

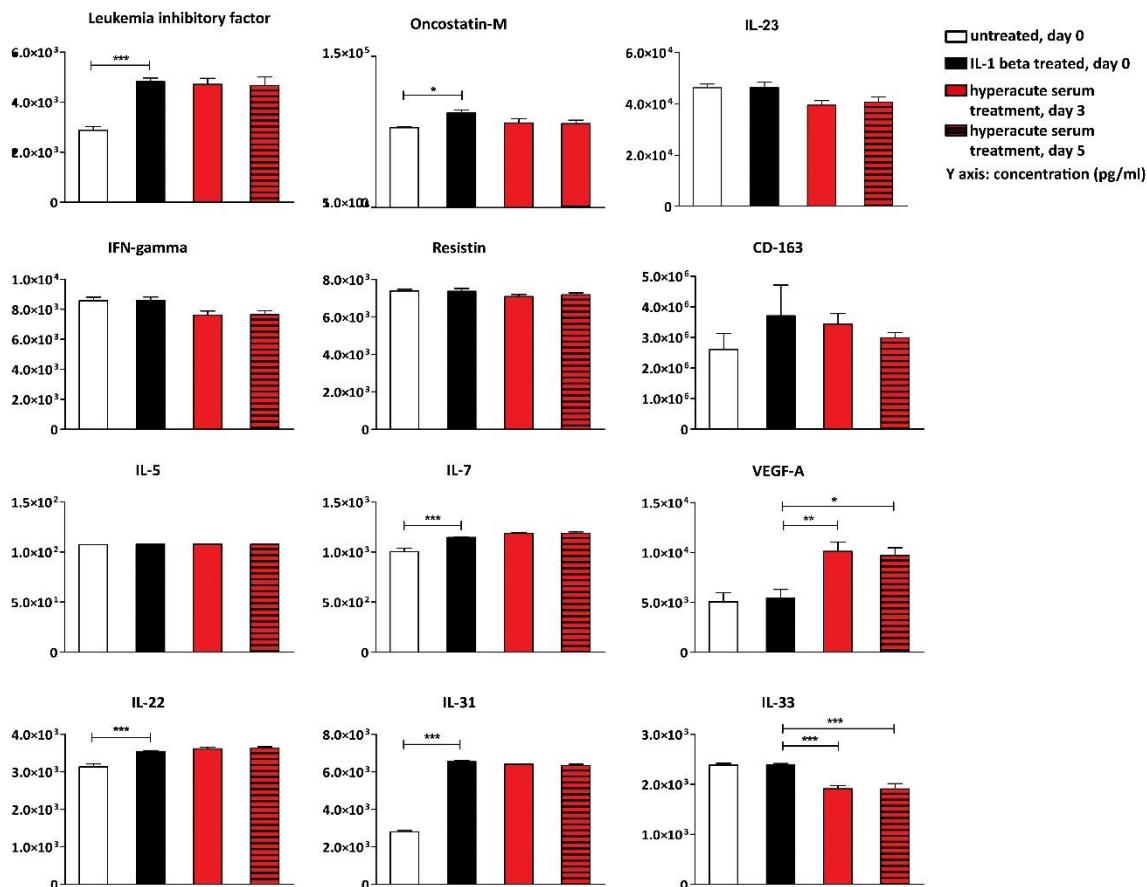
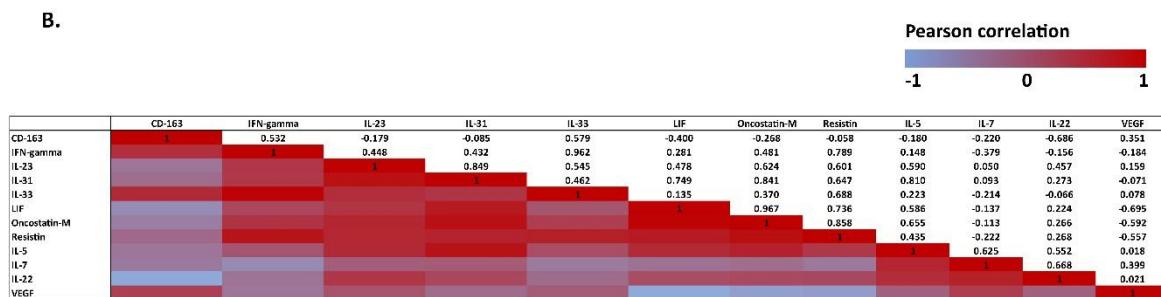
**A.**

