MuSCs from trunk, forelimb and hindlimb muscles, using an antibodies-based strategy (CD45-; Ter119-; Sca-1-; CD34+ and integrin α7+) (Stantzou et al., 2017). Total RNA isolation and protein extraction from MuSCs was performed to evaluate *AHR* gene expression and AHR protein expression by quantitative Polymerase Chain Reaction (qRT-PCR) and western-blot, respectively.
(B) Evaluation of deletion evaluation of AHR exon2 by qPCR. Relative expression of *AHR* mRNA containing (primers #1) or lacking (primers #2 or #3) exon 2 in MuSCs from AHR cKO and AHR Ctrl mice are shown normalized by *Tbp* and *Hprt1* expression Means ± SEM (n=3), Mann-Whitney test.
(C) Representative western-blot and quantification of AHR protein in MuSCs from AHR cKO and AHR Ctrl mice normalized by TBP protein expression. Means ± SEM (n=4), Mann-Whitney test.
(D) Box plot showing the relative expression of AHR target genes (*Nqo1*, *Cyp1a2* and *AHRR*) normalized to *Tbp* and *Hprt1* in MuSCs isolated from AHR Ctrl and AHR cKO mice treated with vehicle (nonane) or TCDD (4µg/kg). Means ± SEM (n=4), two-way ANOVA. *P* values calculated by Sidak's post-test. N.S., not significant.
(E) Experimental design: *Pax7Cre*$^{ERT2/+}$*; AHR*$^{flox/flox}$ mice received tamoxifen food (AHR cKO) or control diet (AHR Ctrl) during 10 days followed by 5 days of normal diet prior to intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks. Isolation of freshly single myofibers from *extensor digitorum longus* (EDL) was performed to examine the myogenic status of MuSCs using co-immunostaining.
(F) Representative co-immunofluorescence staining of single myofibers from *extensor digitorum longus* (EDL) isolated from AHR Ctrl and AHR cKO mice receiving vehicle (nonane) or TCDD (4µg/kg), using antibodies against PAX7 (green), MYOD (red) and nuclei (DAPI, blue). Scale bars, 20 µm (overview) and 10 µm (inset).
(G) Quantification of **(F)** showing quiescent (PAX7+/MYOD-), activated (PAX7+/MYOD+) and differentiated (PAX7-/MYOD+) MuSCs within single myofibers of EDL isolated from AHR Ctrl (top) and AHR cKO (bottom) mice receiving vehicle (nonane) or TCDD (4µg/kg). Means ± SEM (n=4), two-way ANOVA. *P* values calculated by Sidak's post-test. N.S., not significant.

