

SUPPLEMENTAL MATERIAL

Table S1. Top enriched gene function networks of the proteomic analysis from porcine coronary sinus blood obtained 3 days after MI.

Enriched function networks	Count	%	p-value	List Total	Pop Hits	Pop Total	Fold enrichment	Bonferroni p-value	Benjamini p-value	FDR
Inflammatory response	52	16.25	5.55E-29	318	379	16792	7.245	1.45E-25	1.45E-23	9.84E-26
Cell-Cell signaling	44	13.75	1.15E-28	318	254	16792	9.147	3.01E-25	1.5E-25	2.04E-25
Positive regulation of cell proliferation	54	16.86	1.70E-26	318	466	16792	6.119	4.45E-23	1.11E-23	3.01E-23
Monocyte chemotaxis	22	6.86	1.19E-25	318	42	16792	27.660	3.11E-22	6.21E-23	2.11E-22
Cellular response to TNF	24	7.5	6.21E-18	318	110	16792	11.521	1.62E-14	1.35E-15	1.10E-14
Neutrophil chemotaxis	20	6.25	7.59E-18	318	66	16792	16.001	1.99E-14	1.53E-15	1.35E-14
Cellular response to IL-1	17	5.31	2.24E-13	318	71	16792	12.643	5.85E-10	2.93E-11	3.97E-10
Lymphocyte chemotaxis	12	3.75	1.47E-12	318	28	16792	22.631	3.85E-09	1.68E-10	2.61E-09
Positive regulation of inflammatory response	16	5	5.37E-12	318	73	16792	11.574	1.40E-08	5.40E-10	9.52E-09
Negative regulation of angiogenesis	13	4.06	1.55E-09	318	62	16792	11.072	4.04E-06	1.12E-07	2.74E-06

MI, myocardial infarction; TNF, tumor necrosis factor; IL, interleukin; FDR, false detection rate

Table S2. Network pathway genes.

