



Figure S1 Guinea pig description. Monthly body weights (A) over the course of the study duration. Total body weight (B) in 7-month Hartley guinea pig controls (n=8) and infrapatellar fat pad/synovium complex (IFP/SC) removal groups (n=16). (C) Femur lengths in IFP/SC (left) and fibrous connective tissue (FCT, right) containing hindlimbs. Mean values are represented by black lines.

Table S1 Complete custom guinea pig NanoString gene panel

Gene	Accession number	IFP/SC	FCT	P value
ACAN	XM_013158932.2	31.08 [14.25,48.01]	33.15 [12.59,53.71]	0.7615 [†]
ADIPOQ	XM_003476936.2	211.4 [137.5,285.3]	42.86 [25.17,60.55]	*0.0156 [×]
AKT	XM_003463112.3	275.8 [201.0,350.7]	181.7 [126.3,237.1]	*0.0231 [†]
BAD	XM_013150725.2	24.42 [14.31,34.53]	14.59 [10.97, 18.22]	0.0582 [†]
BAK	XM_013156999.2	12.60 [8.457,16.74]	18.40 [9.546,27.26]	0.3300 [†]
BAX	XM_003465527.4	33.67 [24.97,42.37]	37.67 [22.41,52.93]	0.7827 [†]
BCL-2	XM_003474076.3	33.26 [22.49,44.03]	29.87 [21.86,37.88]	0.6924 [†]
BECN1	XM_005002460.3	119.9 [86.80,152.9]	76.92 [55.14,98.70]	*0.0216 [†]
BIM	XM_013147388.2	23.24 [12.61,33.86]	18.42 [8.477,28.35]	0.4099 [†]
BMP-7	XM_003463644.4	9.357 [3.480,15.23]	11.03 [1.591,20.47]	0.5781 [×]
C3	NM_001172903.1	45.50 [23.65,67.34]	13.79 [4.972,22.61]	*0.0312 [×]
CASP1	XM_013155657.1	12.30 [9.236, 15.36]	15.15 [11.30, 19.00]	0.2787 [†]
CASP3	XM_003469171.4	BDL	BDL	BDL
CASP8	XM_013145226.2	7.430 [3.964, 10.90]	9.766 [2.623, 16.91]	0.6523 [×]
CASP9	XM_003471180.4	BDL	BDL	BDL
CAT	NM_001172925.1	74.27 [55.71, 92.84]	62.82 [49.28, 76.35]	*0.0131 [†]
CBS	XM_003463923.4	BDL	BDL	BDL
CCL-2	NM_001172926.1	85.11 [39.52, 130.70]	41.91 [25.81, 58.00]	*0.0117 [×]
CD163	XM_005003802.2	32.15 [14.51, 49.79]	29.00 [19.16, 38.84]	0.9102 [×]
CGRP	NM_001172933.1	BDL	BDL	BDL
CISH	XM_003476702.3	10.07 [6.95, 13.20]	9.198 [4.77,13.64]	0.36721 [†]
COL10A1	XM_013148983.1	5.97 [3.33, 8.61]	14.05 [1.25, 26.84]	0.1289 [×]
COL2A1	XM_005006506.3	13.79 [8.32, 19.25]	50.88 [12.68, 89.07]	*0.0178 [†]
CUL3	XM_003463982.3	BDL	BDL	BDL
Cidec	XM_023562573.1	16.15 [13.32, 18.97]	7.921 [3.927, 11.93]	*0.0140 [†]
Csnk2a1	XM_003476763.4	71.93 [42.12, 101.70]	59.19 [43.48, 74.90]	0.4746 [†]
FGF-18	XM_003473332.4	203.8 [115.2, 292.5]	128.4 [74.94, 181.80]	*0.0485 [†]
FTH-1	NM_001172847.1	930.90 [750.40, 1111]	687.10 [450.1,924.2]	0.1018 [†]