Figure S4. Related to Figure 6

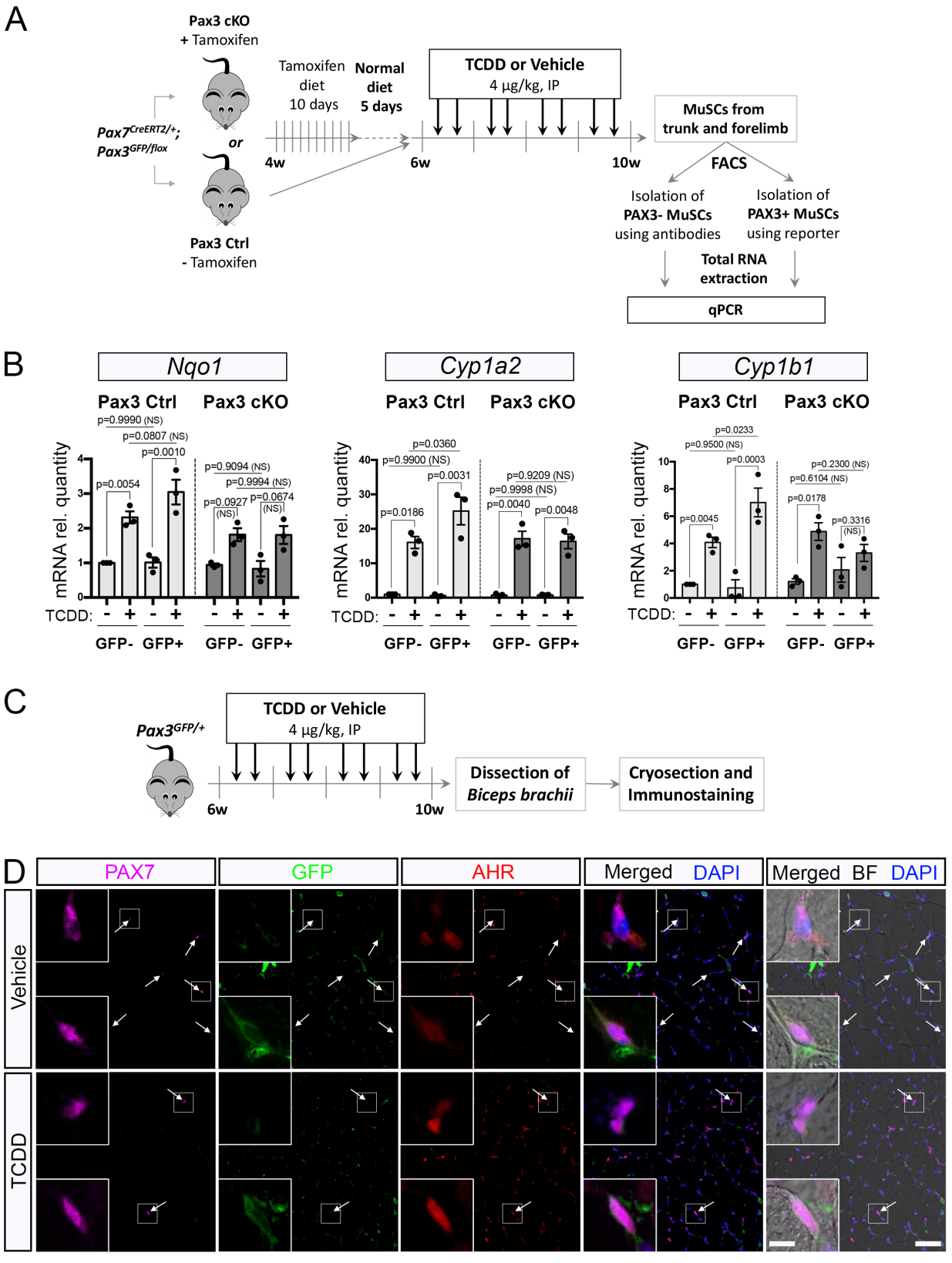

Figure S4. Related to Figure 6

(A) Experimental design: *Pax7*$^{creERT2/+}$*; Pax3*$^{GFP/flox}$ received normal diet (Pax3 Ctrl) or tamoxifen food (Pax3 cKO) for 10 days followed by 5 days of normal diet prior to intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks. PAX3+ (GFP+) and PAX3- (GFP-) MuSCs were isolated by flow cytometry for gene expression studies.
(B) MuSCs were isolated from Pax3 Ctrl or Pax3 cKO trunk and forelimb muscles by antibody-based flow cytometry combined with GFP reporter to distinguish PAX3+ (GFP+) from PAX3- (GFP-) MuSCs. Total RNA was extracted and gene expression study performed by quantitative Polymerase Chain Reaction (qPCR). Relative expression to *Tbp* and *Hprt1* of AHR-target genes (*Nqo1, Cyp1a2, Cyp1b1*) in MuSCs from GFP- (PAX3-) or GFP+ (PAX3+) MuSCs. Means ± SEM (n=3), two way ANOVA. *P* values calculated from Sidak's post-test. N.S.,not significant.
(C) Experimental design: Pax3$^{GFP/+}$ mice fed with or without tamoxifen received intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks before immunohistological analysis on biceps cryosections.
(D) Representative co-immunofluorescence staining of PAX7 (pink), GFP (PAX3 reporter, green), AHR (red) and nuclei (DAPI, blue) from biceps muscle sections from Pax3$^{GFP/+}$ mice
receiving vehicle (nonane, top) or TCDD (4µg/kg, bottom) as indicated. Arrows show PAX7+ MuSCs. BF, Brightfield. Scale bars, 100 µm (overview), 10 µm (insets).

