# Supplementary Table

## Protein Phosphorylation Alterations in Myotonic Dystrophy Type 1: A Systematic Review

**Adriana Costa, Ana C. Cruz, Filipa Martins * and Sandra Rebelo ***

Institute of Biomedicine (iBiMED), Department of Medical Sciences, University of Aveiro,
3810-193 Aveiro, Portugal
* Correspondence: samartins@ua.pt (F.M.); srebelo@ua.pt (S.R.)

**Table S1.** Summary data of the included studies of the systematic review.

| *Author, Year, Country* | *Sample type and characterization* | *Evaluation method* | *Phosphorylation associated proteins* | *Main findings* |
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| **André et al. 2019, The Netherlands** [23] | <u>DM1:</u> Human congenital DM1 proliferating myoblasts; CTG repeat length: 2600<br><u>CTL:</u> Human congenital DM1 proliferating myoblasts with excision of CTG repeats | Mass spectrometry | CDK6 | <u>Total CDK6 level:</u> Significantly **increased** in DM1 (fold change: 0.66; p<0.05) vs CTL. |
| | | | INPP4B | <u>Total INPP4B level:</u> Significantly **increased** in DM1 (fold change: 0.66; p<0.05) vs CTL. |
| | | | PRKAR1B | <u>Total PRKAR1B level:</u> Significantly **decreased** in DM1 (fold change: -0.59; p<0.05) vs CTL. |
| | | | PTPRF | <u>Total PTPRF level</u>: Significantly **increased** in DM1 (fold change: 0.64; p<0.05) vs CTL. |
| **Beffy et al. 2010, Italy** [24] | <u>DM1:</u> Human fetus-derived myoblasts; CTG repeat length: 3200<br><u>CTL:</u> Human fetus-derived myoblasts; CTG repeat length: 20 | Western blot | DMPK | <u>Total DMPK level:</u> **Decreased** in DM1 during all the differentiation process (d0-d6).<br><u>Semi-quantitative total DMPK level (fold change):</u><br><u>d0:</u> DM1: 0.3; CTL: 0.5; <u>d2:</u> DM1: 0.3; CTL: 0.7; <u>d4:</u> DM1: 0.3; CTL: 0.6; <u>d6:</u> DM1: 0.3; CTL: 0.5 (p: NR) |
| | | | ERK1 | <u>p-ERK1 level:</u> Significantly **increased** levels of p-ERK1 (Tyr204) in DM1 vs CTL from d0 to d4 of differentiation. At d6, the levels p-ERK1 (Tyr204) **decrease** to the same background level as CTL. (p: NR) |
| | | | ERK2 | <u>p-ERK2 level:</u> **Increased** p-ERK2 in DM1 vs CTL, in d0 and d2 of differentiation.<br><br><u>p-ERK2/Total ERK2 ratio:</u><br><u>d0:</u> DM1 > CTL (p<0.01); <u>d2:</u> DM1 > CTL (p<0.01); <u>d4:</u> DM1 >CTL (p=ns); <u>d6:</u> DM1 >CTL (p=ns)<br><u>DM1:</u> d0> d2 > d4 > d6; <u>CTL:</u> d0 < d2 < d4 > d6 |
| | | | MEK | <u>p-MEK level:</u> **Increased** p-MEK (Ser 218/Ser222) in DM1 vs CTL, in d0 and d2 of differentiation. |

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| | | | | p-MEK/Total MEK ratio:<br>d0: DM1 > CTL (p<0.01); d2: DM1 > CTL (p<0.05); d4: DM1 > CTL (p=ns); d6: DM1 > CTL (p=ns)<br>DM1: d0>d2>d4>d6; CTL: d0<d>d4~d6 |
| | | | p38MAPK | Total p38MAPK level: **Similar** between DM1 vs CTL during differentiation.<br>p-p38MAPK level: **Decreased** (50%) p-p38MAPK (Thr180/Tyr182) in DM1 during differentiation.<br><br>p-p38MAPK/Total p38MAPK ratio:<br>d0: DM1 < CTL (p<0.05); d2: DM1 < CTL (p<0.05); d4: DM1 < CTL (p<0.05);<br>d6: DM1 < CTL (p<0.05)<br>DM1: d0 > d2 > d4 > d6; CTL: d0 < d2 > d4 < d6 |
| | | | Rb | p-Rb level: **Increased** in p-Rb during day 0 and day 2 of differentiation in DM1 vs CTL. **In both** DM1 and CTL differentiation, Rb protein is completely **dephosphorylated** at day 4 and 6 upon incubation with differentiating medium.<br><br>p-Rb/dp-Rb ratio (fold change):<br>d0: DM1: 0.78 vs CTL: 0.34 (p:NR); d2: DM1: 0.56 vs CTL: 0.27 (p:NR);<br>d4: DM1: n.d vs CTL: 0.15 (p:NR); d6: DM1: n.d vs CTL: n.d (p:NR) |
| | | | S6K1 | p-S6K1 level: Significantly **reduced** levels of p-S6K1 (Thr421/Ser424) during day 0,2, and 4 of differentiation in DM1 vs CTL.<br><br>p-S6K1/Total S6K1 ratio:<br>d0: DM1 < CTL (p<0.05); d2: DM1 < CTL (p<0.01); d4: DM1 < CTL (p<0.01); d6: DM1 < CTL (p=ns)<br>DM1: d0 < d2 ~ d4 > d6; CTL: d0 < d2 > d4 > d6 |
| **Botta et al. 2013, Italy** [25] | DM1: Human *vastus lateralis* differentiated myotubes; n=2; CTG Repeat length (range): 800-1500 (n=8)<br><br>CTL: Human *vastus lateralis* differentiated myotubes from subjects without neuromuscular disorders; n=3 | Western Blot; Immunofluorescence | Lyn kinases | Total Lyn level: Significantly **increased** Lyn protein levels and nuclear localization (570%) in DM1 vs CTL.<br><br>Lyn activity: Significantly **increased** nuclear activity and Tyr phosphorylation activity (250%) in DM1 vs CTL.<br><br>Semi-quantitative total Lyn level: DM1 > CTL (p<0.02)<br>Semi-quantitative p-Tyr phosphorylation: DM1 > CTL (p<0.02) |
| **Brockhoff et al. 2017, Switzerland** [26] | DM1: $HSA^{LR}$ mice skeletal muscle tissue biopsies; Age: 2-month-old; CTG repeat Length: 250<br>CTL: Background strain (FVB/N) mice skeletal muscle tissue biopsies | Western blot | AKT | p-AKT level: **Similar** p-AKT (Ser473) levels between fed and 24h starvation mice in DM1 vs CTL.<br><br>p-AKT/Total AKT ratio:<br>Fed: DM1 ~ CTL (p=ns); 24hStarvation: DM1 > CTL (p=ns) |

