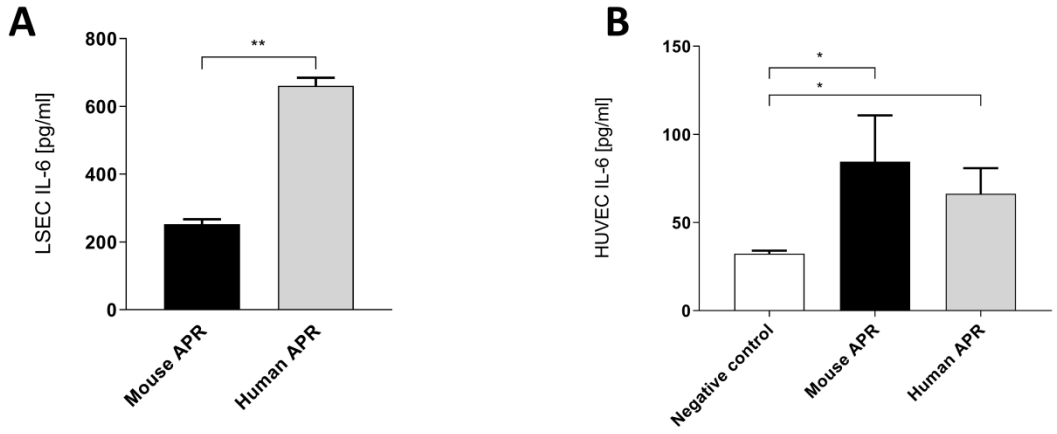


**Figure S1.** Human and mouse activated platelet releasates were both able to induce the production of interleukin-6 by liver sinusoidal endothelial cells or human umbilical vein endothelial cells. A: Human APR showed a stronger effect on LSEC IL-6 production than mouse APR. B: Cultured HUVEC incubated with mouse or human APR. NC: negative control, culture medium. Presented data are representative of 2 independent experiments. ** $p$ value between 0.001 and 0.01. * $p$ value between 0.01 and 0.05 ($t$-test).