Fasn	XM_013147192.1	48.03 [15.29, 80.77]	19.74 [12.63, 26.85]	*0.0469 [×]
GPS2	XM_003466264.4	16.25 [11.14, 21.35]	13.44 [9.052, 17.82]	0.3490 [†]
GPx	XM_003476448.4	2267 [1557, 2976]	1632 [1105,2159]	*0.0319 [†]
GPx4	NM_001256319.1	14.11 [6.82, 21.40]	12.10 [7.67, 16.53]	0.7699 [†]
GSK3b	XM_003469225.4	10.22 [4.969, 15.47]	17.89 [4.481, 31.29]	0.4568 [†]
Gap43	XM_013151711.2	9.576 [4.581, 14.57]	10.18 [4.684,15.68]	0.8988 [†]
HAMP	XM_003466576.3	6.430 [2.187, 10.67]	13.24 [2.314, 24.17]	0.2969 [×]
HIF1-a	XM_013155206.1	10.63 [6.578, 14.69]	11.32 [8.494,14.15]	0.8125 [×]
HMGB1	XM_013141181.2	42.56 [29.58, 55.54]	68.98 [22.40,115.50]	0.5132 [†]
HMOX-1	XM_003462326.3	73.11 [26.63, 119.60]	110.40 [29.29,201.60]	0.5781 [×]
IFN-g	NM_001172874.1	BDL	BDL	BDL
IL-10	NM_001260485.1	BDL	BDL	BDL
IL-1b	NM_001172968.1	10.57 [2.852, 18.29]	10.72 [1.771,19.67]	0.7376 [†]
IL-4	NM_001257263.1	BDL	BDL	BDL
IL-5	NM_001172970.1	7.191 [1.610, 12.77]	16.75 [-2.352,35.85]	0.8081 [†]
IL-6	XM_013152399.1	8.10 [1.135, 15.06]	17.06 [0.4270,33.68]	0.6557 [†]
JAK2	XM_003472261.4	8.264 [3.337,13.19]	11.33 [2.916, 19.74]	0.5182 [†]
KEAP1	XM_003460852.3	331.1 [235.6, 426.6]	220.1 [163.9, 276.2]	*0.0309 [†]
LEP	XM_003475050.2	39.23 [17.96, 60.51]	14.08 [5.534, 22.63]	**0.0078 [†]
MAPK	XM_003478061.3	62.64 [36.85,88.43]	45.56 [26.50,64.63]	0.1917 [†]
MAPK3	XM_003478227.4	22.74 [12.81,32.66]	16.25 [9.086,23.41]	*0.0200 [†]
MCL1	XM_023561171.1	11.31 [5.316,17.30]	11.77 [5.281,18.25]	0.8893 [†]
MMP-2	XM_003477541.3	128.20 [62.85,193.60]	296.40 [171.80,420.90]	*0.0312 [×]
MMP-3	XM_003472809.3	BDL	BDL	BDL
MMP-9	XM_003467793.2	13.65 [5.911,21.39]	12.08 [5.850,18.31]	0.8125 [×]
MMP-13	XM_003472818.2	BDL	BDL	BDL
mTOR	XM_003471204.3	20.95 [12.68, 29.21]	22.24 [10.59, 33.89]	0.9184 [†]
MAPK14	XM_023563297.1	41.71 [24.21,59.21]	34.05 [22.09,46.01]	0.3775 [†]
NFE-2	XM_003476239.2	6.019 [4.052, 7.985]	12.91 [1.986, 23.83]	0.4688 [×]
NF-kB p50	XM_003468027.3	50.98 [36.10, 65.86]	45.62 [29.96, 61.28]	0.5283 [†]
NFE2L2	XM_003478542.4	16.83 [11.88, 21.78]	18.84 [4.862,32.82]	0.6309 [†]
NGF	XM_023561339.1	9.930 [5.56, 14.30]	17.60 [2.45, 32.75]	0.6666 [†]
NOS1	XM_013141712.2	BDL	BDL	BDL
NOS2	NM_001172984.1	BDL	BDL	BDL
NOS3	NM_001172985.1	8.61 [5.87, 11.35]	3.35 [1.375, 5.33]	*0.0173 [†]
NURR1	XM_003478688.4	6.82 [2.67, 10.96]	12.51 [5.33,19.69]	0.2218 [†]
