

1 **SUPPLEMENTARY TABLES**

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3 **Supplementary Table 1. PTOA severity scoring guidelines, as published previously(1, 2)**

Feature	0	1	2	3	4	5	6	7
Structural Damage (0-7)	Normal Cartilage	Roughened surface with small fibrillations	Fibrillations immediately below superficial layer or some loss of laminal surface	Horizontal cracks or separations between calcified and noncalcified cartilage	Mild loss of non-calcified cartilage (<10% surface area)	Moderate loss of non-calcified cartilage (10-50% surface area)	Severe loss of non-calcified cartilage (>50% surface area)	Erosion of cartilage to subchondral bone (any percent of surface area)
Proteoglycan Loss (0-3)	Normal cartilage	Decreased but not complete loss of Safo staining in non-calcified area	Focal loss of Safo staining in non-calcified cartilage (<30% surface area)	Diffuse loss of Safo staining in non-calcified cartilage (>30% surface area)				
Chondrocyte Hypertrophy (0-1)	None	Enlarged chondrocyte lacunae with lack of Safo stain around a collapsed cell						
Osteophyte Size (0-3)	None	Small- same thickness as adjacent cartilage	Medium- 1 to 3 times thick as adjacent cartilage	Large- >3 times thicker than adjacent cartilage				
Osteophyte Maturity (0-3)	None	Predominately cartilage	Mixed cartilage and bone with vascular invasion	Predominately bone				
SCB Thickening (0-3)	Normal cartilage	Mild thickening, <50% increase	Moderate thickening, 50-100% increase	Severe thickening, >100% increase				

5 **Supplementary Table 2. Synovitis scoring guidelines, as published previously(2, 3), with the addition of a fibrosis**
 6 **criterion**

Feature	Description	0	1	2	3
Pannus	Defined as fibrous tissue/synovium/ inflammatory cell outgrowth spreading over the surface of the bone and/or cartilage at the joint margins.	No pannus	Mild: Pannus has migrated on bone but not encroaching on cartilage.	Moderate: Pannus has migrated < 1x cartilage depth.	Severe: Pannus has migrated > 1x cartilage depth.
Bone erosion	Score the margin of the femur at or adjacent to the joint capsule attachment (between joint capsule attachment and cartilage margin – above the junction of the growth plate with the femoral cortex).	No Cortical Bone Erosion	Partial thickness loss of cortical bone only.	Focal complete loss of cortical bone – communication with marrow cavity at one small “vascular” communication site.	Widespread complete loss of cortical bone – communication with marrow cavity at multiple sites or broad area loss of cortical bone.
Synovial lining hyperplasia	Score this superior to the meniscal remnant. Do not score the cells actually attached to the tibia or femur or cells on the surface of the meniscus itself and avoid peri-meniscal plica. Score the maximum hyperplasia seen anywhere along this area.	1 cell thick	Mild: 2-3 cells thick	Moderate: 4-5 cells thick	Severe: > 6 cells thick
Sub-synovial inflammation	Score this superior to the meniscal remnant. The infiltration of inflammatory cells (neutrophils, macrophages and/or lymphocytes) is evaluated.	No inflammatory cells	Occasional scattered inflammatory cells – or perivascular	Focal areas of dense sub-synovial WBC infiltrate – but still predominantly normal sub-synovial areolar connective tissue present.	Widespread dense sub-synovial WBC infiltrate – markedly reduced or little/no normal areolar connective tissue evident or lymphoid follicle formation.
Synovial fibrosis	Score this as a function of synovial area exhibiting pathological fibrosis, characterized by blue staining of collagen (from FastGreen) and reduction of areolar-like adipocytes in fat pad.	No fibrosis	Dispersed fibrosis (<10% of synovial area)	Moderate fibrosis (10-30% of synovial area)	Severe fibrosis (>30% of synovial area)
Synovial exudate	Infiltration of inflammatory cells (neutrophils, macrophages and/or lymphocytes) in the synovial cavity.	No inflammatory cells or fibrin in the synovial cavity.	Inflammatory cells and/or fibrin clot in the synovial cavity – may be restricted to recesses.		