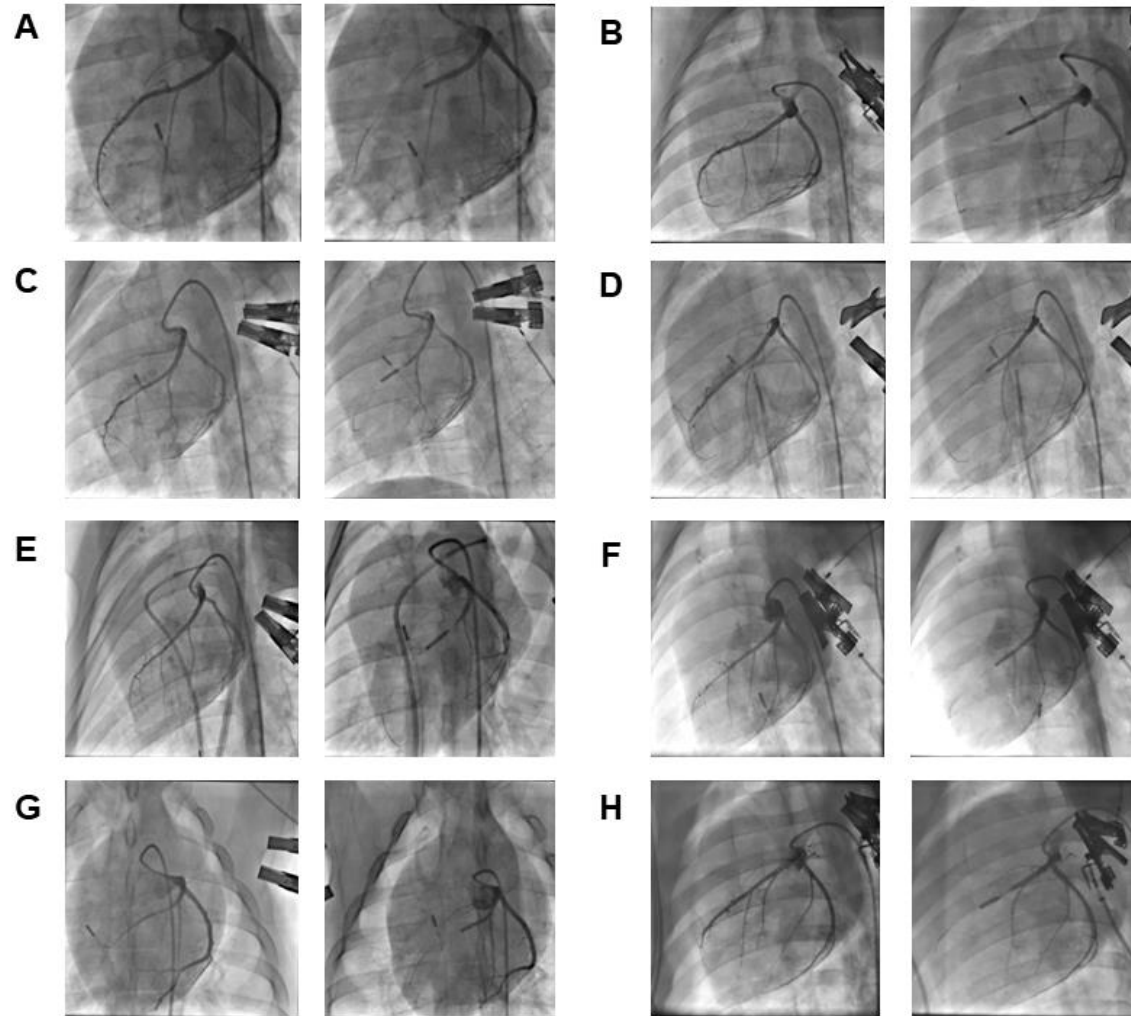
Enriched function networks	Genes
Inflammatory response	RARRES2, S100A8, CXCR3, CXCL10, TNFRSF11B, TNFRSF11A, SERPINA3, SYK, KNG1, LTBR, IL27, ADGRE5, ACKR2, IL26, IL22, TNFAIP6, CCR7, PPBP, CCR4, CCR3, CCR2, NAIP, CCL1, TNFRSF21, CCL3, CSF1, CCL8, PF4, KIT, CCL5, CCL7, CCL26, CALCA, CCL24, TNFRSF1A, CCL22, CCL23, CCL20, ZAP70, THBS1, PTX3, CSF1R, BMP2, IL23R, CCL19, SMAD1, CCL15, EPHA2, CCL17, BMPR1B, IGFBP4, BMP6
Cell-Cell signaling	FGF18, INSL3, NAMPT, CCL3, PPY, PGF, CTF1, CCL8, TSHB, FGF12, POMC, CCL5, CCL7, SHH, CCL26, TGFB2, CXCL10, NOV, CALCA, CCL24, CCL22, TNFRSF11A, CCL23, CCL20, CTGF, LTB, FGFBP1, IL3, BMP3, BMP2, AVP, NTF3, ADGRE5, IL26, CCL15, IL22, CCL17, TNFAIP6, CD80, EREG, PYY, GDF15, MERTK, XCL1
Positive regulation of cell proliferation	NAMPT, FGF18, FGF8, PDGFB, PGF, CXCR3, PDX1, FER, GDNF, SHH, IL31RA, TGFB2, CXCL10, EPCAM, TNFRSF11A, CTGF, NRG1, FGF2, MATK, AVP, CST3, DLL1, IL6R, OSM, VEGFD, EREG, PROK1, F2, ERBB4, CTF1, CSF1, KIT, CALR, LIF, IGF1R, KRAS, PTK2B, THBS1, EGF, FGFBP1, CSF1R, IL3, FLT1, TNFSF4, NTF3, TGFB1, TGFB2, IGF1, KDR, LEP, NOTCH1, SFRP1, HBEGF, FABP1
Monocyte chemotaxis	CCL1, CCL3, FLT1, LGALS3, PDGFB, CCL19, CCL8, CX3CL1, IL6R, CCL5, CCL15, CCL7, CCL26, CCL17, CCL24, CALCA, CCL22, CCL23, TNFRSF11A, TNFSF11, CCL20, XCL1
Cellular response to TNF	CCL1, TNFRSF21, ICAM1, CCL3, ADAMTS13, CCL19, CCL8, CX3CL1, CCL5, CCL15, CCL7, CCL26, CCL17, CCL24, VCAM1, CALCA, CCL22, APOB, CCL23, SFRP1, CCL20, HAMP, THBS1, XCL1
Neutrophil chemotaxis	CCL1, CCL3, S100A8, LGALS3, CCL8, CX3CL1, CCL5, CCL15, CCL7, CCL26, CCL17, TGFB2, CCL24, CCL22, CCL23, PPBP, CCL20, TREM1, XCL1, SYK
Cellular response to IL-1	CCL1, ICAM1, CCL3, CCL19, CCL8, CX3CL1, CCL5, CCL15, CCL7, CCL26, CCL17, CCL24, CCL22, CCL23, CCL20, SFRP1, XCL1
Lymphocyte chemotaxis	CCL24, CCL1, CCL22, CCL3, CCL23, CCL20, CCL8, CCL19, CX3CL1, CCL15, CCL26, CCL17
Positive regulation of inflammatory response	CCL1, CCL3, TNFSF4, S100A8, CCL8, CX3CL1, CCL5, CCL15, CCL7, CCL26, CCL24, TNFRSF1A, CCL23, CCR2, HSPD1, XCL1
Negative regulation of angiogenesis	GDF2, SERPINF1, CCR2, APOH, PF4, CXCR3, TIE1, DCN, SPARC, THBS1, EPHA2, CXCL10, ANGPT4

Figure S1. Antibody array target list.