Nrf1	XM_013158203.2	14.25 [2.86,25.64]	13.23 [7.09, 19.38]	0.8909 [†]
NQO1	NM_001172986.1	BDL	BDL	BDL
PCSK9	XM_023562560.1	BDL	BDL	BDL
PPARG	XM_013144495.1	7.85 [4.56, 11.14]	9.53 [2.48, 16.57]	0.4375 [×]
PRDX1	XM_013144242.1	26.61 [17.24, 35.98]	32.39 [17.48, 47.30]	0.6805 [†]
PTGS-1/COX-1	XM_003470662.3	7.23 [5.21, 9.25]	11.15 [1.09, 21.21]	0.8945 [†]
PTGS-2/COX-2	NM_001173007.1	7.39 [0.86, 13.93]	11.95 [2.66, 21.23]	0.5395 [†]
Pik3r1	XM_003462679.4	38.11 [27.21, 49.00]	46.83 [16.53, 46.57]	0.5858 [†]
Protein Kinase C Zeta	XM_013153031.1	BDL	BDL	BDL
RIPK1	XM_003468780.4	11.37 [5.41, 17.34]	20.63 [-0.86, 42.11]	0.8267 [†]
RUNX2	XM_013156585.1	BDL	BDL	BDL
SESN2	XM_003471268.4	BDL	BDL	BDL
SLC39A14/ZIP14	XM_005008109.2	BDL	BDL	BDL
SLC7A11	XM_003476798.4	BDL	BDL	BDL
SLC40A1/FPN1	XM_005008713.2	15.63 [3.96,27.30]	21.93 [5.68,38.19]	0.3282 [†]
SOCS3	XM_013147101.2	97.63 [48.41,146.90]	90.47 [38.89,142.10]	0.6496 [†]
SOD-1	XM_003467248.3	40.49 [27.46,53.25]	41.83 [33.85,49.82]	0.6692 [†]
SOD-2	XM_003466367.3	44.21 [30.32,58.11]	62.20 [27.18,97.23]	0.3542 [†]
SOD-3	XM_003467399.3	116.70 [73.08,160.20]	144.60 [79.86,209.40]	0.1812 [†]
Substance P	NM_001172899.1	BDL	BDL	BDL
STAT1	XM_003478777.4	37.90 [30.16,45.63]	32.89 [20.67,45.10]	0.3160 [†]
STAT2	XM_005006399.3	22.89 [16.34, 29.44]	14.29 [14.29, 24.43]	0.4282 [†]
STEAP4	XM_003474977.4	14.28 [10.00,18.56]	14.01 [1.85,26.16]	0.5781 [×]
Serpine1	XM_003469906.3	44.59 [26.88, 62.31]	57.80 [19.62, 95.98]	0.8972 [†]
TFRC	NM_001251822.1	13.45 [5.27, 21.63]	15.43 [5.72, 25.15]	0.8292 [†]
TGF-β	NM_001173023.1	40.04 [24.34, 54.74]	27.26 [16.10,38.42]	0.1539 [†]
TIMP-1	XM_005000239.2	16.43 [7.92, 24.94]	12.15 [5.99,18.31]	0.4558 [†]
TIMP-2	NM_001173024.1	12.77 [8.97, 16.57]	18.45 [14.22,22.67]	*0.0344 [†]
TNF	NM_001173025.1	BDL	BDL	BDL
TRPA1	NM_001198770.1	6.28 [-0.28, 12.85]	17.02 [0.46, 33.59]	0.2298 [†]
TRPV 1	NM_001172652.1	BDL	BDL	BDL
TRPV 4	XM_023560824.1	BDL	BDL	BDL
TXN	XM_003463781.4	13.58 [7.81, 19.35]	19.75 [6.67, 32.84]	0.4930 [†]
ULK1	XM_004999396.3	12.35 [6.55, 18.15]	8.50 [5.71,11.29]	0.2867 [†]
VGF	XM_013152538.2	BDL	BDL	BDL
WNT	XM_013159109.1	BDL	BDL	BDL
b-CAT	XM_003477001.3	87.99 [65.76, 110.20]	77.62 [62.66,92.58]	0.4034 [†]
p65 (RELA)	XM_003468074.4	86.14 [66.04, 106.20]	50.13 [50.13, 68.44]	**0.0055 [†]