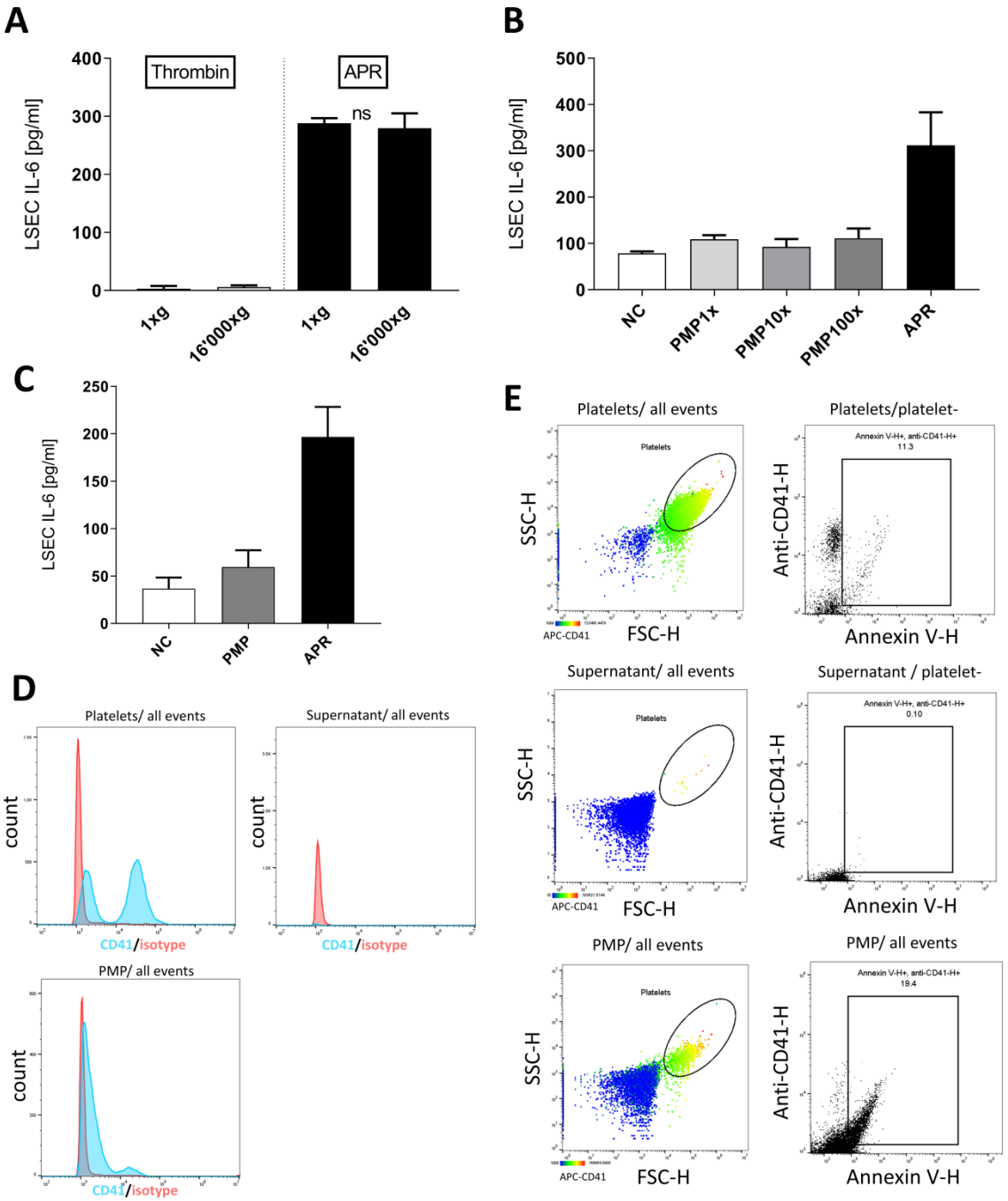


**Figure S2.** Platelet microparticles are not implicated in interleukin-6 secretion by liver sinusoidal endothelial cells. **A:** Mouse APR depleted of PMP induced the secretion of IL-6 by LSEC. NC: negative control, PBS, ns: not significant (t-test) **B:** TRAP-6 generated PMP at various concentration did not affect the release of IL-6 by LSEC, $n = 2$. NC: negative control, PBS. **C:** Platelet freeze-thawing-derived PMP did not induce the secretion of IL-6 by LSEC. NC: negative control, PBS. Ran in 4 to 5 replicas. **D:** Histogram of Isotype control and anti-human CD41 staining of human platelets, human PMP and their supernatant. E: platelets were identified by their side scatter and forward scatter morphology and high expression of CD41. Right: after inverted platelet gate (platelet-) selection, expression of CD41 was plotted against phosphatidylserine (annexin V) expression. PMP were identified as double positive for CD41 and annexin V. If not otherwise specified, presented data are representative of 2 to 4 independent experiments.

**Table S1.** Proteins identified in fraction 09. Dataset matching of mass spectroscopy (MS) dataset with human APR proteome, according to Wijten et al. (24). Listed proteins correspond to protein clusters or individual proteins. Peptide column indicates the number of peptides identified by MS analysis. MW: molecular weight, identity indicates the percentage of common amino acid sequences between human and mouse.

| # | Gene name | Protein | Peptide | MW [kDa] | Identity [%] |
|---|---|---|---|---|---|
| 1 | ECM1 | Extracellular matrix protein 1 | 10 | 61 | 66.8 |
| 2 | TGFB1 | Transforming growth factor beta-1 | 5 | 44 | 89.7 |
| 3 | TGFBI | Transforming growth factor, beta-induced | 8 | 75 | 90.6 |
| 4 | CLEC3B | Tetranectin | 2 | 23 | 79.2 |
| 5 | ITIH3, ITH4 | Inter-alpha-trypsin inhibitor | 22,34 | 100, 103 | 84.9, 64.3 |
| 6 | PLG | Plasminogen | 4 | 91 | 79.1 |
| 7 | SERPINA1 | Alpha-1-antitrypsin | 29 | 47 | 57.52 |
| 8 | SERPINA3 | Alpha-1-antichymotrypsin | 22 | 48 | na |
| 9 | SERPINC1 | Antithrombin-III | 4 | 53 | 87.3 |
| 10 | SRGN | Serglycin | 4 | 18 | 48.1 |
| 11 | C3 | Complement factor 3 | 152 | 187 | 76.8 |
| 12 | C4A | Complement factor 4A | 79 | 193 | 67.8 |
| 13 | C6 | Complement factor 6 | 18 | 105 | na |
| 14 | C8B | Complement factor 8B | 17 | 68 | 75.0 |
| 15 | C9 | Complement factor 9 | 4 | 63 | 57.6 |
| 16 | CFB | Complement factor B | 22 | 86 | 83.6 |
| 17 | CFH | Complement factor H | 33 | 139 | 61.2 |
| 18 | PPBP | Platelet basic protein | 2 | 14 | 47.7% |

