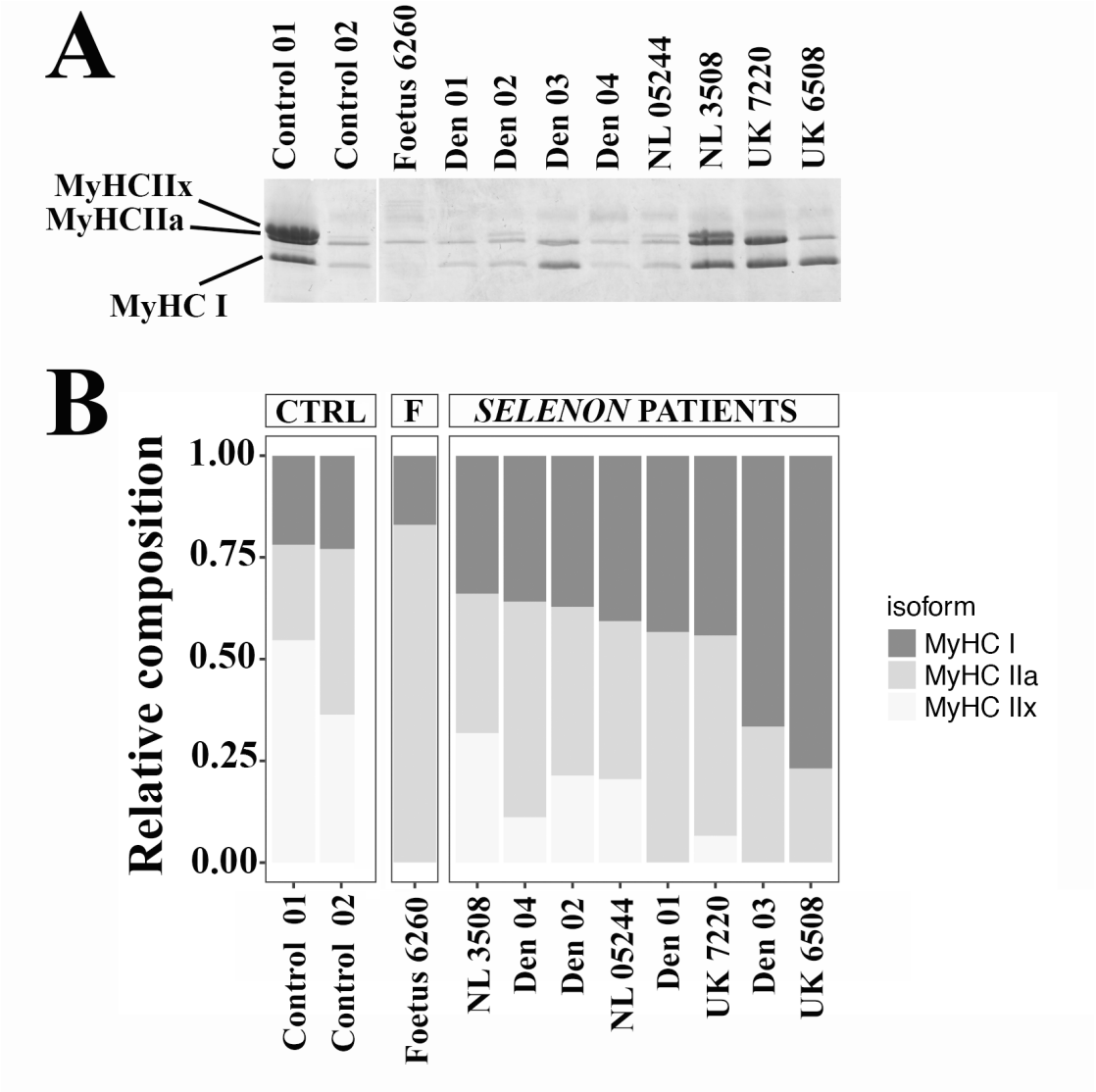
Supporting Tables and Figures

Supplementary Figure S1: **Muscles from *SELENON* patients contain fewer fast glycolytic fibers than muscles from healthy controls. A.** Electrophoretic separation of MyHC isoforms performed according to Talmadge and Roy (1985). Proteins were stained with CBB and the migration of the MyHC isoform bands of proteins in isolated soleus and EDL muscles was used as reference. **B.** Relative composition of MyHC I, IIa and IIx in muscles from controls, foetus and *SELENON* patients.