Figure S5. Related to Figure 7

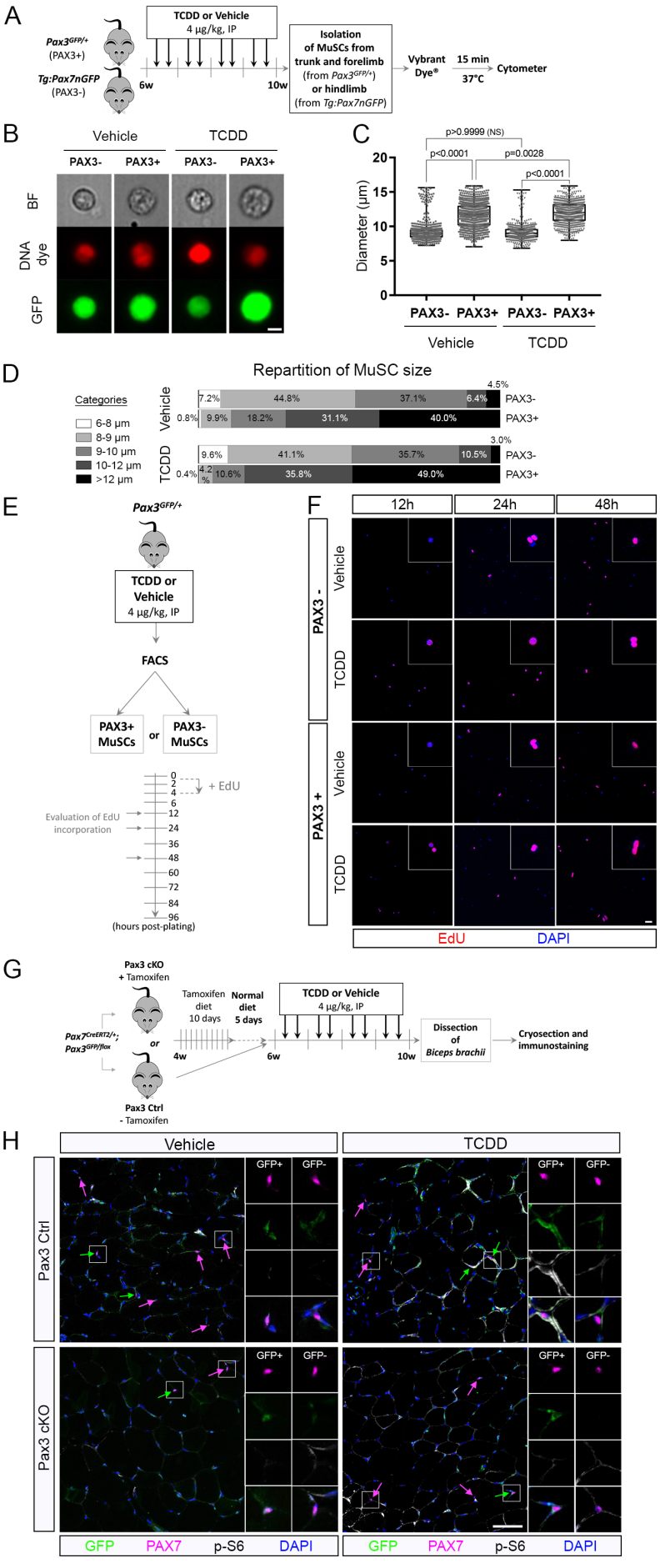

Figure S5. Related to Figure 7

(A) Experimental design: *Pax3*$^{GFP/+}$ or *Tg:Pax7nGFP* mice received intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks before isolation of MuSCs from trunk and forelimb (*Pax3*$^{GFP/+}$, PAX3+ MuSCs) or hindlimb (*Tg:Pax7nGFP*, PAX3- MuSCs) muscles. MuSCs were stained with Vybrant Dye©, a cell permeable DNA dye, before their size characterization by flow cytometry.
(B) Representative picture of brightfield (BF, top), DNA (red, middle) and GFP (green, bottom) staining performed on single isolated PAX3- or PAX3+ MuSCs treated with vehicle (nonane) or TCDD (4µg/kg). Scale bar, 5 µm.
(C) Dot blots showing the diameter (µm) repartition of PAX3- (GFP-) or PAX3+ (GFP+) MuSCs from mice treated with vehicle (nonane) or TCDD (4µg/kg). Means ± SEM (n=5000 cells per conditions), two-way ANOVA. *P* values calculated by Sidak's post-test. N.S., not significant.
(D) Graphs represent the size repartition of MuSCs categorized in 5 groups distributed between 6 to 8 µm, 8 to 9 µm, 9 to 10 µm, 10 to 12 µm and cell diameter superior to 12 µm regarding their expression of PAX3 upon vehicle (top) or TCDD (bottom) treatment.
(E) Experimental design: *Pax3*$^{GFP/+}$ mice received intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks before isolation of PAX3- (GFP-) or PAX3+ (GFP+) MuSCs by FACS. Isolated MuSCs were used to determined EdU incorporation at different time points after a 4h-Edu pulse (10 µM).
(F) Representative co-immunostaining of EdU (red) and nuclear staining (DAPI, blue) in GFP- (PAX3-, top) and GFP+ (PAX3+, bottom) MuSCs from *Pax3*$^{GFP/+}$ mice receiving vehicle or TCDD treatment performed 12, 24 and 48h post-plating.
(G) Experimental design: *Pax3*$^{GFP/+}$ mice *or Pax7Cre*$^{ERT2/+}$*; Pax3*$^{flox/flox}$ mice received normal diet (Pax3 Ctrl) or tamoxifen food (Pax3 cKO) for 10 days followed by 5 days of normal diet prior intraperitoneal administration of vehicle (nonane) or TCDD (4µg/kg) twice a week during four weeks. Cryosections of *biceps brachii* (biceps) were performed at the end of the TCDD treatment (10 weeks) for Pax3 Ctrl and Pax3 cKO mice, and 1 month (14 weeks) or 2 months (18 weeks) post-treatment for *Pax3*$^{GFP/+}$ mice in order to evaluate mTORC1 activation in PAX3-negative (GFP-) and PAX3-positive (GFP+) MuSCs by phospho-S6 ribosomal protein (p-S6) immunostaining.
