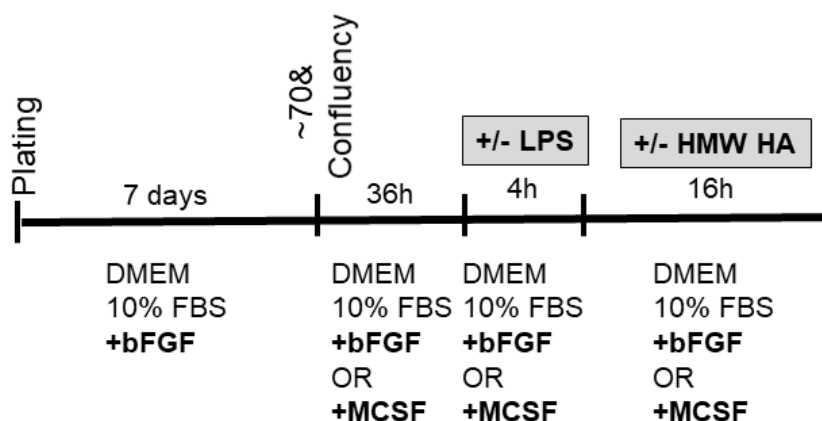


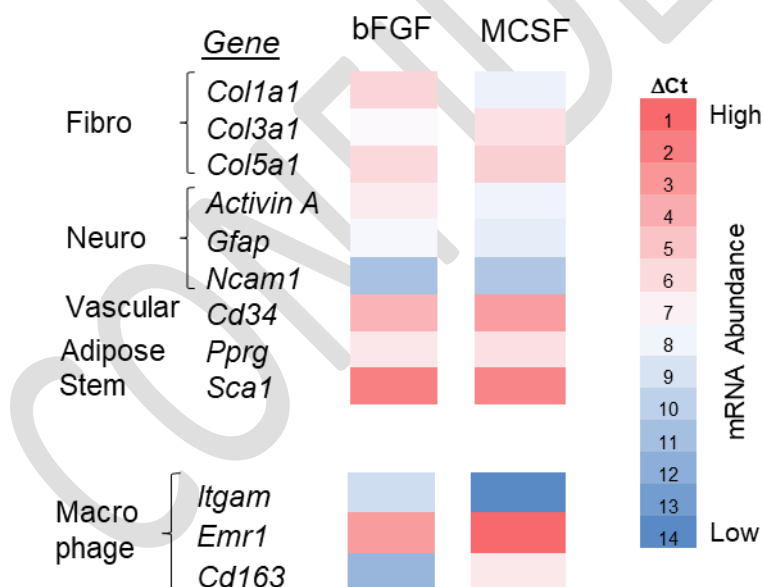
**Supplementary Materials:**

The following are available online at [www.mdpi.com/xxx/s1](http://www.mdpi.com/xxx/s1),

