

Bone & Joint Research



Supplementary Material

10.1302/2046-3758.139.BJR-2023-0398.R1

Table i. Genes significantly correlated with advancing age in both datasets using linear regression analysis.

GeneSymbol	GeneName	GSE180836			GSE26051			Meta-analysis				Heterogeneity		
		Estimate	SE	p-value*	Estimate	SE	p-value*	Meta estimate	Meta SE	Meta p-value†	FDR	QE	QE p	I ² , %
<i>KLHL41</i>	kelch like family member 41	-0.015	0.004	0.001	-0.020	0.007	0.017	-0.016	0.004	3.20E-06	0.0122	0.28	0.60	0
<i>MYH3</i>	myosin heavy chain 3	-0.015	0.004	0.001	-0.021	0.007	0.012	-0.016	0.003	3.07E-06	0.0122	0.52	0.47	0
<i>LINC00888</i>	small nucleolar RNA host gene 33	-0.014	0.005	0.009	-0.021	0.008	0.016	-0.016	0.004	1.21E-04	0.0444	0.68	0.41	0
<i>TNNC2</i>	troponin C2, fast skeletal type	-0.014	0.004	0.002	-0.018	0.008	0.044	-0.015	0.004	5.48E-05	0.0348	0.19	0.67	0
<i>IFT88</i>	intraflagellar transport 88	-0.014	0.005	0.005	-0.016	0.007	0.038	-0.015	0.004	2.00E-4	0.0466	0.07	0.79	0
<i>PDZRN3</i>	PDZ domain containing ring finger 3	-0.012	0.005	0.019	-0.021	0.009	0.031	-0.014	0.004	0.001	0.0855	0.80	0.37	0

<i>MAP3K7CL</i>	MAP3K7 C-terminal like	-0.012	0.005	0.021	-0.020	0.008	0.035	-0.014	0.004	0.001	0.0939	0.68	0.41	0
<i>TTN-AS1</i>	TTN antisense RNA 1	-0.013	0.004	0.002	-0.018	0.007	0.034	-0.014	0.003	3.64E-05	0.0308	0.34	0.56	0
<i>CLYBL</i>	citramalyl-CoA lyase	-0.012	0.005	0.038	-0.016	0.006	0.023	-0.014	0.004	0.001	0.0909	0.29	0.59	0
<i>MALSU1</i>	mitochondrial assembly of ribosomal large subunit 1	-0.011	0.004	0.020	-0.018	0.006	0.009	-0.013	0.004	2.00E-4	0.0466	1.03	0.31	2.56
<i>CRYBG3</i>	crystallin beta-gamma domain containing 3	-0.011	0.005	0.035	-0.018	0.008	0.038	-0.013	0.004	0.002	0.005	0.61	0.43	0
<i>PCM1</i>	pericentriolar material 1	-0.010	0.004	0.017	-0.017	0.008	0.044	-0.011	0.004	0.001	0.095	0.72	0.40	0
<i>ATG4A</i>	autophagy related 4A cysteine peptidase	-0.010	0.004	0.025	-0.016	0.007	0.046	-0.011	0.004	0.002	0.005	0.55	0.46	0
<i>EIF5B</i>	eukaryotic translation initiation factor 5B	-0.008	0.004	0.034	-0.015	0.007	0.046	-0.009	0.003	0.003	0.006	0.80	0.37	0
<i>DGUOK</i>	deoxyguanosine kinase	0.009	0.003	0.009	0.014	0.006	0.042	0.010	0.003	4.00E-4	0.0671	0.62	0.43	0
<i>KANK2</i>	KN motif and ankyrin repeat domains 2	0.009	0.004	0.031	0.017	0.007	0.034	0.011	0.004	0.003	0.007	1.06	0.30	6.09
<i>ERN1</i>	endoplasmic reticulum to nucleus signaling 1	0.009	0.004	0.041	0.018	0.008	0.038	0.011	0.004	0.004	0.009	1.05	0.30	4.96
<i>LRP1</i>	LDL receptor related protein 1	0.009	0.004	0.037	0.018	0.008	0.046	0.011	0.004	0.006	0.011	1.08	0.30	7.06
<i>SCART1</i>	scavenger receptor family member expressed on T cells 1	0.010	0.004	0.010	0.015	0.006	0.038	0.011	0.003	4.00E-4	0.0665	0.40	0.53	0
<i>FMOD</i>	fibromodulin	0.009	0.004	0.035	0.016	0.006	0.023	0.011	0.003	0.001	0.0949	0.85	0.36	0
<i>RFT1</i>	RFT1 homolog	0.011	0.004	0.020	0.012	0.006	0.047	0.011	0.003	0.001	0.0930	0.03	0.85	0
<i>CAMK1</i>	calcium/calmodulin dependent protein kinase I	0.011	0.005	0.019	0.013	0.006	0.049	0.012	0.004	0.001	0.0936	0.07	0.80	0