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| | Fed Conditions - n= 3<br>24h Starvation Conditions- n= 4 | | | Fed DM1 > 24hStarvation DM1 (p<0.05); Fed CTL > 24hStarvation CTL (p<0.05) |
| | | | CaMKIIβM | <u>Total CaMKIIβM level:</u> **Decreased** levels of CaMKIIβM in DM1 vs CTL. (p: NR)<br><br><u>p-CaMKIIβM level:</u> **Decreased** levels of p-CaMKIIβM (Thr286) in DM1 vs CTL in fed and 24h starvation mice.<br><br><u>p-CaMKIIβM fold change:</u><br>Fed: DM1 < CTL (p<0.05); 24hStarvation: DM1 < CTL (p<0.05)<br>Fed DM1 ~ 24hStarvation DM1 (p=ns); Fed CTL ~ 24hStarvation CTL (p=ns) |
| | <u>DM1:</u> HSA$^{LR}$ mice skeletal muscle tissue biopsies; n=3; Age: 2-month-old; CTG repeat length: 250<br><u>CTL:</u> FVB/N mice skeletal muscle tissue biopsies; n=4 | | AMPK | <u>p-AMPK level:</u> **Similar** p-AMPK (Thr172) levels between fed and 45h starvation DM1 vs CTL. **Reduced** levels of p-AMPK (Thr172) in 24h starvation DM1 mice vs CTL.<br><br><u>p-AMPK/Total AMPK ratio:</u><br>Fed: DM1 > CTL (p=ns); 24h Starvation: DM1 < CTL (p<0.05);<br>45hStarvation: DM1 < CTL (p=ns) |
| | <u>DM1:</u> HSA$^{LR}$ mice skeletal muscle tissue biopsies; Age: 2-month-old; CTG repeat length: 250<br><u>CTL:</u> FVB/N mice skeletal muscle tissue biopsies<br>Fed Conditions -n= 3<br>24hStarvation Conditions - n= 7 | | RpS6 | <u>p-RpS6 level:</u> **Increased** levels of p-RpS6 (Ser235/Ser236; Ser240/Ser244) in DM1 vs CTL in 24h starvation mice. **Similar** levels in fed and 45 h starvation in DM1 vs CTL.<br><br><u>p-RpS6/Total RpS6 ratio:</u><br>Fed: DM1 > CTL (p=ns); 24h Starvation: DM1 > CTL (p<0.001);<br>45h Starvation: DM1 < CTL (p=ns)<br><br>Fed DM1 > 24hStarvation DM1 (p=ns); Fed CTL > 24hStarvation CTL (p<0.01)<br>Fed DM1 > 45hStarvation DM1 (p<0.01); Fed CTL > 45hStarvation CTL (p<0.05) |
| | <u>DM1:</u> HSA$^{LR}$ mice skeletal muscle tissue biopsies; Age: 2-month-old; CTG repeat length: 250<br><u>CTL:</u> FVB/N mice skeletal muscle tissue biopsies | | LKB1 | <u>Total LKB1 level:</u> **Similar** in DM1 vs CTL in fed and 24h starvation mice. (p: NR) |
| | | | TAK1 | <u>Total TAK1 level:</u> **Similar** in DM1 vs CTL in fed and 24h starvation mice. (p: NR) |
| | | | mTOR | <u>p-mTOR level:</u> **Similar** levels of p-mTOR (Ser2448) between fed and 24h starvation mice in DM1 vs CTL.<br><br><u>p-mTOR/mTOR ratio:</u><br>Fed<u>:</u> DM1 > CTL (p=ns); 24h Starvation: DM1 < CTL (p=ns) |
| | | | S6K1 | <u>p-S6K1 level</u>: **Similar** levels of p-S6K1 (Thr389) in fed DM1 vs fed CTL mice. **Increased** levels of p-S6K1 (Thr389) in 24h starvation DM1 vs CTL. (p: NR) |
| | | | TSC2 | <u>p-TSC2 level:</u> **Similar** levels of p-TSC2 (Ser1387) in DM1 vs CTL fed and 24h starvation mice. (p: NR) |

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| | | | ULK1 | p-ULK1 level: **Slight but not significant increase** of p-ULK1 (Ser757) in DM1 vs CTL in 24h starvation mice (p: NR). **Similar** levels of p-ULK1 (Ser317) in DM1 vs CTL in fed and 24h starved mice. (p: NR)<br><br>p-ULK1/Total ULK1 ratio (Ser757):<br>Fed: DM1 < CTL (p=ns); 24h Starvation: DM1 > CTL (p=ns);<br><br>Fed DM1 > 24hStarvation DM1 (p=ns); Fed CTL > 24hStarvation CTL (p<0.01)<br><br>p-ULK1/Total ULK1 ratio (Ser317):<br>Fed: DM1 < CTL (p=ns); 24h Starvation: DM1 < CTL (p=ns);<br><br>Fed DM1 < 24hStarvation DM1 (p=ns); Fed CTL < 24hStarvation CTL (p=ns) |
| | DM1: Human patients skeletal muscle tissue biopsies; n=3<br>CTL: Human skeletal muscle tissue biopsies; n=5 | | AMPK | Total AMPK level: **Similar** levels in DM1 vs CTL (p: NR)<br><br>p-AMPK level: **Similar** levels of p-AMPK (Thr172) in DM1 vs CTL. (p: NR) |
| | | | AKT | Total AKT level: **Similar** levels in DM1 vs CTL. (p: NR)<br><br>p-AKT level: **Similar** levels of p-AKT (Ser473) in DM1 vs CTL. (p:NR) |
| | | | S6K1 | p-S6K1 level: **Increased** levels of p-S6K1 (Thr389) in DM1 vs CTL. (p: NR) |
| | | | RpS6 | p-RpS6 level: **Increased** levels of p-RpS6 (Ser235/Ser236; Ser240/Ser244) in DM1 vs CTL. (p: NR) |
| | DM1: Human patients fibroblast-derived myotubes; n=3<br>CTL: Human fibroblast-derived myotubes | | AKT | p-AKT level: **Similar** levels of p-AKT (Ser473) in DM1 vs CTL upon starvation. (p: NR) |
| | | | AMPK | p-AMPK level: **Similar** levels of p-AMPK (Thr172) in DM1 vs CTL upon starvation. (p: NR) |
| | | | RpS6 | p-RpS6 level: **Increased** levels of p-RpS6 (Ser235/Ser236; Ser240/Ser244) in DM1 vs CTL upon starvation (p: NR). |
| **Denis et al. 2013, France** [27] | DM1: Human neural stem cells with large CTG expansions; n=2<br><br>CTL: Human neural stem cells; n=1 | Western blot | AKT | Total AKT levels: **Similar** levels between DM1 vs CTL.<br><br>p-AKT levels: **Similar** levels of p-AKT (Ser473) between DM1 vs CTL<br><br>p-AKT/Total AKT ratio: DM1 < CTL (p=ns) |
| | | | AMPK | Total AMPK levels: **Similar** levels between DM1 vs CTL.<br><br>p-AMPK levels: **Similar** levels of p-AMPK (Thr172) between DM1 vs CTL.<br><br>p-AMPK/ Total AMPK ratio: DM1 < CTL (p=ns) |
| | | | GSK3α/β | Total GSK3α/β level: **Similar** levels between DM1 vs CTL. |

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| | | | | p-GSK3α/β level: **Decreased** levels of p-GSK3α/β (Ser21/Ser9) between DM1 vs CTL.<br><br>p-GSK3α/ Total GSK3α ratio: DM1 < CTL ($p<0.05$)<br><br>p- GSK3β/Total GSK3β ratio: DM1 < CTL ($p<0.05$) |
| | | | Rb | p-Rb level: **Decreased** levels of p-Rb (Ser801/Ser811) in DM1 vs CON.<br><br>p-Rb/Total Rb ratio: DM1 < CTL ($p<0.05$) |
| | | | RpS6 | Total RpS6 level: **Similar** levels between DM1 vs CTL.<br><br>p-RpS6 level: **Decreased** levels of p-RpS6 (Ser235/Ser236 and Ser240/Ser245) between DM1 vs CTL.<br><br>p-RpS6 (Ser235/Ser236)/Total RpS6 ratio: DM1 < CTL ($p<0.001$)<br><br>p-RpS6 (Ser240/Ser245)/Total RpS6 ratio: DM1 < CTL ($p<0.05$) |
| **Furling et al. 2003, France and UK** [28] | DM1: Human fetal congenital DM1 skeletal muscle tissue biopsies; n=5; CTG repeat length (range): 1800-3700<br>CTL: Human fetal skeletal muscle tissue biopsies; n=9 | Western blot | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL.<br><br>Semi-quantitative DMPK levels (fold change): DM1: 0.89 vs CTL: 1.57 (Reduction to 57% of control; p=0.006) |
| | DM1: Human fetal congenital DM1 myotubes;<br>CTL: Human fetal myotubes without neuromuscular diseases | | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL (Reduction of 53% of control values; p: NR) |
| **Gao et al. 2013, USA** [29] | DM1: Human DM1 skeletal muscle tissue biopsies; n=9<br>CTL: Human skeletal muscle tissue biopsies; n=7 | Western blot<br>Immunohistochemistry | PKM2 | Total PKM2 levels: **Increased** levels in DM1 vs CTL. **Increased** presence in type 1 myofibers. (p: NR) |
| | DM1: Mouse C2C12 myoblasts with CUGexp RNA<br>CTL: Mouse C2C12 myoblasts | | | Total PKM2 levels: **Increased** levels in DM1 vs CTL. (p: NR) |
| **García-Puga et al. 2020, Spain** [30] | DM1: Patient skin-derived fibroblasts; n=3; Age (Range): 34-71; CTG repeat length (Range): 167-1650 (n=7) | Western blot | AKT | p-AKT levels: **Decreased** levels of p-AKT (Ser473) in DM1 vs CTL.<br><br>Semi-quantitative p-AKT levels: DM1 < CTL (p: NR) |