**B.**


Figure S1. Additional biomarkers of osteoarthritic inflammation. The level of leukemia inhibitory factor, oncostatin-M, IL-7, IL-13, IL-22 and IL-31 was significantly elevated in response to IL-1 $\beta$  treatment. Hyperacute serum affected only the concentration of VEGF-A and IL-33 (Part A.), n= 12. The significance level was p < 0.05, where \* means that p is between 0.01 and 0.05, \*\* means that p is between 0.01 and 0.001, and \*\*\* means that p is lower than 0.001. Investigating the correlation of changes between day 0 and day 5, strong correlation was found between numerous pairs of cytokines. We considered the correlation very strong if r>0.75, and strong if 0.75>r>0.5 (Part B.), n=12.

Supplementary Table 1. The components of the co-culture supernatant and the osteoarthritic synovial fluid. Mean concentration of each cytokine in the two kind of samples was presented.

| <i>Cytokines</i>                     | <i>Mean of concentration (ng/ml)</i> |                        |
|--------------------------------------|--------------------------------------|------------------------|
|                                      | <b>in vitro (ng/ml)</b>              | <b>in vivo (ng/ml)</b> |
| <i>CD-163</i>                        | 3706,666                             | 2990,840               |
| <i>SPARC/Osteonectin</i>             | 676,268                              | 1421,979               |
| <i>MMP-2</i>                         | 181,201                              | 402,497                |
| <i>Fractalkine</i>                   | 116,307                              | 100,425                |
| <i>OSM</i>                           | 94,744                               | 83,848                 |
| <i>MMP-1</i>                         | 78,103                               | 129,484                |
| <i>CXCL-8/IL-8</i>                   | 77,535                               | 81,125                 |
| <i>MMP-9</i>                         | 67,068                               | 99,811                 |
| <i>CCL-3/MIP1<math>\alpha</math></i> | 58,194                               | 54,371                 |
| <i>CCL-2/MCP-1</i>                   | 56,880                               | 60,093                 |
| <i>IL-13</i>                         | 54,276                               | 51,338                 |
| <i>IL-23</i>                         | 46,271                               | 40,690                 |
| <i>Aggrecan</i>                      | 43,427                               | 45,421                 |
| <i>MMP-13</i>                        | 35,785                               | 40,323                 |
| <i>MMP-3</i>                         | 28,135                               | 30,413                 |
| <i>IL-1RA</i>                        | 21,041                               | 17,403                 |
| <i>IL1-<math>\beta</math></i>        | 17,401                               | 2,772                  |
| <i>IL-2</i>                          | 12,035                               | 11,226                 |
| <i>IL-6R<math>\alpha</math></i>      | 10,535                               | 40,776                 |
| <i>COL1A1</i>                        | 9,697                                | 33,893                 |
| <i>IL-12</i>                         | 9,550                                | 9,157                  |
| <i>IFN-<math>\gamma</math></i>       | 8,576                                | 7,638                  |
| <i>IL-18</i>                         | 7,648                                | 7,549                  |
| <i>Resistin</i>                      | 7,373                                | 7,181                  |
| <i>IL-31</i>                         | 6,541                                | 6,338                  |
| <i>TRANCE/RANKL</i>                  | 6,246                                | 5,494                  |
| <i>VEGF-A</i>                        | 5,430                                | 9,690                  |
| <i>LIF</i>                           | 4,821                                | 4,669                  |
| <i>IL-22</i>                         | 3,545                                | 3,545                  |
| <i>CCL-5/Rantes</i>                  | 3,361                                | 5,966                  |
| <i>EpCAM/TROP1</i>                   | 2,916                                | 3,296                  |

|                      |       |       |
|----------------------|-------|-------|
| <i>IL-33</i>         | 2,386 | 1,909 |
| <i>IL-17A</i>        | 1,624 | 1,356 |
| <i>IL-7</i>          | 1,146 | 1,189 |
| <i>CXCL-10/IP-10</i> | 0,970 | 0,754 |
| <i>TNF-α</i>         | 0,857 | 0,607 |
| <i>IL-4Rα</i>        | 0,612 | 0,618 |
| <i>IL-10</i>         | 0,511 | 0,427 |
| <i>CCL-1/I-309</i>   | 0,434 | 0,416 |
| <i>IL-15</i>         | 0,331 | 0,329 |
| <i>IL-5</i>          | 0,108 | 0,108 |