<i>RNF130</i>	ring finger protein 130	0.011	0.004	0.007	0.015	0.006	0.034	0.012	0.003	2.00E-4	0.0466	0.29	0.59	0
<i>STEAP1</i>	STEAP family member 1	0.011	0.004	0.012	0.019	0.008	0.037	0.012	0.004	0.001	0.0747	0.81	0.37	0
<i>CDO1</i>	cysteine dioxygenase type 1	0.010	0.005	0.039	0.019	0.008	0.025	0.013	0.004	0.002	0.005	1.04	0.31	4.24
<i>DPM2</i>	dolichyl-phosphate mannosyltransferase subunit 2, regulatory	0.013	0.004	0.003	0.015	0.006	0.033	0.013	0.003	7.27E-05	0.0381	0.14	0.70	0
<i>ARHGDI A</i>	Rho GDP dissociation inhibitor alpha	0.013	0.004	0.007	0.018	0.008	0.049	0.014	0.004	4.00E-4	0.0621	0.32	0.57	0

*Independent-samples t-test.

†z-test.

FDR, false discovery rate; I², heterogeneity index; QE, Cochran's Q statistic for Effect; QE_p, p-value for QE value; SE, standard error.

Table ii. Genes differentially expressed in age groups in both datasets using differential expression analysis.

GeneSymb ol	GeneName	GSE180836		GSE26051		Meta-analysis			Heterogeneity	
		log ₂ (FC))	p- value*	log ₂ (FC))	p- value*	Meta log ₂ (FC)	Meta p- value†	FDR	QE	QEp
<i>SYPL2</i>	synaptophysin like 2	-4.39	6.47E-08	-2.06	0.022	-3.522	0.002	0.010	1.99	0.158
<i>FNDC5</i>	fibronectin type III domain containing 5	-2.03	6.53E-05	-1.43	0.012	-2.195	1.97E-09	6.32E-08	0.56	0.456
<i>TTN-AS1</i>	TTN antisense RNA 1	-2.30	4.14E-09	-1.47	0.024	-2.140	5.04E-07	5.37E-06	0.92	0.338
<i>IDH2</i>	isocitrate dehydrogenase (NADP(+)) 2, mitochondrial	-2.33	6.85E-07	-1.25	0.044	-2.079	2.07E-05	2.00E-04	0.10	0.750
<i>MYH3</i>	myosin, heavy chain 3, skeletal muscle, embryonic	-1.96	3.71E-08	-1.75	0.003	-1.927	4.78E-09	7.65E-08	0.05	0.832
<i>SPIB</i>	Spi-B transcription factor	-1.33	0.0152	-1.47	0.020	-1.426	0.010	0.017	0.00	0.955
<i>PACRG-AS1</i>	PACRG antisense RNA 1	-1.09	0.0101	-1.64	0.033	-1.362	0.005	0.010	0.01	0.904
<i>DPYSL5</i>	dihydropyrimidinase like 5	-1.45	0.0272	-1.37	0.034	-1.213	0.009	0.017	0.42	0.516
<i>HOOK1</i>	hook microtubule tethering protein 1	-1.47	0.0163	-0.86	0.050	-1.170	0.011	0.017	0.15	0.700
<i>CBLN2</i>	cerebellin 2 precursor	-1.39	0.0420	-0.77	0.047	-1.150	0.004	0.010	0.17	0.680
<i>KRT80</i>	keratin 80	-1.29	0.0041	-0.80	0.047	-1.132	0.002	0.010	0.37	0.543