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| | CTL: Control skin-derived fibroblasts; n=3; Age (Range): 48-53 | | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL.<br><br>Semi-quantitative total DMPK levels: DM1 < CTL ($p<0.01$) |
| | | | p38MAPK | p-p38MAPK levels: **Increased** levels of p-p38MAPK (Thr180/Tyr182) in 2-fold in DM1 vs CTL.<br><br>p-p38MAPK/Total p38MAPK ratio: DM1 > CTL ($p<0.05$) |
| **Huichalaf et al. 2010, USA** [31] | DM1: Human primary *biceps brachii* myoblasts; n=1; CTG repeat length: 320<br>CTL: Human primary *biceps brachii* myoblast cells | Western blot | CUGBP1 | Total CUGBP1 levels: **Increased** levels in DM1 vs CTL. (p: NR)<br><br>p-CUGBP1 levels: **Reduced** levels of p-CUGBP1 (Ser302) in DM1 vs CTL. (p: NR) |
| | | | eIF2α | p-eIF2α levels: **Increased** levels of p-eIF2α (Ser51) in DM1 vs CTL. (p: NR) |
| | | | PKR | Total PKR levels: **Increased** levels in DM1 vs CTL. (p: NR) |
| | DM1: CHO-tTA cells with 960 CUGexp RNA<br>CTL: CHO cells without CUGexp RNA | | CUGBP1 | Total CUGBP1 levels: **Increased** levels in DM1 vs CTL. (p: NR) |
| | | | eIF2α | p-eIF2α levels: **Increased** levels of p-eIF2α (Ser51) in DM1 vs CTL. (p: NR) |
| **Ikezoe et al. 2007, Japan** [32] | DM1: Human patients *biceps brachii* skeletal muscle tissue biopsies; n=5; CTG repeat length (range): 100-1200 | Immunohistochemistry | eIF2α | p-eIF2α levels: **Increased** levels of p-eIF-2α (Ser51) in 4 of 5 patients. (p: NR) |
| | | | PERK | p-PERK levels: **Increased** levels of p-PERK in 4 of 5 patients. (p: NR) |
| **Jones et al. 2012, USA** [33] | DM1: Human patients *biceps brachii* skeletal muscle tissue biopsies; n=8; Age (range): 42-46<br><br>CTL: Healthy participants *biceps brachii* skeletal muscle tissue biopsies; n=5; Age (range): 46-54 | Western blot | CUGBP1 | Total CUGBP1 levels: **Increased** in DM1 vs CTL.<br><br>Semi-quantitative total CUGBP1 levels: DM1 > CTL (p: NR) |
| | | | Cyclin D3 | Total Cyclin D3 levels: **Decreased** in DM1 vs CTL.<br><br>p-Cyclin D3 levels: **Increased** levels of p-Cyclin D3 (Thr283) in DM1 vs CTL.<br><br>Semi-quantitative total Cyclin D3 levels: DM1 < CTL (p: NR)<br>p-Cyclin D3/Total Cyclin D3 ratio: DM1 > CTL (p: NR) |
| | | | GSK3β | Total GSK3β levels: **Increased** in DM1 vs CTL.<br><br>p-GSK3β levels: **Increased** levels of p-GSK3β (Tyr216) in DM1 vs CTL. **Decreased** levels of p-GSK3β (Ser9) in DM1 vs CTL.<br><br>Semi-quantitative total GSK3β levels: DM1 > CTL (p: NR)<br>Semi-quantitative p-GSK3β (Ser9) levels: DM1 < CTL (p: NR) |

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| | DM1: Human DM1 myoblasts; n=8; Age (range): 42-46<br><br>CTL: Human myoblasts; n=5; Age (range): 46-54 | | GSK3β | Total GSK3β levels: **Increased** levels of cytoplasmic and nuclear GSK3β in DM1 vs CTL during all steps of myoblast differentiation (p: NR). |
| | DM1: $HSA^{LR}$ mice skeletal muscle tissue biopsies; n=6; Age: 6-months-old<br>CTL: WT mice skeletal muscle tissue biopsies; Age: 6-months-old | | CUGBP1 | Total CUGBP1 levels: **Increased** levels in DM1 vs CTL.<br><br>Semi-quantitative total CUGBP1 levels: DM1 > CTL (p:NR) |
| | | | Cyclin D3 | Total Cyclin D3 levels: **Decreased** levels in DM1.<br><br>Semi-quantitative total Cyclin D3 levels: DM1 < CTL (p: NR) |
| | | | GSK3β | Total GSK3β levels: **Increased** levels in DM1 vs CTL.<br><br>Semi-quantitative total GSK3β levels: DM1 > CTL (p: NR) |
| | DM1: $HSA^{LR}$ mice skeletal muscle tissue biopsies; n=6; Age: 1-month-old<br>CTL: WT mice skeletal muscle tissue biopsies; Age: 1-month-old | | GSK3β | Total GSK3β levels: **Increased** levels in DM1 vs CTL.<br>Semi-quantitative total GSK3β: DM1 < CTL (p: NR) |
| **Ketley et al. 2020, UK** [34] | DM1: Human patients *vastus lateralis* skeletal muscle tissue biopsies; n=4<br>CTL: Healthy participants *vastus lateralis* skeletal muscle tissue biopsies; n=4 | Western blot | CDK12 | Total CDK12 levels: **Increased** levels in DM1 vs CTL in 48%.<br>Semi-quantitative total CDK12 levels: DM1 > CTL (p=0.02) |
| **Khajavi et al. 2001, USA** [35] | DM1: Human patients LBCLs; n=18 | Western blot | AKT | Total AKT levels: **Not significantly different** levels across different CTG repeat lengths. (p: NR)<br><br>p-AKT levels: **Not significantly different** levels of p-AKT (Ser473) in DM1 that correlated with CTG Repeat length. (p: NR) |
| | | | ERK 1/2 | Total ERK1/2 levels: **Not significantly different** across different CTG repeat lengths. (p: NR)<br><br>p-ERK 1/2 levels: **Increased levels** of p-ERK 1/2 (Thr202/Tyr204) in DM1 that correlated with CTG Repeat length. (p: NR)<br><br>Semi-quantitative p-ERK1/2 levels (fold change):<br>DM1 550 repeats: 0.27 vs DM1 740 repeats: 0.42 vs DM1 750 repeats: 0.50 vs DM1 770 repeats: 0.63 vs DM1 1150 repeats: 0.95 |

