Parasites and plasma
Cryopreserved parasite isolates (Table S1) from adult Thai patients with well documented *P. falciparum* malaria were thawed and studied during their first cycle in culture as described.[16] Plasma from acutely infected patients was frozen at −80°C. The collection of specimens was approved by the Ethics Committee of the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. Informed consent was obtained from all patients and/or relatives according to the Declaration of Helsinki.

Tissue culture and other reagents
Unless otherwise stated, all tissue culture reagents were obtained from Invitrogen Canada Inc. (Burlington, ON) and chemical reagents were purchased from Sigma Co. (St. Louis, MO). The Src-family kinase inhibitor PP1 and the inactive analog PP3 were purchased from Biomol Research Laboratory (Plymouth Meeting, PA); Rho kinase inhibitor Y-27632, myosin light chain kinase (MLCK) inhibitor ML-7 and protease inhibitor cocktail were from Calbiochem and Novabiochem (San Diego, CA); pan-PKC inhibitor GF109203X was from Biosource International (Invitrogen). Enhanced chemiluminescence substrate (ECL) was purchased from Amersham Pharmacia Biotech (Piscataway, NJ).

Antibodies
Polyclonal antibody to human ZO-1 and MoAb to claudin-5 were purchased from Zymed (Invitrogen). MoAb to VE-cadherin was from Santa Cruz Biotechnology Inc. (Santa Cruz, CA); MoAb to ICAM-1 (84H10) was from R&D Systems, Inc. (Minneapolis, MN); MoAb to TLR2 (clone 2.5) was from Invivogen (San Diego, CA). Fluorescein- or cy3-labeled anti-mouse or anti-rabbit secondary antibodies were from Molecular Probes (Eugene, OR). Horseradish peroxidase (HRP)-conjugated secondary antibodies were purchased from Jackson ImmunoResearch Laboratories (West Grove, PA).

Endothelial Cells
Human dermal microvascular endothelial cells (HDMECs) were harvested from discarded neonatal human foreskins using 0.5 mg/ml Type IA collagenase (Boerhringer Mannheim Biochemicals, Indianapolis, IN) as described.[16] The skin collection was approved by the Conjoint Ethics Board of the Calgary Health Region and University of Calgary, Alberta, Canada. The cells were maintained in endothelial basal medium (EBM) (Cambrex Walkersville Inc., MD) with supplements provided by the manufacturer. Experiments were performed with cells from passages one to five that showed consistent response in transwell permeability assays (see below). Primary human blood lung microvascular endothelial cells at passage 3 were purchased from Cambrex and maintained in the same way as HDMECs. Lung cells were used from passage four to eight.

Detection of apoptosis and cytotoxicity
Endothelial cell death by apoptosis or necrosis was determined by staining with AnnexinV-FITC and propidium iodide (ApoAlert™ Annexin V-FITC Apoptosis Kit, Becton Dickinson Canada, Oakville, Ontario). HDMECs grown in 35 mm dishes were treated with stimuli for 24 hours after which trypsinized cells were stained according to the manufacturer's instructions and analyzed by flow cytometry using FACSCAN (Becton Dickinson). Cellular cytotoxicity was measured by

using the MTS reagent (CellTiter 96 AQueos One Cell Prolif. Kit, Promega Madison, WI) according to the manufacturer's instructions.

ELISA for cytokine detection.
Cytokine production in transwell supernatants and acute plasma from patients was determined by an antibody-capture ELISA using an unlabeled MoAb for capture and a biotinylated MoAb for detection (Endogen, Boston, MA). After incubation with horse radish peroxidase-avidin (Zymed), the reaction was developed using the substrate 3,3′,5,5′-tetramethylbenzidine (TMB) (Dako Corp., Carpinteria, CA). The lower limit of detection of all the assays was 15 pg/ml.