Supplementary Table 1 – A list of muscle biopsies of OPMD patients and controls that were used for RNA expression analyses. All expPABPN1 carriers were confirmed by sequence analysis.

					expPABPN1 Carriers				
Controls				**Pre-Symptomatic**			**Symptomatic**		
Gender	**Age**	**Sex**	**Age**	**Gender**	**Age**	**MRC score***	**Gender**	**Age**	**MRC score***
Female	17	Male	41	Female	37	5	Female	49	4
Male	17	Male	42	Female	37	5	Female	54	5
Female	19	Male	42	Male	38	5	Female	57	4
Female	19	Male	42	Female	39	5	Male	59	5
Male	20	Male	42	Female	39	5	Female	60	4
Female	20	Male	43	Female	41	5	Female	60	4.5
Male	22	Male	43			5	Male	66	4.5
Male	23	Female	43				Male	68	3.5
Female	25	Female	43				Female	69	4.5
Female	27	Female	44						
Male	27	Male	44						
Female	27	Male	45						
Male	28	Female	48						
Male	28	Male	49						
Male	29	Female	49						
Male	29	Male	55						
Female	31	Female	56						
Female	31	Female	56						
Male	32	Male	56						
Female	32	Male	58						
Female	32	Female	58						
Female	34	Female	60						
Female	34	Female	60						
Male	34	Female	60						
Female	35	Male	60						
Female	35	Male	61						
Female	35	Male	66						
Male	36	Female	67						
Female	36	Male	67						
Male	36	Female	67						
Female	37	Female	67						
Female	38	Male	68						
Male	39	Female	70						
Female	39	Male	70						
Male	39	Male	73						
Male	40	Male	77						
Male	40	Female	85						
Male	40	Female	87						
Female	40	Female	89						

* MRC score in left and right quadriceps was determined at the same day when biopsies were sampled. Values show an average of both sides. MRC in age-matching controls and in pre-symptomatic is 5, indicating normal muscle strength; <5 indicates clinical muscle weakness.

Supplementary Table 2 - Functional Analysis of ageing and OPMD associated transcriptional changes. Biological processes are defined and clustered according to KEGG. The proportion of deregulated genes are depicted by %D.E. Genes.