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| **Kim et al. 2016, USA** [36] | <u>DM1:</u> DM5 mice skeletal muscle tissue biopsies with CUGexp RNA and doxycycline induction; n (range)= 3-5<br><br><u>CTL:</u> DM5 mice skeletal muscle tissue biopsies with CUGexp RNA and without doxycycline induction; n (range)=3-5 | Western blot | CUGBP1 | <u>Total protein levels:</u> **Increased** levels in DM1 vs CTL.<br><br><u>Semi-quantitative total CUGBP1 levels:</u> DM1 > CTL (p=0.05) |
| | | | GSK3β | <u>Total GSK3β:</u> **Increased** in DM1 vs CTL<br><br><u>Semi-quantitative total GSK3β relative levels (fold change):</u> DM1: 2.4 vs CTL: 1 (p: NR) |
| | | | PKC | <u>Total PKCα levels:</u> **Similar** in DM1 vs CTL.<br><br><u>Total PKCθ levels:</u> **Similar** in DM1 vs CTL.<br><br><u>p-PKCα/βII levels:</u> **Similar** in p-PKCα/βII (Thr638/Thr641) in DM1 vs CTL.<br><br><u>p-PKCθ levels:</u> **Increase** in p-PKCθ (Thr538) in DM1 vs CTL.<br><br><u>Semi-quantitative total PKCα levels:</u> DM1 < CTL (p=ns)<br><u>Semi-quantitative total PKCθ levels:</u> DM1 < CTL (p=ns)<br><u>Semi-quantitative p-PKCα/βII levels:</u> DM1 < CTL (p=ns)<br><u>Semi-quantitative p-PKCθ levels:</u> DM1 > CTL (p=0.05) |
| **Kuyumcu-Martinez et al. 2007, USA** [37] | <u>DM1:</u> Human patients heart tissue<br><u>CTL</u>: Human heart tissue from unaffected individuals | Western blot | CUGBP1 | <u>p-CUGBP1 levels:</u> **Increased** phosphorylation in DM1 vs CTL. (p: NR) |
| | | | PKC | <u>p-PKC levels:</u> 3 out of 4 DM1 patients with **activation** of p-PKCα and p-PKCβII in compared to CTL. (p: NR) |
| | <u>DM1:</u> Human patients fibroblast-derived myotubes; CTG repeat length: 2000<br><u>CTL:</u> Human fibroblast-derived myotubes from unaffected individuals | | CUGBP1 | <u>p-CUGBP1 levels:</u> **Increased** rphosphorylation in DM1 vs CTL. (p: NR) |
| | <u>DM1:</u> TAM mice cardiac tissue<br><u>CTL:</u> Mice cardiac tissue | | CUGBP1 | <u>Total CUGBP1 levels:</u> **Increased** steady-state levels in DM1 vs CTL. (p: NR)<br><br><u>p-CUGBP1 levels:</u> **Increased** phosphorylation in DM1 vs CTL. (p: NR) |
| | <u>DM1:</u> COS M6 cells with 960 CUGexp RNA<br><u>CTL</u>: COS M6 cells without CUGexp RNA | Western blot; Kinase Assay | PKC | <u>p-PKC levels:</u> **Increased** levels of p-PKCα and p-PKCβII in DM1 vs CTL. (p: NR) |
| **Llagostera et al. 2007, Spain** [38] | <u>DM1:</u> DMPK knockout mice cardiac tissue<br><u>CTL:</u> WT mice cardiac tissue | Western blot | AKT | <u>p-AKT levels:</u> **Decreased** levels in 39±5% of p-AKT (Ser473) in DM1 vs CTL upon activation of the insulin pathway (p<0.05). |
| | | | GSK3β | <u>p-GSK3β levels</u>: **Decreased** levels in 67±9% of p-GSK3β (Ser9) in DM1 vs CTL upon activation of the insulin pathway (p<0.05). |
| | | | InsR/IGF-1R | <u>p-Insulin/IGF-1 receptor levels</u>: **Decreased** levels in 54±10% of p-InsR (Tyr1150/Tyr1151) and p-IGF-IR (Tyr1135/Tyr1136) in DM1 vs CTL upon activation of the insulin pathway (p<0.05). |

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| | DM1: DMPK knockout mice skeletal muscle tissue biopsies<br>CTL: WT mice skeletal muscle tissue biopsies | | InsR/IGF-1R | p-Insulin/IGF-1 receptor levels: **Decreased** levels in 44±10% of p-InsR (Tyr1150/Tyr1151) and p-IGF-IR (Tyr1135/Tyr1136) in DM1 vs CTL upon activation of the insulin pathway ($p<0.05$). |
| **Llagostera et al. 2012, Spain** [39] | DM1: DMPK knockout mice cardiac tissue<br>CTL: WT mice cardiac tissue | Western blot | PLN | p-PLN levels: **Increase** in 4-fold in the levels of p-PLN (Ser16) in CTL in response to isoproterenol (β-adrenegic agonist). In DMPK knockout mice, p-PLN (Ser16) levels were **unaltered**.<br><br>p-PLN/Total PLN ratio:<br>Without isoproterenol activation: DM1 < CTL ($p<0.05$)<br>With isoproterenol activation: DM1 < CTL ($p<0.05$) |
| **Morriss et al. 2018, USA** [40] | DM1: TREDT960I mice skeletal muscle tissue biopsies + dox; n=12<br>DM1 mice with moderate muscle wasting - n= 7<br>DM1 mice with severe muscle wasting - n= 5<br><br>CTL: TREDT960I mice skeletal muscle tissue biopsies lacking the reverse transactivator + dox; n=8<br>CTL mice with moderate muscle wasting - n= 4<br>CTL mice with severe muscle wasting -n= 4 | RPPA analysis/Western blot | AMPKα | Total AMPKα levels: **Similar** levels in DM1 vs CTL mice with moderate muscle wasting. **Increased** levels of AMPKα (F6) in severe muscle wasting mice in DM1 vs CTL.<br><br>p-AMPKα levels: **Increased** levels of p-AMPKα (Thr172) in DM1 vs CTL mice with severe muscle wasting. **Similar** levels of p-AMPKα (Thr172) in DM1 vs CTL mice with moderate muscle wasting.<br><br>Semi-quantitative total AMPKα (23A3) levels:<br>Moderate muscle wasting: DM1 < CTL (p=ns)<br>Severe muscle wasting: DM1 < CTL (p=ns)<br><br>Semi-quantitative total AMPKα (F6) levels:<br>Moderate muscle wasting: DM1 < CTL (p=ns)<br>Severe muscle wasting: DM1 > CTL ($p=0.05$)<br><br>Semi-quantitative p-AMPKα levels:<br>Moderate muscle wasting: DM1 < CTL (p=ns)<br>Severe muscle wasting: DM1 < CTL ($p<0.01$)<br><br>p-AMPKα (23A3)/Total AMPKα ratio:<br>Moderate muscle wasting: DM1 > CTL (p=ns)<br>Severe muscle wasting: DM1 > CTL ($p<0.01$)<br><br>p-AMPKα (F6)/Total AMPKα ratio:<br>Moderate muscle wasting: DM1 > CTL ($p<0.01$)<br>Severe muscle wasting: DM1 > CTL (p=ns) |
| | | RPPA | c-Jun | p-c-Jun levels: **Decreased** levels of p-c-Jun (Ser63) in DM1 vs CTL. (p: NR) |

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| | | RPPA | CDKN1B | <u>p-CDKN1B levels:</u> **Increased** levels of p-CDKN1B (Thr198) in DM1 vs CTL. (p: NR) |
| | | RPPA analysis/Western blot | PDGFRβ | <u>Total PDGFRβ levels:</u> **Increased** levels in DM1 vs CTL mice with severe muscle wasting. **Similar** in DM1 vs CTL mice with moderate muscle wasting.<br><br><u>p-PDGFRβ levels:</u> **Increased** levels of p-PDGFRβ (Tyr751) in DM1 vs CTL mice with severe muscle wasting. **Similar** in DM1 vs CTL mice with moderate muscle wasting.<br><br><u>Semi-quantitative total PDGFRβ levels:</u><br>Moderate muscle wasting: DM1 > CTL (p=ns)<br>Severe muscle wasting: DM1 > CTL ($p<0.01$)<br><br><u>Semi-quantitative p-PDGFRβ levels:</u><br>Moderate muscle wasting: DM1 < CTL (p=ns)<br>Severe muscle wasting: DM1 > CTL ($p<0.05$)<br><br><u>p-PDGFRβ/Total PDGFRβ ratio:</u><br>Moderate muscle wasting: DM1 < CTL (p=ns)<br>Severe muscle wasting: DM1 < CTL ($p<0.05$) |
| | | RPPA analysis/Western blot | Stat3 | <u>Total Stat3 levels:</u> **Increased** levels in DM1 vs CTL mice with severe muscle wasting. **Similar** levels in DM1 vs CTL mice with moderate muscle wasting.<br><br><u>p-Stat3 levels:</u> **Increased** levels of p-Stat3 (Ser727) in DM1 vs CTL mice with severe muscle wasting. **Reduced** levels of p-Stat3 in proportion to total Stat3 levels in DM1 vs CTL mice with severe muscle wasting.<br><br><u>Semi-quantitative total Stat3 levels:</u><br>Moderate muscle wasting: DM1 ~ CTL (p=ns)<br>Severe muscle wasting: DM1 > CTL ($p<0.01$)<br><br><u>Semi-quantitative p-Stat3 levels:</u><br>Moderate muscle wasting: DM1 > CTL ($p<0.05$)<br>Severe muscle wasting: DM1 > CTL ($p<0.05$)<br><br><u>p-Stat3/Total Stat3 ratio:</u><br>Moderate muscle wasting: DM1 > CTL (p=ns)<br>Severe muscle wasting: DM1 < CTL ($p<0.05$) |
| | <u>DM1:</u> Human skeletal muscle tissue biopsies from patients with DM1: n=7 | Western blot | AMPKα | <u>Total AMPKα levels:</u> **Similar** levels in DM1 vs CTL.<br><br><u>p-AMPKα levels:</u> **Similar** levels of p-AMPKα (Thr172) in DM1 vs CTL |