(H) Representative co-immunofluorescence staining of GFP (PAX3 reporter, green), PAX7 (pink), p-S6 (white) and nuclear staining (DAPI, blue) in biceps sections from Pax3 Ctrl (top) and Pax3 cKO (bottom) mice receiving vehicle (nonane) or TCDD (4µg/kg) treatment. Insets show co-immunostaining of GFP+ (left) and GFP- (right) MuSCs. Pink arrows designate PAX3- MuSCs. Green arrows indicate PAX3+ MuSCs. Scale bar, 50 µm.

Supplementary Table

Table S1: List of qPCR oligonucleotides used in this study related to STAR Methods**.**

Gene	Sequence	Name
AHRR	5’ - GACTTCTGCAGACAGCTACA - 3’	Aryl Hydrocarbon Receptor Repressor
	5’ - TGTCAAGAAGGCCGAGTACT - 3’	
Cyp1a1	5' - CAGCCTTCCCAAATGGTTTA - 3'	P450 Cytochrome 1A1
	5' - GCCTGGGCTACACAAGACTC - 3'	
Pax3	5' - TGCCCTCAGTGAGTTCTATCAGC -3'	Paired Box 3
	5' - GCTAAACCAGACCTGCACTCGGGC- 3'	
MyoD	5' - TAGTAGGCGGTGTCGTAGCC - 3'	Myogenic Differentiation 1
	5' - TACAGTGGCGACTCAGATGC - 3'	
Hprt1	5’ - AGGGCATATCCAACAACAAACTT - 3’	Hypoxanthine Phosphoribosyltransferase 1
	5’ - GTTAAGCAGTACAGCCCCAAA - 3’	
Tbp	5’ - ATCCCAAGCGATTTGCTG - 3’	TATA Box Protein
	5’ - CCTGTGCACACCATTTTTCC - 3’	
AHR	5' - TTCCAGGTTCTCAGGCATTC - 3'	Aryl hydrocarbon receptor
	5' - TGGGAGCTACAGGAATCCAC - 3'	
AHR primers 1	5' - ATGTTTCGTCGGTAGAGCAGT - 3'	Aryl hydrocarbon receptor
	5' - ACACCAAATCCTCTCTCGTCC - 3'	
AHR primers 2	5' - AACATCACCTATGCCAGCCG - 3'	Aryl hydrocarbon receptor
	5' - GGTCTCTGTGTCGCTTAGAAGG - 3'	
AHR primers 3	5' - AAGCTGGACAAACTCTCTGTTCTT - 3'	Aryl hydrocarbon receptor
	5' - GCCAGTCTCTGATTTGTGCTCTA - 3'	
Cyp1a2	5' - ACAACGAGGGACACCTCAC - 3'	P450 Cytochrome 1A2
	5' - GGGATCTCCCCAATGCAC - 3'	
Cyp1b1	5' - AGGATGTGCCTGCCACTATT - 3'	P450 Cytochrome 1B1
	5' - AGCTGGAGAATCGCATTGAT - 3'	
Nqo1	5' - TCTGCAGCTTCCAGCTTCTTG - 3'	NAD(P)H Quinone Dehydrogenase 1
	5'- TATCCTTCCGAGTCATCTCTAGCA - 3'	