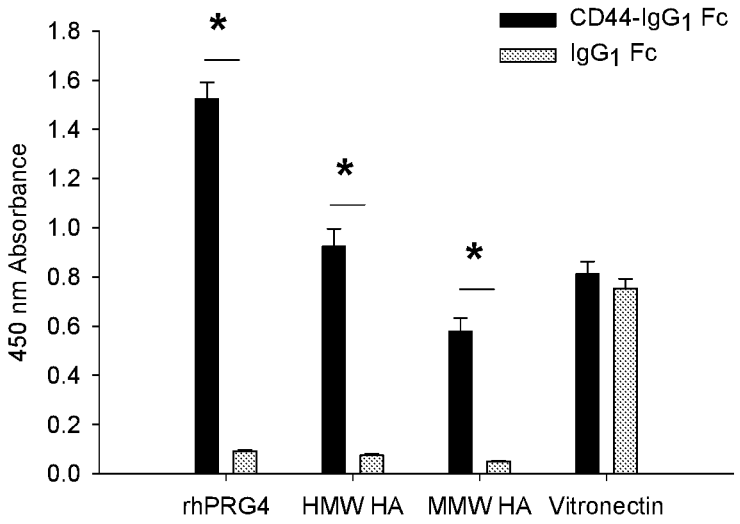

CD44-IgG1 Fc
IgG1 Fc
450 nm Absorbance
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
*
*
*
rhPRG4
HMW HA
MMW HA
Vitronectin

FIG. 1A

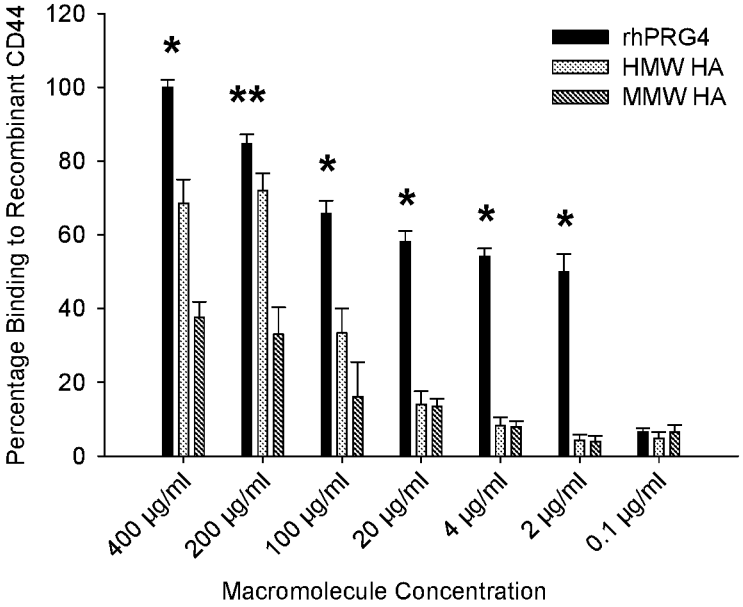

rhPRG4
HMW HA
MMW HA
Percentage Binding to Recombinant CD44
120
100
80
60
40
20
0
*
**
*
*
*
*
400 µg/ml
200 µg/ml
100 µg/ml
20 µg/ml
4 µg/ml
2 µg/ml
0.1 µg/ml
Macromolecule Concentration

FIG. 1B

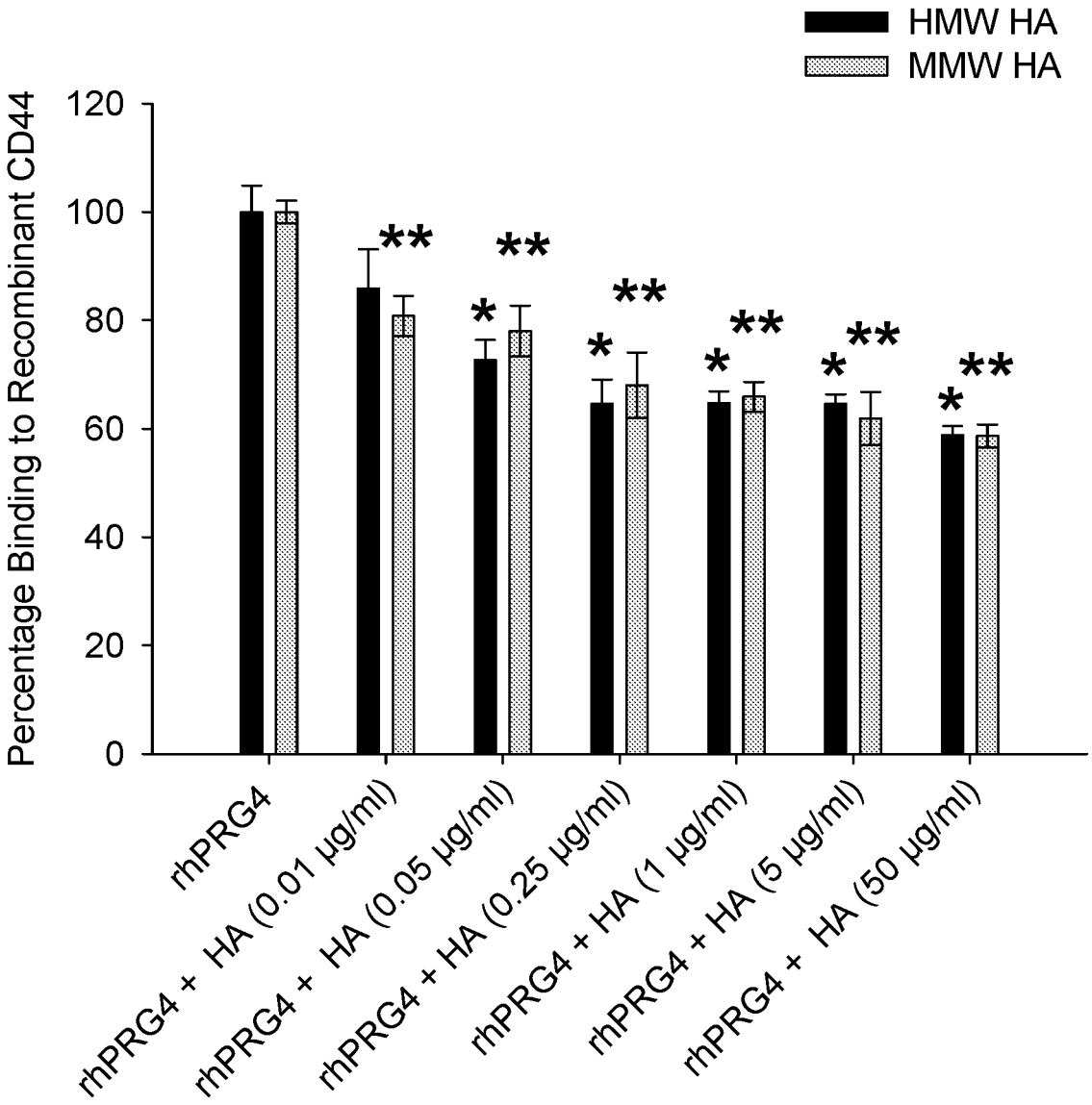

HMW HA
MMW HA
Percentage Binding to Recombinant CD44
120
100
80
60
40
20
0
**
**
*
**
*
**
*
**
*
**
rhPRG4
rhPRG4 + HA (0.01 µg/ml)
rhPRG4 + HA (0.05 µg/ml)
rhPRG4 + HA (0.25 µg/ml)
rhPRG4 + HA (1 µg/ml)
rhPRG4 + HA (5 µg/ml)
rhPRG4 + HA (50 µg/ml)