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| | <u>CTL:</u> Human skeletal muscle tissue biopsies from unaffected individuals; n=4 | | | <u>Semi-quantitative total AMPKα levels:</u> DM1 < CTL (p=ns)<br><u>Semi-quantitative p-AMPKα levels:</u> DM1> CTL (p=ns)<br><br><u>p-AMPKα /Total AMPKα ratio:</u> DM1 > CTL (p=ns) |
| | | | PDGFRβ | <u>Total PDGFRβ levels:</u> **Increased** levels in DM1 vs CTL.<br><br><u>p-PDGFRβ levels:</u> **Increased** levels of p-PDGFRβ (Tyr751) in DM1 vs CTL.<br><br><u>Semi-quantitative total PDGFRβ levels:</u>DM1 > CTL (p<0.001)<br><u>Semi-quantitative p-PDGFRβ levels:</u> DM1 > CTL (p<0.05)<br><br><u>p-PDGFRβ/Total PDGFRβ ratio:</u> DM1 < CTL (p=ns) |
| | | | Stat3 | <u>Total Stat3 levels:</u> **Similar** levels in DM1 vs CTL.<br><br><u>p-Stat3 levels:</u> **Similar** levels of p-Stat3 (Ser727) in DM1 vs CTL<br><br><u>Semi-quantitative total Stat3 levels:</u> DM1 > CTL (p=ns)<br><u>Semi-quantitative p-Stat3 levels:</u> DM1 > CTL (p=ns)<br><u>p-Stat3/Total Stat3 ratio:</u> DM1 < CTL (p=ns) |
| **Nakamori et al. 2017, Japan** [41] | <u>DM1:</u> Mice C2C12 myoblasts with 800 CUGexp RNA<br><br><u>CTL:</u> Mice C2C12 myoblasts without CUGexp RNA | Western blot | IkBα | <u>Total IkBα levels:</u> **Decreased** levels in DM1 vs CTL.<br><br><u>p-IkBα levels:</u> **Increased** levels of p-IkBα (Ser32) in DM1 vs CTL.<br><br><u>Semi-quantitative total IkBα levels:</u> DM1 < CTL (p<0.01)<br><u>Semi-quantitative p-IkBα levels (% to CTL):</u> DM1 > CTL (p<0.01) |
| | | Western blot/ELISA | NF-kB | <u>Total NF-kB levels:</u> **Similar** in DM1 vs CTL.<br><br><u>p-NF-kB levels:</u> **Increased** levels of p-NF-kB (Ser536) in DM1 vs CTL.<br><br><u>NF-kB activity:</u> **Increased** nuclear localization and **increased** binding activity.<br><br><u>Semi-quantitative total NF-kB levels:</u> DM1 > CTL (p=ns)<br><br><u>Semi-quantitative p-NF-kB levels:</u> DM1 > CTL (p<0.01)<br><br><u>Semi-quantitative Nuclear NF-kB levels:</u> DM1 > CTL (p<0.01) |

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| | | | | Semi-quantitative NF-kB binding activity: DM1 > CTL (<p<0.01) |
| | | Western blot | PKR | Total PKR levels: **Similar** in DM1 vs CTL.<br><br>p-PKR levels: **Increase** in p-PKR in DM1 vs CTL.<br><br>Semi-quantitative total PKR levels: DM1 > CTL (p=ns)<br><br>Semi-quantitative p-PKR levels: DM1 > CTL (p<0.01) |
| **Peric et al. 2014, Serbia** [42] | jDM1: Human CSF; n=27; Sex: 10F/17M; Age: 35±9.1 (Mean±SD); CTG Repeat Length: 859.2±311.8 (Mean±SD)<br><br>aDM1: Human CSF; n=47; Age: 46.7±7.6 (Mean±SD); Sex: 27F/20M; CTG Repeat Length: 703.2±248.0 (Mean±SD)<br><br>CTL: Human CSF; n=26; Age: 50.9±8.3 (Mean±SD); Sex: 16F/10M | Sandwich ELISA | Tau | Total Tau levels: Adult-onset with **similar** levels of Tau vs CTL and jDM1.<br><br>p-tau levels: Adult-onset with **slight but not significant increase** in p-Tau (Thr181) vs CTL and jDM1.<br><br>Quantitative total Tau concentration (Mean±SD):<br>jDM1: 175.5±90.2 ng/l vs aDM1: 218.4±108.2 ng/l vs CTL: 178.9±38.6 ng/l (p=0.156)<br><br>Quantitative p-tau concentration (Mean±SD):<br>jDM1: 43.1±21.0 ng/l vs aDM1: 54.6±23.4 ng/l vs CTL: 47.8±23.7 ng/l (p=0.057) |
| **Ravel-Chapuis et al. 2017, Canada** [43] | DM1: $HSA^{LR}$ mice EDL skeletal muscle tissue biopsies; n=4 (n for evaluation of activity=8) CTG repeat length: 250<br><br>CTL: $HSA^{SR}$ mice EDL skeletal muscle tissue biopsies | Western blot | Calcineurin | Total Calcineurin levels: **Increase** in ~2 fold in DM1 vs CTL (p<0.001)<br><br>Calcineurin activity: **Increase** of ~2.5 fold in the phosphatase activity (p<0.001) |
| **Ravel-Chapuis et al. 2018, Canada** [44] | DM1: $HSA^{LR}$ mice EDL skeletal muscle tissue biopsies; n range= 4-5; CTG repeat length: 250 n range= 4-5<br><br>CTL: WT mice EDL skeletal muscle tissue biopsies; n range)= 4-5 | Western blot | AMPK | Total AMPK levels: **Similar** in DM1 vs CTL (p=ns)<br><br>p-AMPK levels: **Decrease** (~70%) in p-AMPK (Thr172) in DM1 vs CTL (p=0.02)<br><br>Semi-quantitative total AMPK levels: DM1~CTL (p=ns)<br><br>p-AMPK/Total AMPK ratio: DM1 < CTL (p=0.02) |
| | DM1: Human fibroblast cell line-derived myoblasts with DM1<br><br>CTL: Human fibroblast cell line-derived myoblasts | | AMPK | Total AMPK levels: **Similar** in DM1 vs CTL.<br><br>p-AMPK levels: **Decrease** (~35%) in p-AMPK (Thr172) in DM1 vs CTL.<br><br>Semi-quantitative total AMPK levels: DM1 > CTL (p=ns) |