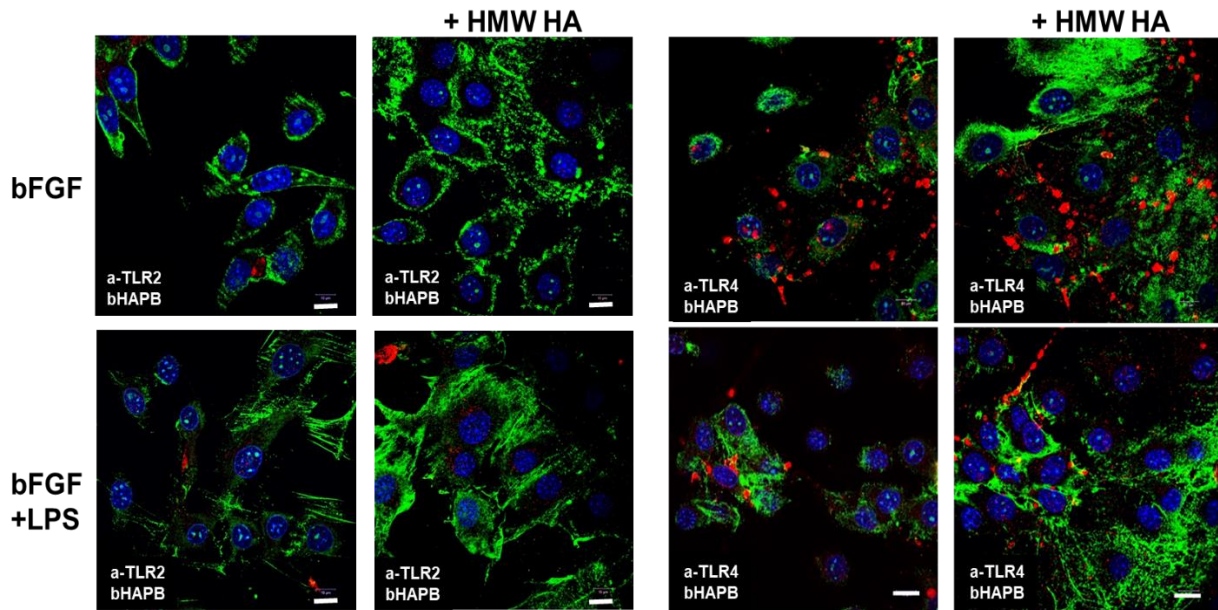
**Figure S1:** Schematic of Culture Timeline and Treatment Methods, **Figure S2:** Expression of Multipotent Progenitor Cell and Macrophage Markers in FLSC cultures maintained in bFGF or MCSF. **Figure S3:** Schematic of Epitope locations on Versican and Aggrecan Core Proteins for Peptide-Specific Antibodies used in western blots and confocal localization. **Figure S4:** Western Blotting of HC1 in commercially available preparations of Fetal Bovine Serum used in this study. **Table S1:** Listing of single gene Taqman Primers (a), Phagocytosis gene array (b) and TLR Signaling gene array. **Table S2:** Listing of Abbreviations used throughout the manuscript.



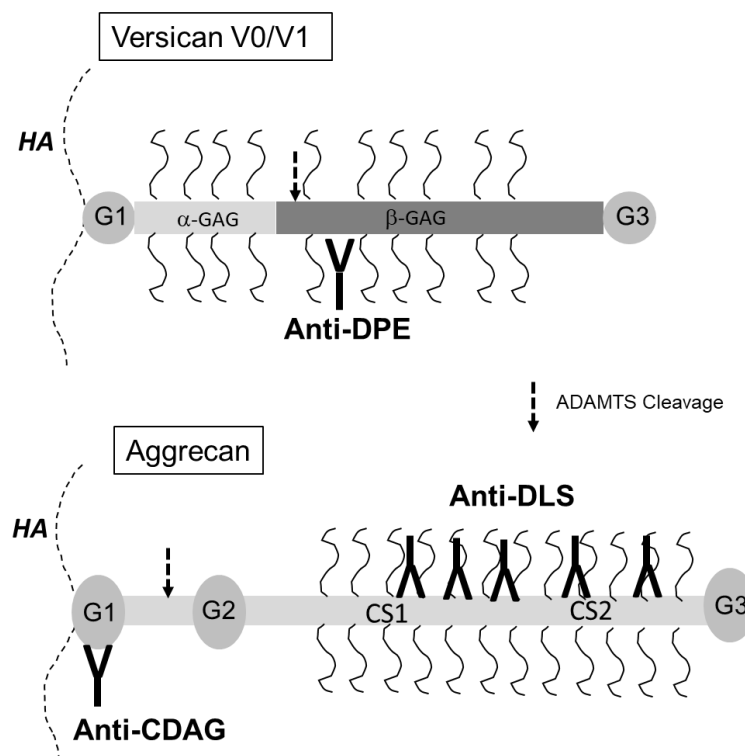
**Figure S1.** Schematic of Culture Timeline and Treatment Methods.



