**Table S1. Antibodies used for flow cytometry**

| Antibodies | Isotype | Conjugate | Supplier Catalog No. |
|---|---|---|---|
| **Isotype control** | | | |
| Mouse $IgG_1$ κ | - | FITC | BD Bioscience 555909 |
| Mouse $IgG_1$ κ | - | PE | BD Pharmingen ™ 555749 |
| Mouse IgM κ | - | None | Biolegend 401601 |
| Rabbit polyclonal | - | None | Biolegend 910801 |
| **Primary antibodies** | | | |
| Anti-CD31/PCAM-1 | Mouse $IgG_1$ | FITC | BD Pharmingen™ 555445 |
| Anti- CD54/ICAM-1 | Mouse $IgG_1$ | PE | BD Bioscience 555511 |
| Anti-CD62P/P-selectin | Mouse $IgG_1$ | FITC | BD Pharmingen™ 555523 |
| Anti-CD62E/E-selectin | Mouse $IgG_1$ | PE | BD Pharmingen™ 551145 |
| Anti-CD45 | Mouse $IgG_1$ | FITC | BD Pharmingen™ 555482 |
| Anti-CD105/Endoglin | Mouse $IgG_1$ | PE | R&D Systems FAB10971P |
| Anti-CD106/VCAM-1 | Mouse $IgG_1$ | PE | BD Pharmingen™ 555647 |
| Anti-heparan sulfate (10E4) | Mouse IgM κ | None | Amsbio 370255-1 |
| Anti-glypican-4 | Rabbit polyclonal | None | Acris AP02029SU |
| Anti-chondroitin sulfate (CS-56) | Mouse IgM | None | ThermoScientific MA1-83055 |
| Anti-biglycan | Rabbit polyclonal | None | ThermoScientific PA5-13700 |
| **Secondary antibodies** | | | |
| Anti-mouse IgM | - | FITC | BioLegend® 406506 |
| Anti-rabbit IgG | - | PE | BioLegend® 406421 |

**Table S2. Correlation matrix between MMP2 and HSPG/CSPG genes in fold differences on day 7 over day 0**

| Group | BGN | GPC1 | GPC3 | GPC4 | HSPG2 | MXRA5 | SDC1 | SDC2 | SDC4 |
|---|---|---|---|---|---|---|---|---|---|
| **HUVECs without TNF-α stimulation** | 0.64 | -0.15 | 0.11 | 0.64 | 0.45 | 0.10 | 0.05 | 0.88 | 0.40 |
| **p-value** | 0.062 | 0.685 | 0.802 | 0.097 | 0.230 | 0.832 | 0.952 | 0.003* | 0.297 |
| **HUVECs with TNF-α stimulation** | 0.55 | 0.15 | -0.02 | 0.07 | 0.34 | -0.24 | 0.30 | 0.46 | 0.42 |
| **p-value** | 0.128 | 0.699 | 0.955 | 0.863 | 0.372 | 0.542 | 0.428 | 0.211 | 0.265 |
| **HUAECs without TNF-α stimulation** | 0.81 | -0.56 | -0.04 | 0.30 | -0.22 | 0.59 | -0.39 | 0.65 | -0.04 |
| **p-value** | 0.009* | 0.120 | 0.923 | 0.429 | 0.563 | 0.095 | 0.306 | 0.059 | 0.912 |
| **HUAECs with TNF-α stimulation** | 0.95 | 0.10 | 0.13 | -0.35 | 0.61 | -0.42 | 0.52 | 0.40 | 0.40 |
| **p-value** | 0.000* | 0.997 | 0.834 | 0.393 | 0.148 | 0.850 | 0.310 | 0.276 | 0.311 |

BGN, biglycan; GPC1, glypican-1; GPC3, glypican-3; GPC4, glypican-4; HSPG2, heparan sulphate proteoglycan-2; HUAECs, human umbilical artery endothelial cells; HUVECs, human umbilical vein endothelial cells; MXRA5, matrix-remodeling-associated protein 5; SDC1, syndecan-1; SDC2, syndecan-2; SDC4, syndecan-4; TNF-α, tumor necrosis factor-α.
* significant difference