Number	Name	Number	Name	Number	Name	Number	Name	Number	Name	Number	Name	Number	Name
1	ACK1	74	DNF alpha	147	FGF-18	220	IGFBP-4	295	IL-2 R	366	MMP-14	439	SH-PT
2	Activin A	75	FB	148	FGF-20	221	IGFBP-6	294	IL-23 R	367	MMP-25	440	SPARC
3	Activin B	76	CRIM 1	149	FGF-21	222	IGFBP-ep2	295	IL-23	368	MusK	441	Spinesin
4	Activin C	77	Cripto-1	150	FGF-23	223	IGF-I	296	IL-23 R	369	MSH	442	TAC1
5	Activin R1A	78	CRTH-2	151	PLRG	224	IGF-I R	297	IL-24	370	MICA	443	TarC
6	Activin R1B	79	Cryptic	152	Fib-3 Ligand	225	IGF-II	298	IL-26	371	NAP-2	444	TCR
7	EYA2	80	CTACK	153	Follistatin	226	IGF-II R	299	IL-27	372	NCAM-1	445	TECK
8	Activin R1IA	81	CTGF	154	Follistatin-like 1	227	IL-1 alpha	300	IL-28A	373	Neurin	446	TRP1
9	Adiponectin	82	CTLA-4	155	Fractalkine	228	IL-1 beta	301	IL-29	374	NeuroD1	447	TGF-alpha
10	AgRP	83	CV-2	156	Frizzled-1	229	IL-1 F5	302	IL-31	375	Neuropilin-2	448	TGF-beta 1
11	ALCAM	84	CXCL14	157	Frizzled-3	230	IL-1 F6	303	IL-31 RA	376	Neurturin	449	TGF-beta 2
12	Angiogenin	85	CXCL16	158	Frizzled-4	231	IL-1 F7	304	BACE-1	377	NGF R	450	TGF-beta 3
13	Angiopoietin-1	86	CXCR1	159	Frizzled-5	232	IL-1 F8	305	FACK	378	NOV	451	ATP2B1
14	Angiopoietin-2	87	CXCR2	160	Frizzled-6	233	IL-1 F9	306	Insulin	379	GGF2	452	TGF-beta R1
15	Angiopoietin-4	88	CXCR3	161	Frizzled-7	234	IL-1 F10	307	Insulin R	380	Nidogen-1	453	TGF-beta RII
16	ANGPT1	89	CXCR4	162	Galectin-9	235	IL-1 R3	308	Insulysin	381	NrCam	454	GRI2
17	ANGPT2	90	CXCR5	163	GASP-1	236	IL-1 RA	309	IP-10	382	NG2	455	TGF-beta RIII
18	ANGPT3	91	CXCR6	164	GASP-2	237	IL-1 R6	310	I-TAC	383	NRG3	456	Thrombospondin
19	Angiotensin	92	D6	165	GCP-2	238	IL-1 R8	311	Kininogen	384	NT-3	457	Thyroid Peroxidase
20	APJ	93	DAN	166	GCSF	239	IL-1 R9	312	Kremen-1	385	NT-4	458	Thrombospondin-1
21	Amphiregulin	94	DANCE	167	G-CSF R	240	IL-1 ra	313	Kremen-2	386	Orexin A	459	Thrombospondin-2
22	APRIL	95	DCR3	168	GDF1	241	IL-1 R1	314	Lck	387	Orexin B	460	Thrombospondin-4
23	Artemin	96	Decorin	169	GDF3	242	IL-1 RII	315	LTBP1	388	OSM	461	Thymospondin
24	Ar	97	DNA-1	170	GDF5	243	IL-2	316	LRP	389	Osteonectin	462	Tie-1
25	BT-1	98	DNA-3	171	GDF8	244	IL-2 R alpha	317	LECT2	390	Dibecoron	463	Tie-2
26	BAFF R	99	DNA-4	172	GDF9	245	IL-2 R beta	318	Lefty-A	391	Osteoprotegerin	464	TIMP-1
27	BCMA	100	DNA	173	GDF11	246	IL-2 R gamma	319	Leptin B	392	OXA0 Ligand	465	TIMP-2
28	BD-1	101	DR6	174	GDF15	247	IL-3	320	Leptin	393	PABC	466	TIMP-3
29	BDNF	102	Dlx	175	GDNF	248	IL-3 R alpha	321	LFA-1 alpha	394	PD-ECGF	467	TIMP-4
30	beta-Catenin	103	EDA-A2	176	GFR alpha-1	249	IL-4	322	LIF	395	PDGF R alpha	468	DEFA5
31	Bcl-1	104	EDAR	177	GFR alpha-2	250	IL-4 R	323	LIF R alpha	396	PDGF R beta	469	TSP1
32	beta-NGF	105	EDG-1	178	GFR alpha-3	251	IL-5	324	LIGHT	397	PDGF-AA	470	TLR2
33	Bcl-2	106	EGF	179	GFR alpha-4	252	IL-5 R alpha	325	Lipocalin-1	398	PDGF-AB	471	TLR3
34	Bcl-3	107	EGF R	180	GITR	253	IL-6	326	LRP-1	399	PDGF-BB	472	TLR4
35	BMP-2	108	EG-VEGF	181	GITR Ligand	254	IL-6 R	327	LRP-6	400	PDGF-C	473	TMEFF1
36	BMP-3	109	EMAP-II	182	CBR1	255	IL-7	328	L-selectin	401	PDGF-D	474	TMEFF2
37	BMP-3b	110	ENA-78	183	Glut1	256	IL-7 R alpha	329	Lipocalin-2	402	PEGAM-1	475	TNF-alpha
38	BMP-4	111	Endocan	184	Glut2	257	IL-8	330	Lymphotactin	403	Pentraxin3	476	TNF-beta
39	BMP-5	112	Endoglin	185	Glut3	258	IL-9	331	LTB	404	Persephin	477	TNF R1
40	BMP-6	113	Endostatin	186	Glut5	259	IL-10	332	LTBR	405	PF4	478	TNF RII
41	BMP-7	114	EN-RAGE	187	Glypican 3	260	IL-10 R alpha	333	MAC-1	406	PIGF	479	TRADD
42	BMP-8	115	Entaxin	188	Glypican 5	261	IL-10 R beta	334	MCP-1	407	PLUNC	480	TRAIL
43	BMP-15	116	Entaxin-2	189	GM-CSF	262	IL-11	335	MCP-2	408	Pref-1	481	TRAIL R1
44	BMPRI-IA	117	Entaxin-3	190	GM-CSF R alpha	263	IL-12 p40	336	MCP-3	409	Progranulin	482	TRAIL R2
45	BMPRI-IB	118	Epregrulin	191	Granzyme A	264	IL-12 p70	337	MCP-4	410	Prolactin	483	TRAIL R3
46	BMPRI-III	119	ErbB2	192	GREMLIN	265	IL-12 R beta 1	338	MA-CSF	411	P-selectin	484	TRAIL R4
47	BTC	120	ErbB3	193	GRO	266	IL-12 R beta 2	339	MA-CSF R	412	RAGE	485	TRAMP
48	Cardiotrophin-1	121	ErbB4	194	GRO-a	267	IL-13	340	MDC	413	RANK	486	TREM-1
49	CC14	122	Erythropoietin	195	GRI	268	IL-13 R alpha 1	341	MFG-E8	414	RANTES	487	TRCV
50	CC18	123	E-selectin	196	GRII	269	IL-13 R alpha 2	342	MFRP	415	RELM beta	488	TSG-6
51	CCR1	124	Endostatin	197	HR-EGF	270	IL-15	343	MIF	416	RELT	489	TSR P R
52	CCR2	125	FADD	198	HCC-4	271	IL-15 R alpha	344	MIG	417	ROBO4	490	TWEAK
53	CCR3	126	FAM3B	199	HCR	272	IL-16	345	MIP-1a	418	\$100 AB/AB	491	TWEAK R
54	CCR4	127	Fox	200	Hepassocin	273	IL-17	346	MIP-1b	419	\$100A10	492	Ubiquitin+1
55	CCR5	128	Fas Ligand	201	GLO-1	274	IL-17B	347	MIP-1d	420	SAA	493	uPA
56	CCR6	129	FGF Basic	202	HGF	275	IL-17B R	348	MIP-2	421	SCF	494	uPAR
57	CCR7	130	FGF-8P	203	HGFR	276	IL-17C	349	MIP-3 alpha	422	SCF R	495	Vasorin
58	CCR8	131	FGF R3	204	HRG-alpha	277	IL-17D	350	MIP-3 beta	423	SDP-1	496	VCAM-1
59	CCR9	132	FGF R4	205	HRG-beta 1	278	IL-17E	351	MMP-1	424	sFRP-1	497	VE-Cadherin
60	CD14	133	FGF R5	206	HVEM	279	IL-17F	352	MMP-2	425	sFRP-3	498	VEGF
61	CD27	134	FGF-4	207	I-SOB	280	IL-17R	353	MMP-3	426	sFRP-4	499	VEGF R2
62	CD30	135	FGF-5	208	ICAM-1	281	IL-17RC	354	MMP-7	427	sgp130	500	VEGF R3
63	CD30 Ligand	136	FGF-6	209	ICAM-2	282	IL-17RD	355	MMP-8	428	SigIRR	501	VEGF-R
64	CD40	137	FGF-7	210	ICAM-3	283	IL-18 Rpa	356	MMP-9	429	Siglec-5	502	VEGF-C
65	CD40 Ligand	138	FGF-8	211	ICAM-5	284	IL-18 R alpha	357	MMP-10	430	Siglec-9	503	VEGF-D
66	CD 163	139	FGF-9	212	IFN-alpha/beta R1	285	IL-18 R beta	358	MMP-11	431	SLP1	504	VEGI
67	Cerberus 1	140	FGF-10	213	IFN-alpha/beta R2	286	IL-19	359	MMP-12	432	Smad 1	505	WIF-1
68	Chem R23	141	FGF-11	214	IFN-beta	287	IL-20	360	MMP-13	433	Smad 6	506	WISP-1
69	Chordin-Like 1	142	FGF-12	215	IFN-gamma	288	IL-20 R alpha	361	MMP-14	434	Smad 5	507	XEDAR
70	Chordin-Like 2	143	FGF-13 1B	216	IFN-gamma R1	289	IL-20 R beta	362	MMP-15	435	Smad 7		
71	Csk	144	FGF-16	217	IGFBP-1	290	IL-21	363	MMP-16	436	Smad 8		
72	CLC	145	FGF-17	218	IGFBP-2	291	IL-21 R	364	MMP-19	437	Prdx6		
73	CNTF	146	FGF-18	219	IGFBP-3	292	IL-22	365	MMP-20	438	Soggy-1		

