SUPPLEMENTAL METHODS

Commercial ELISA kits were used to measure levels of plasma lactadherin in mice (Boster Biological Technology, Pleasanton, CA) according to the manufacturer's instructions.

BDMV transmigration through the endothelial cell barrier

Human umbilical vein endothelial cells (HUVECs, Lonza, Basel, Switzerland) were grown in endothelial growth basal medium (Lonza) until confluent on a collagen-coated polytetrafluoroethylene membrane (Corning, Tewksbury, MA).[1] Confluent endothelial cells were activated with 25 μM of histamine[2] and, after washing with PBS, were incubated with 1 x 10^7/ml of PKH26-labeled BDMVs (5 μM, Sigma-Aldrich, St. Louis, MO), 300,000/μl of human platelets, and 1,000/μl of human $CD45^+$ monocytes in the presence and absence of purified lactadherin (10 μg/ml) for 3 hrs at 37°C. The medium in the bottom chamber was collected and PKH26-labeled BDMVs were counted by flow cytometry as previously described.[1]

Genotyping lactadherin mice

The protocol is provided by the RIKEN BioSource Center (Ibaraki 305-0074, Japan). Tails (~3 mg from each mouse) were collected from lactadherin null mice (B6;129-Mfge8<tm1Osa>/OsaRbrc Mice, No.RBRC01726)[3] and wild-type littermates into clean 1.5 ml Eppendorf tubes. Genomic DNA was extracted using the MyTaq Extract-PCR kit

(Bioline, Taunton, MA) according to the manufacturer's instructions. The genomic DNA was amplified with PCR using the following primers: MFG-E8 sense-GTGAACCTTCTGCGGAAGAT, MFG-E8 antisense- GGGCATAAACTCCAGCTCAC and Nor R- CGTGGGATCATTGTTTTTCT (Integrated DNA Technologies, Coralville, Iowa). For the polymerase chain reaction (PCR), the template was first denatured at 94^{o}C for 120 sec and then amplified by 30 cycles: 10 sec denaturing at 95^{o}C, 30 sec annealing at 65^{o}C and 60 sec extension at 68^{o}C. The PCR produced a 570 kb band from wild-type and a 310 kb band from the lactadherin null mice (Figure S7).

SUPPLEMENTAL FIGURES

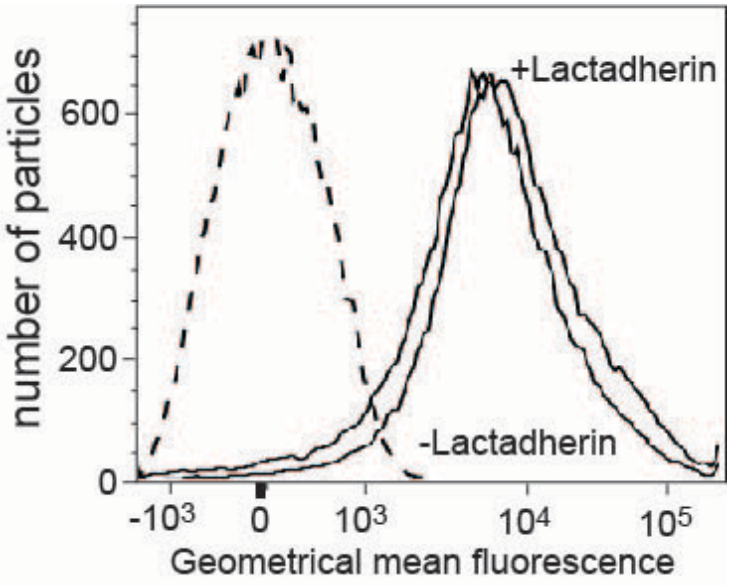

Figure S1: A representative histogram of 3 separate experiments shows that the binding FITC-streptavidin to biotinylated BDMVs does not affect lactadherin binding to the microvesicle. This experiment is necessary to ensure an equal detection of biotinylated BDMVs in mice receiving lactadherin and those receiving saline.