FIG. 1C

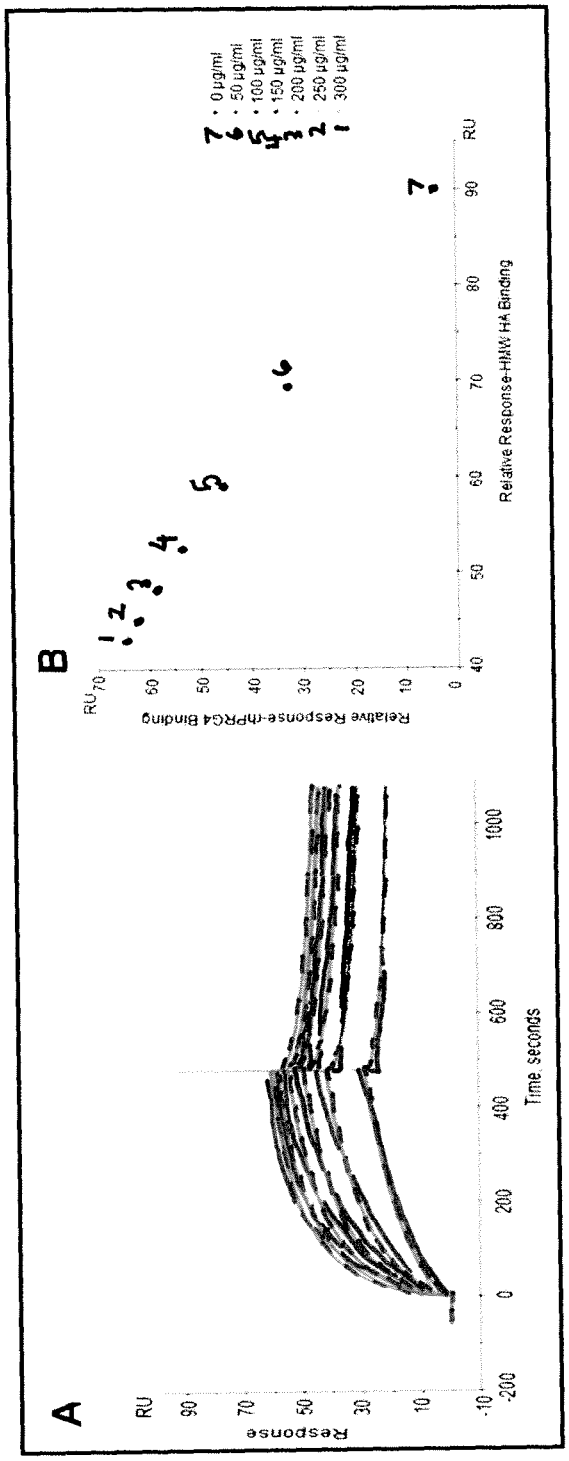

A
Response
RU
90
70
50
30
10
-10
-200
0
200
400
600
800
1000
Time seconds
B
Relative Response-rhPRG4 Binding
RU
70
60
50
40
30
20
10
0
40
50
60
70
80
90
RU
Relative Response-HMW HA Binding
7 • 0 µg/ml
6 • 50 µg/ml
5 • 100 µg/ml
4 • 150 µg/ml
3 • 200 µg/ml
2 250 µg/ml
1 300 µg/ml

FIG. 2A

FIG. 2B

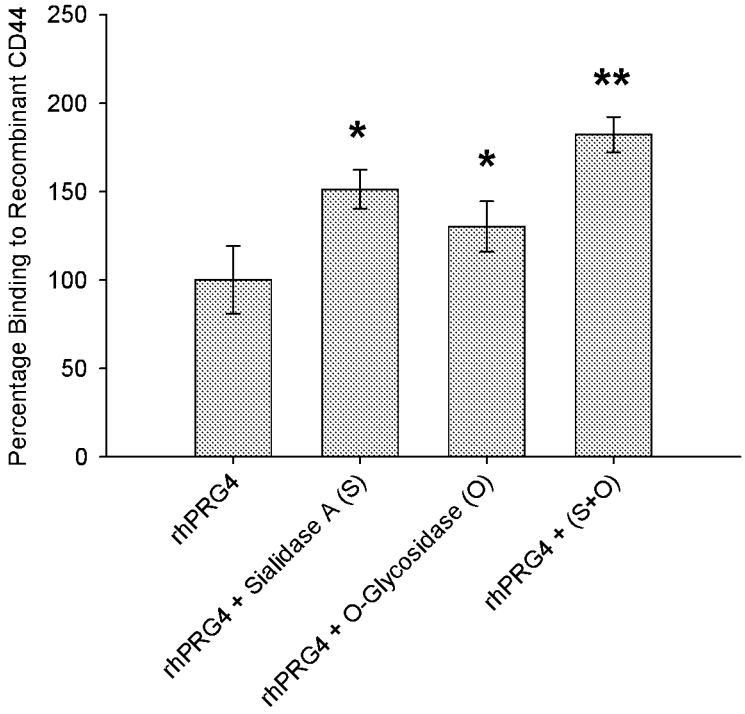

Percentage Binding to Recombinant CD44
250
200
150
100
50
0
*
*
**
rhPRG4
rhPRG4 + Sialidase A (S)
rhPRG4 + O-Glycosidase (O)
rhPRG4 + (S+O)

FIG. 3A

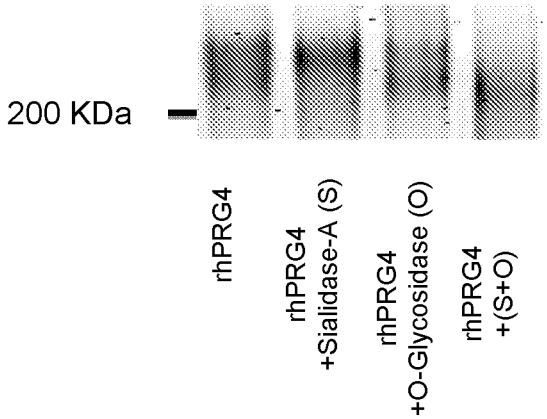

200 KDa
rhPRG4
rhPRG4 +Sialidase-A (S)
rhPRG4 +O-Glycosidase (O)
rhPRG4 +(S+O)

FIG. 3B

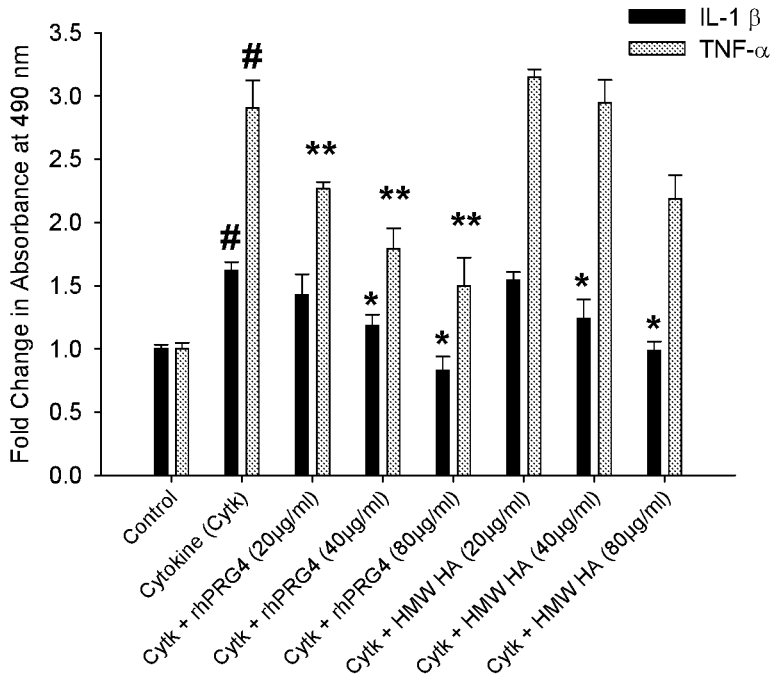

IL-1 β
TNF-α
Fold Change in Absorbance at 490 nm
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
#
#
**
**
**
*
*
*
*
Control
Cytokine (Cytk)
Cytk + rhPRG4 (20µg/ml)
Cytk + rhPRG4 (40µg/ml)
Cytk + rhPRG4 (80µg/ml)
Cytk + HMW HA (20µg/ml)
Cytk + HMW HA (40µg/ml)
Cytk + HMW HA (80µg/ml)