| | | | | | |
|---|---|---|---|---|---|
| 19 | FGA, FGB,FGG | Fibrinogen | 3, 4, 3 | 95, 56, 52 | 66,1, 81.4, 79.5 |
| 20 | FN1 | Fibronectin | 62 | 263 | 88.2 |
| 21 | HRG | Histidine-rich glycoprotein | 12 | 60 | 60.9 |
| 22 | LGALS3BP | Galectin-3-binding protein | 7 | 65 | 67.7 |
| 23 | NID1 | Nidogen-1 | 26 | 136 | 85 |
| 24 | NID2 | Nidogen-2 | 13 | 151 | 78.5 |
| 25 | THBS1 | Thrombospondin-1 | | | 94.8 |
| 26 | TNXB | Tenascin-X | 5 | 458 | 71.9 |
| 27 | VTN | Vitronectin | 8 | 54 | 73.6 |
| 28 | VWF | Von Willebrand factor | 29 | 309 | 83.2 |
| 29 | AHSG | Alpha-2-HS-glycoprotein | 3 | 39 | 57.2 |
| 30 | APOA1 | Apolipoprotein A-I | 53 | 31 | 65.2 |
| 31 | CALU | Calumenin | 3 | 37 | 98.1 |
| 32 | CP | Ceruloplasmin | 49 | 122 | 83.1 |
| 33 | GC | Vitamin D-binding protein | 14 | 53 | 77.7 |
| 34 | HB | Haptoglobin | 25 | 45 | 68.2 |
| 35 | HPX | Hemopexin | 18 | 52 | 73.4 |
| 36 | SPARC | Basement-membrane protein 40 | 4 | 35 | 92.4 |
| 37 | TF | Serotransferrin | 31 | 77 | 72.5 |
| 38 | TTR | Transthyretin | 7 | 16 | 81.6 |
| 39 | A1BG | Alpha-1B-glycoprotein | 13 | 54 | 44.2 |
| 40 | APCS | Serum amyloid P-component | 9 | 25 | 68.8 |
| 41 | APLP2 | Amyloid-like protein 2 | 8 | 87 | 85.5 |
| 42 | CLU | Clusterin | 15 | 52 | 76.4 |

| | | | | | |
|---|---|---|---|---|---|
| 43 | FSTL1 | Follistatin-related protein 1 | 2 | 35 | 91.9 |
| 44 | MAN2A1 | Alpha-mannosidase 2 | 2 | 131 | 80.4 |
| 45 | ORM2 | Alpha-1-acid glycoprotein 2 | 5 | 24 | 42.5 |
| 46 | PSAP | Prosaposin | 4 | 58 | 63.4 |
| 47 | QSOX1 | Sulfhydryl oxidase 1 | 8 | 83 | 72.2 |
| 48 | SEPP1 | Selenoprotein P | 2 | 43 | 70.2 |
| 49 | PROS1 | protein S | 12 | 75 | 79.6 |
| 50 | SERPINA4 | Kallistatin | 2 | 49 | na |
| 51 | F5 | Coagulation factor V | 13 | 252 | 69.73 |
| 52 | F13B | Coagulation factor XIIIB | 4 | 76 | 76.4 |

**Table S2.** Summary of proteins tested. ANG-1: angiopoietin-1, ECM-1: extracellular matrix protein 1, PDGF-BB : platelet derived growth factor BB, SDF-1: stromal derived factor 1, TSP1: thrombospondin 1, TGF-β1: transforming growth factor β 1, vWf: Von Willebrand factor.

| Protein | Tested concentrations | IL-6 modulation |
|---|---|---|
| CD154 | Antibody blockade of APR | No |
| VEGF | 5-100 [ng/mL] | No |
| SDF-1 | 25-100 [ng/mL] | No |
| ECM-1 | 2-200 [ng/mL] | No |
| PDGF-BB | 1 to 100 [ng/mL] | No |
| ANG-1 | 1 to 1000 [ng/mL] | No |
| TSP1 | 0.1 to 1000 [ng/mL] | No |
| vWf | 1 to 10 [µg/mL] | Yes |
| TGF-β1 | 0.01 to 500 [ng/mL] | Yes |