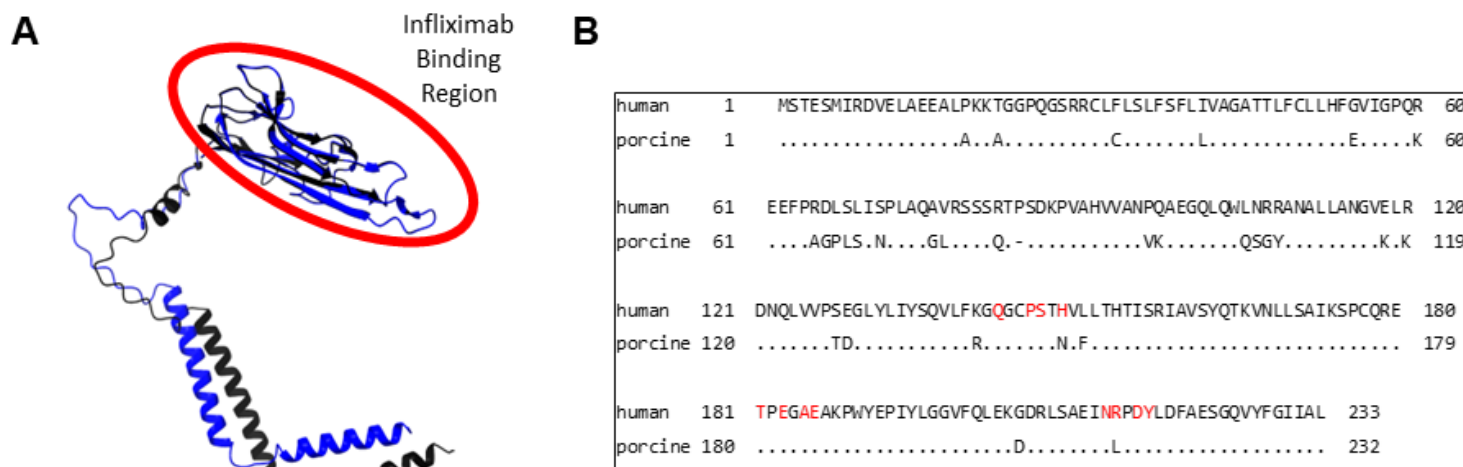
RayBiotech Label-Based (L-Series) Human L507 Array Membrane Kit: Antibody array target list.