Metabolism

			Muscle Ageing						**OPMD**, Anvar et al. (2011)							
			Human, Welle et al. (2004)			**Human**			**Human**		**Mouse**			**Drosophila**		
			# Genes	P-value	% D.E. Genes	# Genes	P-value	% D.E. Genes	P-value	% D.E. Genes	# Genes	P-value	% D.E. Genes	# Genes	P-value	% D.E. Genes
Carbohydrate	620	Pyruvate metabolism	41	1.13E-07	36.59	40	1.24E-04	37.50	-		50	6.26E-09	32.00	43	6.75E-04	25.58
	51	Fructose and mannose metabolism	35	3.02E-03	20.00	35	2.11E-04	48.57	2.28E-02	28.57	40	1.18E-10	37.50	31	9.43E-04	16.13
	562	Inositol phosphate metabolism	49	3.12E-02	16.33	47	8.22E-04	31.91	2.98E-03	17.02	63	2.37E-07	31.75	32	1.89E-03	21.88
Energy	190	Oxidative phosphorylation	112	1.87E-05	54.46	108	7.87E-03	28.70	1.37E-02	17.59	123	4.63E-06	32.52	97	6.17E-04	49.48
	910	Nitrogen metabolism	24	6.76E-05	25.00	24	2.79E-02	50.00	1.13E-02	20.83	23	1.23E-11	43.48	27	1.21E-03	22.22
Lipid	564	Glycerophospholipid metabolism	67	3.39E-03	19.40	64	5.03E-07	48.44	1.67E-03	18.75	67	8.17E-09	35.82	113	8.84E-04	11.50
	1030	Glycan structures - biosynthesis 1	118	8.77E-03	23.73	106	4.30E-03	37.74	3.27E-03	14.15	137	2.54E-07	31.39	49	4.87E-02	12.24
	590	Arachidonic acid metabolism	54	1.28E-02	14.81	50	2.94E-04	40.00	1.46E-02	18.00	69	3.74E-11	24.64		-	
Nucleotide	230	Purine metabolism	145	5.06E-04	23.45	139	5.59E-05	43.88	5.47E-03	28.78	164	3.14E-08	35.37	246	9.39E-04	21.14
	240	Pyrimidine metabolism	89	1.56E-03	20.22	86	1.14E-03	36.05	1.94E-02	22.09	104	2.05E-08	36.54	68	1.33E-03	14.71
Amino Acid	260	Glycine, serine and threonine metabolism	42	3.58E-06	23.81	39	1.28E-03	30.77	4.38E-02	20.51	46	5.92E-08	23.91	34	6.36E-04	17.65
	251	Glutamate metabolism	24	1.06E-04	29.17	23	4.15E-03	47.83	4.15E-02	17.39	27	4.65E-09	40.74	26	1.25E-03	34.62
	271	Methionine metabolism	21	1.44E-02	28.57	20	1.19E-02	40.00	4.27E-02	25.00	22	4.71E-08	59.09		-	
Glycan Biosynthesis	1032	Glycan structures - degradation	31	2.53E-02	22.58	29	1.69E-02	37.93	3.01E-03	24.14	31	2.61E-07	29.03		-	
Cofactors and Vitamins	760	Nicotinate and nicotinamide metabolism	23	1.74E-06	34.78	23	2.19E-04	56.52	6.21E-03	34.78	25	1.05E-06	32.00	8	2.74E-03	12.50
Genetic Information Processing																
Transcription	3020	RNA polymerase	25	9.28E-04	28.00	22	3.94E-04	36.36	2.11E-02	27.27	31	1.21E-06	32.26	19	1.14E-03	21.05
Translation	970	Aminoacyl-tRNA biosynthesis	41	1.19E-03	24.39		-		1.23E-02	28.95	53	2.34E-06	35.85	26	2.92E-03	23.08
	3010	Ribosome		-		83	5.86E-03	37.35	-		67	1.73E-08	37.31	78	6.99E-04	53.85
Folding, Sorting and Degradation	3050	Proteasome	43	4.67E-04	32.56		-		9.27E-03	34.09	52	3.72E-06	30.77	42	7.71E-04	57.14
	4120	Ubiquitin mediated proteolysis	131	1.64E-03	27.48	126	5.41E-06	45.24	1.52E-03	30.16	177	3.61E-10	38.98	80	8.66E-04	21.25
	4130	SNARE interactions in vesicular transport	37	1.88E-03	27.03	38	5.83E-03	34.21	3.54E-02	26.32	36	2.86E-09	50.00	22	3.38E-02	9.09
Replication and Repair	3030	DNA replication	36	1.40E-03	33.33	34	1.25E-03	41.18	1.54E-02	23.53	38	2.97E-08	42.11	28	1.02E-03	14.29
	3420	Nucleotide excision repair	43	2.87E-02	18.60	41	1.56E-03	36.59	8.88E-04	24.39	43	3.36E-10	53.49	33	1.06E-03	24.24

Environmental Information Processing

Membrane Transport	2010	ABC transporters - General	41	8.85E-03	24.39	44	2.06E-04	43.18	4.08E-03	25.00	41	5.22E-09	39.02	3	3.81E-02	66.67
Signal Transduction	4330	Notch signaling pathway	46	1.12E-05	41.30	-			2.81E-03	18.60	49	2.70E-08	22.45	21	6.99E-03	19.05
	4150	mTOR signaling pathway	50	2.39E-05	42.00	49	1.92E-03	44.90	1.71E-02	28.57	64	3.78E-08	39.06	23	7.76E-04	34.78
	4370	VEGF signaling pathway	73	1.68E-03	23.29	67	2.48E-06	43.28	5.52E-03	20.90	82	8.69E-11	40.24	32	7.22E-04	31.25
	4010	MAPK signaling pathway	265	1.91E-03	24.91	253	7.50E-05	39.13	5.50E-03	18.18	283	1.49E-10	33.92	not available		
	4012	ErbB signaling pathway	87	1.97E-03	27.59	83	3.14E-06	33.73	2.33E-02	27.71	107	2.21E-09	35.51	26	1.31E-03	34.62
	4310	Wnt signaling pathway	148	4.43E-03	25.68	147	1.47E-04	39.46	7.60E-04	21.09	171	1.78E-10	35.09	64	8.77E-04	23.44
	4350	TGF-beta signaling pathway	83	7.54E-03	25.30	82	8.16E-05	39.02	9.51E-03	26.83	84	1.70E-10	38.10	29	1.36E-02	17.24
	4340	Hedgehog signaling pathway	53	1.95E-02	16.98	56	3.30E-02	26.79	3.69E-03	16.07	56	7.04E-09	21.43	18	1.15E-03	33.33
	4070	Phosphatidylinositol signaling system	76	2.16E-02	18.42	75	4.29E-03	34.67	3.44E-03	20.00	94	3.85E-10	34.04	45	2.64E-03	13.33
	4630	Jak-STAT signaling pathway	150	2.24E-02	19.33	145	3.92E-05	39.31	5.59E-03	19.31	170	7.91E-09	25.29	20	1.80E-03	35.00
	4020	Calcium signaling pathway	176	4.28E-02	21.59	169	3.05E-04	41.42	1.36E-03	18.34	220	6.19E-10	26.36	43	6.54E-04	32.56
Signaling Molecules and Interaction	4512	ECM-receptor interaction	84	3.93E-02	20.24	79	5.33E-03	43.04	5.01E-04	27.85	97	1.72E-05	31.96	not available		