**Table S3. Correlation matrix between GPC4 and genes for cholesterol transport in fold changes from day 0 to day 7 and differenced after TNF-α stimulation**

| Group | ABCA1 | ABCG1 | LCAT | LDL-R | PCSK9- | VLDL-R |
|---|---|---|---|---|---|---|
| Fold changes from day 0 to day 7 | | | | | | |
| HUVECs without TNF-α | 0.02 | 0.12 | 0.55 | 0.25 | -0.23 | 0.08 |
| p-value | 0.612 | 0.644 | 0.052 | 0.408 | 0.585 | 0.753 |
| HUVECs with TNF-α | -0.64 | -0.52 | 0.44 | -0.57 | -0.36 | 0.05 |
| p-value | 0.063 | 0.155 | 0.237 | 0.107 | 0.348 | 0.893 |
| HUAECs without TNF-α | 0.36 | 0.68 | 0.22 | -0.23 | -0.04 | 0.33 |
| p-value | 0.348 | 0.042* | 0.565 | 0.558 | 0.927 | 0.382 |
| HUAECs with TNF-α | 0.22 | -0.11 | 0.05 | -0.50 | -0.52 | 0.45 |
| p-value | 0.596 | 0.795 | 0.914 | 0.211 | 0.189 | 0.263 |
| Fold changes after TNF-α stimulation | | | | | | |
| HUVECs day 0 | 0.36 | 0.11 | -0.42 | 0.29 | -0.60 | -0.01 |
| p-value | 0.342 | 0.771 | 0.264 | 0.444 | 0.086 | 0.975 |
| HUVECs day 7 | -0.07 | 0.12 | 0.39 | 0.03 | -0.14 | 0.60 |
| p-value | 0.838 | 0.759 | 0.297 | 0.970 | 0.742 | 0.097 |
| HUAECs day 0 | -0.60 | -0.70 | 0.62 | -0.67 | -0.55 | -0.70 |
| p-value | 0.089 | 0.034* | 0.076 | 0.047* | 0.125 | 0.035* |
| HUAECs day 7 | 0.18 | 0.58 | 0.39 | -0.03 | 0.47 | 0.22 |
| p-value | 0.672 | 0.129 | 0.342 | 0.949 | 0.241 | 0.599 |

ABCA1, ATP binding cassette subfamily A member 1; ABCG1, ATP binding cassette subfamily G member 1; HUAECs, human umbilical artery endothelial cells; HUVECs, human umbilical vein endothelial cells; LCAT, lecithin-cholesterol acyltransferase; LDL-R, low-density lipoprotein receptor; PCSK9, proprotein convertase subtilisin kexin type 9; VLDL-R, very low-density lipoprotein receptor. * significant difference

**Table S4. Primers used for qPCR analysis**

| Function | Gene | mRNA sequence accession number | Primer sequence | Amplicon |
|---|---|---|---|---|
| Sulfotransferase | CHST7 | NM_019886.3 | F: ATGCGTCTGCTCGCCTAC<br>R: GAGAGTGTGACAGATTGCCCC | 216 |
| | CHST15 | NM_015892.4 | F: CTGGACCTCTTTGACCTGGC<br>R: CCATCCGTGCTGTTGTCGTA | 164 |
| HSPC or CSPG | GPC1 | NM_002081.2 | F: AGAAGCTGGTCTCCGAAGC<br>R: ACCTCGGGGTTGTTGATCTG | 199 |
| | GPC3 | NM_001164617.1 | F: CCAAAAGGCAGCAAGGAATGG<br>R: ACCGCAGTCTCCACTTTCAA | 199 |
| | GPC4 | NM_001448.2 | F: GTCTCGTGACTGTGAAGCCA<br>R: TCTGCCACCATCAGCATAGC | 124 |
| | HSPG2 | NM_001291860.1 | F: CAGCATCTCAGGAGACGACC<br>R: CTCCAGCGTGTCTACCACAG | 175 |
| | BGN | NM_001711.5 | F: GACAACAACAAGTTGGCCAGG<br>R: GACAGAAGTCGTTGACACCCA | 112 |
| | MXRA5 | NM_015419 | F: ATCCTTGTGCCTGCTACGTC<br>R: TCCAACTTGGTCAGTCCTGC | 160 |
| | SDC1 | NM_001006946.1 | F: GGTGCTGGGAGGGGTCATTG<br>R: TTGTTTCGGCTCCTCCAAGG | 127 |