Figure S2. Additional angiograms of the porcine MI model to highlight anatomical consistency.



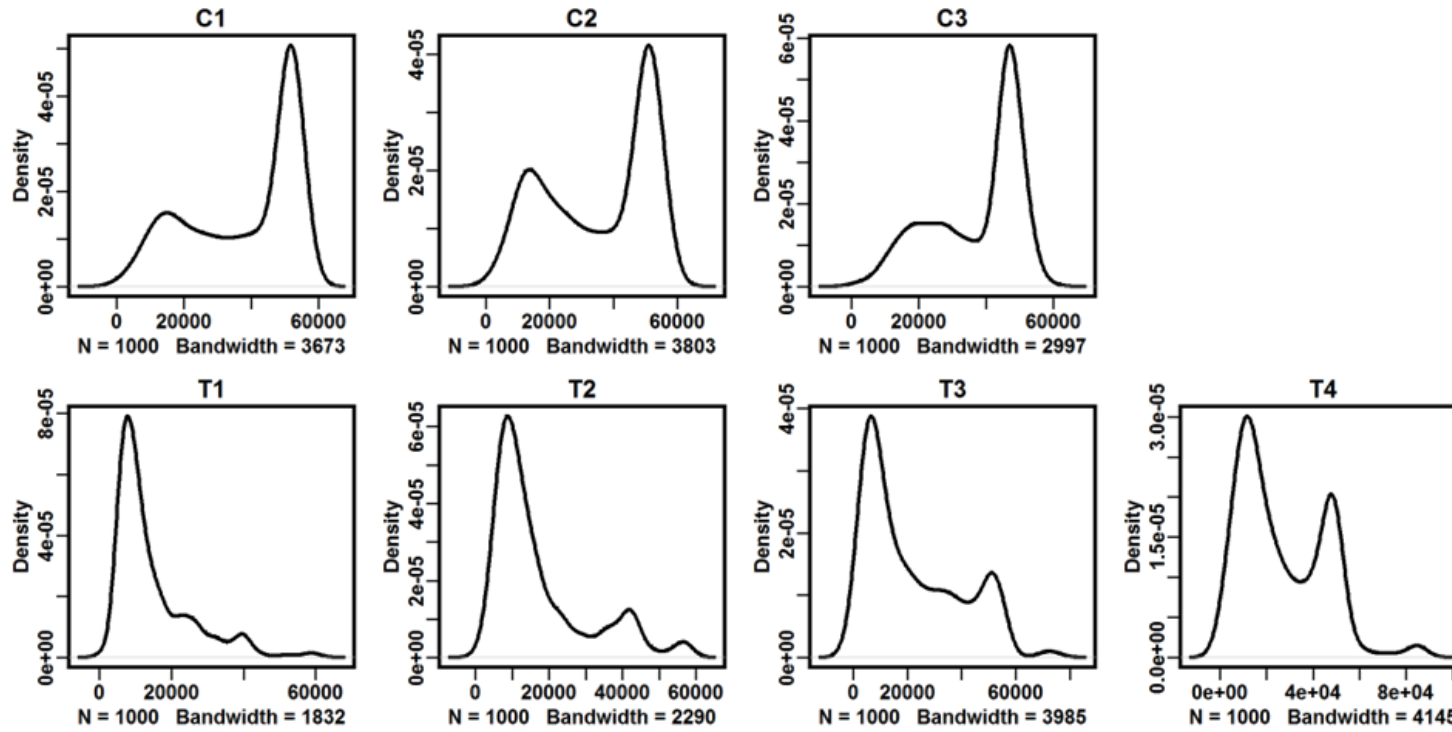
(A-H) Images displayed at baseline (left panels) and following balloon inflation distal to the first diagonal branch of the LAD (right panels). MI, myocardial infarction; LAD, left anterior descending.