<i>ARFGEF3</i>	ARFGEF family member 3	-0.95	0.0138	-1.08	0.022	-1.056	0.023	0.025	0.44	0.507
<i>FKBP6</i>	FK506 binding protein 6	-1.09	0.0297	-1.57	0.027	-0.977	0.004	0.010	0.02	0.876
<i>KLHDC8B</i>	kelch domain containing 8B	-0.80	0.0119	-0.82	0.045	-0.808	0.005	0.010	0.00	0.982
<i>CEBPD</i>	CCAAT/enhancer binding protein delta	0.86	0.0276	0.62	0.045	0.764	0.005	0.010	0.15	0.700
<i>STEAP1</i>	six transmembrane epithelial antigen of the prostate 1	0.73	0.0100	1.10	0.049	0.767	0.013	0.018	0.14	0.705
<i>ELL2</i>	elongation factor for RNA polymerase II 2	0.87	0.0290	0.76	0.038	0.837	0.012	0.017	0.03	0.873
<i>MT1E</i>	metallothionein 1E	1.09	0.0323	0.79	0.040	0.844	0.003	0.010	0.25	0.615
<i>CACNA1C</i>	calcium voltage-gated channel subunit alpha1 C	0.79	0.0089	1.26	0.022	0.871	0.013	0.018	0.09	0.764
<i>COMP</i>	cartilage oligomeric matrix protein	1.04	0.0442	1.04	0.041	0.968	0.014	0.018	0.14	0.713
<i>FIBIN</i>	fin bud initiation factor homolog (zebrafish)	0.82	0.0337	1.10	0.034	1.017	0.004	0.010	0.11	0.742
<i>SLC22A18A S</i>	solute carrier family 22 member 18 antisense	0.97	0.0107	1.31	0.026	1.038	0.016	0.020	0.14	0.704
<i>GALNT15</i>	polypeptide N-acetylgalactosaminyltransferase 15	0.98	0.0342	1.90	0.019	1.044	0.018	0.021	0.00	0.999
<i>MT1X</i>	metallothionein 1X	1.51	0.0072	1.06	0.041	1.332	0.002	0.010	0.43	0.512
<i>E2F2</i>	E2F transcription factor 2	1.23	0.0077	2.10	0.009	1.372	0.003	0.010	0.20	0.658
<i>CDO1</i>	cysteine dioxygenase type 1	1.51	0.0101	1.88	0.014	1.583	0.003	0.010	0.08	0.783

*t-test.

†z-test.

FDR, false discovery rate; QE, Cochran's Q statistic for Effect; QEp, p-value for QE value; SE, standard error.

Table iii. Gene Ontology (GO) gene set enrichment analysis revealing potential function of age-related genes.

Correlation with age	Category	GO term	Age-related genes	NE S	p-value *	p-adjust	Gene ratio, %	Highlight†
Downregulated	Biological process	Aerobic respiration	<i>IDH2</i>	2.73	1.00E-10	5.00E-08	72	
		Cellular respiration	<i>IDH2</i>	2.46	1.00E-10	5.00E-08	55	
		Energy derivation by oxidation of organic compounds	<i>IDH2</i>	2.37	1.00E-10	5.00E-08	50	
		Actin mediated cell contraction	<i>MYH3</i>	2.14	2.83E-05	0.002	42	
		Sarcomere organization	<i>MYH3</i>	2.07	8.39E-05	0.004	50	
		Mitochondrial translation	<i>MALSU1</i>	2.04	1.99E-05	0.001	57	
		Mitochondrial gene expression	<i>MALSU1</i>	1.94	5.09E-06	4.00E-04	49	Highlight
		Muscle cell development	<i>MYH3, SYPL2</i>	1.92	5.86E-05	0.003	33	Highlight
		ATP metabolic process	<i>MYH3</i>	1.92	2.00E-04	0.007	71	Highlight
		Muscle contraction	<i>MYH3</i>	1.83	1.73E-05	0.001	28	Highlight
		Muscle cell differentiation	<i>MYH3, SYPL2</i>	1.60	2.00E-04	0.008	27	
		Dendrite development	<i>DPYSL5</i>	1.51	0.002	0.038	19	
		Muscle structure development	<i>MYH3, SYPL2</i>	1.48	0.001	0.013	23	
		Nucleobase containing small molecule metabolic process	<i>MYH3, IDH2, DPYSL5</i>	1.43	0.001	0.017	39	Highlight