FIG. 4A

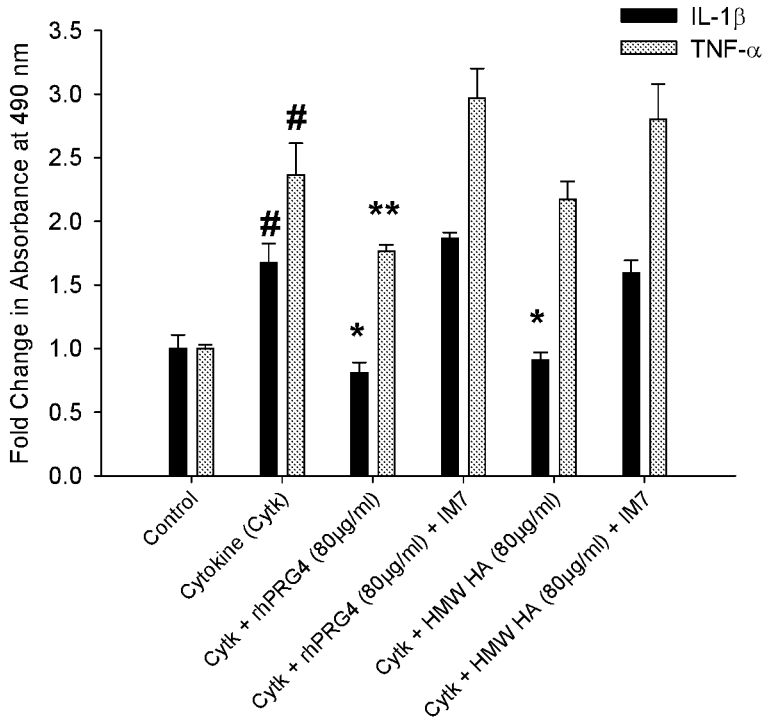

IL-1β
TNF-α
Fold Change in Absorbance at 490 nm
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
#
#
**
*
*
Control
Cytokine (Cytk)
Cytk + rhPRG4 (80µg/ml)
Cytk + rhPRG4 (80µg/ml) + IM7
Cytk + HMW HA (80µg/ml)
Cytk + HMW HA (80µg/ml) + IM7

FIG. 4B

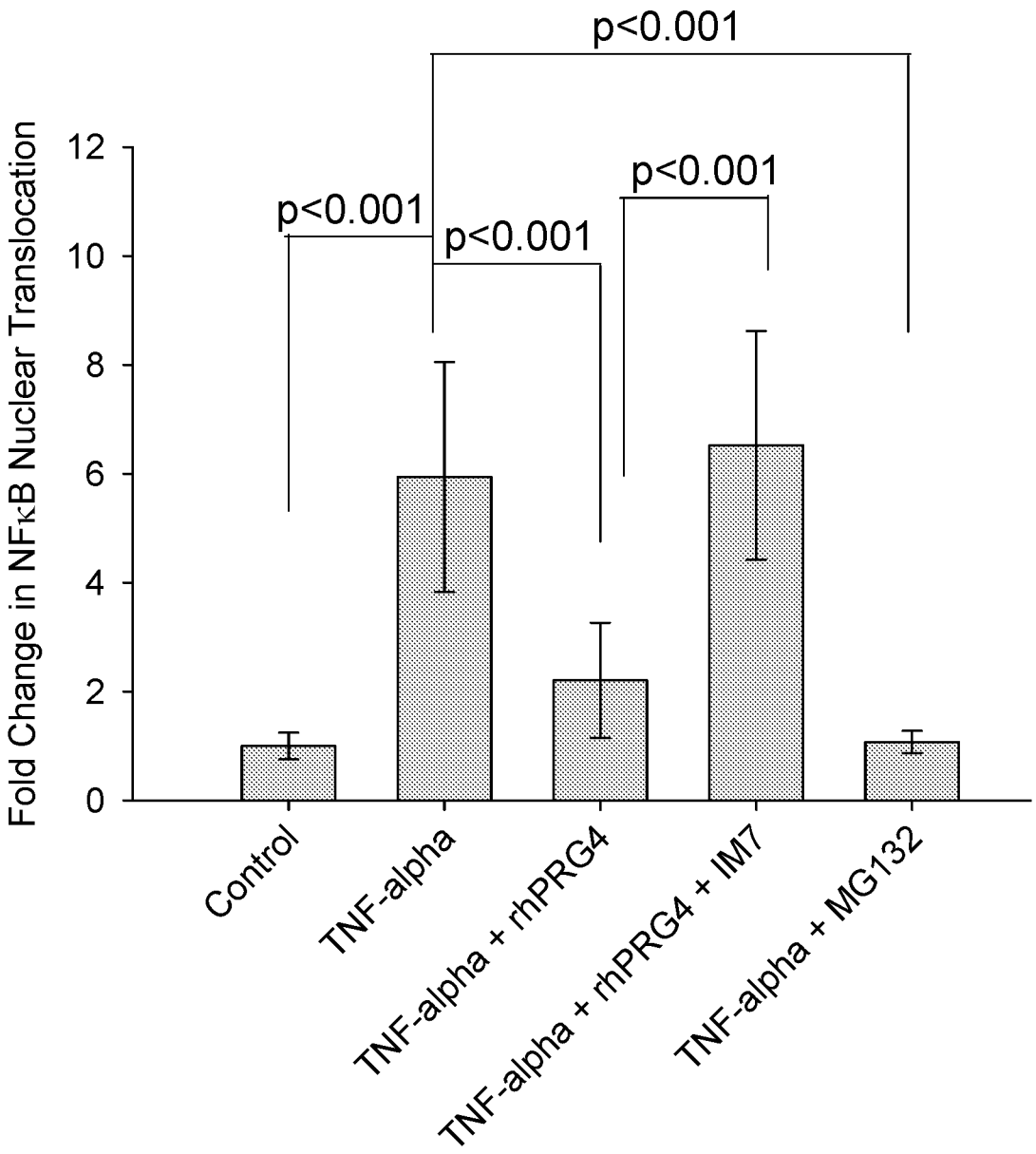
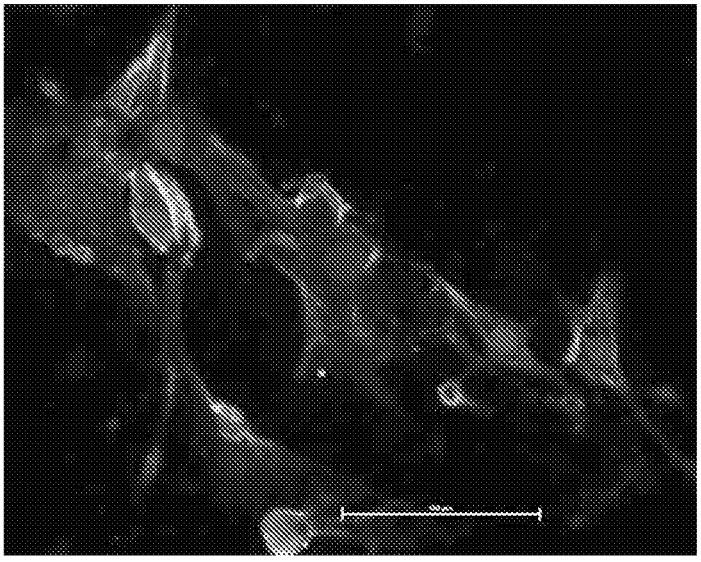

p<0.001
p<0.001
p<0.001
p<0.001
Fold Change in NFκB Nuclear Translocation
0
2
4
6
8
10
12
Control
TNF-alpha
TNF-alpha + rhPRG4
TNF-alpha + rhPRG4 + IM7
TNF-alpha + MG132