Figure S3. Structural Comparison of Human and Porcine TNF- α using ChimeraX (University of California, San Francisco) and BLAST (NCBI, Bethesda, MD).



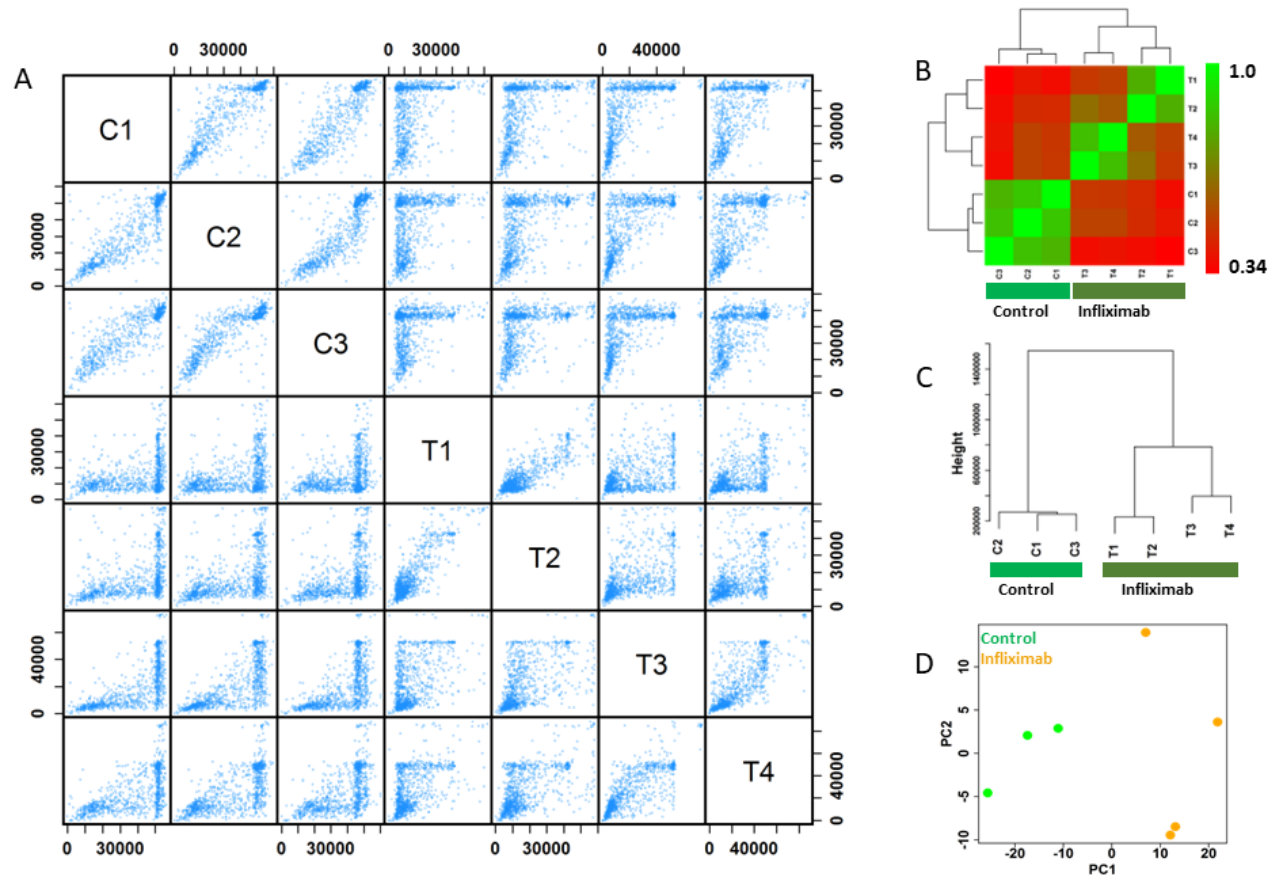
(A) Alpha fold was used to predict the three-dimensional structure of both human (AF-P01375-F1) and porcine (AF-P23563-F1) TNF- α . Matchmaker was used within ChimeraX to align the two structures. (B) BLAST was used to align the two sequence and determine homology of antigenic residues of TNF- α involved in Infliximab binding. Residues interacting with Infliximab are displayed in red. Method: Compositional matrix adjust. Identities:202/233(87%), Positives:215/233(92%), Gaps:1/233(0%).

Figure S4. Protein data distribution density curves.