| | | | | |
|---|---|---|---|---|
| | SDC2 | NM_002998.3 | F: GACTACGCTTCTGCGTCTGG<br>R: TATTCAGCGTCGTGGTTTCCA | 130 |
| | SDC4 | NM_002999.3 | F: ACAAGGTGTCAATGTCCAGCA<br>R: ACGATGCCACCCACAATCAG | 88 |
| Degradation enzyme | HSPE1 | NM_006665.5 | F: TGGCACCAAGACAGACTTCC<br>R: AGGGCCATTCCAACCGTAAC | 152 |
| | GALNS | NM_000512.4 | F: AGCTCAACGTGTGCAACTGG<br>R: AGAGGCACTTCTTGGGAATGG | 105 |
| | MMP2 | NM_001127891 | F: GTGGATGCCGCCTTTAACTG<br>R: TTCCAGGCATCTGCGATGAG | 131 |
| Collagen | COL4A5 | NM_000495.4 | F: TTCAAGCATTGGTCTTCCAGG<br>R: CCAGGAGGGCCACTAATACC | 210 |
| Cholesterol transport | LCAT | NM_000229.1 | F: AAGGACCGCTTTATTGATGGC<br>R: TGGTGGTTATGCGCTGCTC | 148 |
| | ABCA1 | NM_005502.3 | F: TCTGAGCTTTGTGGCCTACC<br>R: CTTGCTCGGGAAGGGAGATG | 123 |
| | ABCG1 | NM_004915.3 | F: AGCGCCAAACTCTTCGAGC<br>R: CAGCCGACTGTTCTGATCACC | 192 |
| | LDL-R | NM_000527.4 | F: ACTCGCTGGTGACTGAAAACA<br>R: GGCGGTTGGCACTGAAAATG | 243 |
| | VLDL-R | NM_003383.4 | F: GTGCACAAATGGTCGCTGTA<br>R: TTCCATCGGCTGGGAACAC | 153 |
| | PCSK9-2 | NR_110451.1 | F: TCAAGGAGCATGGAATCCCG<br>R: ACACACGTGTTGTCTACGGC | 136 |

| | | | | |
|---|---|---|---|---|
| Non-sulfated GAG | LYVE1 | NM_006691.3 | F: TCCAGTGAGCCGACAGTTTG<br>R: GCCACCGAGTAGGTACTGTC | 162 |
| | CD44 | NM_000610 | F: GGACAAGTTTTGGTGGCACG<br>R: TCCGTCCGAGAGATGCTGTA | 141 |
| | HYAL1 | NM_153285.2 | F: TGGGAAAATACAAGAACCAAGGAAT<br>R: TCACGTTCAGGATGAAGGGC | 85 |
| | HYAL2 | NM_003773.4 | F: CGGGGCTTAGTGAGATGGAC<br>R: GTCTCCGTGCTTGTGGTGTA | 109 |
| Housekeeping | YWHAZ | NM_003406.3 | F: AACAGCAGATGGCTCGAGAA<br>R: GCAACCTCAGCCAAGTAACG | 175 |