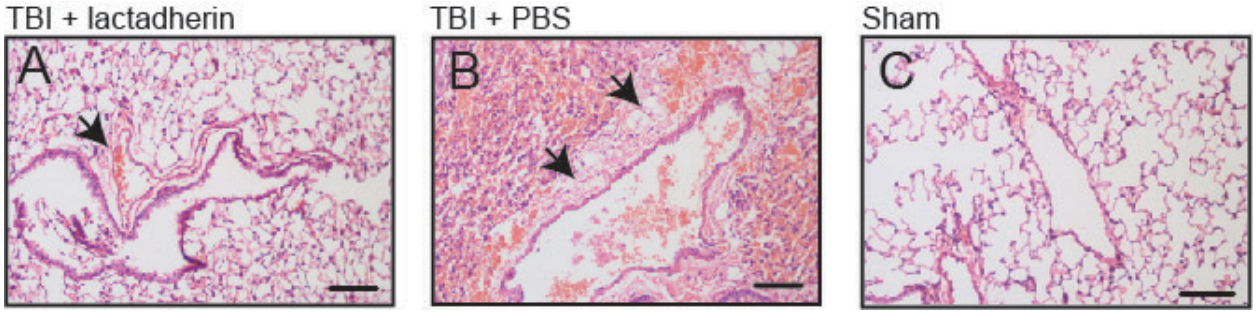

Figure S2: H&E staining of pulmonary tissues from FPI mice preconditioned with lactadherin (**A**) or PBS (**B**), and from a sham mouse (C, bars in A-C = 100 μm). Arrows indicate perivascular space that is enlarged in FPI mice receiving PBS, but not receiving lactadherin. The images are representative of 26 separate experimental mice.

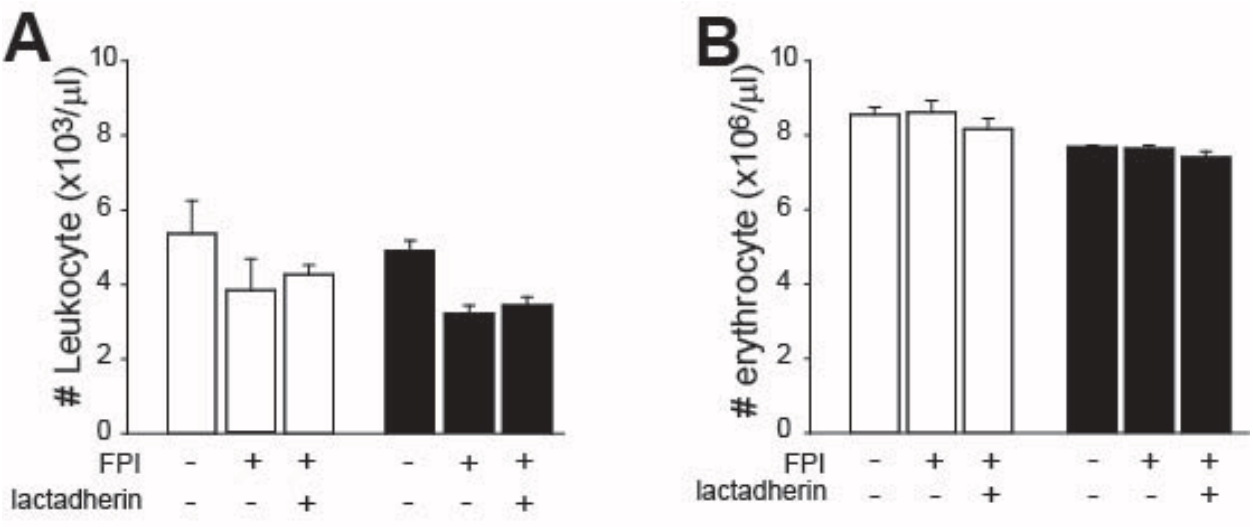

Figure S3: Counts of blood leukocytes (**A**) and erythrocytes (**B**) measured before (white bars) and 3 hrs after (black bars) FPI of mice preconditioned with lactadherin or PBS (n = 16, one-way ANOVA). Control mice received PBS