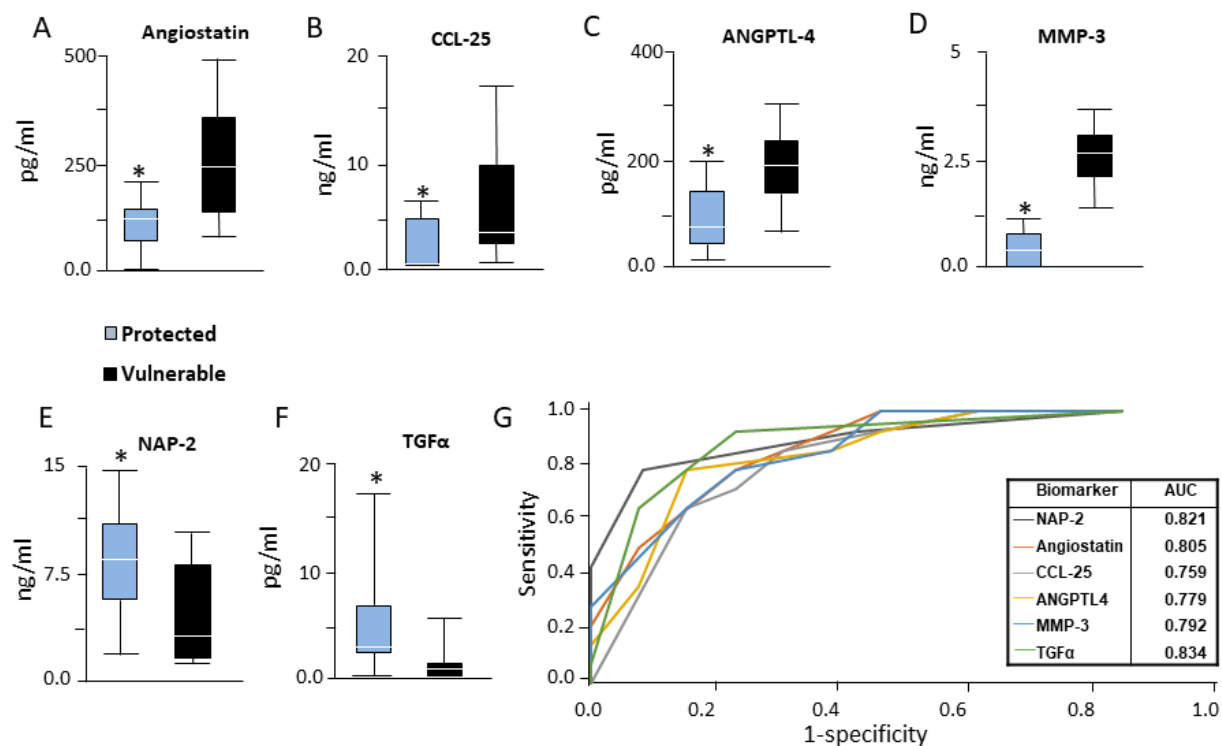
Protein data distribution density curves highlighting the difference between control (top row) and treated samples (bottom row).

Figure S5. Protein array data in control and treated porcine coronary sinus samples collected from the great cardiac vein at 3-days postinfarction.



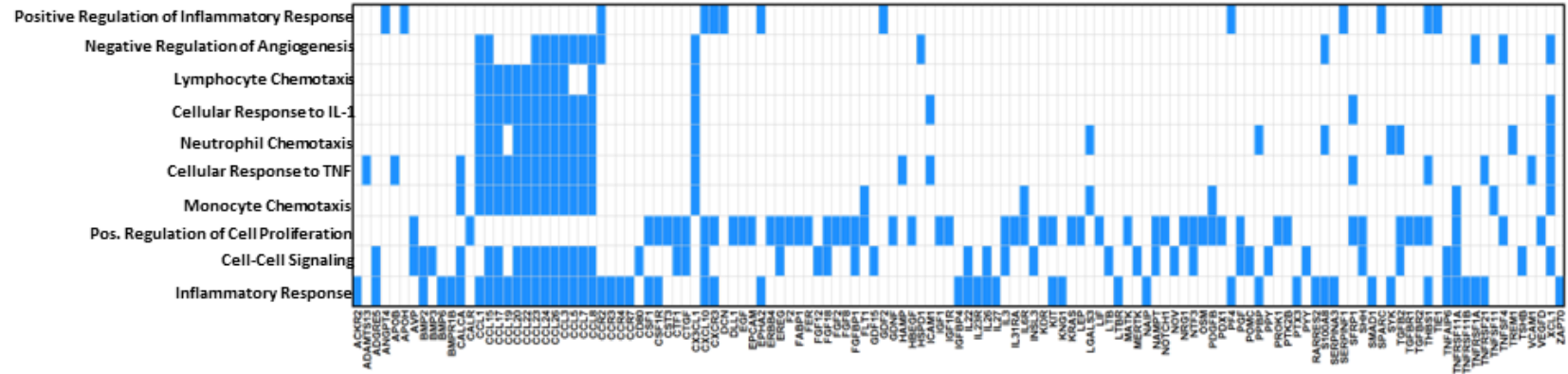
(A) Correlation scatter plot of protein data in control and treated samples. **(B)** Principal component analysis based on all protein expression profiles reveals a good separation of control and treated samples. **(C)** Hierarchical clustering highlights the difference between control and treated groups. **(D)** Correlation heatmap confirms the difference between Treated and Control and similarity within each group.

Figure S6. Coronary aspirate differentially expressed proteins.