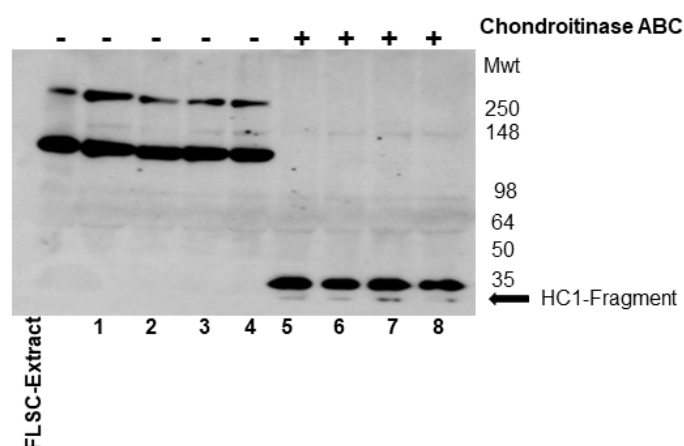
**Figure S2.** Expression of multipotent progenitor cell and macrophage markers in IFP cultures maintained in bFGF or MCSF.



**Figure S3.** Confocal Localization of TLR2 or TLR4 Proteins (Red Fluorescence) and HA (green fluorescence) in FLSC Cultures treated or not with LPS followed by treatment or not with exogenous HMW HA. TLR2 protein was associated with very few cells (5-10% of cells +ve within an imaged field), whereas TLR4 protein was more abundant, (40-50% of cells +ve within and imaged field). Neither protein abundances nor distributions were altered by addition of LPS and/or HMW HA. .



**Figure S4.** Schematic of Epitope locations on Versican and Aggrecan Core Proteins for Peptide-Specific Antibodies used in western blots and confocal localization. The versican antibody anti-DPE recognizes a regions in the  $\beta$ -GAG domain of V0/V1 isoform in both, the intact core protein and the ADAMTS-G1 cleavage product. The aggrecan antibody anti-CDAG recognize the globular G1 (HA binding) domain in the intact core protein and the ADAMTS-G1 cleavage product. The anti-DLS recognizes multiple epitope regions in the chondroitin sulfate (CS) domains 1 and 2.



**Figure S4.** Western Blotting of HC1 in commercially available preparations of Fetal Bovine Serum used in this study. Ten uL of FBS were diluted with 90 uL 0.1 M ammonium acetate, pH 7.5. 50uL portions were incubated at 37 C for 20 min in the absence (-) or presence (+) of Proteinase free Chondroitinase ABC, prior to SDS PAGE and western blotting with anti-HC antibody. Lanes 1, 2, 5, 6 show 2 different batches of FBS from Atlanta Biologics and lanes 3, 4, 7, 8 show 2 different batches of FBS from Sigma Aldrich.