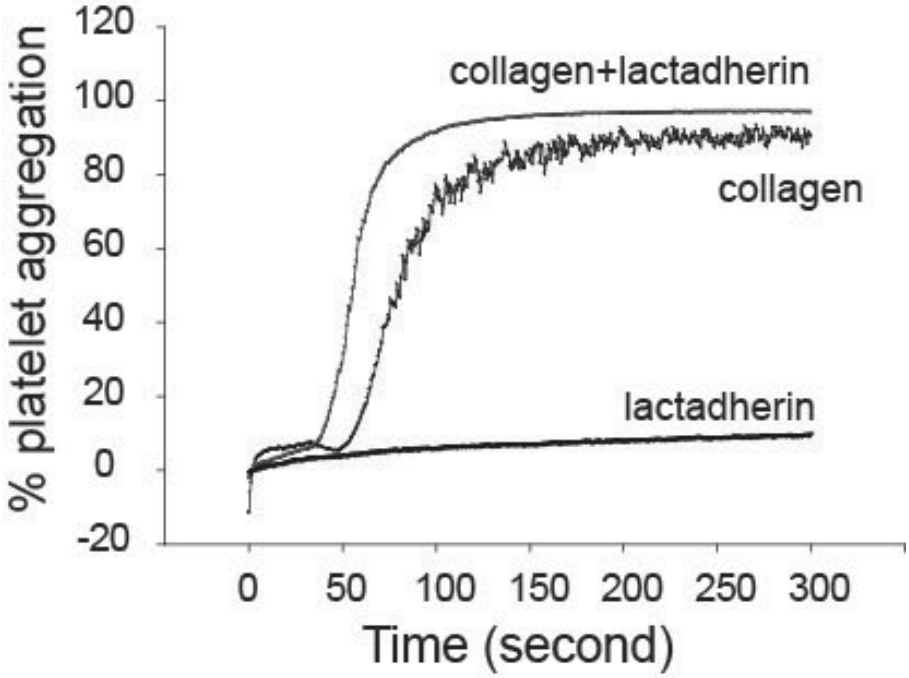

Figure S4: Lactadherin neither induced platelet aggregation nor affected platelet aggregation induced by collagen.