	Cellular component	Contractile fibre	<i>MYH3</i>	2.40	2.13E-08	6.21E-06	40	Highlight
		Mitochondrial matrix	<i>MALSU1, IDH2</i>	2.38	0.000	0.000	48	Highlight
		Myosin complex	<i>MYH3</i>	1.92	0.001	0.021	35	
		Supramolecular polymer	<i>MYH3, HOOK1, KRT80</i>	1.31	0.003	0.041	18	Highlight
	Molecular function	Microfilament motor activity	<i>MYH3</i>	1.84	0.002	0.036	33	Highlight
		Calmodulin binding	<i>MYH3</i>	1.65	0.001	0.014	36	
	Human phenotype	Elevated urinary carboxylic acid	<i>IDH2</i>	2.08	1.00E-04	0.003	50	
		Abnormality of acid base homeostasis	<i>IDH2</i>	2.03	3.72E-09	0.000	45	
		Abnormal urine carboxylic acid level	<i>IDH2</i>	1.95	1.00E-04	0.004	46	
		Hypertrophic cardiomyopathy	<i>FKBP6</i>	1.89	1.46E-05	0.001	45	
		Elevated circulating follicle stimulating hormone level	<i>FKBP6</i>	1.84	0.002	0.035	57	
		Abnormality of circulating enzyme level	<i>FKBP6</i>	1.83	0.000	0.001	31	
		Impulsivity	<i>DPYSL5</i>	1.64	0.002	0.037	25	
		Focal onset seizure	<i>DPYSL5</i>	1.52	0.002	0.027	24	
		Bilateral tonic clonic seizure	<i>DPYSL5</i>	1.44	0.002	0.037	26	
		Muscle weakness	<i>MYH3</i>	1.36	1.00E-04	0.004	24	Highlight

Upregulated	Biological process	Cellular response to cadmium ion	<i>MT1E, MT1X</i>	-2.25	1.40E-07	2.80E-05	56	
		Response to cadmium ion	<i>MT1E, MT1X</i>	-2.23	6.06E-07	1.00E-04	39	
		Bone development	<i>COMP</i>	-2.21	7.83E-09	2.57E-06	43	
		Skeletal system development	<i>COMP</i>	-2.19	1.00E-10	5.00E-08	36	
		Response to zinc ion	<i>MT1E, MT1X</i>	-2.18	3.26E-06	3.00E-04	50	
		Chondrocyte differentiation	<i>COMP</i>	-2.11	1.57E-06	2.00E-04	43	
		Defence response to bacterium	<i>LRP1</i>	-2.04	6.40E-07	1.00E-04	38	
		Myeloid leucocyte migration	<i>CAMK1</i>	-2.03	7.96E-07	1.00E-04	49	
		Inflammatory response	<i>LRP1, CAMK1, CDO1</i>	-2.00	1.00E-10	5.00E-08	34	Highlight
		Collagen fibril organization	<i>FMOD, COMP</i>	-1.98	3.00E-04	0.008	42	Highlight
Phagocytosis	<i>LRP1, CAMK1</i>	-1.97	8.44E-06	0.001	51			

		Immune effector process	<i>LRP1, SCART1</i>	- 1.9 7	2.67E -09	1.17E -06	38	
		Ossification	<i>CEBPD, COMP</i>	- 1.9 4	1.28E -07	2.71E -05	33	Highlig ht
		External encapsulating structure organization	<i>LRP1, FMOD, COMP</i>	- 1.9 2	4.31E -06	4.00E -04	30	
		Transforming growth factor beta receptor signalling pathway	<i>FMOD</i>	- 1.9 2	2.26E -05	0.001	33	
		Regulation of vasculature development	<i>E2F2</i>	- 1.9 1	1.33E -05	0.001	30	
		Adaptive immune response	<i>SCART1</i>	- 1.9 0	1.39E -06	2.00E -04	39	
		Leucocyte mediated immunity	<i>SCART1</i>	- 1.8 9	1.96E -06	2.00E -04	38	
		Negative regulation of vasculature development	<i>E2F2</i>	- 1.8 8	2.00E -04	0.007	35	
		Positive regulation of MAPK cascade	<i>ERN1</i>	- 1.8 0	8.62E -06	0.001	36	
		Regulation of Ras protein signal transduction	<i>KANK2, ARHGDI A</i>	- 1.7 9	3.00E -04	0.008	32	
		Epithelial cell apoptotic process	<i>E2F2</i>	- 1.7 8	0.001	0.018	27	

