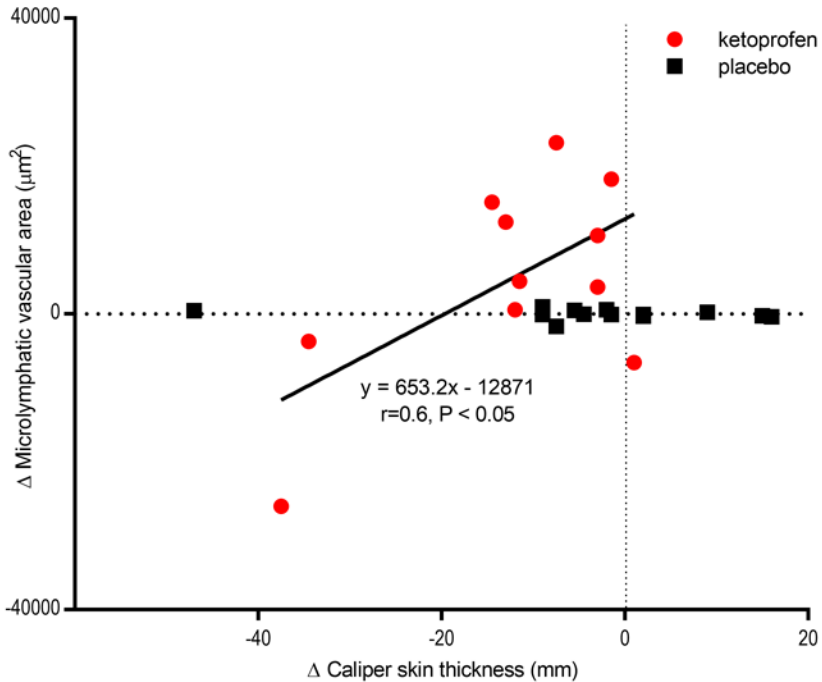


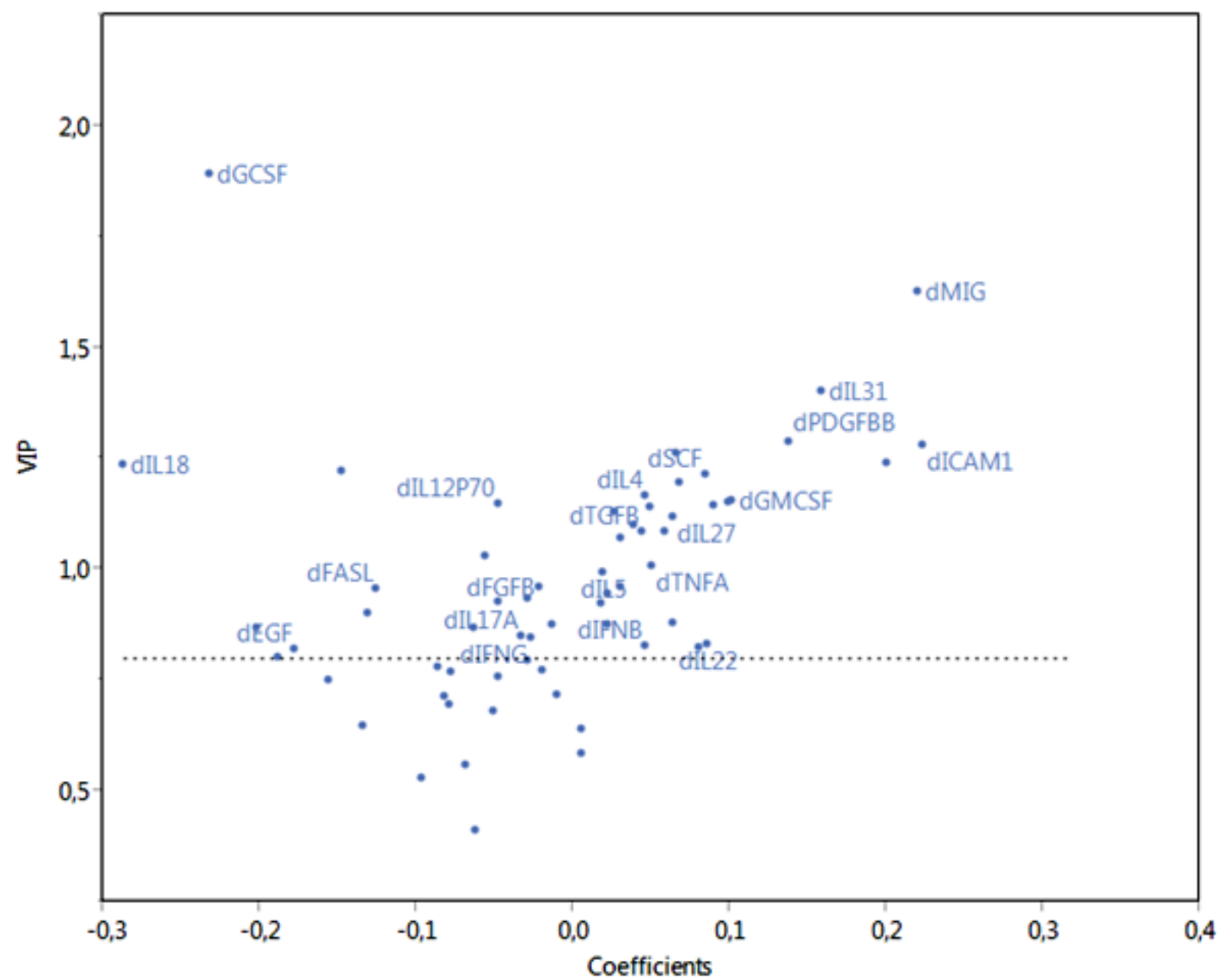
Supplementary Figure Legends

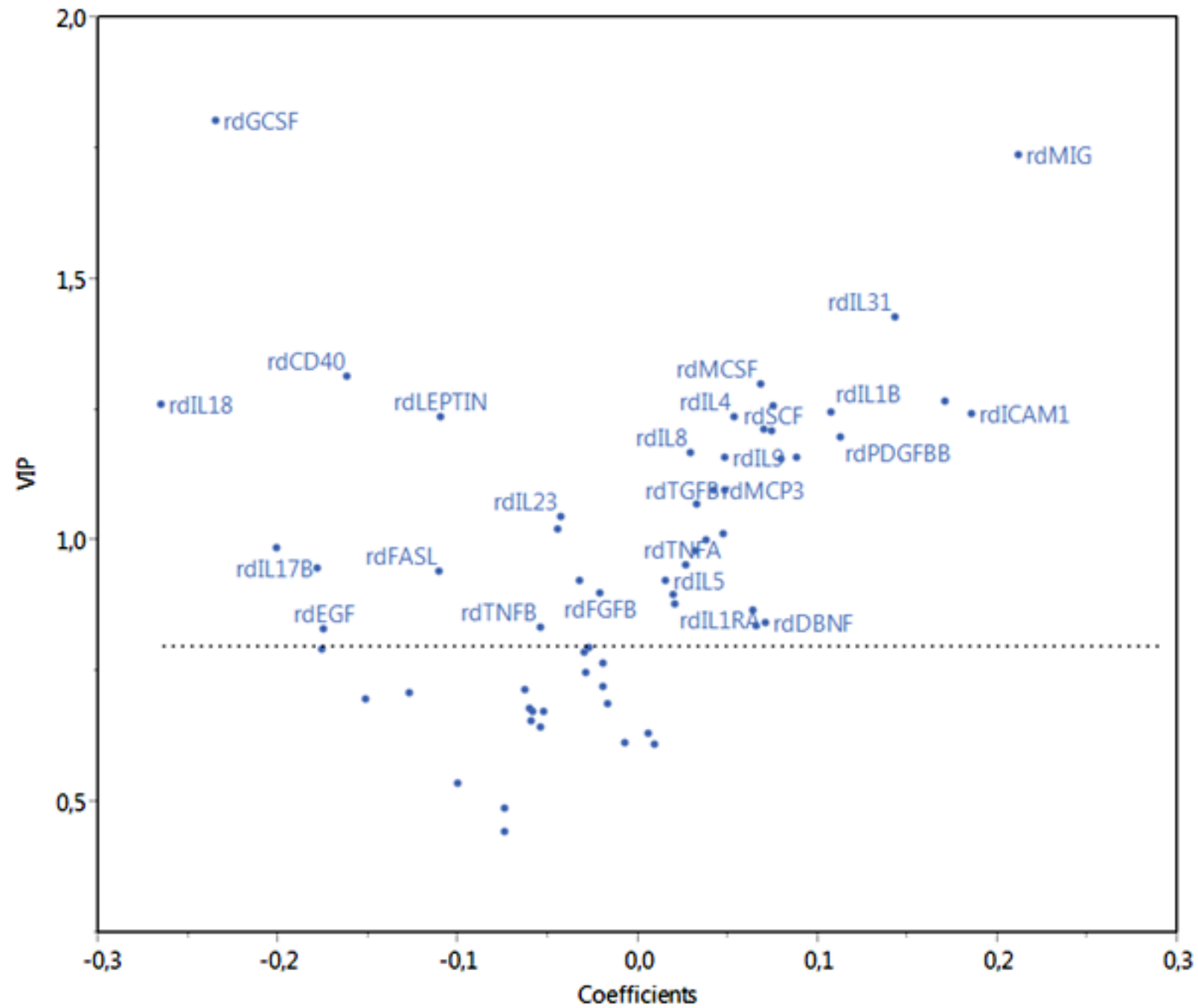
Supplementary Figure 1. Correlation between changes in skin thickness and cutaneous microvascular lymphatic vascular area. Skin thickness was measured by caliper (post-treatment minus pre-treatment) and lymphatic vascular cross-sectional area was determined by immunohistochemical analysis of podoplanin staining in the cutaneous biopsy specimens at the same time points. The two variables were positively correlated ($r=0.6$, $P<0.05$). The ketoprofen recipients are depicted in red and placebo recipients in black. Values to the left of the vertical line represent an improvement in skin thickness and values above the horizontal line represent a net increase in lymphatic vascular area.