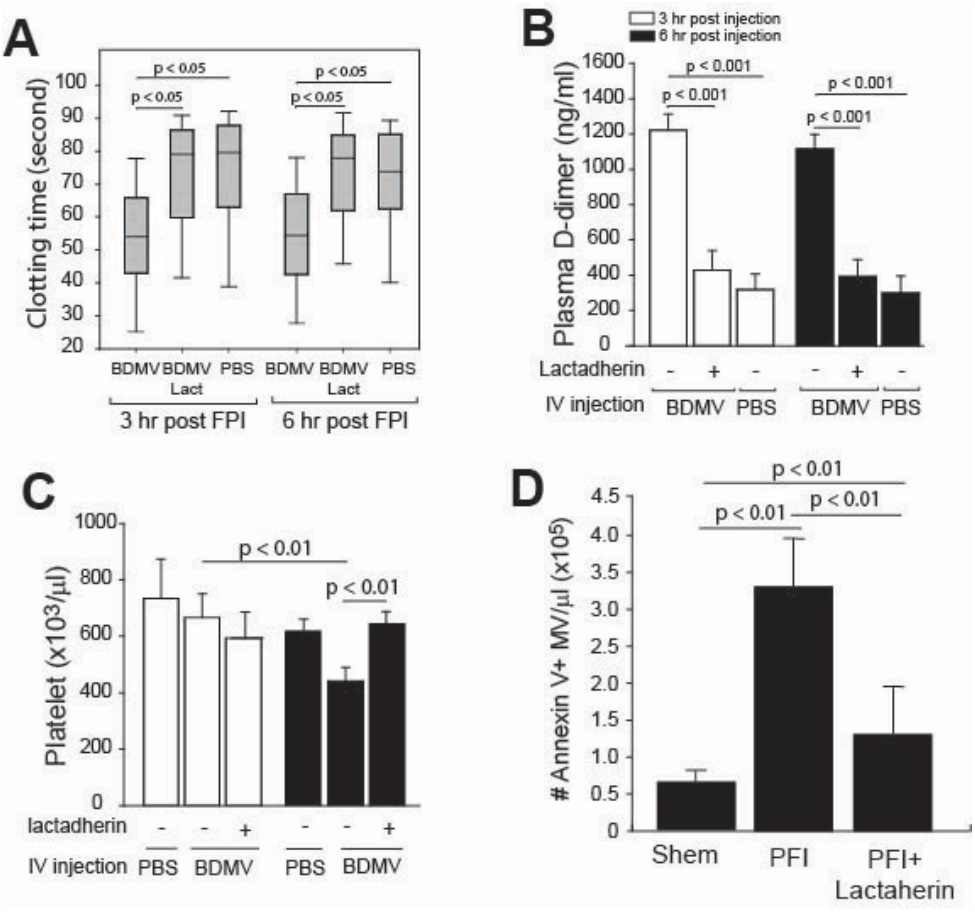

Figure S5: (**A**) Clotting time, (**B**) plasma D-dimer and (**C**) platelet counts of non-injured mice infused with $1.5x10^7$ BDMVs/ml followed by infusion of either 400 μg/kg of lactadherin or an equal volume of PBS and mice without BDMV infusion as control (n = 16, one-way ANOVA). (**D**) Total counts of annexin V-binding microvesicles measured by flow cytometry (n = 12, one-way ANOVA).

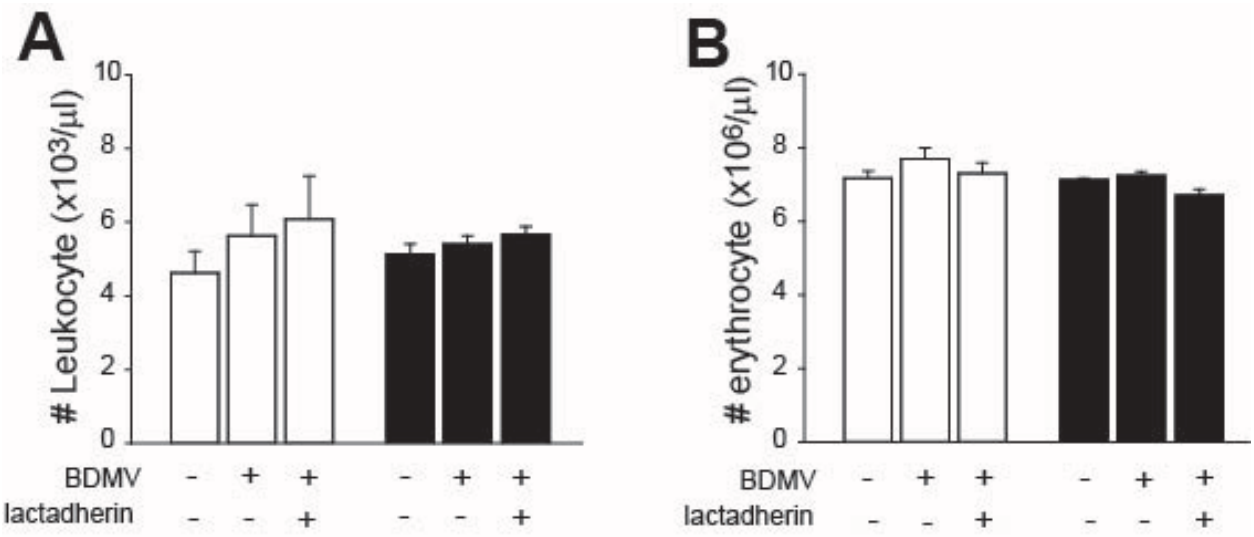

Figure S6: Counts of leukocytes (**A**) and erythrocytes (**B**) in non-injured mice before (white bars) and 3 hrs after (black bars) infusion with purified BDMVs followed by lactadherin or PBS (n = 16, one-way ANOVA). Control mice received PBS without BDMVs.