**Table S1.** Listing of single gene Taqman Primers (a), TLR Signaling gene array (b) and Phagocytosis gene array.

| Protein:   | Gene:          | Taqman Primer: |
|--|----------------|----------------|
| Activin A  | <i>Acvr1</i>   | Mm01331069_m1  |
| Aggrecan   | <i>Acan</i>    | Mm00545794_m1  |
| CD163 Molecule                                   | <i>Cd163</i>   | Mm00474091_m1  |
| CD34 Molecule                                    | <i>Cd34</i>    | Mm00519283_m1  |
| CD44 Molecule                                    | <i>Cd44</i>    | Mm01277161_m1  |
| Cell Migration Inducing Hyaluronidase            | <i>Cemip</i>   | Mm00472921_m1  |
| Cell Surface Hyaluronidase                       | <i>Tmem2</i>   | Mm00459599_m1  |
| Collagen Type 1 alpha 1                          | <i>Col1a1</i>  | Mm00801666_g1  |
| Collagen Type 3 alpha 1                          | <i>Col3a1</i>  | Mm00802300_m1  |
| Collagen Type 5 alpha 1                          | <i>Col5a1</i>  | Mm00489299_m1  |
| EGF module-containing mucin-like receptor        | <i>Emr1</i>    | Rn01527631_m1  |
| Glial Fibrillary Acidic Protein                  | <i>Gfap</i>    | Mm01253033_m1  |
| Hyaluronan Synthase 1                            | <i>Has1</i>    | Mm03048195_m1  |
| Hyaluronan Synthase 2                            | <i>Has2</i>    | Mm00515089_m1  |
| Hyaluronan Synthase 3                            | <i>Has3</i>    | Mm00515092_m1  |
| Hyaluronidase 1                                  | <i>Hyal1</i>   | Mm00476206_m1  |
| Hyaluronidase 2                                  | <i>Hyal2</i>   | Mm01230688_g1  |
| Integrin Subunit Alpha M                         | <i>Itgam</i>   | Mm00434455_m1  |
| Interleukin 6                                    | <i>Il6</i>     | Mm00446190_m1  |
| Lubricin   | <i>Prg4</i>    | Mm01284582_m1  |
| Neural Cell Adhesion Molecule 1                  | <i>Ncam1</i>   | Mm01149710_m1  |
| Nitric Oxide Synthase 2                          | <i>Nos2</i>    | Mm00440502_m1  |
| Pentraxin 3                                      | <i>Ptx3</i>    | Mm00477268_m1  |
| Peroxisome proliferator-activated receptor gamma | <i>Pparg</i>   | Mm00440940_m1  |
| TSG6 (TNF-inducible gene 6 protein)              | <i>Tnfaip6</i> | Mm00493736_m1  |
| Versican   | <i>Vcan</i>    | Mm01283063_m1  |

(a)