***Supplementary Table S1*: List of primary antibodies and suppliers**

	Target	**Supplier**	**Catalogue #**
1	RyR1	Thermo Fischer	MA3-925
2	Ca_V 1.1	Santa Cruz	sc-8160
3	SERCA1	LS Bio	LS-C351853
4	SERCA2	Thermo Fischer	MA3-910
5	Desmin	Santa Cruz	sc-14026
6	MyHC (all isoforms)	Millipore	05-716
7	HDAC-4	Cell Signaling	2072S
8	HDAC-5	Abcam	ab1439
9	H3K9ac	Abcam	ab10812
10	H3K9me3	Abcam	ab8898
11	Acetylated Lysine	Abcam	ab21623
12	CasQ-1	Sigma	C0743
13	CalR	Abcam	ab92516

***Supplementary Table S2*: Sequences of primers used for qPCR**

Gene	Forward	Reverse
SEPN1/ SELENON	5'-CTGGGGACAGATGGCCTTTTT-3'	5'-AATGGGTTTGAACTCCTCAGG-3'
RYR1	5'-GGACCTCTACGCCCTGTATC-3'	5'-ATCTCCCGCCTTAGCCATTTT-3'
CACNA1S	5'-TTGCCTACGGCTTCTTATTCCA-3'	5'-GTTCCAGAATCACGGTGAAGAC-3'
STAC3	5'- AATGGTGGCGGGGGAAAATC-3'	5'- CCCGCTTCGTCTCCTTTCTG-3'
ATP2A1	5'-GGTGCTGGCTGACGACAACT-3'	5'-AAGAGCCAGCCACTGATGAG-3'
ATP2A2	5'-CTCCATCTGCCTGTCCAT-3'	5'-GGCTGACGGCTTCCAAGT-3'
ATP2B2	5'-CTGCTGTGGGTGTGAACTCT-3'	5'- CCGTCCTGTTGTTTGGCTTT-3'
HDAC1	5'-TCAAGCCGGTCATGTCCAAA-3'	5'-CCTCCCAGCATCAGCATAGG-3'
HDAC3	5'-TAATGCCTTCAACGTAGGCGA-3'	5'-AGCCAGAGGCCTCAAACTTCT-3'
HDAC4	5'-AGGCTCAGACTTGCGAGAAC-3'	5'-ATCTGGTCTCTTTTCGGCGG-3'
HDAC5	5'-GGCAGAAGCTAGACAGCAAG-3'	5'-TCCATTCTTGAGCTCTCCTG-3'
HDAC9	5'-CTCTCCACCCCTTAGTGGAAC-3'	5'-TTGGGCTCAGAGGCAGTTTT-3'
DNMT1	5′-AGAACGGTGCTCATGCTTACA-3′	5′-CTCTACGGGCTTCACTTCTTG-3'
TRDMT1	5′-TGCCAAGACGATTGAAGGCAT-3′	5′-GCAGGGAGGGCTCATTAAAAT-3'
DES	5'-AACCAGGAGTTTCTGACCACG-3'	5'-TTGAGCCGGTTCACTTCGG-3'

qPCR conditions were as follows: 2 minutes at 50°C, 2 minutes at 95°C, 40 x (15 seconds at 95°C, 1 minute at 60°C) using PowerUp Sybr Green master mix.

***Supplementary Table S3*: miRNA specifications and primer sequences used for miRNA quantification**

miRNA	Human miRBase ID	Sequence
1	hsa-miR-1-3p	5'-UGGAAUGUAAAGAAGUAUGUAU-3'
22	hsa-miR-22-3p	5'-AAGCUGCCAGUUGAAGAACUGU-3'
23	hsa-miR-23b-3p	5'-AUCACAUUGCCAGGGAUUACC-3'
124	hsa-miR-124a-3p	5'-UAAGGCACGCGGUGAAUGCC-3'
128	hsa-miR-128a-3p	5'-UCACAGUGAACCGGUCUCUUU-3'
133	hsa-miR-133a-3p	5'-UUUGGUCCCCUUCAACCAGCUG-3'
193	hsa-miR-193b-3p	5'-AACUGGCCCUCAAAGUCCCGCU-3'
206	hsa-miR-206	5'-UGGAAUGUAAGGAAGUGUGUGG-3'
224	hsa-miR-224-3p	5'-AAAAUGGUGCCCUAGUGACUACA-3'
486	hsa-miR-486-3p	5'-CGGGGCAGCUCAGUACAGGAU-3'
RNU44	housekeeping gene	5'-CCTGGATGATGATAGCAAATGCTGAC TGAACATGAAGGTCTTAATTAGCTCTAA CTGACT-3'

Amplification was performed using an Applied Biosystems 7500 Fast Real-time PCR System running 7500 software version 2.3 (program: 1 second at 50°C, 10 minutes at 95°C, 40 x (15 seconds at 95°C, 1 minute at 60°C)). Quantification was based on the comparative ΔΔCt method.