FIG. 4C

Fig. 5A

Prg4 -/- Synoviocytes



Prg4 +/+ Synoviocytes

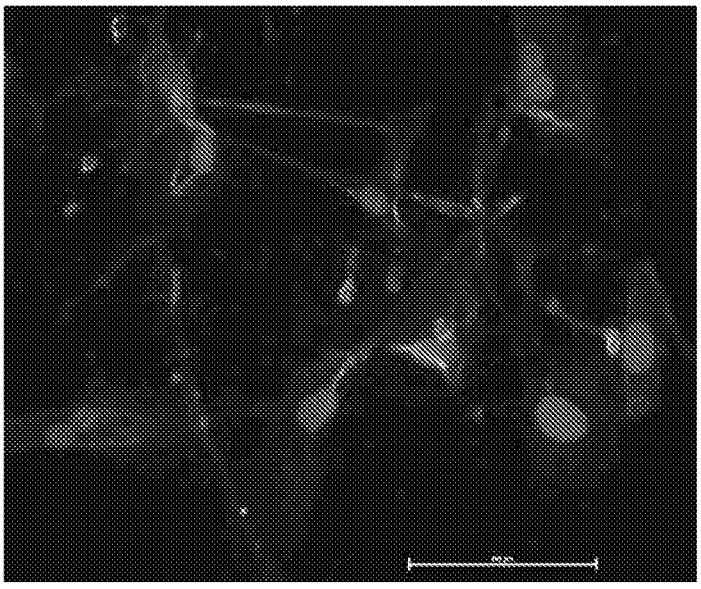


FIG. 5B

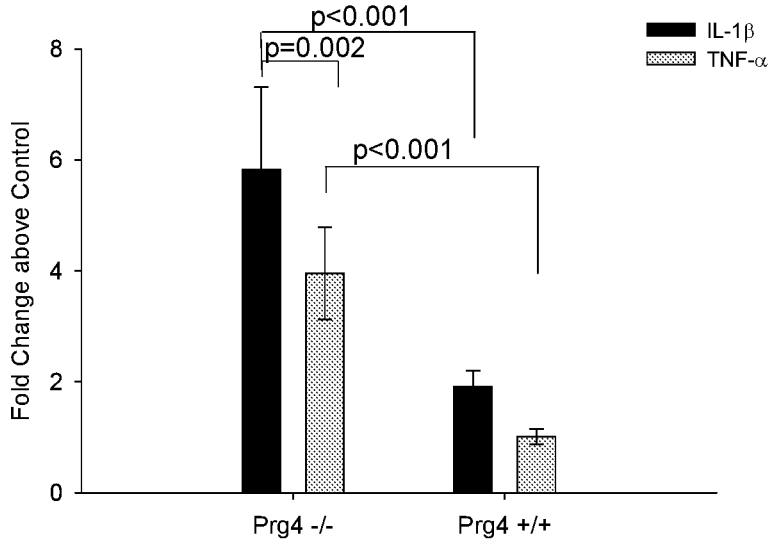

p<0.001
p=0.002
p<0.001
IL-1β
TNF-α
Fold Change above Control
0
2
4
6
8
Prg4 -/-
Prg4 +/+

FIG. 5C

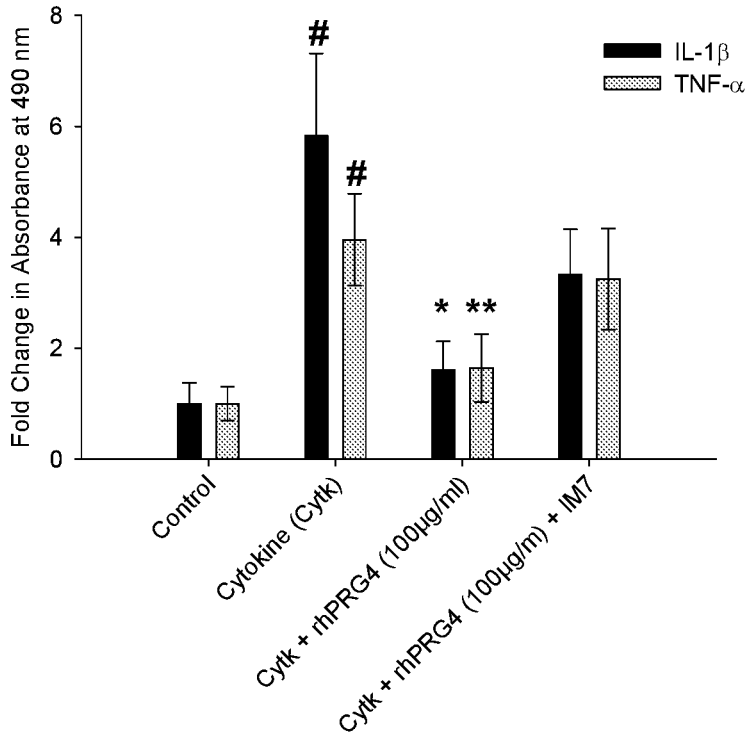

IL-1β
TNF-α
Fold Change in Absorbance at 490 nm
0
2
4
6
8
#
#
*
**
Control
Cytokine (Cytk)
Cytk + rhPRG4 (100µg/ml)
Cytk + rhPRG4 (100µg/m) + IM7

FIG. 6

SEQ ID NO: 1, LENGTH: 1404, ORGANISM: Homo sapiens, UniProt Accession No. Q92954:

MAWKTLPIYL LLLLSVFVIQ QVSSQDLSSC AGRCGEGYSR DATCNCDYNC QHYMECCPDF
KRVCTAELSC KGRCFESFER GRECDCDAQC KKYDKCCPDY ESFCAEVHNP TSPPSSKKAP
PPSGASQTIK STTKRSPKPP NKKKTKKVIE SEEITEEHSV SENQESSSSS SSSSSSSTIR
KIKSSKNSAA NRELQKKLKV KDNKKNRTKK KPTPKPPVVD EAGSGLDNGD FKVTTPDTST
TQHNKVSTSP KITTAKPINP RPSLPPNSDT SKETSLTVNK ETTVETKETT TTNKQTSTDG
KEKTTSAKET QSIEKTSAKD LAPTSKVLAK PTPKAETTTK GPALTTPKEP TPTTPKEPAS
TTPKEPTPTT IKSAPTTPKE PAPTTTKSAP TTPKEPAPTT TKEPAPTTPK EPAPTTTKEP
APTTTKSAPT TPKEPAPTTP KKPAPTTPKE PAPTTPKEPT PTTPKEPAPT TKEPAPTTPK
EPAPTAPKKP APTTPKEPAP TTPKEPAPTT TKEPSPTTPK EPAPTTTKSA PTTTKEPAPT
TTKSAPTTPK EPSPTTTKEP APTTPKEPAP TTPKKPAPTT PKEPAPTTPK EPAPTTTKKP
APTTPKEPAP TTPKETAPTT PKKLTPTTPE KLAPTTPEKP APTTPEELAP TTPEEPTPTT
PEEPAPTTPK AAAPNTPKEP APTTPKEPAP TTPKEPAPTT PKETAPTTPK GTAPTTLKEP
APTTPKKPAP KELAPTTTKE PTSTTCDKPA PTTPKGTAPT TPKEPAPTTP KEPAPTTPKG
TAPTTLKEPA PTTPKKPAPK ELAPTTTKGP TSTTSDKPAP TTPKETAPTT PKEPAPTTPK
KPAPTTPETP PPTTSEVSTP TTTKEPTTIH KSPDESTPEL SAEPTPKALE NSPKEPGVPT
TKTPAATKPE MTTTAKDKTT ERDLRTTPET TTAAPKMTKE TATTTEKTTE SKITATTTQV
TSTTTQDTTP FKITTLKTTT LAPKVTTTKK TITTTEIMNK PEETAKPKDR ATNSKATTPK
PQKPTKAPKK PTSTKKPKTM PRVRKPKTTP TPRKMTSTMP ELNPTSRIAE AMLQTTTRPN
QTPNSKLVEV NPKSEDAGGA EGETPHMLLR PHVFMPEVTP DMDYLPRVPN QGIIINPMLS
DETNICNGKP VDGLTTLRNG TLVAFRGHYF WMLSPFSPPS PARRITEVWG IPSPIDTVFT
RCNCEGKTFF FKDSQYWRFT NDIKDAGYPK PIFKGFGGLT GQIVAALSTA KYKNWPESVY
FFKRGGSIQQ YIYKQEPVQK CPGRRPALNY PVYGETTQVR RRRFERAIGP SQTHTIRIQY
SPARLAYQDK GVLHNEVKVS ILWRGLPNVV TSAISLPNIR KPDGYDYYAF SKDQYYNIDV
PSRTARAITT RSGQTLSKVW YNCP

FIG. 7

SEQ ID NO: 2 LENGTH: 5041, TYPE: DNA, ORGANISM: Homo sapiens, GenBank Accession No. U70136.1:

