**Supplementary Results**

**Gene expression of IL-6**

***HLMVEC - IL-6 gene expression***

Gene expression levels of IL-6 were significantly increased with LPS treatment which was downregulated 5.8 fold with rhPRG4 (Supplementary Fig. 1, Supplemental Digital Content 3, http://links.lww.com/CCX/A183; legend, Supplemental Digital Content 7, http://links.lww.com/CCX/A187). Cell culture media treated with patient samples and then subsequently given 100 µg/mL rhPRG4 after 30 minutes only showed IL-6 downregulation in one sample of 15 (SEA 8 = 2.4 fold). On the contrary, one sample had upregulated IL-6 gene expression with rhPRG4 treatment (SEA 14 = 2 fold).

When gene expression from cells treated with patient samples or LPS were compared to gene expression levels of media controls, the samples treated with LPS had significantly upregulated IL-6 gene expression (4.8 fold) which was not reversed with 50 µg/mL rhPRG4 but was reversed with 100 µg/mL rhPRG4 (1.1 fold and 2.8 fold respectively) (Supplementary Fig. 2, Supplemental Digital Content 4, http://links.lww.com/CCX/A184; legend, Supplemental Digital Content 7, http://links.lww.com/CCX/A187). However, when comparing media controls to patient treated cell culture samples, 5 patient plasma treated cell culture samples had increased gene expression levels whereas 3 patient plasma treated cell culture samples had decreased gene expression. Compared to media controls, the following samples showed significantly upregulated gene expression of IL-6: LPS, LPS+50 µg/mL rhPRG4, sea 11, sea 23 + 50 µg/mL rhPRG4, and sea 41 (4.8, 2.8, 2.0, 2.5, and 2.0 fold respectively). On the contrary, compared to media controls, sea 8 + 50 µg/mL rhPRG4, sea 12 + 100 µg/mL rhPRG4, and sea 22 + 50 µg/mL rhPRG4 had significantly downregulated IL-6 gene expression (each 2.1 fold).

**VE-Cadherin imaging**

All four genotypes of MLMVECs were immunostained for VE-cadherin and then imaged to verify that all cells were of endothelial phenotype. All genotypes had cells that were 99-100% positive for VE-cadherin (Supplementary Fig. 3, Supplemental Digital Content 5, http://links.lww.com/CCX/A185; legend, Supplemental Digital Content 7, http://links.lww.com/CCX/A187) based upon ImageJ analysis. Cellular borders can be faintly seen with the red VE-cadherin staining and cell nuclei exhibit pink colors due to overlapping VE-cadherin and DAPI staining.

**ELISA PRG4 levels in sepsis patient plasma**

Patient sepsis versus control samples were tested for levels of PRG4. Overall, sepsis patient plasma had significantly higher levels of PRG4 (30.8 ± 13.2 µg/mL) compared to control patient plasma (3.2 ± 1.5 µg/mL) (p<0.05) (Supplementary Fig. 4, Supplemental Digital Content 6, http://links.lww.com/CCX/A186; legend, Supplemental Digital Content 7, http://links.lww.com/CCX/A187).

**PRG4 and IL-6 correlation in sepsis patient plasma**

There was a non-significant correlation between PRG4 and IL-6 levels (r = 0.30, p = .30, R2 = 0.09). Removing an outlier IL-6 data point did not significantly change the correlation coefficient (r = 0.32, p = .28, R2 = 0.10).