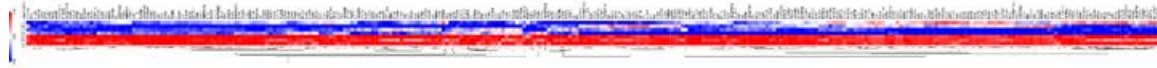
Top 6 differentially expressed proteins in the coronary aspirate samples are delineated with (A) Angiostatin, (B) Chemokine ligand 25 (CCL-25), (C) Angiopoietin like-4 (ANGPTL-4), and (D) Matrix metalloproteinase-3 (MMP-3), all significantly upregulated in vulnerable. (E) Neutrophil Activating Peptide-2 (NAP-2) and (F) Transforming Growth Factor alpha (TGF α) significantly downregulated in vulnerable. (G) Corresponding receiver operating characteristic curve (ROC) for each of the biomarkers provided, showing a high degree of correspondence with outcomes.

Figure S7. Differential expressed proteins involved in the top 10 enriched function pathways.



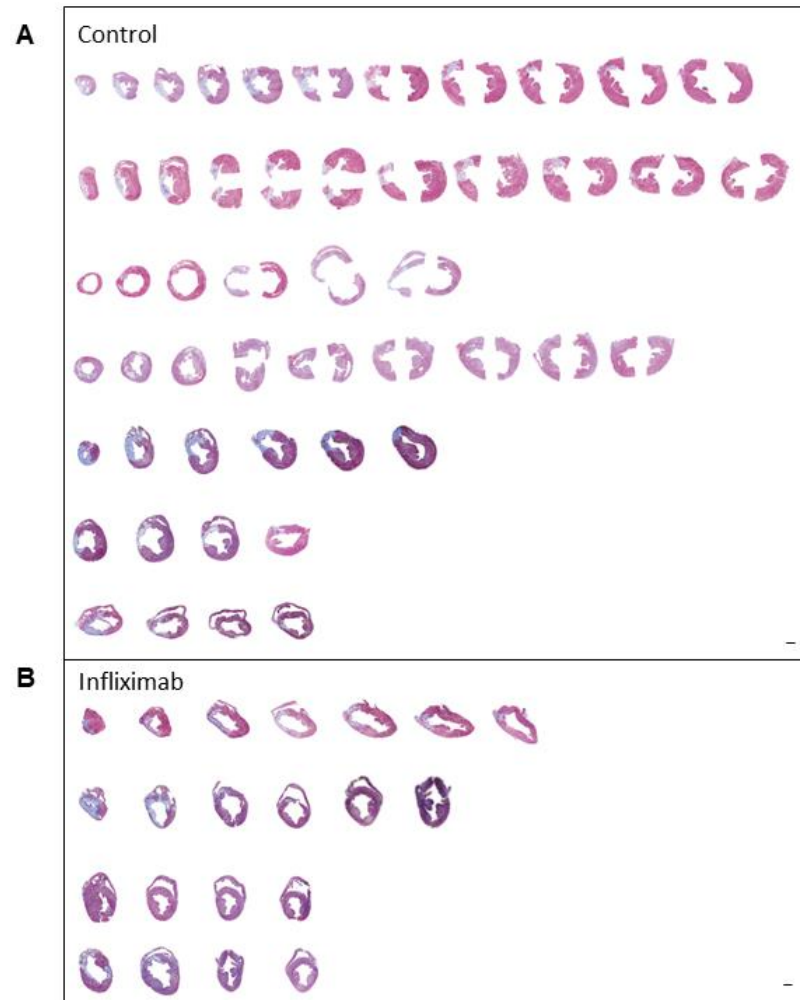
Individual genes involved in top 10 pathways. Overlapped genes are in charge of the crosstalk between different pathways.

Figure S8. Heat map.



Heatmap of 323 significantly differential proteins obtained from coronary sinus blood 3 days after myocardial infarction in infliximab-treated (n=4) and control (n=3) cohorts.

Figure S9. Representative histological cross sections.



Additional representative histological cross-sections of pig hearts 4-weeks post infarction stained with Masson's Trichrome to visualize collagen (blue) and myocardium (red/purple) in (A) Control (n=7) and (B) Infliximab-treated (n=4) cohorts. Scale bar represents 10 mm.

Supplemental Video Legends:

Video S1. Structural Comparison of Human and Porcine TNF- α . 3D reconstruction of the TNF α comparing human versus porcine structure and its infliximab binding region as defined in Figure S3. Best viewed with Windows Media Player.

Video S2. Reconstruction of untreated porcine heart. 3D reconstruction of hearts using serial cross-sectional histology documents a larger scar territory in the untreated porcine hearts versus those treated with infliximab. Cross sectional short axis images were digitally superimposed (26 slices for untreated heart) and given a 5 mm dimensional digital width in the Zeiss Zen software. Blue represents collagen and red muscle as per the Masson's trichome staining pattern. Digitized images were rendered as a z-stack and a movie was generated from manipulation of the z-stacked image. Best viewed with Windows Media Player.

Video S3. Reconstruction of infliximab-treated porcine heart. 3D reconstruction of hearts using serial cross-sectional histology documents a smaller scar territory in the hearts treated with infliximab versus in the untreated porcine hearts. Cross sectional short axis images were digitally superimposed (20 slices for infliximab treated heart) and given a 5mm dimensional digital width in the Zeiss Zen software. Blue represents collagen and red muscle as per the Masson's trichome staining pattern. Digitized images were rendered as a z-stack and a movie was generated from manipulation of the z-stacked image. Best viewed with Windows Media Player.