		Regulation of small GTPase mediated signal transduction	<i>KANK2, ARHGDI</i> A	-1.75	2.00E-04	0.007	33	
		Appendage development	<i>CACNA1C, COMP</i>	-1.74	0.001	0.016	42	
		Rho protein signal transduction	<i>KANK2, ARHGDI</i> A	-1.73	0.001	0.026	38	
		Appendage morphogenesis	<i>CACNA1C</i>	-1.71	0.002	0.035	43	
		Osteoblast differentiation	<i>CEBPD</i>	-1.71	0.001	0.016	27	
		Response to ketone	<i>FIBIN</i>	-1.70	0.001	0.024	32	
		Response to lipid	<i>KANK2, CDO1, FIBIN</i>	-1.65	9.36E-06	0.001	31	
		Glycoprotein metabolic process	<i>DPM2, GALNT15</i>	-1.64	4.00E-04	0.011	34	Highlight
		Positive regulation of catalytic activity	<i>ERN1, LRP1, CACNA1C</i>	-1.63	5.17E-06	0.000	35	
		Positive regulation of cell population proliferation	<i>ERN1, CAMK1, COMP</i>	-1.62	9.12E-07	0.000	29	
		Response to metal ion	<i>MT1E, FIBIN, MT1X</i>	-1.62	0.001	0.017	25	Highlight

		Haemopoiesis	<i>CEBPD</i>	-1.61	0.000	0.001	34	
		Gland development	<i>CDO1</i>	-1.59	0.001	0.023	34	
		Negative regulation of cell population proliferation	<i>DGUOK, KANK2</i>	-1.48	0.001	0.016	34	
	Cellular component	External encapsulating structure	<i>FMOD, COMP</i>	-2.27	1.00E-10	5.00E-08	37	
		Collagen containing extracellular matrix	<i>FMOD, COMP</i>	-2.22	1.00E-10	5.00E-08	38	Highlight
		Lysosomal lumen	<i>FMOD</i>	-2.08	2.73E-05	0.001	56	
		Endocytic vesicle	<i>LRP1</i>	-1.67	0.001	0.016	36	
		Vacuole	<i>LRP1, FMOD</i>	-1.64	1.00E-04	0.003	43	
	Molecular function	Glycosaminoglycan binding	<i>COMP</i>	-2.18	2.35E-08	6.56E-06	44	
		Extracellular matrix structural constituent	<i>FMOD, COMP</i>	-2.14	2.51E-07	4.74E-05	44	Highlight
		Collagen binding	<i>COMP</i>	-2.11	1.39E-05	0.001	38	

		Cargo receptor activity	<i>LRP1</i>	- 2.0 6	3.87E -05	0.002	72	
		Proteoglycan binding	<i>LRP1, COMP</i>	- 1.9 9	1.00E -04	0.004	77	
		Scavenger receptor activity	<i>LRP1</i>	- 1.9 1	0.001	0.013	85	
		Extracellular matrix structural constituent conferring compression resistance	<i>FMOD</i>	- 1.9 1	4.00E -04	0.011	73	
		Tetrapyrrole binding	<i>STEAP1</i>	- 1.8 2	0.001	0.013	37	
		Acetylgalactosaminyl transferase activity	<i>GALNT15</i>	- 1.8 1	0.003	0.045	54	
		Carbohydrate binding	<i>GALNT15</i>	- 1.6 1	0.002	0.038	32	
		Structural molecule activity	<i>FMOD, COMP</i>	- 1.5 1	0.002	0.033	20	
		Molecular function activator activity	<i>LRP1, DPM2, ARHGDI1</i>	- 1.4 4	0.002	0.032	32	
	Human phenotype	Lumbar hyperlordosis	<i>COMP</i>	- 1.9 4	1.00E -04	0.003	49	
		Hip osteoarthritis	<i>COMP</i>	- 1.9 2	0.001	0.013	75	