Supplementary Table 2. The protein concentrations in human serum albumin treated co-culture supernatants. The mean concentration and standard error of mean (SEM) of each protein, measured on day 3 and day 5 was presented in this table.

| <i>Cytokines</i>     | <i>Mean of concentration (pg/ml)</i>          |            |   |            |
|----------------------|---|------------|---|------------|
|                      | <b>Albumin,<br/>control day 3<br/>(pg/ml)</b> | <b>SEM</b> | <b>Albumin,<br/>control day 5<br/>(pg/ml)</b> | <b>SEM</b> |
| <i>Aggrecan</i>      | 41 791  | 2 601      | 44 170  | 1 659      |
| <i>CCL-1/I-309</i>   | 417   | 9          | 403   | 5          |
| <i>CCL-2/MCP-1</i>   | 36 341  | 6 961      | 28 249  | 6 558      |
| <i>CCL-3/MIP1a</i>   | 56 344  | 1 022      | 55 415  | 1 014      |
| <i>CD-163</i>        | 2 359 511                                     | 302 351    | 2 080 235                                     | 145 780    |
| <i>COL1A1</i>        | 9 384   | 2 226      | 15 946  | 10 764     |
| <i>Fractalkine</i>   | 101 186                                       | 2 412      | 96 228  | 1 642      |
| <i>CXCL-10/IP-10</i> | 584   | 33         | 563   | 54         |
| <i>IFN-γ</i>         | 8 494   | 239        | 8 281   | 190        |
| <i>IL1-β</i>         | 5 368   | 1 485      | 2 155   | 561        |
| <i>IL-1RA</i>        | 16 091  | 3 007      | 15 433  | 3 399      |
| <i>IL-2</i>          | 11 310  | 199        | 11 443  | 270        |
| <i>IL-6Rα</i>        | 8 596   | 945        | 13 364  | 5 600      |
| <i>IL-10</i>         | 421   | 7          | 417   | 5          |
| <i>IL-12 p70</i>     | 9 148   | 134        | 9 286   | 140        |
| <i>IL-13</i>         | 49 752  | 687        | 47 954  | 734        |
| <i>IL-15</i>         | 300   | 6          | 296   | 12         |
| <i>IL-17A</i>        | 1 409   | 193        | 1 276   | 165        |
| <i>IL-18</i>         | 7 405   | 88         | 7 578   | 100        |
| <i>IL-23</i>         | 45 007  | 1 667      | 43 442  | 1 273      |

|                          |         |        |         |         |
|--------------------------|---------|--------|---------|---------|
| <i>IL-31</i>             | 6 253   | 48     | 6 140   | 73      |
| <i>IL-33</i>             | 2 375   | 73     | 2 246   | 57      |
| <i>LIF</i>               | 3 729   | 108    | 3 266   | 204     |
| <i>MMP-1</i>             | 76 628  | 6 559  | 84 505  | 16 452  |
| <i>MMP-2</i>             | 202 509 | 13 385 | 228 459 | 54 832  |
| <i>OSM</i>               | 82 078  | 2 117  | 77 915  | 1 974   |
| <i>Resistin</i>          | 7 222   | 132    | 7 146   | 107     |
| <i>SPARC/Osteonectin</i> | 594 120 | 46 465 | 675 913 | 240 283 |
| <i>TNF-α</i>             | 590     | 27     | 596     | 32      |
| <i>TRANCE/RANKL</i>      | 8 604   | 2 492  | 6 188   | 119     |
| <i>CCL-5/Rantes</i>      | 3 277   | 263    | 3 517   | 339     |
| <i>CXCL-8/IL-8</i>       | 75 482  | 2 613  | 73 968  | 2 455   |
| <i>IL-4Rα</i>            | 614     | 2      | 592     | 7       |
| <i>IL-5</i>              | 108     | 0      | 108     | 0       |
| <i>IL-7</i>              | 1 155   | 6      | 1 136   | 14      |
| <i>IL-22</i>             | 3 531   | 10     | 3 447   | 38      |
| <i>MMP-3</i>             | 28 697  | 247    | 27 820  | 568     |
| <i>MMP-9</i>             | 79 403  | 11 364 | 78 537  | 15 459  |
| <i>MMP-13</i>            | 36 895  | 731    | 36 608  | 622     |
| <i>VEGF-A</i>            | 5 457   | 567    | 5 740   | 755     |