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| | | | | <u>p-AMPK/Total AMPK ratio:</u> DM1 < CTL (p=0.02) |
| **Renna et al. 2017, Italy** [45] | <u>DM1:</u> Human patients' *biceps brachii* (BB) (n=4) and *tibialis anterior* (TA) (n=4) skeletal muscle tissue biopsies<br><br><u>CTL:</u> Healthy participants' BB (n=4) and TA (n=3) skeletal muscle tissue biopsies | Western blot | AKT | ***Biceps brachii* (BB)**<br><u>Total AKT levels:</u> **Similar** levels in DM1 vs CTL.<br><u>p-AKT levels:</u> **Similar** levels of p-AKT (Thr308) in DM1 vs CTL.<br><br><u>Semi-quantitative total AKT levels:</u> DM1 > CTL (p=ns)<br><u>Semi-quantitative p-AKT levels:</u> DM1 > CTL (p=ns)<br><br>***Tibialis Anterior* (TA)**<br><u>Total AKT levels</u>: **Increased** in DM1 vs CTL.<br><u>p-AKT levels:</u> **Increased** values of p-AKT (Thr308) in DM1 vs CTL.<br><br><u>Semi-quantitative total AKT levels:</u> DM1 > CTL (p=0.02)<br><u>Semi-quantitative p-AKT levels:</u> DM1 > CTL (p=0.04) |
| | | | ERK1/2 | ***Biceps brachii* (BB)**<br><u>Total ERK1/2 levels</u>: **Increased** in DM1 vs CTL.<br><u>p-ERK1/2 levels:</u> **Similar** levels of p-ERK1/2 (Thr202/Tyr204) in DM1 vs CTL.<br><br><u>Semi-quantitative total ERK1/2 levels:</u> DM1 > CTL (p=0.02)<br><u>Semi-quantitative p-ERK1/2 levels:</u> DM1 > CTL (p=ns)<br><br>***Tibialis Anterior* (TA)**<br><u>Total ERK1/2 levels:</u> **Increased** in DM1 vs CTL.<br><u>p-ERK1/2 levels:</u> **Increased** levels of p-ERK1/2 (Thr202/Tyr204) in DM1 vs CTL<br><br><u>Semi-quantitative total ERK1/2 levels:</u> DM1 > CTL (p=0.01)<br><u>Semi-quantitative p-ERK1/2 levels:</u> DM1 > CTL (p=0.03) |
| | | | GSK3β | ***Biceps brachii* (BB)**<br><u>Total GSK3β levels:</u> **Similar** values in DM1 vs CTL.<br><u>p-GSK3β levels:</u> **Similar** levels of p-GSK3β (Tyr216) in DM1 vs CTL.<br><br><u>Semi-quantitative total GSK3β levels:</u> DM1 > CTL (p=ns)<br><u>Semi-quantitative p-GSK3β levels:</u> DM1 > CTL (p=ns)<br><br>***Tibialis Anterior* (TA)**<br><u>Total GSK3β values</u>: **Decreased** in DM1 vs CTL.<br><u>p-GSK3β values:</u> **Increased** levels of p-GSK3β (Tyr216) in DM1 vs CTL. |

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| | | | | Semi-quantitative total GSK3β levels: DM1 < CTL (p=0.03)<br>Semi-quantitative p-GSK3β levels: DM1 > CTL (p=0.004) |
| | | | S6K1 | ***Biceps brachii* (BB)**<br>Total S6K1 levels: **Similar** values in DM1 vs CTL.<br>p-S6K1 levels: **Similar** levels of p-S6K1 (Thr421/Ser424) in DM1 vs CTL.<br><br>Semi-quantitative total S6K1 levels: DM1 < CTL (p=ns)<br>Semi-quantitative p-S6K1 levels: DM1 > CTL (p=ns)<br><br>***Tibialis Anterior* (TA)**<br>Total S6K1 levels: **Similar** levels in DM1 vs CTL<br>p-S6K1 levels: **Similar** levels values of p-S6K1 (Thr421/Ser424) in DM1 vs CTL<br><br>Semi-quantitative total S6K1 levels: DM1 > CTL (p=ns)<br>Semi-quantitative p-S6K1 levels: DM1 > CTL (p=ns) |
| | DM1: Human patients satellite cell-derived myotubes; n=5<br><br>CTL: Healthy participants satellite cell-derived myotubes; n=6 | | AKT | p-AKT levels: **Slower increase** in the activation of AKT (Thr308) upon insulin stimulation in DM1 vs CTL.<br><br>p-AKT/Total AKT ratio:<br>0 min.: DM1 ~ CTL (p=ns); 5 min.: DM1 < CTL (p=ns)<br>15 min.: DM1 < CTL (p=0.04); 30 min.: DM1 < CTL (p=ns)<br>Between DM1 vs CTL groups: p=0.04 |
| | | | ERK 1 | p-ERK 1 levels: **Similar** levels of p-ERK 1 (Thr202) upon insulin stimulation in DM1 vs CTL.<br><br>p-ERK 1/Total ERK 1 ratio:<br>0 min.: DM1 ~ CTL (p=ns); 5 min.: DM1 < CTL (p<0.05)<br>15 min.: DM1 < CTL (p=ns); 30 min.: DM1 < CTL (p=ns)<br>Between DM1 vs CTL groups: p=ns |
| | | | ERK 2 | p-ERK 2 levels: **Decreased** levels of p-ERK 2 (Tyr204) upon insulin stimulation in DM1 vs CTL.<br><br>p-ERK 2/Total ERK 2 ratio:<br>0 min.: DM1 ~ CTL (p=ns); 5 min.: DM1 < CTL (p<0.05)<br>15 min.: DM1 < CTL (p=ns); 30 min.: DM1 < CTL (p=ns)<br>Between DM1 vs CTL groups: p=0.05 |

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| | | | GSK3β | <u>p-GSK3β levels:</u> **Not significant but increased** levels of p-GSK3β (Tyr216) <u>upon insulin stimulation</u> in DM1 vs CTL.<br><br><u>p-GSK3β/Total GSK3β ratio:</u><br>0 min.: DM1 ~ CTL (p=ns); 5 min.: DM1 > CTL (p=ns)<br>15 min.: DM1 > CTL (p=ns); 30 min.: DM1 > CTL (p=ns)<br>Between DM1 vs CTL groups: p=ns |
| | | | IRS1 | <u>p-IRS1 levels:</u> **No increase** in p-IRS1 (Tyr612) <u>upon insulin stimulation</u> in DM1 vs **increase** in CTL. **Not significant but decreased** levels of p-IRS1 (Tyr896) in DM1 vs CTL.<br><br><u>p-IRS1/Total IRS1 (Tyr612) ratio:</u><br>0 min.: DM1 ~CTL (p=ns); 5 min.: DM1 < CTL (p=0.002)<br>15 min.: DM1 < CTL (p=0.01); 30 min.: DM1 ~CTL (p=ns)<br>Between DM1 vs CTL groups: p=0.01<br><br><u>p-IRS1/Total IRS1 (Tyr896) ratio:</u><br>0 min.: DM1 ~ CTL (p=ns); 5 min.: DM1 < CTL (p=0.04)<br>15 min.: DM1 < CTL (p=0.01); 30 min.: DM1 < CTL (p=ns)<br>Between DM1 vs CTL groups: p=ns |
| | | | S6K1 | <u>p-S6K1 levels:</u> **Not significant but decreased** levels of p-S6K1 (Thr421/Ser424) <u>upon insulin stimulation</u> in DM1 vs CTL.<br><br><u>p-S6K1/Total S6K1 ratio:</u><br>0 min.: DM1 ~ CTL (p=ns); 5 min.: DM1 < CTL (p=ns)<br>15 min.: DM1 < CTL (p=ns); 30 min.: DM1 < CTL (p=ns)<br>Between DM1 vs CTL groups: p=ns |
| **Renna et al. 2019, Italy** [46] | <u>DM1:</u> Human patients' *biceps brachii* (BB) and *tibialis anterior* (TA) skeletal muscle tissue biopsies (n=8)<br><br><u>CTL:</u> Healthy participants BB and TA skeletal muscle tissue biopsies (n=6) | Western blot | AKT | <u>p-AKT levels:</u> **Decreased activation** of AKT (Thr308/Ser473) <u>upon insulin stimulation</u> in DM1 vs CTL.<br><br><u>p-AKT fold change on basal level (Thr308):</u> DM1 < CTL (p<0.01)<br><br><u>p-AKT fold change on basal level (Ser473):</u> DM1 < CTL (p<0.01) |
| | | | AS160 | <u>p-AS160 levels:</u> **Decreased** levels of p-AS160 (Thr642) <u>upon insulin stimulation</u> in DM1 vs CTL.<br><br><u>p-AS160 fold change on basal level:</u> DM1 < CTL (p<0.01) |
| | | | ERK 1/2 | <u>p-ERK 1/2 levels:</u> **Decreased** levels of p-ERK 1/2 (Thr202/Tyr204) <u>upon insulin stimulation</u> in DM1 vs CTL. |