		Osteoarthritis	<i>COMP</i>	-1.89	0.001	0.017	48	
		Squamous cell carcinoma	<i>LRP1</i>	-1.82	0.003	0.043	59	
		Abnormality of humoral immunity	<i>LRP1</i>	-1.80	2.56E-05	0.001	37	Highlight
		Inflammatory abnormality of the eye	<i>LRP1</i>	-1.78	4.00E-04	0.011	34	
		Nephritis	<i>KANK2, ARHGDI1</i>	-1.77	0.001	0.024	49	
		Abnormal bone structure	<i>DPM2, COMP</i>	-1.60	1.00E-04	0.003	32	
		Abnormal frontal bone morphology	<i>CACNA1C</i>	-1.58	0.001	0.024	28	
		Increased inflammatory response	<i>KANK2, LRP1, ARHGDI1, CACNA1C</i>	-1.53	2.93E-05	0.002	27	Highlight
		Abnormality of bone mineral density	<i>DPM2</i>	-1.52	0.001	0.021	31	Highlight
		Abnormal lung morphology	<i>DPM2, ARHGDI1, CACNA1C</i>	-1.45	0.001	0.012	28	

*Permutation test.

†Terms labelled with 'Highlight' are represented in Figure 4.

ATP, adenosine triphosphate; GO, Gene Ontology; NES, normalized enrichment score.

Table iv. Enrichment network and clusters of age-related genes.

Hub function term	Hit gene	Gene, %	$-\log_{10}(P)$	Function term in cluster	Similarity Kappa score	Genes in cluster
GO:0006936 ~ Muscle contraction	6	10.53	-5.24	GO:0048736 ~ Appendage development	0.62	CACNA1C COMP MYH3 TNNC2 P2RX6 KLHL41 SYPL2 FMOD PCM1 HOOK1 KRT80
				GO:0050905 ~ Neuromuscular process	0.62	
				GO:0042692 ~ Muscle cell differentiation	0.52	
				GO:0055001 ~ Muscle cell development	0.52	
				GO:0097435 ~ Supramolecular fiber organization	0.31	
				GO:0050879 ~ Multicellular organismal movement	0.62	
				GO:0006941 ~ Striated muscle contraction	0.76	
				GO:0050881 ~ Musculoskeletal movement	0.62	
				GO:0003012 ~ Muscle system process	1.00	
WP3286 ~ Copper homeostasis	3	5.26	-3.91	hsa04978 ~ Mineral absorption	1.00	ERN1 MT1E MT1X IFT88 FIBIN STEAP1
				GO:0010035 ~ Response to inorganic substance	0.43	
hsa04020 ~ Calcium signalling pathway	4	7.02	-2.88	GO:0006936 ~ Muscle contraction	0.52	CACNA1C TNNC2 CAMK1 P2RX6 COMP MYH3 KLHL41
				GO:0006941 ~ Striated muscle contraction	0.42	
				GO:0003012 ~ Muscle system process	0.52	
	4	7.02	-2.73	GO:0070085 ~ Glycosylation	0.84	

GO:0009101 ~ Glycoprotein biosynthetic process				GO:0043413 ~ Macromolecule glycosylation	0.84	DGUOK DPM2 HS3ST2 RFT1 GALNT15 FMOD LRP1
				GO:1901137 ~ Carbohydrate derivative biosynthetic process	0.87	
				R-HSA-3781865 ~ Diseases of glycosylation	0.52	
				GO:0006486 ~ Protein glycosylation	0.84	
				GO:0009100 ~ Glycoprotein metabolic process	1.00	
				GO:0006720 ~ Isoprenoid metabolic process	0.52	
GO:0044272 ~ Sulphur compound biosynthetic process	3	5.26	-2.47	N/A	N/A	CDO1 HS3ST2 LIAS
GO:0140694 ~ Non-membrane-bounded organelle assembly	4	7.02	-2.40	GO:0042692 ~ Muscle cell differentiation	0.42	CACNA1C COMP MYH3 EIF5B FARP2 KLHL41 SYPL2 TNNC2
				GO:0055001 ~ Muscle cell development	0.42	
				GO:0006941 ~ Striated muscle contraction	0.42	
WP5420 ~ ADHD and autism ASD linked metabolic pathways and SNP	4	7.02	-2.28	N/A	N/A	CACNA1C CDO1 DGUOK ATG4A
GO:0030705 ~ Cytoskeleton-dependent	3	5.26	-2.24	GO:0097435 ~ Supramolecular fibre organization	0.30	PCM1 IFT88 COMP FMOD MYH3 KLHL41 HOOK1 KRT80