Supplementary Table 3. The components of hyperacute serum and human serum albumin containing medium. The mean concentration of the measured proteins in 10% hyperacute serum, and 5% human serum albumin containing culture medium was presented in this table.

| <i>Cytokines</i>     | <i>Mean of concentration (pg/ml)</i>              |  |
|----------------------|---|--|
|                      | <b>Hyperacute serum containing medium (pg/ml)</b> | <b>Human serum albumin containing medium (pg/ml)</b> |
| <i>Aggrecan</i>      | 6785,508  | 198,682  |
| <i>CCL-1/I-309</i>   | 19,270  | 0,000  |
| <i>CCL-2/MCP-1</i>   | 200,819   | 21,508   |
| <i>CCL-3/MIP1a</i>   | 2881,027  | 5,559  |
| <i>CD-163</i>        | 135213,974  | 1091,271   |
| <i>COL1A1</i>        | 360,290   | 32,691   |
| <i>Fractalkine</i>   | 4649,019  | 120,716  |
| <i>CXCL-10/IP-10</i> | 17,349  | 0,485  |
| <i>IFN-γ</i>         | 438,833   | 0,583  |
| <i>IL1-β</i>         | 44,376  | 1,526  |

|                                 |           |          |
|---------------------------------|-----------|----------|
| <i>IL-1RA</i>                   | 200,674   | 1,225    |
| <i>IL-2</i>                     | 614,999   | 8,006    |
| <i>IL-6R<math>\alpha</math></i> | 3097,122  | 268,567  |
| <i>IL-10</i>                    | 19,517    | 1,774    |
| <i>IL-12</i>                    | 459,922   | 33,039   |
| <i>IL-13</i>                    | 2410,747  | 218,770  |
| <i>IL-15</i>                    | 12,111    | 1,075    |
| <i>IL-17A</i>                   | 87,949    | 0,000    |
| <i>IL-18</i>                    | 382,946   | 8,196    |
| <i>IL-23</i>                    | 2412,957  | 2,225    |
| <i>IL-31</i>                    | 304,853   | 1,133    |
| <i>IL-33</i>                    | 104,366   | 0,881    |
| <i>LIF</i>                      | 113,073   | 0,000    |
| <i>MMP-1</i>                    | 204,341   | 16,157   |
| <i>MMP-2</i>                    | 9416,864  | 1360,354 |
| <i>OSM</i>                      | 3268,440  | 266,980  |
| <i>Resistin</i>                 | 361,025   | 50,539   |
| <i>SPARC/Osteonectin</i>        | 40571,472 | 180,257  |
| <i>TNF-<math>\alpha</math></i>  | 24,744    | 2,064    |
| <i>TRANCE/RANKL</i>             | 311,739   | 3,095    |
| <i>CCL-5/Rantes</i>             | 588,443   | 92,465   |
| <i>CXCL-8/IL-8</i>              | 7,277     | 2,464    |
| <i>IL-4R<math>\alpha</math></i> | 0,938     | 4,788    |
| <i>IL-5</i>                     | 5,339     | 0,000    |
| <i>IL-7</i>                     | 8,852     | 1,378    |
| <i>IL-22</i>                    | 105,286   | 8,693    |
| <i>MMP-3</i>                    | 76,393    | 4,783    |
| <i>MMP-9</i>                    | 3967,262  | 251,319  |
| <i>MMP-13</i>                   | 45,656    | 0,000    |
| <i>VEGF-A</i>                   | 101,643   | 23,477   |