Mean values (with 95% confidence interval) for normalized mRNA counts for infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) hindlimbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution ([×]). *, P<0.05; **, P<0.005. Normalized mRNA counts less than detectable limits. BDL, below detectable limit.

Table S2 Methods exclusion justifications: rationale for excluding individual values from data sets

Outcome	Number of animals	Exclusion justification
AnyMaze	13/16	Not amendable for movement on some but not all collection dates
Tekscan	16/16	N/A
Digigait	12/16	Not amendable for walking on some but not all collection dates
NanoString Gene Expression	7/8	Insufficient total RNA concentration for analysis
IHC TIMP2	7/8	One animal did not have additional slides for IHC analysis
IHC ADAMST-4	6/8	Two guinea pigs did not have additional slides for IHC analysis
Biomechanical Analyses	7/8	One hind limb was compromised during initial testing
OARSI histology	6/8	Two guinea pigs had flipped tissue or inadequate cuts for OARSI scoring.
AAS	8/8	N/A

Table S3 Voluntary weight-bearing parameters

Parameter	Left hind (sham)	Right hind (IFP removal)	Left vs. right hind (P value)	Time (P value)
Maximum Force (%BW)	32 [29, 36]	33 [27, 39]	0.4614	****<0.0001
Stride Velocity (cm/sec)	39 [31, 47]	37 [29, 46]	0.7437	****<0.0001
Maximum Peak Pressure (kPA)	45.39 [38.48, 52.30]	44.73 [38.34, 51.11]	0.8240	****<0.0001
Maximum Force (kg)	0.2305 [0.201, 0.261]	0.2284 [0.199, 0.258]	0.8562	****<0.0001
Force Time Integral [FTI (%bw*sec)]	6.948 [5.551, 8.345]	7.484 [5.443, 9.526]	0.6372	**0.0047
Force Time Integral [FTI (kg*sec)]	0.051 [0.031, 0.072]	0.056 [0.031, 0.81]	0.0819	****<0.0001
Stride Length (cm)	13.57 [12.21, 14.93]	13.73 [12.32, 15.13]	0.6810	****<0.0001
Stride Time (sec)	0.45 [0.35, 0.54]	0.48 [0.36, 0.59]	0.5136	****<0.0001
Stance Time (sec)	0.34 [0.25, 0.44]	0.36 [0.24, 0.48]	0.6720	****<0.0001
Swing Time (sec)	0.11 [0.10, 0.12]	0.13 [0.12, 0.14]	0.1503	0.8268

Hindlimb differences [mean \pm 95% confidence interval (CI) interval upper and lower limits] from final timepoint taken prior to study termination at 7 months of age. Statistical analyses of time represent longitudinal differences in time during study duration. Italicized P values represent statistical significance of Two-Way analysis of variance (ANOVA) or Mixed Model with a Tukey post hoc test analysis. **, P<0.005; ****, P<0.0001.

Table S4 Biomechanical tests for the infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT)

Biomechanical tests	Unit of measure	IFP/SC (sham)	FCT (IFP removal)	P value
Cranial/anterior drawer		5.73 [5.06, 6.39]	6.95 [4.74, 9.16]	0.6406 ^x
Patellar tendon	Width (mm)	3.26 [2.79, 3.73]	3.53 [3.16, 3.91]	0.2109 ^x
	Thickness (mm)	1.42 [1.14, 1.70]	1.63 [1.16, 2.09]	0.4806 [†]
Pull to Failure	Cross-sectional Area (mm ²)	14.92 [10.35, 19.49]	18.30 [12.02, 24.59]	0.3395 [†]
	Elastic Modulus (MPa)	24.93 [15.34, 34.52]	14.76 [7.106, 22.41]	**0.0078 ^x
	Ultimate Load (N)	86.06 [59.95, 112.20]	89.07 [64.19, 113.90]	0.7954 [†]
	Ultimate Stress	7.24 [4.76, 9.73]	5.57 [2.62, 8.85]	0.1094 ^x
	Ultimate Strain	0.51 [0.31, 0.72]	0.59 [0.31, 0.44]	0.2994 [†]