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| | | | | p-ERK1/2 fold change on basal level: DM1 < CTL ($p<0.01$) |
| | | | FOXO1 | p-FOXO1 levels: **Decreased** levels of p-FOXO1 (Thr24) upon insulin stimulation in DM1 vs CTL.<br><br>p-FOXO1 fold change on basal level: DM1 < CTL ($p<0.01$) |
| | | | IRS1 | p-IRS1: **Decreased** levels of p-IRS1 (Tyr612) upon insulin stimulation in DM1 vs in CTL.<br><br>p-IRS1 fold change on basal level: DM1 < CTL ($p<0.0001$) |
| | | | mTOR | p-mTOR: **Decreased** levels of p-mTOR (Ser2448) upon insulin stimulation in DM1 vs CTL.<br><br>p-mTOR fold change on basal level: DM1 < CTL ($p<0.01$) |
| | | | S6K1 | p-S6K1: **Decreased** levels of p-S6K1 (Thr421/Ser424) upon insulin stimulation in DM1 vs CTL<br><br>p-S6K1 fold change on basal level: DM1 < CTL ($p<0.05$) |
| **Rizzo et al. 2018, Italy** [47] | DM1: Human fetus-derived congenital DM1 myoblasts and myotubes; n=2; CDM13 CTG repeat length: 1800; CDM15 CTG repeat length: 3200<br><br>CTL: Human fetus-derived myoblasts and myotubes | Western blot | AKT | Total AKT levels: **Significantly decreased** levels in CDM15 vs CTL in day 0 of differentiation. **Similar** levels in CDM13 vs CTL in day 0 of differentiation.<br><br>Semi-quantitative total AKT levels: CDM13 < CTL (p=ns); CDM15 < CTL ($p<0.05$) |
| | | | S6K1 | p-S6K1 levels: **Decreased** levels of p-S6K1 (Thr421/Ser424) at day 0 and day 3 of differentiation in DM1 (CDM15) vs CTL. However, there was an **increase** of p-S6K1 (Thr421/Ser424) at day 0 and day 3 of differentiation in DM1 (CDM13) vs CTL.<br><br>Semi-quantitative p-S6K1 levels:<br>d0: CDM15 < CDM13 > CTL; d3: CDM15 < CDM13 > CTL (p: NR) |
| **Sabater-arcis et al. 2020, Spain** [48] | DM1: Human fibroblast-derived myotubes with scrambled oligonucleotides; CTG repeat length: 1300<br><br>CTL: Human fibroblast-derived myotubes with scrambled oligonucleotides | Western blot | AKT | p-AKT levels: **Decreased** levels of p-AKT (Ser473) in DM1 vs CTL.<br><br>p-AKT/Total AKT ratio:<br>DM1: 0.910 ± 0.127 (Mean±SEM); CTL: 1.861 ± 0.140 (Mean±SEM) (p: NR) |
| | | | AMPK | p-AMPK levels: **Similar** levels of p-AMPK (Thr172) in DM1 and CTL.<br><br>p-AMPK/Total AMPK ratio:<br>DM1: 0.7906±0.1316 (Mean±SEM); CTL: 0.5272±0.1316 (Mean±SEM) (p: NR) |

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| **Salisbury et al. 2008, USA** [49] | DM1: human patients' primary myoblasts and myotubes<br><br>CTL: human primary myoblasts and myotubes | Western blot<br>EMSA assay | AKT | Total AKT levels: **Similar** levels in DM1 vs CTL (p: NR)<br><br>p-AKT levels: **Increased** levels of p-AKT (Ser473) in the cytoplasm of DM1 vs CTL proliferating myoblasts. **Decreased** levels in DM1 vs CTL differentiating myotubes. (p: NR)<br><br>AKT activity: **Increased** interaction with CUGBP1 in DM1 vs CTL myoblasts. (p: NR) |
| | | | CDK4 | Total CDK4 levels: **Increased** levels in CTL differentiating myotubes, while levels remain **unchanged** in DM1 during differentiation. (p: NR) |
| | | | CUGBP1 | Total CUGBP1 levels: **Decreased** levels in DM1 differentiating myotubes vs proliferating myoblasts. In CTL, CUGBP1 is **increased** in differentiating myotubes. (p: NR)<br><br>p-CUGBP1 levels: **Increased** levels of p-CUGBP1 (Ser28) in DM1 vs CTL proliferating myoblasts. **Decreased levels** of p-CUGBP1 (Ser302) in DM1 vs CTL differentiating myotubes (p: NR)<br><br>CUGBP1 activity: **Decreased** formation of CUGBP1–eIF2 complex during differentiation in DM1 vs CTL **Increased** interaction with Cyclin D1 mRNA in DM1 vs CTL myoblasts and myotubes. **Decreased** interaction with cyclin D3 in myotubes. (p: NR) |
| **Salvatori et al. 2005, Italy** [50] | DM1: Human patients skeletal muscle tissue biopsies; n=16<br><br>CTL: Healthy participants skeletal muscle tissue biopsies; n=6 | Immunohistochemistry<br>Western blot | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL.<br><br>Semi-quantitative total DMPK levels (fold change):<br>DM1: 1.96±0.24 (Mean±SEM) vs CTL: 3.62±0.69 (Mean±SEM) ($p=0.004$) |
| **Song et al. 2020, China** [51] | DM1: IPSC-derived satellite skeletal muscle cells (n=2) (DM1-03, DM1-13-3)<br><br>CTL: IPSC-derived satellite skeletal muscle cells (n=1) | Western Blot | mTOR | p-mTOR levels: **Decreased** levels of p-mTOR (Ser2448) in DM1 vs CTL<br><br>p-mTOR/Total mTOR relative expression: DM1-03 < DM1-13-3 < CTL: 1.0 ($p<0.05$) |
| | DM1: Human patients satellite skeletal muscle cells; n=3; Sex: 1M/2F; Age: 46±2 y (mean ± SD)<br><br>CTL: Healthy participants satellite skeletal muscle cells; n=3; Sex: 2M/1F; Age: 48±3 years (mean ± SD) | | | p-mTOR levels: **Decreased** levels of p-mTOR (Ser2448) in DM1 vs CTL<br><br>p-mTOR/Total mTOR relative expression: DM1 < CTL ($p<0.05$) |
| **Wang et al. 2009, USA** [52] | DM1: TAM+EpA960 RNA mice heart tissue | 2D Gel/ Western Blot | CUGBP1 | Total CUGBP1 levels: **Increased** in DM1 vs CTL. (p: NR)<br><br>p-CUGBP1 levels: **Increased** phosphorylation levels of p-CUGBP1 in DM1. (p: NR) |

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| | CTL: MCM mice heart tissue | | PKCα/βII | p-PKCα/βII levels: **Increased** levels of p-PKC (Thr638/Thr641) in DM1 vs CTL. (p: NR) |
| **Wang et al. 2019, Taiwan** [53] | DM1: DMSXL mice brain tissue; CTG repeat length: >1000 CUG<br><br>CTL: WT mice brain tissue | Western blot | CUGBP1 | p-CUGBP1 levels: **Decreased** levels of p-CUGBP1 (Ser302) in DM1 vs CTL. (p: NR) |
| | DM1: DMSXL adult mice diaphragm muscle tissue biopsies; CTG repeat length: >1000 CUGexp RNA<br><br>CTL: WT mice diaphragm muscle tissue biopsies | | GSK3β | Total GSK3β levels: **Increased** in DM1 vs CTL. (p: NR) |
| | DM1: Human congenital DM1 myoblasts; n=3; CTG Repeat Length: ~2000<br><br>CTL: Healthy participants' myoblasts; n=3 | | GSK3β | Total GSK3β levels: **Increased** in DM1 vs CTL. (p: NR) |
| **González-Barriga et al. 2021, France** [54] | DM1: DMSXL mice primary oligodendrocytes<br><br>CTL: WT mice primary oligodendrocytes | Mass-spectrometry<br>2D Gel/ Western Blot | Capzb | p-CAPZB levels: **Increased** levels of p-CAPZB (Ser 263) in DM1 vs CTL (fold change: 2.778; p = 0.0089) |
| **Panaite et al. 2011, Switzerland** [55] | DM1: DMSXL mice spinal cord<br><br>CTL: WT mice primary spinal cord | Immunohistochemistry | Tau | Total Tau levels: **Decreased** in DM1 vs CTL. (p: NR)<br><br>p-Tau levels: **Increased** phosphorylation levels of p-Tau (Ser 396, Ser 404, Ser 199 and Ser 202) in DM1 vs CTL. (p: NR) |
| **Takahashi et al. 2001, Japan** [56] | DM1: COS-7 cells transiently expressing mutant DMPK $(CTG)_{130}$ cDNA<br><br>CTL: COS-7 cells transiently expressing WT DMPK $(CTG)_5$ cDNA | Western blot | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL in 20-30% (p<0.05). |
| **Fu et al. 1993, USA** [57] | DM1: Human adult DM1 patients skeletal muscle tissue biopsies; n=20<br><br>CTL: Human normal adult skeletal muscle tissue biopsies; n=7 | Western Blot | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL. (p: NR) |