intracellular transport						
WP4352 ~ Ciliary landscape	3	5.26	-2.11	N/A	N/A	ARHGDI1 IFT88 EIF5B

ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; N/A, not applicable.

Table v. Reviews on differential expression genes in lesion tendon in GeneCards database.

GeneSymbol	Gene name	Summary	Function	Related disease
<i>CEBPD</i>	CCAAT Enhancer Binding Protein Delta	CEBPD is a bZIP transcription factor involved in immune and inflammatory responses.	Regulates genes associated with immune responses, inflammation, and macrophage activation and differentiation.	Speech and communication disorders and developmental coordination disorder.
<i>ARFGEF3</i>	ARFGEF Family Member 3	ARFGEF3 is predicted to enable guanyl nucleotide exchange factor activity, and is involved in actin cytoskeleton organization.	Integral to the transport vesicle membrane and may influence systemic glucose homeostasis, insulin granule biogenesis, and more.	Hermansky-Pudlak syndrome 3 and breast cancer.
<i>MT1X</i>	Metallothionein 1X	MT1X is associated with copper and zinc ion binding and is responsive to various cellular stimuli.	Metallothioneins such as MT1X are known to bind heavy metals and are involved in cellular responses.	Deficiency anaemia.
<i>DPYSL5</i>	Dihydropyrimidinase Like 5	DPYSL5 is a member of the CRMP protein family associated with neural development.	Negatively regulates dendrite outgrowth and is relevant to neurological disorders.	Ritscher-Schinzel syndrome 4 and non-specific syndromic intellectual disability.
<i>KLHDC8B</i>	Kelch Domain Containing 8B	KLHDC8B forms a unique beta propeller protein structure of kelch domains for protein-protein interactions.	Involved in cytokinesis, chromosomal stability, and the integrity of mitosis.	Lymphoma, Hodgkin, Classic.

Table vi. Reviews on differential expression genes of lesion tendon in Aging Atlas database.

GeneSymbol	Correlation in present study		Correlation with age or aging in Aging Atlas			PMID
	Age	Lesion	Species	Cell/tissue	Fold-change	
CEBPD	up	down	<i>Macaca fascicularis</i>	aorta[1], brain[2]	up	[1]32729022; [2]35102134
			<i>Mus musculus</i>	kidney	up	33408182
				limb muscle[1], skin[1], knee joint[2], cerebellum[3]	down	[1]30283141 ; [2]31935848; [3]31935848
ARFGEF3	down	up	<i>Mus musculus</i>	knee joint[1], cerebellum[2], skin[3]	down	[1]31935848; [2]29298427; [3]30283141
				hypothalamus	up	29298427
			<i>Homo sapiens</i>	umbilical vein endothelial cells	down	37117524
MT1X	up	down	<i>Homo sapiens</i>	hepatocyte	up	33408182
				umbilical vein endothelial cells	down	37117524
			<i>Macaca fascicularis</i>	brain	up	35102134
DPYSL5	down	down	<i>Macaca fascicularis</i>	heart, kidney, liver	down	32729022
			<i>Mus musculus</i>	knee joint[1], lung[2], mat[2]	down	[1]31935848; [2]30283141
				gonadal adipose tissue, small_intestine, spleen, bone	up	30283141
KLHDC8B	down	up	<i>Macaca fascicularis</i>	lung	up	32729022
				skin	down	32729022
			<i>Mus musculus</i>	liver[1], lung[2], bat[2], mat[2]	down	[1]33408182; [2]30283141
				small_intestine	up	30283141
			<i>Homo sapiens</i>	umbilical vein endothelial cells	up	37117524

BAT, brown adipose tissue; MAT, mesenteric adipose tissue.