Mean values (with 95% confidence interval) for biomechanical measurements for infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) hindlimbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (^x). **, P<0.005.

Table S5 Atomic absorption spectroscopy (AAS) trace element concentrations of infrapatellar fat pad/synovium complex (IFP/SC) and fibrous connective tissue (FCT)

Trace Elements	Concentration (ppm)		P value
	IFP/SC (sham)	FCT (IFP removal)	
Calcium (Ca)	3778 [1480, 6075]	8469 [2062, 15875]	0.3125 ^x
Magnesium (Mg)	635.6 [-388.0, 1659]	3176 [-3926, 10279]	0.8632 [†]
Zinc (Zn)	22.54 [9.064, 36.01]	35.41 [-2.099, 68.72]	0.8470 [†]
Iron (Fe)	76.13 [10.24, 142.0]	177.9 [-49.39, 405.2]	0.3828 ^x
Phosphorous (P)	1012 [-157.7, 2182]	1580 [-689.1, 3849]	0.9453 ^x

Mean values (with 95% confidence interval) for IFP/SC and FCT collected from IFP/SC vs. FCT limbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (^x).

Table S6 Atomic absorption spectroscopy (AAS) trace element concentrations of infrapatellar fat pad/synovium complex (IFP/SC) and fibrous connective tissue (FCT) patellae

Trace Elements	Concentration (ppm)		P value
	IFP/SC (sham)	FCT (IFP removal)	
Calcium (Ca)	172,333 [161037, 183630]	165,000 [144286, 185714]	0.4857 [†]
Magnesium (Mg)	3793 [3453, 4133]	3583 [3181, 3986]	0.3125 ^x
Zinc (Zn)	216.4 [199.7, 233.1]	197.4 [169.6, 225.2]	*0.0503 [†]
Iron (Fe)	48.72 [37.30, 60.13]	48.35 [41.35, 55.32]	0.5625 ^x
Phosphorous (P)	88,117 [78849, 97384]	104,083 [82568, 125599]	0.0820 [†]

Mean values (with 95% confidence interval) for patellae collected from IFP/SC vs. FCT limbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (^x). *, P<0.05.

Table S7 Atomic absorption spectroscopy (AAS) trace element concentrations of infrapatellar fat pad/synovium complex (IFP/SC) and fibrous connective tissue (FCT) patellar tendons

Trace Elements	Concentration (ppm)		P value
	IFP/SC (sham)	FCT (IFP removal)	
Calcium (Ca)	11460 [5945, 6975]	26855 [-8869, 62579]	0.9453 ^x
Magnesium (Mg)	240.5 [105.9, 375.0]	480.2 [-26.97, 987.3]	0.8632 [†]
Zinc (Zn)	30.20 [20.94, 39.46]	52.90 [40.68, 65.12]	*0.0143 [†]
Iron (Fe)	21.58 [9.986, 33.17]	29.98 [9.912, 50.04]	0.4609 ^x
Phosphorous (P)	4028 [2615, 5440]	9133 [-1620, 19886]	0.9453 ^x

Mean values (with 95% confidence interval) for patellar tendons. collected from IFP/SC vs. FCT limbs. Data with similar variance and normal distribution were compared using parametric *t*-tests (†). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (x). *, P<0.05.