Cellular Processes

Transport and Catabolism	4140	Regulation of autophagy	34	1.34E-03	26.47	32	1.95E-02	31.25	3.59E-02	18.75	39	8.13E-08	30.77	16	1.07E-03	25.00
Cell Motility	4810	Regulation of actin cytoskeleton	210	7.61E-03	22.38	204	9.77E-03	33.33	2.43E-02	16.67	229	2.44E-08	32.75	not available		
Cell Growth and Death	4110	Cell cycle	111	1.39E-04	28.83	109	4.98E-06	42.20	6.02E-03	21.10	119	3.80E-09	36.97	-		
	4115	p53 signaling pathway	68	1.39E-03	27.94	63	1.12E-06	34.92	-		75	7.69E-11	37.33	15	7.20E-04	6.67
	4210	Apoptosis	88	4.61E-03	23.86	78	5.43E-06	42.31	1.09E-02	21.79	104	1.74E-10	31.73	19	6.06E-04	36.84
Cell Communication	4510	Focal adhesion	199	9.03E-04	26.13	190	3.13E-04	44.21	3.38E-03	24.74	215	4.04E-08	37.21	not available		
	4520	Adherens junction	74	9.49E-04	28.38	75	1.57E-02	34.67	3.83E-03	25.33	84	1.17E-07	32.14	not available		
	4530	Tight junction	129	1.72E-03	22.48	127	1.87E-03	40.16	2.13E-02	21.26	145	2.15E-09	37.93	not available		
	4540	Gap junction	94	8.11E-03	23.40	92	1.62E-03	40.22	9.79E-04	31.52	105	2.40E-09	31.43	not available		

Organismal Systems

Immune System	4660	T cell receptor signaling pathway	94	5.71E-03	23.40	86	7.00E-03	45.35	3.53E-02	15.12	112	1.11E-09	27.68	not available		
	4670	Leukocyte transendothelial migration	113	1.29E-02	17.70	107	6.69E-03	45.79	-		125	1.25E-08	25.60	not available		
	4664	Fc epsilon RI signaling pathway	76	1.87E-02	17.11	73	4.12E-04	45.21	1.37E-03	17.81	86	1.21E-10	30.23	not available		
	4650	Natural killer cell mediated cytotoxicity	130	2.38E-02	17.69	121	1.49E-03	42.15	3.19E-02	11.57	138	3.86E-10	26.09	not available		
	4620	Toll-like receptor signaling pathway	101	3.70E-02	17.82	93	1.22E-02	45.16	1.62E-02	19.35	108	1.06E-10	30.56	not available		
Endocrine System	4910	Insulin signaling pathway	136	8.43E-04	30.88	135	3.26E-05	39.26	1.62E-03	29.63	161	2.36E-08	38.51	not available		
	4912	GnRH signaling pathway	98	1.05E-02	23.47	95	4.96E-05	40.00	7.40E-04	30.53	116	3.47E-10	32.76	not available		
	4916	Melanogenesis	99	1.74E-02	20.20	101	5.49E-03	30.69	6.92E-04	25.74	108	2.54E-10	35.19	not available		
Nervous System	4720	Long-term potentiation	70	9.74E-03	25.71	68	5.89E-03	36.76	2.58E-03	25.00	85	2.00E-11	36.47	not available		