GCGGCCGCGACTATTCGGTACCTGAAAACAACGATGGCATGGAAAACACTTCCCATTTACCTGT
TGTTGCTGCTGTCTGTTTTCGTGATTCAGCAAGTTTCATCTCAAGATTTATCAAGCTGTGCAGG
GAGATGTGGGGAAGGGTATTCTAGAGATGCCACCTGCAACTGTGATTATAACTGTCAACACTAC
ATGGAGTGCTGCCCTGATTTCAAGAGAGTCTGCACTGCGGAGCTTTCCTGTAAAGGCCGCTGCT
TTGAGTCCTTCGAGAGAGGGAGGGAGTGTGACTGCGACGCCCAATGTAAGAAGTATGACAAGTG
CTGTCCCGATTATGAGAGTTTCTGTGCAGAAGTGCATAATCCCACATCACCACCATCTTCAAAG
AAAGCACCTCCACCTTCAGGAGCATCTCAAACCATCAAATCAACAACCAAACGTTCACCCAAAC
CACCAAACAAGAAGAAGACTAAGAAAGTTATAGAATCAGAGGAAATAACAGAAGAACATTCTGT
TTCTGAAAATCAAGAGTCCTCCTCCTCCTCCTCCTCTTCCTCTTCTTCTTCAACAATTTGGAAA
ATCAAGTCTTCCAAAAATTCAGCTGCTAATAGAGAATTACAGAAGAAACTCAAAGTAAAAGATA
ACAAGAAGAACAGAACTAAAAAGAAACCTACCCCCAAACCACCAGTTGTAGATGAAGCTGGAAG
TGGATTGGACAATGGTGACTTCAAGGTCACAACTCCTGACACGTCTACCACCCAACACAATAAA
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CACCACTCCCAAGGAGCCTGCATCTACCACACCCAAAGAGCCCACACCTACCACCATCAAGTCT
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AGCCTGCACCCACCACCACCAAGGAGCCTGCACCCACCACTCCCAAGGAGCCTGCACCCACCAC
CACCAAGGAGCCTGCACCCACCACCACCAAGTCTGCACCCACCACTCCCAAGGAGCCTGCACCC
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CTACACCCACCACTCCCAAGGAGCCTGCACCCACCACCAAGGAGCCTGCACCCACCACTCCCAA
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ACTCCCAAGGAGCCTGCACCCACCACCACCAAGGAGCCTTCACCCACCACTCCCAAGGAGCCTG
CACCCACCACCACCAAGTCTGCACCCACCACTACCAAGGAGCCTGCACCCACCACTACCAAGTC

TGCACCCACCACTCCCAAGGAGCCTTCACCCACCACCACCAAGGAGCCTGCACCCACCACTCCC
AAGGAGCCTGCACCCACCACCCCCAAGAAGCCTGCCCCAACTACCCCCAAGGAGCCTGCACCCA
CCACTCCCAAGGAACCTGCACCCACCACCACCAAGAAGCCTGCACCCACCGCTCCCAAAGAGCC
TGCCCCAACTACCCCCAAGGAGACTGCACCCACCACCCCCAAGAAGCTCACGCCCACCACCCCC
GAGAAGCTCGCACCCACCACCCCTGAGAAGCCCGCACCCACCACCCCTGAGGAGCTCGCACCCA
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AAGGAGCCTGCTCCAACTACCCCTAAGGAGACTGCTCCAACTACCCCTAAAGGGACTGCTCCAA
CTACCCTCAAGGAACCTGCACCCACTACTCCCAAGAAGCCTGCCCCCAAGGAGCTTGCACCCAC
CACCACCAAGGAGCCCACATCCACCACCTCTGACAAGCCCGCTCCAACTACCCCTAAGGGGACT
GCTCCAACTACCCCTAAGGAGCCTGCTCCAACTACCCCTAAGGAGCCTGCTCCAACTACCCCTA
AGGGGACTGCTCCAACTACCCTCAAGGAACCTGCACCCACTACTCCCAAGAAGCCTGCCCCCAA
GGAGCTTGCACCCACCACCACCAAGGGGCCCACATCCACCACCTCTGACAAGCCTGCTCCAACT
ACACCTAAGGAGACTGCTCCAACTACCCCCAAGGAGCCTGCACCCACTACCCCCAAGAAGCCTG
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GGAGCCTACCACTATCCACAAAAGCCCTGATGAATCAACTCCTGAGCTTTCTGCAGAACCCACA
CCAAAAGCTCTTGAAAACAGTCCCAAGGAACCTGGTGTACCTACAACTAAGACTCCTGCAGCGA
CTAAACCTGAAATGACTACAACAGCTAAAGACAAGACAACAGAAAGAGACTTACGTACTACACC
TGAAACTACAACTGCTGCACCTAAGATGACAAAAGAGACAGCAACTACAACAGAAAAAACTACC
GAATCCAAAATAACAGCTACAACCACACAAGTAACATCTACCACAACTCAAGATACCACACCAT
TCAAAATTACTACTCTTAAAACAACTACTCTTGCACCCAAAGTAACTACAACAAAAAAGACAAT
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GTGCTGAAGGAGAAACACCTCATATGCTTCTCAGGCCCCATGTGTTCATGCCTGAAGTTACTCC
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GAGACCAATATATGCAATGGTAAGCCAGTAGATGGACTGACTACTTTGCGCAATGGGACATTAG
TTGCATTCCGAGGTCATTATTTCTGGATGCTAAGTCCATTCAGTCCACCATCTCCAGCTCGCAG

AATTACTGAAGTTTGGGGTATTCCTTCCCCCATTGATACTGTTTTTACTAGGTGCAACTGTGAA
GGAAAAACTTTCTTCTTTAAGGATTCTCAGTACTGGCGTTTTACCAATGATATAAAAGATGCAG
GGTACCCCAAACCAATTTTCAAAGGATTTGGAGGACTAACTGGACAAATAGTGGCAGCGCTTTC
AACAGCTAAATATAAGAACTGGCCTGAATCTGTGTATTTTTTCAAGAGAGGTGGCAGCATTCAG
CAGTATATTTATAAACAGGAACCTGTACAGAAGTGCCCTGGAAGAAGGCCTGCTCTAAATTATC
CAGTGTATGGAGAAATGACACAGGTTAGGAGACGTCGCTTTGAACGTGCTATAGGACCTTCTCA
AACACACACCATCAGAATTCAATATTCACCTGCCAGACTGGCTTATCAAGACAAAGGTGTCCTT
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CACTGCCCAACATCAGAAAACCTGACGGCTATGATTACTATGCCTTTTCTAAAGATCAATACTA
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AAAGTCTGGTACAACTGTCCTTAGACTGATGAGCAAAGGAGGAGTCAACTAATGAAGAAATGAA
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CAGTTGTTATTGTTTACAGACCATTTAATTAATATTTCCTCTGTTTATTCCTCCTCTCCCTCCC
ATTGCATGGCTCACACCTGTAAAAGAAAAAAGAATCAAATTGAATATATCTTTTAAGAATTCAA
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GAGATACAACAAATGAATATAACACTATAACACTTCATATTTTCCAAATCTTAATTTGGATTTA
AGGAAGAAATCAATAAATATAAAATATAAGCACATATTTATTATATATCTAAGGTATACAAATC
TGTCTACATGAAGTTTACAGATTGGTAAATATCACCTGCTCAACATGTAATTATTTAATAAAAC
TTTGGAACATTAAAAAAATAAATTGGAGGCTTAAAAAAAAAAAAAAAAA

	Saline	LPS	% Change
IL2	0	0	0.0
IL4	1.06	1.4	32.1
IL6	11	30	172.7
IL8	206	560	171.8
IL10	0.38	0.48	26.3
VEGF	21	46	119.0
IFNg	0.3	0.3	0.0
TNFa	128	327	155.5
IL1a	0.5	0.5	0.0
IL1b	1.46	1.7	16.4
MCP1	79	91	15.2
EGF	4.1	3.4	-17.1