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| **Furling et al. 2001, Canada** [58] | DM1: primary human DM1 skeletal muscle cell culture<br><br>CTL: primary human normal skeletal muscle cell culture | Western Blot | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL. (p: NR) |
| **Koga et al. 1994, Japan** [59] | DM1: Human adult DM1 patients skeletal muscle tissue biopsies; n=14<br><br>CTL: Human normal adult skeletal muscle tissue biopsies; n=NR | Western Blot | DMPK | Total DMPK levels: **Decreased** levels in DM1 vs CTL in about 36±36.9% (p: NR). |
| **Usuki et al. 2000, Japan** [60] | DM1: C2C12 cells stably expressing mutant DMPK $(CTG)_{160}$ cDNA<br><br>CTL: C2C12 cells stably expressing WT DMPK $(CTG)_5$ cDNA | Western Blot | c-Jun | Total c-Jun levels: **Similar** in DM1 vs CTL upon MeHg-induced cytotoxicity. (p: NR)<br><br>p-c-Jun levels: **Increased** phosphorylation levels of p-c-Jun (Ser 63) in DM1 vs CTL upon MeHg-induced cytotoxicity. (p: NR) |
| | | | Elk1 | p-Elk1 levels: **Decreased** phosphorylation levels of p-Elk1 (Ser 383) in DM1 vs CTL upon MeHg-induced cytotoxicity. (p: NR) |
| **Timchenko et al. 2001, USA** [61] | DM1: human DM1 skeletal muscle cells<br><br>CTL: human normal skeletal muscle cells | Western Blot<br>Kinase assay | Cdk4 | Total Cdk4 levels: **Similar** in DM1 vs CTL during myoblasts differentiation. (p: NR)<br><br>Cdk4 activity: **Increased** in DM1 vs CTL during myoblasts differentiation. (p: NR) |
| **Narang et al. 2000, Canada** [62] | DM1: Human adult DM1 patients skeletal muscle tissue biopsies; n=4<br><br>CTL: Human adult age-matched control skeletal muscle tissue biopsies; n=4 | Western Blot | DMPK | Total DMPK levels: Significantly **Decreased** in DM1 vs CTL. ($p<0.005$) |
| | DM1: Human post-mortem congenital DM1 patients skeletal muscle tissue; n=4<br><br>CTL: Human post-mortem age-matched control skeletal muscle tissue; n=4 | | | Total DMPK levels: **Similar** in DM1 vs CTL. (p: NR) |
| **Hernandez-Hernandez et** | DM1: PC12 cells stably expressing mutant DMPK $(CTG)_{190}$ cDNA | Western Blot | Tau | Total Tau levels: Slightly but significantly **Decreased** in DM1 vs CTL. ($p<0.05$) |

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| **al. 2006, Mexico** [63] | <u>CTL:</u> PC12 cells stably expressing WT DMPK $(CTG)_5$ cDNA | | | <u>p-Tau levels:</u> Significantly **Increased** phosphorylation levels of p-Tau (Ser 396, Ser 404 and Thr231) in DM1 vs CTL. ($p<0.05$) |

**Abbreviatures: aDM1** – Adult phenotype; **AKT -** Protein kinase B; **AMPK** - 5' AMP-activated protein kinase; **AS160 -** TBC1 domain family member 4; **CaMKIIβM** - $Ca^{2+}$/calmodulin dependent protein kinase; **Capzb** - F-actin-capping protein subunit beta; **CDKN1B** - Cyclin-dependent kinase inhibitor 1B; **CDK4** – Cyclin-dependent kinase 4; **CDK6** - Cyclin-dependent kinase 6; **CHO-tTA** – chinese hamster ovary cells transfected with the TRE-GFP-$CTG_{914}$ plasmid; **CSF** - Cerebrospinal fluid; **CTG** – Cytosine-Thymine-Guanine triplet; **CTL** – Control or Wild-type group; **CUGBP1** - CUG triplet repeat RNA binding protein 1; **CUGexp** – Expanded CUG; **DMPK -** Dystrophia myotonica protein kinase; **DMSXL -** Transgenic mice carrying >1,000 CTG repeats; **DM1**- Myotonic Dystrophy type 1 model group; **DM5 mice** - RNA toxicity model; **Dox** – Doxycycline; **dp-protein -** dephosphorylated protein; **d0** – Before exposure to differentiating medium; **d2/d3/d4/d6** – 2/3/4/6 days after exposure to differentiation medium; **EDL** - Extensor digitorum longus muscle; **eIF2α** - Eukaryotic translation initiation factor 2 subunit 1; **EpA960** – interrupted 960-CTG expansion model; **ERK 1/2** - Extracellular signal-regulated kinases 1/2; **Fed** – Mice food deprived for 12 hours followed by 4 hours of free access to food before sacrifice; **FOXO1** - Forkhead box protein O1; **GSK3** - Glycogen synthase kinase 3; **HSA$^{LR}$** - Transgenic mice expressing the human skeletal actin gene with long CUG repeat Length; **HSA$^{SR}$** - Transgenic mice expressing the human skeletal actin gene with short CUG repeat Length; **IGF-1** - Insulin-like growth factor 1; **IkBα** - Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha; **INPP4B** - Type II inositol 3,4-bisphosphate 4-phosphatase; **InsR** – Insulin Receptor; **IRS1** – Insulin Receptor Substrate 1; **jDM1** – Childhood/juvenile phenotype; **LBCLs** - Lymphoblastoid cell lines; **LKB1** - Liver kinase B1; **MCM** - MerCreMer (MCM) model; **MEK** - Mitogen-activated protein kinase kinase; **MeHg –** Methylmercury chloride**; mTOR** - Mammalian target of rapamycin; **n** – sample size; **n.d.** - not detected; **NF-kB** - Nuclear factor kappa-light-chain-enhancer of activated B cells; **PDGFRβ** - Platelet-derived growth factor receptor beta; **PERK** - Protein kinase R (PKR)-like endoplasmic reticulum kinase; **PKC** – Protein Kinase C; **PKM2** - Pyruvate kinase isozyme M2; **PKR** - Protein kinase R; **PLN** – Phospholamban; **p-protein -** phosphorylated protein; **PRKAR1B** - cAMP-dependent protein kinase type I-beta regulatory subunit; **p-state** - phosphorylation state; **PTPRF** - Receptor-type tyrosine-protein phosphatase F; **p38MAPK** - p38 Mitogen-activated protein kinase; **Rb** – Retinoblastoma protein; **RpS6** – Ribosomal protein S6; **SEM** - Standard error of the mean; **Stat3** - Signal transducer and activator of transcription 3; **S6K1** - Ribosomal protein S6 kinase beta-1; **TAK1** - Mitogen-activated protein kinase kinase kinase 7; **TAM** - Tamoxifen-inducible and heart-specific EpA960(R) RNA expression model; **TREDT960I -** Tetracycline-inducible transgene model; **TSC2** - Tuberous Sclerosis Complex 2; **ULK1** - Unc-51 like autophagy activating kinase; **WT** – Wildtype; **24hStarved/45hStarved** – Mice with 24/45 hours of food deprivation but free access to water before sacrifice.