Table S8 Clinical microcomputed tomography (microCT)

Measurement	IFP/SC	FCT	P value
Location of Osteophytes	2.250 [-0.0177, 4.518]	2.250 [0.3673, 4.133]	>0.9999 ^x
Size of Osteophytes	1.000 [-0.0946, 2.095]	1.375 [0.1980, 2.552]	0.1970 [†]
Subchondral Bone Sclerosis	0.00 [0.00, 0.00]	0.1250 [-0.1706, 0.4206]	0.3506 [†]
Total MicroCT Score	3.250 [0.035, 6.465]	3.750 [0.5353, 6.965]	0.5000 ^x

Mean values (with 95% confidence interval) for clinical microCT measurements for infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) hindlimbs. Data with similar variance and normal distribution were compared using parametric *t*-tests (†). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (x).

Table S9 Osteophyte volumes

Osteophyte Volume	IFP/SC	FCT	P value
Femur	0.6917 [0.4615, 0.9218]	0.6213 [0.3655, 0.8771]	0.3207 [†]
Tibia	0.2964 [0.05269, 0.5400]	0.1574 [-0.0031, 0.3179]	0.0938 ^x
Patella	0.2287 [-0.0312, 0.07695]	0.02126 [-0.029, 0.07154]	>0.9999 ^x

Mean values (with 95% confidence interval) for osteophyte volume measurements for infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) hindlimbs. Data with similar variance and normal distribution were compared using parametric *t*-tests (†). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (x).

Table S10 Quantitative microcomputed tomography (microCT)

Measurement	Compartment	IFP/SC	FCT	P value
Trabecular vBMD (g/cm ³)	MT	0.4186 [0.3541, 0.4832]	0.4360 [0.3290, 0.5430]	0.8701 [†]
	LT	0.4535 [0.3558, 0.5513]	0.5001 [0.4276, 0.5726]	0.3125 [×]
	MF	0.3541 [0.3036, 0.4045]	0.2941 [0.2369, 0.3513]	0.0667 [†]
	LF	0.2298 [0.1838, 0.2758]	0.2376 [0.1749, 0.3003]	0.7188 [†]
Trabecular Bone Volume/Total Volume (BV/TV%)	MT	31.01 [25.42, 36.60]	29.39 [25.84, 32.93]	0.6404 [×]
	LT	31.55 [24.72, 38.39]	32.84 [25.34, 40.33]	0.3828 [×]
	MF	26.18 [22.30, 30.07]	22.56 [19.23, 25.90]	0.1479 [†]
	LF	16.86 [14.64, 19.08]	18.87 [16.49, 22.77]	0.1094 [†]
Trabecular Number (Tb.N)	MT	2.369 [2.131, 2.606]	2.338 [2.143, 2.533]	0.9453 [×]
	LT	2.611 [2.234, 2.987]	2.754 [2.373, 3.135]	0.5103 [×]
	MF	1.945 [1.709, 2.180]	1.796 [1.515, 2.077]	0.3932 [†]
	LF	1.601 [1.446, 1.757]	1.680 [1.403, 1.957]	0.3889 [†]
Trabecular Thickness (Tb.Th)	MT	0.1299 [0.1195, 0.1403]	0.1257 [0.1152, 0.1361]	0.8438 [†]
	LT	0.1158 [0.1074, 0.1243]	0.1249 [0.1142, 0.1357]	0.1094 [×]
	MF	0.1344 [0.1244, 0.1444]	0.1270 [0.1165, 0.1375]	*0.0114 [†]
	LF	0.1051 [0.09708, 0.1132]	0.1118 [0.1039, 0.1197]	0.0771 [†]
Trabecular Space (Tb.Sp)	MT	0.2809 [0.2549, 0.3069]	0.3023 [0.2775, 0.3272]	0.3125 [×]
	LT	0.2771 [0.2436, 0.3106]	0.2438 [0.2127, 0.2749]	0.1014 [×]
	MF	0.3297 [0.3124, 0.3471]	0.3335 [0.3052, 0.3619]	0.8717 [†]
	LF	0.3477 [0.3362, 0.3592]	0.3322 [0.3005, 0.3639]	0.2409 [†]
Cortical vBMD (g/cm ³)	MT	0.9050 [0.8677, 0.9422]	0.8716 [0.8156, 0.9277]	0.2582 [†]
	LT	0.8855 [0.8613, 0.9096]	0.8617 [0.8161, 0.9073]	0.1862 [×]
	MF	0.8863 [0.8289, 0.9436]	0.8821 [0.8128, 0.9514]	0.9112 [†]
	LF	0.9625 [0.8985, 1.026]	0.9003 [0.8278, 0.9727]	0.2463 [†]
Cortical Thickness (Ct.Th)	MT	0.2968 [0.2396, 0.3540]	0.3059 [0.2606, 0.3512]	0.8438 [†]
	LT	0.3208 [0.2824, 0.3592]	0.3574 [0.2985, 0.4162]	0.3346 [×]
	MF	0.2789 [0.2391, 0.3186]	0.3056 [0.2455, 0.3658]	0.5809 [†]
	LF	0.3874 [0.3305, 0.4443]	0.3608 [0.3095, 0.4121]	0.3684 [†]
Cortical Porosity (%)	MT	1.430 [0.4352, 2.424]	1.463 (0.5249, 2.401)	0.6829 [†]
	LT	0.8483 [-0.05361, 1.750]	0.9498 [0.02034, 1.879]	0.8438 [×]
	MF	2.051 [0.2971, 3.804]	2.360 (0.1606, 4.560)	>0.9999 [†]
	LF	0.6389 [-0.01874, 1.297]	0.8195 [-0.5365, 2.176]	0.8438 [†]