Human Diseases

Cancer	5211	Renal cell carcinoma	69	3.72E-05	34.78	67	1.85E-05	40.30	3.06E-02	20.90	74	2.42E-09	40.54	not available
	5216	Thyroid cancer	29	1.65E-04	41.38	28	4.66E-04	42.86	1.18E-02	25.00	28	2.75E-04	35.71	not available
	5215	Prostate cancer	90	2.30E-04	26.67	84	5.94E-03	45.24	4.69E-03	29.76	103	7.82E-08	36.89	not available
	5218	Melanoma	71	5.25E-04	30.99		-		3.93E-02	19.12	75	2.88E-08	44.00	not available
	5214	Glioma	64	7.85E-04	32.81	62	1.19E-02	38.71	5.39E-03	24.19	76	2.20E-09	50.00	not available
	5220	Chronic myeloid leukemia	74	8.54E-04	36.49	70	3.40E-05	32.86	2.81E-02	22.86	87	1.43E-08	39.08	not available
	5223	Non-small cell lung cancer	54	1.16E-03	29.63	51	1.42E-02	33.33	3.35E-02	17.65	62	4.73E-09	43.55	not available
	5210	Colorectal cancer	83	1.42E-03	31.33	81	2.71E-03	38.27	1.71E-02	20.99	92	9.70E-09	42.39	not available
	5222	Small cell lung cancer	86	2.19E-03	27.91	78	2.71E-04	53.85	1.31E-02	25.64	108	3.74E-07	35.19	not available
	5213	Endometrial cancer	52	2.36E-03	26.92	50	2.30E-03	40.00	3.81E-02	24.00	60	8.46E-08	40.00	not available
	5221	Acute myeloid leukemia	57	4.54E-03	29.82	53	1.83E-05	47.17	2.99E-02	28.30	71	5.10E-07	30.99	not available
	5217	Basal cell carcinoma	53	2.66E-02	18.87	53	4.26E-03	33.96	2.31E-04	16.98	54	1.08E-06	27.78	not available
Immune System	5340	Primary immunodeficiency	34	1.24E-02	14.71		-		3.51E-02	12.50	36	2.02E-08	11.11	not available
Neurodegenerative	5010	Alzheimer's disease	158	5.04E-06	46.84	151	6.45E-05	29.80	2.57E-03	21.85	187	1.00E-09	33.16	not available
	5012	Parkinson's disease	113	1.35E-05	58.41	104	2.33E-03	27.88	2.11E-02	18.27	138	1.93E-09	35.51	not available
	5040	Huntington's disease	31	2.93E-03	32.26	28	9.57E-03	42.86	5.01E-03	35.71	38	6.79E-08	36.84	not available
	5014	Amyotrophic lateral sclerosis (ALS)	55	6.35E-03	27.27	51	7.47E-05	37.25	1.04E-02	23.53	67	5.40E-10	26.87	not available
Metabolic	4930	Type II diabetes mellitus	42	2.49E-03	35.71	41	7.43E-05	36.59	2.58E-02	19.51	51	1.97E-09	33.33	not available
Infectious	5130	Pathogenic Escherichia coli infection - EHEC	49	1.28E-03	38.78	48	4.76E-02	45.83	2.28E-02	22.92		-		not available
	5110	Vibrio cholerae infection	56	2.39E-03	25.00	57	5.07E-03	45.61	3.67E-03	28.07		-		not available
	5120	Epithelial cell signaling in Helicobacter …	65	1.16E-02	20.00	62	1.58E-05	53.23	2.53E-02	29.03		-		not available

eTable 2 -

A list of genes that exhibit accelerated expression trends in OPMD compared with skeletal muscle aging.