FIG. 8A

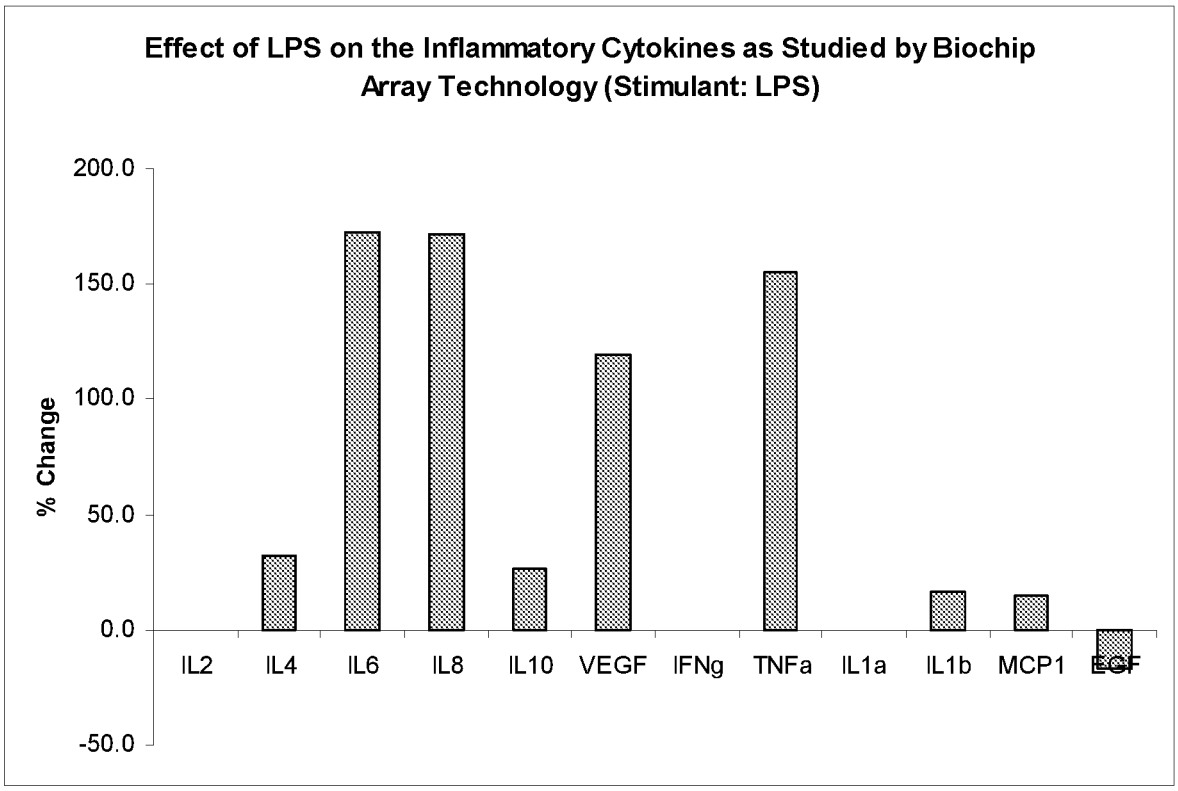

Effect of LPS on the Inflammatory Cytokines as Studied by Biochip Array Technology (Stimulant: LPS)
% Change
200.0
150.0
100.0
50.0
0.0
-50.0
IL2
IL4
IL6
IL8
IL10
VEGF
IFNg
TNFa
IL1a
IL1b
MCP1
EGF

FIG. 8B

	Saline	Lubricin	% Change
IL2	0	0	0.0
IL4	0.99	0.92	-7.1
IL6	89	68	-23.6
IL8	382	260	-33.7
IL10	2.76	2.14	-23.0
VEGF	12.69	6.95	-45.2
IFNg	0.22	0.29	31.8
TNFa	9.5	9	-5.3
IL1a	0.25	0.25	0.0
IL1b	7.53	6.92	-8.1
MCP1	223	201	-9.9
EGF	1.75	1.23	-29.7

FIG. 9A

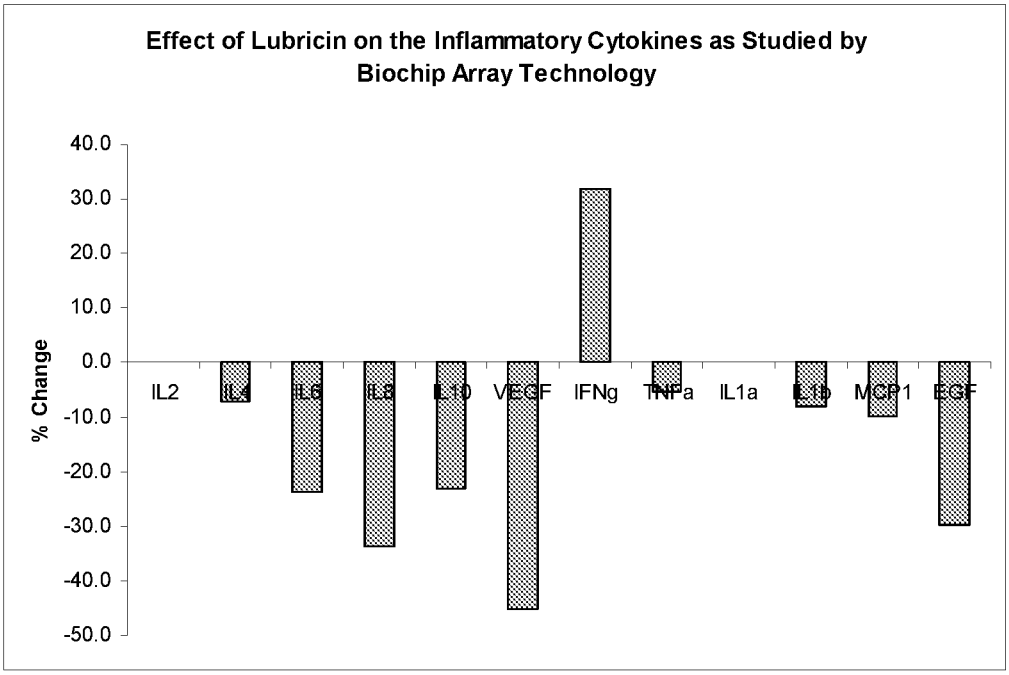

Effect of Lubricin on the Inflammatory Cytokines as Studied by Biochip Array Technology
% Change
40.0
30.0
20.0
10.0
0.0
-10.0
-20.0
-30.0
-40.0
-50.0
IL2
IL4
IL6
IL8
IL10
VEGF
IFNg
TNFa
IL1a
IL1b
MCP1
EGF

FIG. 9B

	LPS	LPS/Lubricin	% Change
IL2	0	0	0.0
IL4	1.4	1.2	-14.3
IL6	30	29	-3.3
IL8	570	504	-11.6
IL10	0.48	0.32	-33.3
VEGF	48	34	-29.2
IFNg	0.52	0.52	0.0
TNFa	327	301	-8.0
IL1a	0.62	0.62	0.0
IL1b	1.62	1.21	-25.3
MCP1	91	68	-25.3
EGF	4.1	2	-51.2

FIG. 10A

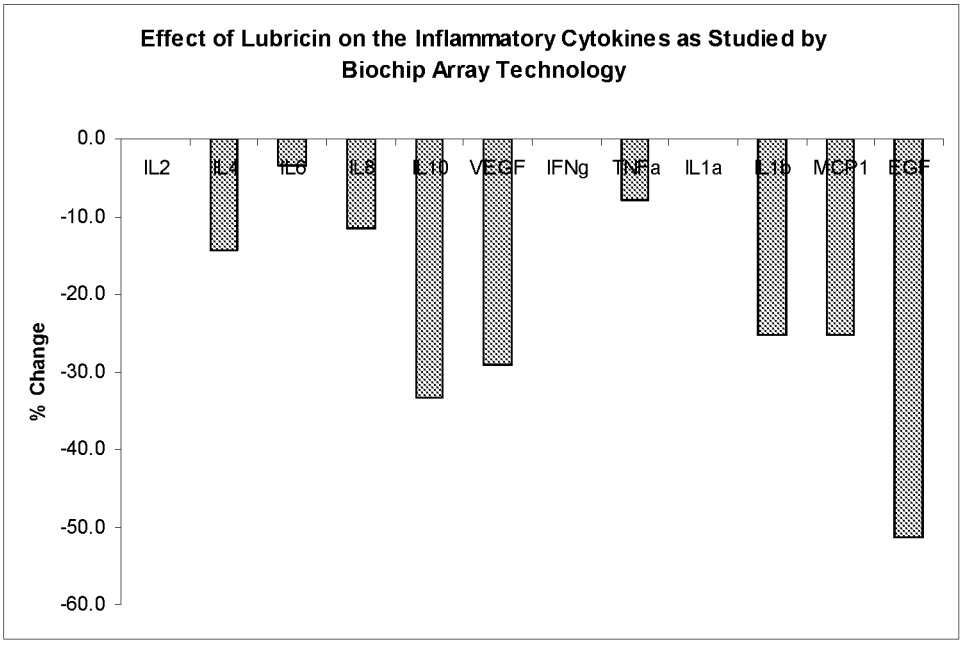

Effect of Lubricin on the Inflammatory Cytokines as Studied by Biochip Array Technology
% Change
0.0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
IL2
IL4
IL6
IL8
IL10
VEGF
IFNg
TNFa
IL1a
IL1b
MCP1
EGF

