



Figure S1 Pilot data towards determination of vancomycin dose and concentrations in synovial fluid in treated *vs.* control horses. (A) Effect of VAN on viability of equine bone marrow-derived mesenchymal stromal cells in monolayer culture. Cell viability (mean±SD) was assessed in MSC from each of three donor horses, each in triplicate, using trypan blue dye exclusion staining to determine percentage of live cells following antibiotic exposure for 24 hours. X-axis represents antibiotic concentration; y-axis represents percentage of live cells. Dose response for each concentration was normalized to control, and the data transformed to ‘normalized dose response *vs.* log₁₀ (concentration)’ at which point the half maximal inhibitory concentration (IC₅₀) was estimated by nonlinear regression implemented in GraphPad Prism8 (GraphPad Software Prism8). (B) VAN (100 mg) was injected in the tibiotarsal joint of a 3-year-old Quarter Horse mare and synoviocenteses performed at baseline and 1, 4, 8, 24, 48, and 72 hours following injection to obtain synovial fluid samples (1 to 2 mL). VAN concentrations in synovial fluid were assessed via immunoassay (BioVision, Milpitas, CA, USA 95035)), and (C) remained above MIC for the targeted pathogen (1 µg/mL) at 72 hours following injection. (D) VAN levels in synovial fluid were determined and (E) remained above 1 µg/mL in both treatment and control horses at each of the time points following administration (days 4, 7, 14). VAN levels varied widely between individuals but were not significantly different overall between VAN or TLR-MS-C-VAN treated horses at any time point.

Table S1 Microsatellite haplotype data for MSC donor and treatment recipient horses.

Horse	Microsatellite haplotype	Intra-MHC Microsatellite Alleles											
		Class I				Class III			Class II				
		UMNJH-38	COR110	305-93	CZM002	ABGe9019	UMNe65	ABGe9030	EQMHC1	COR112	COR113	UM011	COR114
MSC Donor Horses													
A	ELA-A9a	156	217	0	247	307	255	215	190	264	272	169	255
	ELA-A5a	156	221	0	261	299	257	212	190	254	260	172	243
B	ELA-A5a	156	221	0	261	299	257	212	190	254	260	172	243
	ELA-A10a	156	221	0	259	312	261	207	190	237	264	180	243
C	ELA-A5a	156	221	0	261	299	257	212	190	254	260	172	243
	ELA-A3b	163	207	0	251	312	261	211	192	262	268	176	247
Treatment Recipient Horses													
Control													
A	Not phased	156	211	342	249	301	259	205	192	250	266	169	245
	Not phased	156	221	345	232	310	263	217	199	254	266	170	249
B	ELA-A5a	156	221	340	261	299	257	212	190	254	260	172	243
	Novel	161	211	341	255	314	259	219	190	262	270	184	245
C	Not phased	156	215	345	253	312	257	221	180	252	274	171	243
	Not phased	156	211	345	259	299	261	215	190	260	266	169	249
D	Novel	161	211	341	255	312	261	207	190	237	264	180	243
	ELA-A3b	163	207	343	251	312	261	211	192	262	268	176	247
Treatment (MSC Recipients)													
E	ELA-A3b	163	207	343	251	312	259	211	192	262	268	176	247
	Novel	156	215	345	251	312	259	221	180	252	274	171	243
F	COR-188	156	221	342	230	318	257	219	190	254	270	172	249
	Novel	156	219	347	230	316	263	215	190	237	268	176	247
G	Not Phased	156	207	340	230	314	257	215	190	262	260	172	243
	Not Phased	156	207	346	261	316	259	215	196	268	268	176	247
H	ELA-A2	156	211	343	249	301	259	209	192	262	268	174	234
	ELA-A5a	156	221	340	261	299	257	212	190	254	260	172	243

Table S2 Histological scoring system for synovium tissues

Fibrin exudate (0-4)	Cellular infiltrate (neutrophils)	Vascularity	Intimal ulceration
0 = none	0 = none	0 = normal	0 = none
1 = occasional small scattered foci	1 = occasional small foci / infiltrates	1 = slight increase vessels in focal areas	1 = occasional small scattered foci
2 = confluent mats <25% total surface	2 = neutrophils 25% inflammatory infiltrate	2 = mild increase number and dilation throughout	2 = 25–50% total surface area
3 = mats 25 to 50% total surface	3 = neutrophils 25% to 50% infiltrates	3 = moderate increase number and dilation <50% section	3 = >50–75% total surface area
4 = mats >50% total surface	4 = neutrophils >50% infiltrates	4 = marked increase >50% of section	4 = >75% total surface area
Intimal hyperplasia	Subintimal edema	Subintimal fibrosis/Granulation tissue	
0 = none	0 = no edema	0 = normal	
1 = villi with 2 to 4 rows intimal cells	1 = slight edema detected in section	1 = slight increase in fibrosis within section	
2 = villi with 4 to 5 rows intimal cells over 25 to 50% section	2 = mild edema 25% of section	2 = mild increased fibrosis within 25% section	
3 = villi with 4 to 5 rows intimal cells >50% section	3 = moderate edema with 25–50% section	3 = moderate increased fibrosis within 25–50% section	
4 = villi with >5 rows intimal cells over 50% section	4 = marked edema >50% section	4 = marked increased fibrosis within >50% section	
5 = diffusely ulcerated intima			

Table S3 Histological scoring system for osteochondral tissues

Cartilage parameters				
Chondrocyte necrosis	Chondrones	Fibrillation/fissures	Focal cell loss	SafO stain uptake
0 = none	0 = none	0 = no fibrillation/fissures	0 = 0%	0 = 0%
1 = 1 necrotic cell near surface per 20x objective	1 = 2 chondrone nuclei (doublets)	1 = fibrillation/fissures restricted to surface, superficial zone	1 = 10–20% acellularity per 20x field	1 = <25%
2 = 1 to 2 necrotic cells	2 = 2 to 3 chondrone nuclei	2 = fissures extend to middle zone	2 = 20–30% acellularity	2 = 25–50%
3 = 2 to 3 necrotic cells	3 = 3 to 4 chondrone nuclei	3 = fissures extend to level of deep zone	3 = 40–50% acellularity	3 = 50–75%
4 = 3 to 4 necrotic cells	4 = >4 chondrone nuclei	4 = fissures extend to deep zone	4 = >50% acellularity per 20x field	4 = >75%
Bone parameters				
Osteochondral lesions	Subchondral bone remodeling	Subchondral bone activation	Osteochondral splitting	
0 = no visible changes in cartilage or bone	0 = no remodeling	0 = no remodeling	0 = no splitting	
1 = minor disruption of subchondral bone matrix <25% of condylar surface, no cartilage fibrillation	1 = scalloped remodeling, no tidemarks crossed	1 = hyperemic/edematous osteonal spaces	1 = splitting involves tidemark and subchondral bone but simple linear defects	
	2 = remodeling crosses deep tidemarks, superficial tidemark intact	2 = OB activation	2 = fragments and debris within splits and connections between splits	
	3 = remodeling crosses tidemark front	3 = OCL activation/scalloped margins of osteons 4 = subchondral OCL and OB activation with inflammation	3 = involve articular cartilage with displacement of fragments	