Mean values (with 95% confidence interval) for quantitative microCT measurements for infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) limbs. Values are derived from the medial and lateral tibial and femoral subchondral trabecular bone. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (×). *, P<0.05. MT, medial tibia; LT, lateral tibia; MF, medial femur; LF, lateral femur.

Table S11 Cortical and Subchondral atomic absorption spectroscopy AAS for trace minerals/elements

Trace Element	Compartment	IFP/SC	FCT	P value
Calcium (Ca)	MF	219,125 [208424, 229826]	211,750 [204465, 219035]	0.1630 [†]
	LF	199,429 [189542, 209316]	204,429 [192781, 216076]	0.2188 [×]
Magnesium (Mg)	MF	4,373 [4178, 4567]	4,396 [4251, 4541]	0.8076 [†]
	LF	4,213 [3903, 4523]	4324 [4040, 4608]	0.3039 [†]
Zinc (Zn)	MF	285.5 [259.2, 311.8]	292.6 [270.6, 314.7]	0.5106 [†]
	LF	284.0 [263.8, 304.2]	300.0 [277.9, 322.1]	*0.0220 [†]
Iron (Fe)	MF	30.46 [20.73, 40.20]	34.13 [29.30, 38.95]	0.5469 [×]
	LF	32.90 [17.24, 48.56]	37.60 [20.03, 55.17]	0.6875 [×]
Phosphorous (P)	MF	148,125 [125434, 170816]	141,550 [113696, 169404]	0.4819 [†]
	LF	141,571 [127245, 155898]	163,714 [135502, 191927]	0.2225 [†]

Means values (with 95% confidence interval) for trace element concentrations from tissue collected from regions of interest in the subchondral trabecular bone of tibia and femurs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (×). *, P<0.05. Medial Femur (MF); Lateral Femur (LF).