FIG. 10B

	TNFa	TNFa/Lubricin	% Change
IL2	0	0	0.0
IL4	0.96	0.98	2.1
IL6	95	68	-28.4
IL8	400	235	-41.3
IL10	10	9	-10.0
VEGF	65	41	-36.9
IFNg	1.4	0	-100.0
TNFa	863	34	-96.1
IL1a	0.33	0.41	24.2
IL1b	34	18	-47.1
MCP1	250	250	0.0
EGF	19	11	-42.1

FIG. 11A

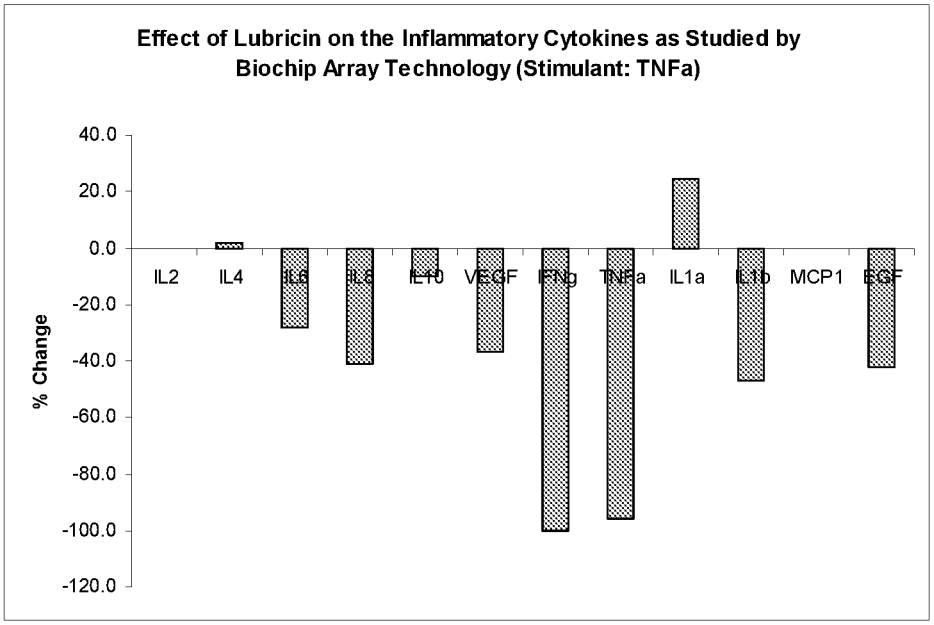

Effect of Lubricin on the Inflammatory Cytokines as Studied by Biochip Array Technology (Stimulant: TNFa)
% Change
40.0
20.0
0.0
-20.0
-40.0
-60.0
-80.0
-100.0
-120.0
IL2
IL4
IL6
IL8
IL10
VEGF
IFNg
TNFa
IL1a
IL1b
MCP1
EGF

FIG. 11B

	TF	TF/Lubricin	% Change
IL2	0	0	0.0
IL4	0.92	0.92	0.0
IL6	71	68	-4.2
IL8	350	233	-33.4
IL10	1.26	2.1	66.7
VEGF	29	12	-58.6
IFNg	0.3	0.3	0.0
TNFa	8.32	0.3	-96.4
IL1a	0.33	0.23	-30.3
IL1b	7.18	7.15	-0.4
MCP1	199	168	-15.6
EGF	2.74	1.99	-27.4

FIG. 12A

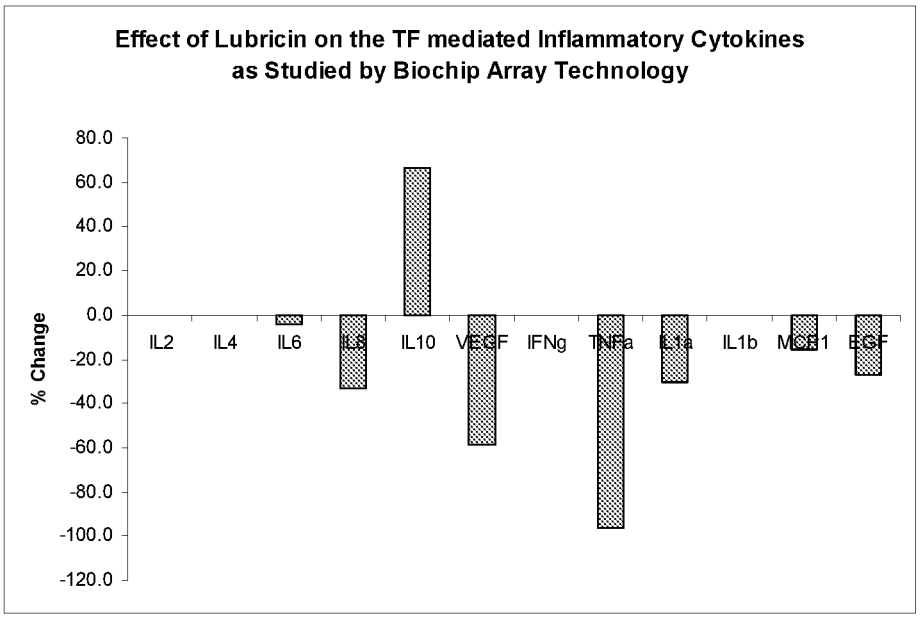

Effect of Lubricin on the TF mediated Inflammatory Cytokines
as Studied by Biochip Array Technology
% Change
80.0
60.0
40.0
20.0
0.0
-20.0
-40.0
-60.0
-80.0
-100.0
-120.0
IL2
IL4
IL6
IL8
IL10
VEGF
IFNg
TNFa
IL1a
IL1b
MCP1
EGF

