Supplementary Fig. S1 Validation of measuring biochemical markers in citrated plasma versus serum. Lactate, C-reactive protein (CRP), albumin, creatinine and urea levels were measured both in serum and citrated plasma samples from 10 individuals by an ARCHITECT ci8200 (Abbott Diagnostics, Hoofddorp, the Netherlands). Serum is the preferred medium for measuring these variables, although the manufacturer has validated the method for plasma (albumin bromocresol purple [BCP] [ref 7D54], creatinine [ref 3L81–22], urea nitrogen [ref 7D75], lactic acid [ref 9D89] and CRP Vario [ref 6K26–30]). Linear regression analysis was performed to establish whether the results in citrated plasma were comparable to serum. Results correlated well for CRP, creatinine and urea, but not lactate and albumin. Because paired statistical analysis was performed in this study, the poor correlation for lactate and albumin values was accepted.

Supplementary Fig. S2 Dose-finding of anti-tissue factor pathway inhibitor (TFPI) C-terminus domain antibodies. For determining the contribution of TFPI to thrombin generation (TG), a modified TG assay was performed. The amount of anti-TFPI C-terminus domain antibodies needed to cause a maximum elevation in peak height was determined. TG was measured in response to 1 pM TF.

Supplementary Fig. S3 Tissue factor pathway inhibitor (TFPI) contribution to thrombin generation (TG). TG was measured in platelet-poor plasma (PPP) samples drawn at 50 and 3,883 m above sea level, with addition of 40 μM anti-TFPI C-terminus domain antibodies or buffer, triggered by 1 pM tissue factor (TF). The ratio of peak height in the absence and presence of anti-TFPI antibodies was calculated to determine the contribution of TFPI activity to the TG. Individual ratios are shown. Statistical significance was determined using the paired t-test, and p-value of < 0.05 was considered statistically significant.