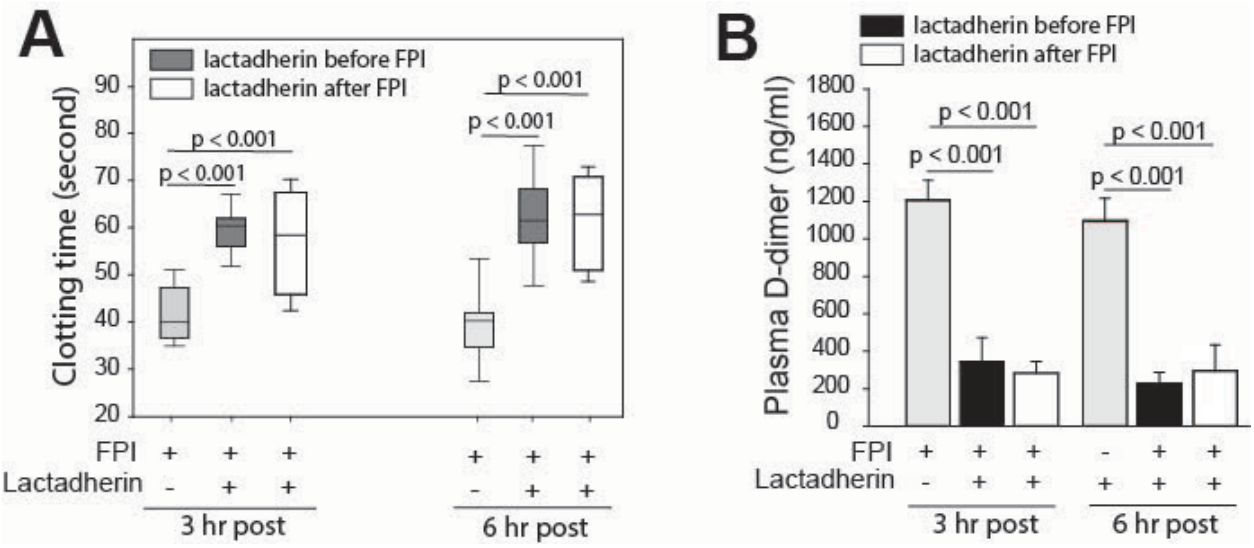

Figure S7: Comparisons of post-FPI clotting times (**A**) and plasma levels of D-dimer (**B**) between mice preconditioned with lactadherin before the injury (dark grey/back bars) and those receiving lactadherin after the injury (white bars). Control mice received PBS before injury (n = 32, one-way ANOVA).

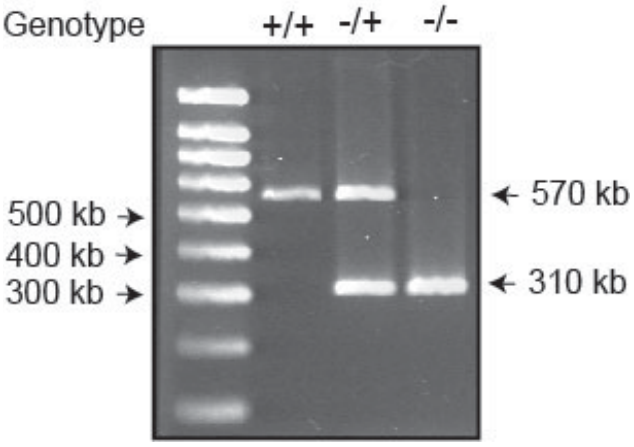

Figure S8: Genotyping lactadherin null and wild-type mice: Genomic DNA was extracted from lactadherin null, heterozygous, and wild-type mice and amplified with specific primers. These primers amplified a 570 kp DNA fragment from the wild-type mice and a 310 kp fragment from the lactadherin null mice.

1. Tian Y, Salsbery B, Wang M, et al. Brain-derived microparticles induce systemic coagulation in a murine model of traumatic brain injury. *Blood*. 2015;125(13):2151-2159.
2. Dong JF, Moake JL, Nolasco L, et al. ADAMTS-13 rapidly cleaves newly secreted ultralarge von Willebrand factor multimers on the endothelial surface under flowing conditions. *Blood*. 2002;100(12):4033-4039.
3. Hanayama R, Tanaka M, Miyasaka K, et al. Autoimmune disease and impaired uptake of apoptotic cells in MFG-E8-deficient mice. *Science*. 2004;304(5674):1147-1150.