|          | 1                         | 2                      | 3                      | 4                       | 5                       | 6                        | 7                         | 8                         | 9                       | 10                       | 11                        | 12                       |
|----------|---------------------------|------------------------|------------------------|-------------------------|-------------------------|--------------------------|---------------------------|---------------------------|-------------------------|--------------------------|---------------------------|--------------------------|
| <b>A</b> | 18s rRNA<br>Hs99999901_s1 | Btk<br>Mm00442712_m1   | Casp8<br>Mm00802247_m1 | Ccl2<br>Mm00441242_m1   | Cd14<br>Mm00438094_g1   | Cd80<br>Mm00711660_m1    | Cd86<br>Mm00444543_m1     | Cebpb<br>Mm00843434_s1    | Chuk<br>Mm00432529_m1   | Clec4e<br>Mm00490870_m1  | Csf2<br>Mm01290062_m1     | Csf3<br>Mm00438334_m1    |
| <b>B</b> | Cxcl10<br>Mm00445235_m1   | Elk1<br>Mm00468230_m1  | Fadd<br>Mm00438861_m1  | Fos<br>Mm00487425_m1    | Hmgb1<br>Mm00849805_gH  | Hras<br>Mm01275929_m1    | Aglf1<br>Mm00802809_m1    | Hspa1a<br>Mm01159846_s1   | Hspd1<br>Mm00849835_g1  | Ilnb1<br>Mm00439552_s1   | Ilnf<br>Mm01168134_m1     | Ikbkb<br>Mm01222247_m1   |
| <b>C</b> | Il10<br>Mm00439614_m1     | Il12a<br>Mm00434165_m1 | Il1a<br>Mm00439620_m1  | Il1b<br>Mm01336189_m1   | Il1r1<br>Mm00434237_m1  | Il2<br>Mm00434256_m1     | Il6<br>Mm00446190_m1      | Il6ra<br>Mm00439653_m1    | Irak1<br>Mm01193538_m1  | Irak2<br>Mm01184677_m1   | Irf1<br>Mm01288580_m1     | Irf3<br>Mm00516779_m1    |
| <b>D</b> | Jun<br>Mm00495062_s1      | Lta<br>Mm00440228_gH   | Muc13<br>Mm00495397_m1 | Ly86<br>Mm00440240_m1   | Ly96<br>Mm01227593_m1   | Map2k3<br>Mm00435950_m1  | Map2k4<br>Mm00436508_m1   | Map3k1<br>Mm00803707_m1   | Map3k7<br>Mm00554516_g1 | Mapk8<br>Mm00489541_m1   | Mapk8ip3<br>Mm01301203_m1 | Mapk9<br>Mm00444239_m1   |
| <b>E</b> | Myd88<br>Mm00440338_m1    | NfkB1<br>Mm00476361_m1 | NfkB2<br>Mm00479807_m1 | NfkBia<br>Mm00477798_m1 | NfkBib<br>Mm00456849_m1 | NfkBil1<br>Mm00447990_m1 | NfkB<br>Mm00555264_m1     | Nr2c2<br>Mm01182440_m1    | Pel1<br>Mm00481051_m1   | Pglyrp1<br>Mm00437150_m1 | Ppara<br>Mm00440939_m1    | Eif2ak2<br>Mm01235643_m1 |
| <b>F</b> | Ptgs2<br>Mm00478374_m1    | Rel<br>Mm01239661_m1   | Rela<br>Mm00501346_m1  | Ripk2<br>Mm00446816_m1  | Tbk1<br>Mm00451150_m1   | Ticam1<br>Mm00844508_s1  | Ticam2<br>Mm01260003_m1   | Tirap<br>Mm00446502_m1    | Tir1<br>Mm00446095_m1   | Tir2<br>Mm00442346_m1    | Tir3<br>Mm00628112_m1     | Tir4<br>Mm00445273_m1    |
| <b>G</b> | Tlr5<br>Mm00546288_s1     | Tlr6<br>Mm02529782_s1  | Tlr7<br>Mm00446590_m1  | Tlr8<br>Mm04209873_m1   | Tlr9<br>Mm00446193_m1   | Tnf<br>Mm00443258_m1     | Tnfrsf1a<br>Mm00437121_m1 | Tnfrsf1a<br>Mm00441883_g1 | Tollip<br>Mm00445841_m1 | Tradd<br>Mm01251031_g1   | Tra6<br>Mm00493836_m1     | Ube2n<br>Mm00779119_s1   |
| <b>H</b> | Ube2v1<br>Mm01249540_g1   | Gapdh<br>Mm99999915_g1 | Hprt<br>Mm00446968_m1  | Gusb<br>Mm00446953_m1   | Actb<br>Mm00607939_s1   | B2m<br>Mm00437762_m1     | Hmbs<br>Mm00660262_g1     | Ipo8<br>Mm01255158_m1     | Pgk1<br>Mm00435617_m1   | Rplp2<br>Mm00782638_s1   | Tbp<br>Mm00446973_m1      | Ttrc<br>Mm00441941_m1    |

(b)