**Table S5. Antibodies used for immunofluorescent staining**

| Antibodies | Isotype | Dilution | Supplier Catalog No. |
|---|---|---|---|
| **Primary antibodies** | | | |
| Anti-glypican-4 | Rabbit polyclonal | 1:100 | Acris/Origene AP02029SU-N |
| Anti-heparan sulfate | Mouse polyclonal | 1:100 | Amsbio 370255-S |
| Anti-Δ-heparan sulfate | Mouse monoclonal | 1:100 | Amsbio 370260-1 |
| Anti-VCAM-1 (BBIG-V1) | Mouse monoclonal | 1:100 | R&D Systems BBA5 |
| Anti-E-selectin (BBIG-E4) | Mouse monoclonal | 1:100 | R&D Systems BBA13 |
| **Secondary antibodies** | | | |
| Anti-rabbit IgG-Alexa 488 | - | 1:500 | Molecular Probes A11008 |
| Anti-mouse IgG-Alexa 555 | - | 1:500 | Molecular Probes A21422 |

**Table S6. Antibodies used for immunohistochemistry staining**

| Antibodies | Isotype | Dilution | Supplier Catalog No. |
|---|---|---|---|
| **Primary antibodies** | | | |
| Anti-Glypican-4 | Rabbit polyclonal | 1:800 | Acris/Origene AP02029SU-N |
| Anti-heparan sulfate | Mouse polyclonal | 1:200 | Amsbio 370255-S |
| Anti-syndecan-4 | Rabbit polyclonal | 1:800 | Biozol |
| Anti-CD68 | Mouse polyclonal | Ready to use | Agilent |
| **Secondary antibodies** | | | |
| Goat-anti-rabbit-Ig | polyclonal | 1:800 | Agilent |
| Rabbit-anti-mouse-Ig | - | Ready to use | Agilent |

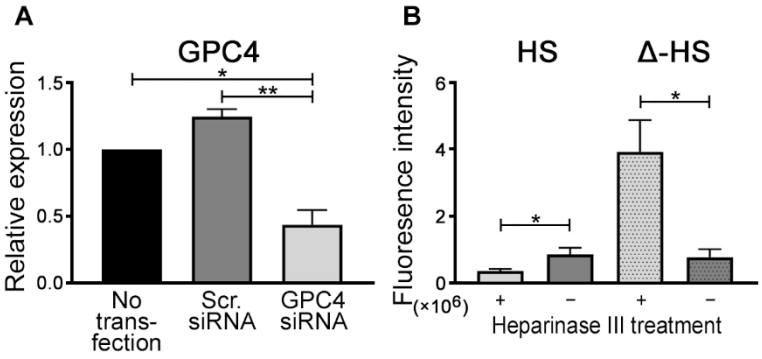


**Figure S1. Verification of GPC4 and HS disruption**

Relative mRNA expression of GPC4 in siRNA-transfected HUVECs over non-transfected HUVECs ($n$ = 3) (A). GPC4 mRNA was significantly reduced in HUVECs transfected with GPC4 siRNA compared with those without transfection ($p < 0.05$) or those transfected with scrambled siRNA (1-way ANOVA with repeated measures with Holm-Sidak post hoc test; $p < 0.01$).

Verification of heparinase III treatment in HUVECs under laminar flow conditions ($n$ = 4) (B). By heparinase III treatment, fluorescence intensities for HS signaling was reduced (left, paired t-test; $p < 0.05$) and those for ΔHS signaling was increased (right, paired t-test; $p < 0.05$), verifying the HS degradation by heparinase III. Data are expressed as mean ± SEM. * $p < 0.05$, ** $p < 0.01$. GPC4: glypican-4, HS: heparan sulfate, Scr. siRNA: scrambled small interfering RNA.