Table S12 Meniscus and cartilage indentation analysis

Indentation Analysis	Location	IFP/SC	FCT	P value
Meniscus	MA I. Modulus (MPa)	38.67 [18.25, 59.09]	27.47 [15.24, 39.69]	0.3922 [†]
	MP I. Modulus (MPa)	19.24 [14.08, 24.39]	19.80 [9.77, 29.83]	0.8176 [†]
	MA E. Modulus (MPa)	9.25 [0.56, 17.93]	3.35 [1.65, 5.04]	0.2626 [†]
	MP E. Modulus (MPa)	1.64 [0.68, 2.61]	2.75 [0.28, 5.78]	0.5338 [†]
	LA I. Modulus (MPa)	23.80 [5.88, 41.71]	20.06 [14.93, 25.19]	0.9337 [†]
	LP I. Modulus (MPa)	23.42 [1.66, 48.51]	16.52 [8.29, 24.77]	0.8595 [†]
	LA E. Modulus (MPa)	5.26 [0.66, 11.18]	2.48 [1.49, 3.47]	0.5781 [×]
	LP E. Modulus (MPa)	2.27 [0.85, 3.69]	2.19 [0.01, 4.37]	0.6810 [†]
Cartilage	MT I. Modulus (MPa)	33.15 [5.49, 60.82]	32.19 [17.11, 47.28]	0.7422 [×]
	MF I. Modulus (MPa)	57.89 [30.60, 85.18]	76.90 [36.82, 117.00]	0.6532 [†]
	MT E. Modulus (MPa)	5.13 [1.59, 8.66]	4.58 [2.25, 6.91]	0.9444 [†]
	MF E. Modulus (MPa)	13.07 [0.99, 27.15]	10.84 [1.67, 20.01]	0.8125 [×]
	LT I. Modulus (MPa)	39.08 [26.15, 52.01]	24.53 [18.82, 30.25]	*0.0234 [×]
	LF I. Modulus (MPa)	60.87 [34.74, 87.00]	66.03 [36.83, 95.23]	0.7269 [†]
	LT E. Modulus (MPa)	5.46 [4.12, 6.79]	3.77 [2.26, 5.28]	*0.0333 [†]
	LF E. Modulus (MPa)	14.59 [5.42, 23.77]	10.33 [2.48, 18.18]	0.3828 [×]

Mean values (with 95% confidence interval) for Biomechanical measurements for infrapatellar fat pad/ synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) limbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution (×). *, P<0.05. Instantaneous Modulus (I. Modulus); Equilibrium Modulus (E. Modulus); MA, medial anterior; MP, medial posterior; LA, lateral anterior; LP, lateral posterior; MT, medial tibia; LT, lateral tibia; MF, medial femur; LF, lateral femur.

Table S13 Atomic absorption spectroscopy (AAS) trace element concentrations of medial cartilage

Trace Element	Concentration (ppm)		P value
	Left Hind (IFP/SC)	Right Hind (FCT)	
Calcium (Ca)	177000 [150585, 203415]	100300 [150467, 199033]	0.7544 [†]
Magnesium (Mg)	3001 [2151, 3852]	2761 [2272, 3250]	0.1016 [×]
Zinc (Zn)	187.6 [167.0, 208.2]	188.1 [164.9, 211.4]	0.9928 [†]
Iron (Fe)	139.5 [39.62, 239.5]	72.04 [46.81, 97.26]	0.2393 [†]
Phosphorous (P)	56855 [48864, 64646]	61257 [51446, 71068]	0.4609 [×]

Mean values (with 95% confidence interval) for medial tibial cartilage collected from the infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) hindlimbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution ([×]).

Table S14 Atomic absorption spectroscopy (AAS) trace element concentrations of lateral cartilage

Trace Element	Concentration (ppm)		P value
	Left Hind (IFP/SC)	Right Hind (FCT)	
Calcium (Ca)	172750 [137453, 208047]	157663 [109007, 206318]	0.2321 [†]
Magnesium (Mg)	3104 [2642, 3565]	2775 [1945, 3605]	0.2811 [†]
Zinc (Zn)	208.1 [170.0, 246.2]	150.6 [117.7, 183.4]	*0.0444 [†]
Iron (Fe)	165.0 [-41.42, 371.3]	61.35 [13.52, 109.2]	0.2500 [×]
Phosphorous (P)	63621 [52012, 75229]	56676 [40100, 73252]	0.1038 [†]

Mean values (with 95% confidence interval) for the lateral tibial cartilage collected from the infrapatellar fat pad/synovium complex (IFP/SC) vs. fibrous connective tissue (FCT) hindlimbs. Data with similar variance and normal distribution were compared using parametric *t*-tests ([†]). Wilcoxon matched pairs signed rank test was used to compare data with non-Gaussian distribution ([×]). *, P<0.05.