FIG. 12B

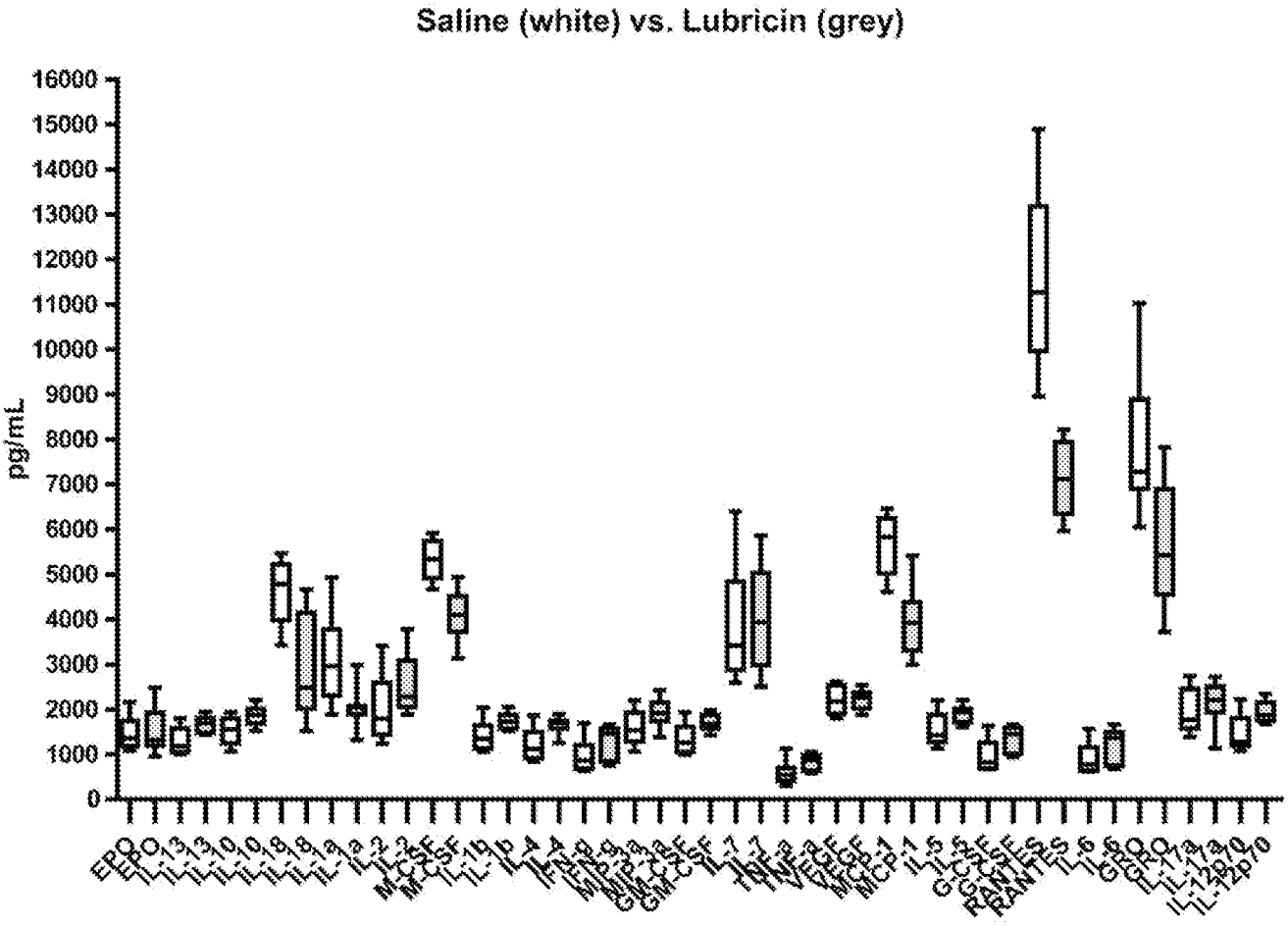

Saline (white) vs. Lubricin (grey)
pg/mL
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
EPO
IL-13
IL-10
IL-8
IL-1a
IL-2
M-CSF
IL-1b
IL-4
IFN-g
MIP-3a
GM-CSF
IL-1
TNF-a
VEGF
MCP-1
IL-5
G-CSF
RANTES
IL-6
GRO
IL-17a
IL-12p70
IL-12p70

FIG. 13

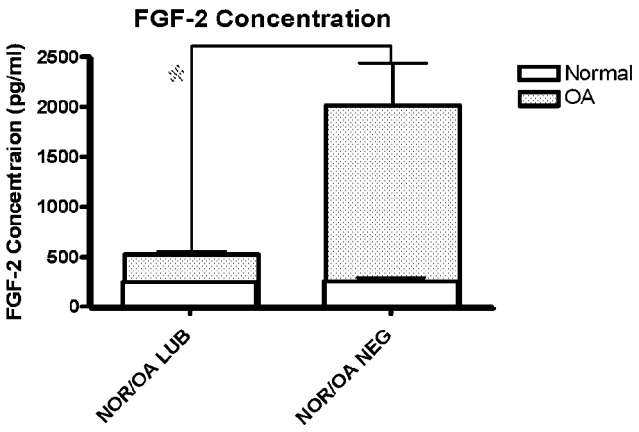


FIG. 14A

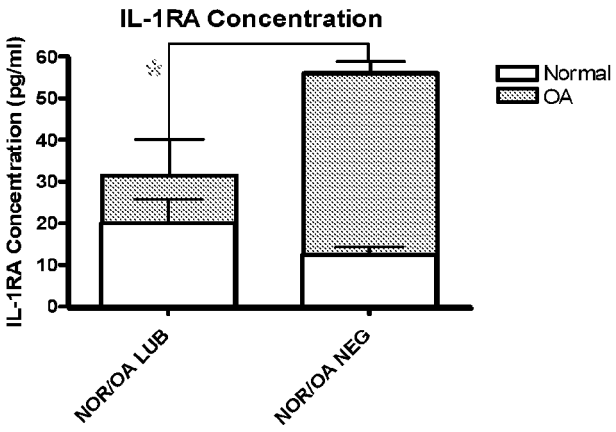


FIG. 14B

FIGURE 15

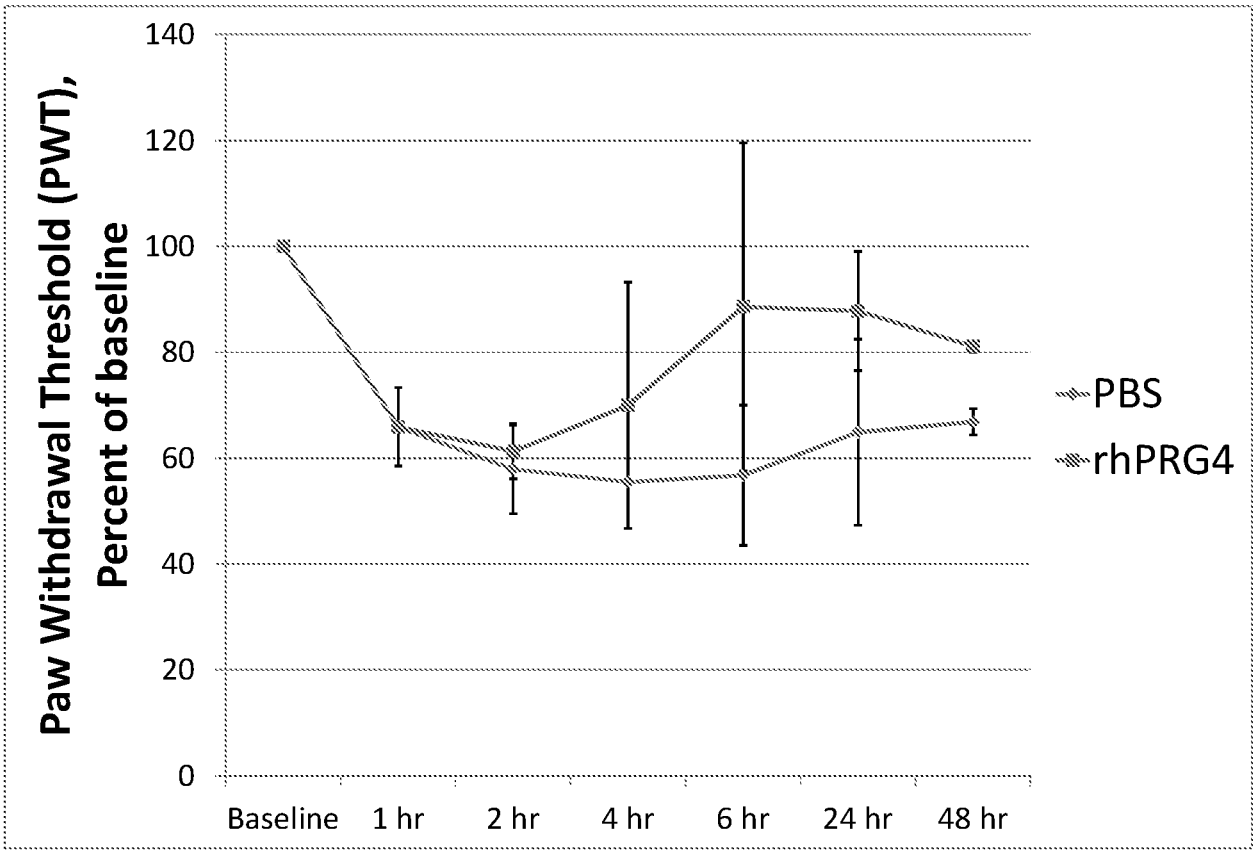


Fig. 15 Impact of intra-articular administration of recombinant human proteoglycan 4 (rhPRG4) on monosodium urate (MSU) crystal induced change in paw withdrawal pressure (PWT) in Male Lewis rats. Male Lewis rats (10 weeks ol; n=4) were injected with MSU suspension (50µl; 5 mg/ml; Invivogen, California) in their knee joints. At 1 hour following MSU injection, rat knee joints were treated with 50 µl phosphate buffered saline (PBS; n=2) or rhPRG4 (50µl; 2 mg/ml) (n=2). Paw withdrawal pressures were measured using an electronic Von Frey instrument, and data is present as percent change from baseline values.