|          | 1                         | 2                       | 3                       | 4                        | 5                        | 6                        | 7                       | 8                       | 9                         | 10                      | 11                       | 12                       |
|----------|---------------------------|-------------------------|-------------------------|--------------------------|--------------------------|--------------------------|-------------------------|-------------------------|---------------------------|-------------------------|--------------------------|--------------------------|
| <b>A</b> | 18s rRNA<br>Hs99999901_s1 | Adipoq<br>Mm00456425_m1 | Ager<br>Mm01134790_g1   | Anxa1<br>Mm00440225_m1   | Axl<br>Mm00437221_m1     | C3<br>Mm00437838_m1      | Calr<br>Mm00482936_m1   | Cd14<br>Mm00438094_g1   | Cd36<br>Mm01135198_m1     | Cd44<br>Mm01277163_m1   | Cd47<br>Mm00495011_m1    | Ceacam3<br>Mm01257219_m1 |
| <b>B</b> | Clec7a<br>Mm01183349_m1   | Clic4<br>Mm01179940_mH  | Cnn2<br>Mm01169510_m1   | Colec12<br>Mm01236242_m1 | Crk<br>Mm00467065_m1     | Crp<br>Mm00432680_g1     | Csf1<br>Mm00432686_m1   | Csf2<br>Mm01290062_m1   | Csk<br>Mm00432751_m1      | Cyp2s1<br>Mm00512037_m1 | Dock1<br>Mm01269874_m1   | Dock2<br>Mm00473720_m1   |
| <b>C</b> | Elmo1<br>Mm000519109_m1   | Fas<br>Mm01204974_m1    | Fcer1g<br>Mm02343757_m1 | Fcgr1<br>Mm00438874_m1   | Fcgr2b<br>Mm00438875_m1  | Fcgr3<br>Mm00438882_m1   | Fyn<br>Mm00433373_m1    | Gulp1<br>Mm00518428_m1  | Ilnf<br>Mm01168134_m1     | Irf1<br>Mm00516117_m1   | Isgec1<br>Mm01182566_m1  | Ilgam<br>Mm00434455_m1   |
| <b>D</b> | Ilgav<br>Mm00434486_m1    | Ilgb2<br>Mm00434513_m1  | Lyn<br>Mm01217488_m1    | Mapk14<br>Mm01301009_m1  | Marco<br>Mm00440265_m1   | Mbl2<br>Mm00487623_m1    | Mcoln3<br>Mm00460328_m1 | Merck<br>Mm00434920_m1  | Mfge8<br>Mm00500549_m1    | Mif<br>Mm03938638_s1    | Msn<br>Mm00447889_m1     | Myd88<br>Mm00440338_m1   |
| <b>E</b> | Nod1<br>Mm00805062_m1     | Pecam1<br>Mm01242584_m1 | Pik3cb<br>Mm00659576_m1 | Pip5k1a<br>Mm00476829_m1 | Pla2g4a<br>Mm00447040_m1 | Pla2g5<br>Mm00448162_m1  | Pid1<br>Mm01289339_m1   | Pid2<br>Mm00447066_m1   | Prkce<br>Mm00440894_m1    | Pros1<br>Mm01343426_m1  | Pten<br>Mm00477208_m1    | Rab5a<br>Mm00727887_s1   |
| <b>F</b> | Rab7<br>Mm01183732_g1     | Rac1<br>Mm01201653_mH   | Rac2<br>Mm00485472_m1   | Rala<br>Mm00450933_m1    | Ralb<br>Mm00469677_m1    | Rapgef3<br>Mm00522941_m1 | Rhoa<br>Mm00834507_g1   | Scarb1<br>Mm00450234_m1 | Serpine1<br>Mm00435860_m1 | Sitpd<br>Mm00486060_m1  | Siglec1<br>Mm00488332_m1 | Sirpb1a<br>Mm02525668_u1 |
| <b>G</b> | Stab2<br>Mm00454684_m1    | Six18<br>Mm00452814_m1  | Syk<br>Mm01333032_m1    | Tgm2<br>Mm004436987_m1   | Ticam1<br>Mm00844508_s1  | Ticam1<br>Mm01207404_m1  | Tir3<br>Mm00446193_m1   | Tnf<br>Mm00443258_m1    | Tnfrsf11<br>Mm00441906_m1 | Vamp7<br>Mm00807071_m1  | Vav1<br>Mm01232047_m1    | Was<br>Mm00494167_m1     |
| <b>H</b> | Wnt5a<br>Mm00437347_m1    | Gapdh<br>Mm99999915_g1  | Hprt<br>Mm00446968_m1   | Gusb<br>Mm00446953_m1    | Actb<br>Mm00607939_s1    | B2m<br>Mm00437762_m1     | Hmbs<br>Mm00660262_g1   | Ipo8<br>Mm01255158_m1   | Pgk1<br>Mm00435617_m1     | Rplp2<br>Mm00782638_s1  | Tbp<br>Mm00446973_m1     | Ttrc<br>Mm00441941_m1    |

(c)