8 **Supplementary Table 3. Antibodies**

Antibody name	Raised in	Manufacturer	RRID	Application (dilution)
BV650 anti-mouse CD45 Clone 30-F11	Rat	Biologend 103151	AB_2565884	Flow cytometry, 1:400
PE/Cy7 anti-mouse CD31 Clone 390	Rat	Biologend 102417	AB_830756	Flow cytometry, 1:200
FITC anti-mouse Podoplanin Clone 8.1.1	Syrian Hamster	Biologend 127416	AB_2629802	Flow cytometry, 1:100
PE/Dazzle594 anti-mouse CD90.2 Clone 30-H12	Rat	Biologend 105340	AB_2632887	Flow cytometry, 1:200
PE/Cy7 anti-mouse CD55 Clone RIKO-3	Armenian Hamster	Biologend 131814	AB_2800634	Flow cytometry, 1:100
BV605 anti-mouse CD11b Clone M1/70	Rat	Biologend 101237	AB_11126744	Flow cytometry, 1:400
TruStain FcX PLUS (anti-mouse CD16/32) Clone S17011E	Rat	Biologend 156604	AB_2783138	Flow cytometry, 1:1000
Anti-mouse R-spondin 2 Polyclonal	Rabbit	ProteinTech 17781-1-AP	AB_2269700	Flow cytometry, 2 µg/sample; IHC/ICC, 1:250
Rabbit IgG Isotype Control Polyclonal	Rabbit	Abcam ab171870	AB_2687657	Flow cytometry, 2 µg/sample
BV421 anti-rabbit IgG secondary Polyclonal	Donkey	Biologend 406410	AB_10897810	Flow cytometry, 1:100
AlexaFluor488 anti-rabbit IgG secondary Polyclonal	Goat	Invitrogen A-11008	AB_143165	IHC/ICC, 1:500
Non-phospho β-Catenin (Ser33/37/Thr41) Clone D13A1	Rabbit	Cell Signaling 8814	AB_11127203	ICC, 1:1600
AlexaFluor488 anti-rabbit IgG secondary Polyclonal	Goat	Invitrogen A-11034	AB_2576217	ICC, 1:500
Normal Rabbit IgG Isotype Control Polyclonal	Rabbit	Santa Cruz sc-2027	AB_737197	ICC, 1:1600

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10 **Supplementary Table 4. Primers**