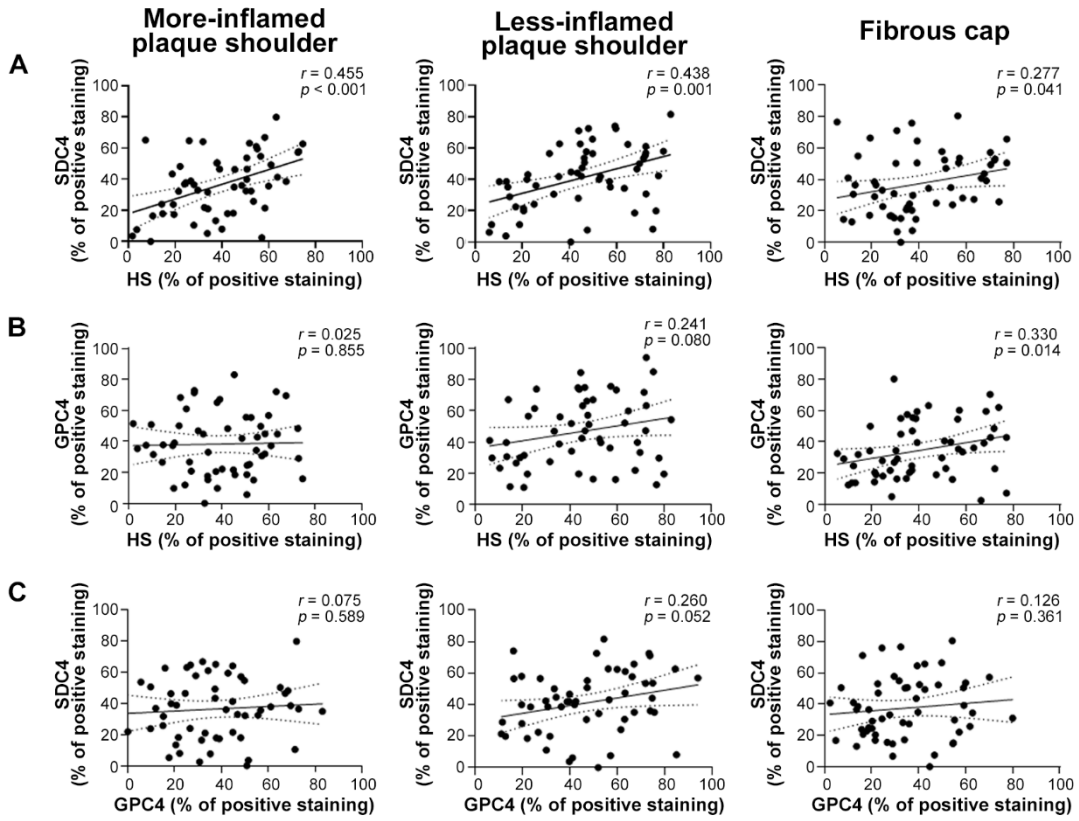


**Figure S2. Correlation analysis between the GCX-components in the two PSs and the FC in all plaque sections**

Pearson correlation was done between SDC4 and HS (A), GPC4 and HS (B) and SDC4 with GPC4 (C) of the percentage results described in Figure 7. Graphs showing simple linear regression with 95% confidence interval (dotted line) r: Pearson coefficient, PS: plaque shoulder, GPC4: glypican-4, HS: heparan sulfate, SDC4: syndecan-4.