Supplementary Figure 2. The results of the multiplex cytokine assays are depicted graphically in a V plot. The analysis reflects the comparison of absolute changes observed in ketoprofen- and placebo-treated patient groups, utilizing a 3-factor model. The formal VIP >1.5 cutoff was exceeded by the two biomarkers highlighted in red. The horizontal dashed line represents a VIP = 0.8.

Supplementary Figure 3. The results of the multiplex cytokine assays are depicted graphically in a V plot. The analysis reflects the comparison of relative changes observed in ketoprofen- and placebo-treated patient groups, utilizing a 3-factor model. The formal VIP >1.5 cutoff was exceeded by the two biomarkers highlighted in red. The horizontal dashed line represents a VIP = 0.8.







SUPPLEMENTARY Table 1

| Class | Biomarker |
|---|--|
| Growth factors | EGF, FGF- β , HGF, NGF, PDGF-BB, PIGF-1, TNF α , TGF- β 1, VEGF, VEGF-D |
| Colony stimulating factors and stem cell factors | G-CSF, GM-CSF, M-CSF, SCF |
| Interleukins | IL-1 α , IL-1 β , IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL12p40, IL12p70, IL-13, IL-15, IL-17A, IL-17F, IL-18, IL-21, IL-23, IL-27, IL-31, and LIF |
| Chemokines | CCL2 (MCP-1), CCL3 (MIP-1 α), CCL4 (MIP-1 β), CCL5 (RANTES) CCL7 (MCP-3), CXCL1 (Gro- α), CXCL5 (ENA78), CXCL9 (MIG), CXCL10 (IP-10), CCL11 (Eotaxin), CXCL12 (SDF-1 α) |
| Interferons | INF- α , INF- β , INF- γ |
| Adhesion Molecule | ICAM-1, VCAM-1 |
| Other factors | BDNF, CD40L, FASL, Leptin, PAI-1, Resistin, TNF- α , TNF- β , TRAIL |

Supplementary Table 1. Inflammatory circulating biomarkers assessed in the multiplex assay.