Gene name	5' – 3' sequence	Organism
<i>Acan</i> Fwd	CCTGCTACTTCATCGACCCC	<i>Mus musculus</i>
<i>Acan</i> Rev	AGATGCTGTTGACTCGAACCT	<i>Mus musculus</i>
<i>Arg1</i> Fwd	ATCGTGTACATTGGCTTGCG	<i>Mus musculus</i>
<i>Arg1</i> Rev	GGCCTTTTCTTCCTTCCCAG	<i>Mus musculus</i>
<i>Atp5b</i> Fwd	CTGGATTCAGGGGCACCAAT	<i>Mus musculus</i>
<i>Atp5b</i> Rev	GCACCTCCAAGAGTCCGAT	<i>Mus musculus</i>
<i>Axin2</i> Fwd	GCGCTTTGATAAGGTCCTGG	<i>Mus musculus</i>
<i>Axin2</i> Rev	TCATGTGAGCCTCCTCTCTTT	<i>Mus musculus</i>
<i>Bsp/lbsp</i> Fwd	TTCGTTTGAAGTCTCCTCTTCC	<i>Mus musculus</i>
<i>Bsp/lbsp</i> Rev	CTCCTCTGAAACGGTTTCCA	<i>Mus musculus</i>
<i>Col2a1</i> Fwd	ACTTGCCAAGACCTGAAACTCTG	<i>Mus musculus</i>
<i>Col2a1</i> Rev	AAACTTTTCATGGCGTCCAAGG	<i>Mus musculus</i>
<i>Col10a1</i> Fwd	TCTCCCAGCACCAGAATCTATC	<i>Mus musculus</i>
<i>Col10a1</i> Rev	CTTTATGCCTGTGGGCGTTT	<i>Mus musculus</i>
<i>Gapdh</i> Fwd	GCCTCTCTTGCTCAGTGCC	<i>Mus musculus</i>
<i>Gapdh</i> Rev	CTCCACTCTTCCACCTTCG	<i>Mus musculus</i>
<i>Il10</i> Fwd	GCGCTGTCATCGATTTCTCC	<i>Mus musculus</i>
<i>Il10</i> Rev	ATGGCCTTGTAGACACCTTGG	<i>Mus musculus</i>
<i>Il1b</i> Fwd	TGCCACCTTTTGACAGTGATG	<i>Mus musculus</i>
<i>Il1b</i> Rev	AAGGTCCACGGGAAAGACAC	<i>Mus musculus</i>
<i>Il6</i> Fwd	GCCTTCTTGGGACTGATGCT	<i>Mus musculus</i>
<i>Il6</i> Rev	TGCCATTGCACAACCTCTTTTCT	<i>Mus musculus</i>
<i>Lef1</i> Fwd	AAGAAATGAGAGCGAATGTCGT	<i>Mus musculus</i>
<i>Lef1</i> Rev	TTCTGGGACCTGTACCTGAAGT	<i>Mus musculus</i>
<i>Lgr4</i> Fwd	GCTGCGGACTCTGGACTTAT	<i>Mus musculus</i>
<i>Lgr4</i> Rev	TGTCCCAAGCTTCGCAAAG	<i>Mus musculus</i>
<i>Lgr5</i> Fwd	ATCAGGTCAATACCGGAGCG	<i>Mus musculus</i>
<i>Lgr5</i> Rev	GGCACCATTCAAAGTCAGTGT	<i>Mus musculus</i>
<i>Lgr6</i> Fwd	GGCATCATGCTGTCCGC	<i>Mus musculus</i>
<i>Lgr6</i> Rev	GGTTGTTCACTAGAGGTCTAGGT	<i>Mus musculus</i>
<i>Mrc1/Cd206</i> Fwd	GGCTGATTACGAGCAGTGGA	<i>Mus musculus</i>
<i>Mrc1/Cd206</i> Rev	ATGCCAGGGTCACCTTTCAG	<i>Mus musculus</i>
<i>Nos2</i> Fwd	AGAGAACGGAGAACGTTGGA	<i>Mus musculus</i>
<i>Nos2</i> Rev	GGATTCTGGAACATTCTGTGCTG	<i>Mus musculus</i>
<i>Ocn/Bglap</i> Fwd	CAGACACCATGAGGACCATCTT	<i>Mus musculus</i>
<i>Ocn/Bglap</i> Rev	GATAGCTCGTCAACAAGCAGG	<i>Mus musculus</i>
<i>Osx/Sp7</i> Fwd	TTCCCCAGGGTTGTTGAGTC	<i>Mus musculus</i>
<i>Osx/Sp7</i> Rev	ATGGCGTCTCTCTGCTTGA	<i>Mus musculus</i>
<i>Rspo2</i> Fwd	ACGTGTAGCAGAAACAACCG	<i>Mus musculus</i>
<i>Rspo2</i> Rev	GCTTCCGCCTCTTCTTCTTG	<i>Mus musculus</i>
<i>Runx2</i> Fwd	CCCAGCCACCTTTACCTACA	<i>Mus musculus</i>
<i>Runx2</i> Rev	TATGGAGTGCTGCTGGTCTG	<i>Mus musculus</i>
<i>Sox5</i> Fwd	AGCACAACACAATGGAAGTCG	<i>Mus musculus</i>
<i>Sox5</i> Rev	TTCAGGGTGTCCACCACATC	<i>Mus musculus</i>
<i>Tnf</i> Fwd	ATGGCCTCCCTCTCATCAGT	<i>Mus musculus</i>
<i>Tnf</i> Rev	TGTTTTGCTACGACGTGGG	<i>Mus musculus</i>

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