Symbol	Entrez IDs	Probe IDs	A	S	P
ABCA11	79963	2320403	🟦	🟦	
ACP6	51205	4670671	🟦	🟦	🟦
ADAM7	8756	1260424	🟦	🟦	
ALDH3A1	218	5560369	🟨	🟨	🟨
ALDH6A1	4329	5820373	🟨	🟨	🟨
AP2A1	160	4390180	🟨	🟨	
BHLHB5	27319	7210551	🟨	🟨	
C21ORF34	388815	70368	🟦	🟦	
C4ORF29	80167	5810192	🟨	🟨	
CDKN1A	1026	4230201	🟨	🟨	
CHRNA1	1134	1410017	🟨	🟨	🟨
CHRNA1	1134	4120717	🟨	🟨	🟨
CHRNA1	1134	4570634	🟨	🟨	🟨
CREB5	9586	4290619	🟨	🟨	🟨
CTDSP1	58190	7150333	🟨	🟨	🟨
DHRS12	79758	3710086	🟦	🟦	🟦
DNAJB6	10049	6580189	🟨	🟨	
DUOX1	53905	3060528	🟦	🟦	
EEF1A1	1915	3450719	🟨	🟨	
EGFLAM	133584	7380092	🟨	🟨	
EMX1	2016	3460390	🟦	🟦	🟦
FRAS1	80144	270358	🟦	🟦	🟦
GRM2	2912	4230673	🟦	🟦	
H2AFX	3014	4120538	🟨	🟨	
HPS4	89781	3170504	🟦	🟦	
IARS	3376	6420397	🟦	🟦	
IGF2BP3	10643	1770243	🟨	🟨	🟨
JARID2	3720	2320286	🟦	🟦	🟦
LMOD1	25802	6760246	🟦	🟦	🟦
LOC100131174	100131174	4670482	🟦	🟦	
LOC400793	400793	5090142	🟨	🟨	
LOC402251	402251	3440670	🟨	🟨	
LOC642795	642795	6100068	🟨	🟨	
LOC644284	644284	2490451	🟨	🟨	
LOC649260	649260	770348	🟨	🟨	
LRTM2	654429	5890243	🟨	🟨	🟨
MAP2K3	5606	4200544	🟦	🟦	
METTL10	399818	6370075	🟦	🟦	
MUTYH	4595	5670037	🟦	🟦	
NEK3	4752	1190504	🟦	🟦	
NFYA	4800	6180072	🟨	🟨	
OSBP	5007	5550296	🟦	🟦	
PDDC1	347862	3420730	🟦	🟦	🟦
PHF19	26147	5550402	🟦	🟦	
POU5F1	5460	5550577	🟦	🟦	
PRODH	5625	5860689	🟨	🟨	
PRRX1	5396	1440601	🟨	🟨	🟨
RAPGEFL1	51195	1940072	🟦	🟦	🟦
RCC1	1104	2570292	🟨	🟨	
RDH5	5959	110326	🟦	🟦	
RFPL3S	10737	1240731	🟦	🟦	
ROPN1B	152015	730521	🟨	🟨	
SF3A3	10946	1230747	🟦	🟦	
SH2B3	10019	6560301	🟨	🟨	
SLC1A4	6509	6350392	🟦	🟦	🟦
SLC36A2	153201	6180711	🟦	🟦	
SLC38A10	124565	6590333	🟨	🟨	
SNHG11	128439	4560332	🟨	🟨	🟨
SPCS2	9789	7040068	🟦	🟦	
STX11	8676	60470	🟨	🟨	
STX5	6811	6450470	🟨	🟨	
TIAM2	26230	7050612	🟨	🟨	🟨
TMEM55B	90809	5220152	🟦	🟦	🟦
TRIM38	10475	3930377	🟨	🟨	
TSC1	7248	4040373	🟦	🟦	
TSPY1	64591	4250097	🟦	🟦	
UBQLN4	56893	2120215	🟨	🟨	🟨
UCP2	7351	6580059	🟨	🟨	🟨
UNC13B	10497	5820121	🟦	🟦	🟦
UPB1	51733	3830735	🟦	🟦	🟦
VAMP1	6843	2350541	🟦	🟦	
WDR20	91833	3130494	🟦	🟦	
ZCCHC11	23318	4260093	🟦	🟦	🟦
ZNF679	168417	3940431	🟨	🟨	

A: Aging
S: Symptomatic
P: Pre-symptomatic

Yellow: Up-regulation 🟨
Blue: Down-regulation 🟦

Supplementary Table 4 – A primer list for qPCR.

Gene	**FW Primer**	**RV Primer**
GUSB	5’ CTCATTTGGAATTTTGCCGATT	5’ CCGAGTGAAGATCCCCTTTTTA
GapDH	5’ CAACGAATTTGGCTACAGCA	5’ AGGGGTCTACATGGCAACTG
PABPN1	5’ CGTTGGCAATGTGGACTATG	5’ ACACGGTTGACTGAACCACA
MYH1	5’ TGGACAAACTGCAAGCAAAG	5’ GACCTGGGACTCAGCAATGT
CAV3	5’ CTGTTGCCTGAGCACAAAAA	5’ GTTAGCCAAAGGGGAGGTTC