***Supplementary Table S4*: Normalized protein content in muscle samples from *SELENON* patients and controls as determined by densitometric staining of immunopositive bands obtained on western blots.**

HDAC	Calcium Homeostasis				Histone Modifications			
HDAC-4	RyR1	$Ca_V1.1$	SERCA1	SERCA2	H3K9ac	H3K9me3	acetylated Lysine	id
0.6869	1.5470	-	-	-	1.000	-	1.2640	ctrl01
1.4427	0.2577	-	-	-	-	-	-	ctrl02
0.8703	1.1953	-	-	-	-	-	-	ctrl03
1.000	1.000	1.0904	0.8841	0.9709	1.1402	1.000	1.0911	ctrl04
-	-	-	-	-	-	-	0.7360	ctrl05
0.5848	-	-	0.9239	1.0900	-	0.7635	-	ctrl06
1.1893	1.7986	1.3304	1.0591	0.8050	1.7596	0.8925	-	ctrl07
0.5041	1.5387	1.3776	1.0170	1.1050	0.2404	1.4272	-	ctrl08
1.0039	0.7534	-	-	-	-	0.7723	-	ctrl09
1.4187	0.4187	0.7311	-	-	-	1.0828	-	ctrl10
1.2992	0.4907	0.5609	-	-	-	1.0617	-	ctrl11
-	-	0.3779	-	-	-	1.3826	-	ctrl12
-	-	1.5316	1.1159	1.0291	0.8598	0.6174	0.9089	ctrl13
7.4887	0.0001	0.0001	0.4835	0.3087	0.0001	-	0.0318	Den 01
5.6065	0.1311	0.4298	0.3668	0.9575	0.0001	0.3580	0.0421	Den 02
8.3053	0.0263	0.3142	0.6549	1.0906	0.4984	0.5321	0.0541	Den 03
5.5923	0.0095	0.5179	0.7332	0.8508	0.2862	16.8241	0.0419	Den 04
6.4781	-	-	0.5375	1.1626	0.0670	-	-	NL 00682
-	-	0.5722	0.5386	1.1213	0.6907	1.1326	0.1452	NL 05244
11.2958	0.0001	-	0.2906	0.5287	-	0.8047	-	NL 3508
-	-	-	0.5215	0.8472	-	-	-	UK 3866
-	-	0.1541	0.6202	0.7010	0.3044	0.0960	-	UK 7220
-	-	-	-	-	0.2133	-	-	UK 6508
7.0543	-	-	-	-	-	-	0.1189	CH 01
7.403	0.033	0.331	0.527	0.841	0.257	3.291	0.072	patient avg.
0.000	0.500	1.000	5.000	10.000	100.000	color code / scale bar		

***Supplementary Table S5*: Genotypes of the patients whose genome was analyzed for methylation using EPIC Bead Chip Array**

Sample ID	Mutated gene	Variant	Age of biopsy (years)
Den 01 (S1) (Ferreiro et al., 2002; Hansen et al., 2011)	*SELENON (NM_020451.2)*	c.446dup c.943G>A, p.G315S	14
Den 02 (S2) (Witting et al., 2017)	*SELENON (NM_020451.2)*	c.893T>C, p.L298P c.1396C>T, p.R466W	7
Den 03 (S3) (Ferreiro et al., 2002)	*SELENON (NM_020451.2)*	Hom c.943G>A, p.G315S	10
Den 04 (S4) (Ferreiro et al. 2002)	*S SELENON (NM_020451.2)*	c.943G>A, p.G315S c.713dup	14
NL 05244 (S5) (Ferreiro et al., 2002)	*SELENON (NM_020451.2)*	Hom c.943G>A p.G315S	2
R1 (MmD patient NL03) (Rokach et al., 2015)	*RYR1 (NM_00540.2)*	c.4711A>G, p.I1571V c.10097G>A, p.R3366H c.11798A>G, p.Y3933C c.14545G>A, p.V4849I	28
R2 (MmD patient SA07)(Rokach et al., 2015)	*RYR1 (NM_00540.2)*	Compound Heterozygous c.3381+1 G>A + c.10348-6C>G+ c.14524G>A, p.V4842M	8 years
R7 (MmD patient NL01) (Rokach et al., 2015)	*RYR1 (NM_00540.2)*	Heterozygous *RYR1* c.11905C>A p.Q3969K	2 years

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