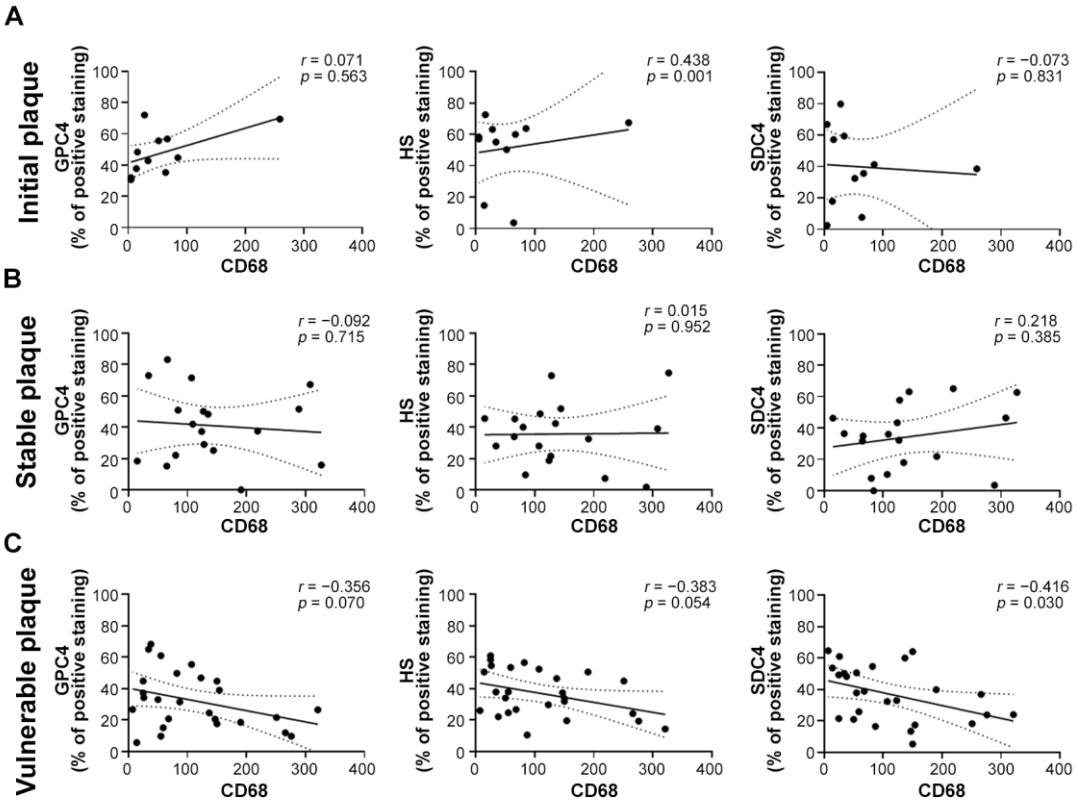


**Figure S3. Correlation analysis between the GCX-components and CD68 positive cells in the more-inflamed PSs in initial (A), stable (B) and vulnerable (C) plaque sections**

Pearson or Spearman correlation between GPC4, HS, and SDC-4 with CD68 were done in the more-inflamed PS region. Graphs showing simple linear regression with 95% confidence interval (dotted line). r: Pearson coefficient; ρ: Spearman coefficient, GPC4: glypican-4.

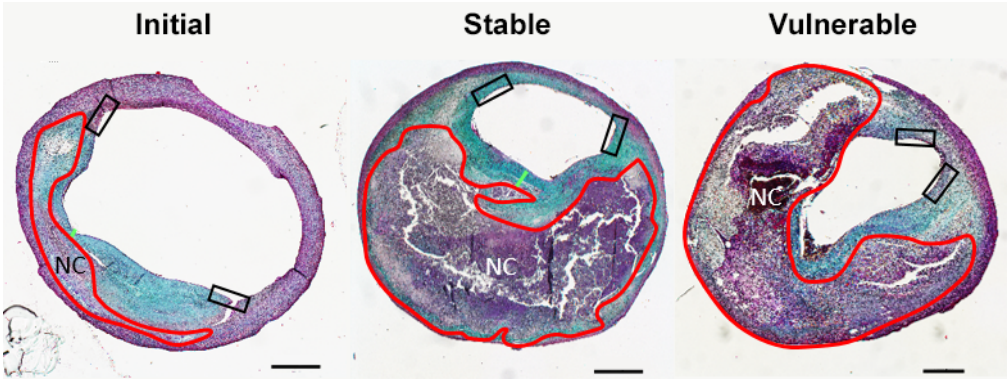


**Figure S4. Representative pictures of plaque sections stained by modified Crossmon's Trichrom staining**

Initial (left), stable (middle), and vulnerable (right) plaque sections. Images were taken at 20x magnification with an Olympus IX70 inverted microscope with NIS elements® software. The necrotic core (NC, red), the two plaque shoulders (black) and the thinnest part of the FC (green) are indicated. Scale bar = 1000 µm.