Appendix S1. Supplementary material

Patient characterisation

Nulliparous or multiparous women with a singleton pregnancy were eligible for the study. Pre-eclampsia was defined as hypertension and proteinuria occurring after 20 weeks of gestation. Hypertension was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg after 20 weeks of gestation. Proteinuria was defined as the urinary excretion of ≥0.3 g protein in a 24-hour specimen, or 0.3 g/l, or two ≥1+ dipstick readings in a random urine determination in the absence of urinary tract infection. The pre-eclamptic and control women did not differ in age or body mass index (BMI). In preeclampsia, the median proteinuria was 3.31 g/L (25, 75 percentiles 1.59, 6.04, median systolic blood pressure was 164 mmHg (152, 177), median diastolic blood pressure was 108 mmHg (103, 114). The preeclamptic women gave birth at median 38 weeks of gestation (35, 39) and 57.3% had vaginal deliveries.

487/500 peeclamptic women and 187/190 controls genotyped, passed quality control. At stage 2 we included in the analyses exomes from 122 preeclamptic women and 1905 non-preeclamptic controls from the national FINRISK study cohort (FINRISK licence # 8/2016)[1]. National FINRISK Study description and ethical approvals are available online: https://www.thl.fi/documents/10531/1921702/2015+FINRISK+description_for_researchers_final.pdf/fc952cba-86f6-4ef5-8ef2-fa13c23173c3.

Plasmid DNA

The cDNA coding for full-length human CD11c in pCDM8 vector was a gift from Carl G. Gahmberg (University of Helsinki, Finland). A251T-CD11c mutation was created to wt-CD11c-pCDM8 by using site-directed mutagenesis and sequenced. The human cDNA of CD11b has been cloned into pCDNA3.1(+) vector (Fagerholm et al, 2006.*Blood*). For preparing the other CD11c mutant W48R, the wt-CD11c insert was transferred to high-copy pCDNA3.1(+) vector to facilitate the cloning step of the plasmid. The integrin mutants W48R-CD11c, M441K-CD11b and T1000N-CD11b were created by using site-directed mutagenesis and the presence of mutation was confirmed by Sanger sequencing of the mutated region in the DNA Dream Lab facility (Helsinki, Finland). CD18 in pCDNA3.1(+) was from Addgene (Cambridge, MA, USA) (plasmid 8640, [2]).

Cell culture and transfection

COS-1 cell line was cultured in DMEM supplemented with 10 % FBS, 2 mM L-glutamine and 100 units/ml penicillin-streptomycin (all of them purchased from GIBCO, Thermo Fisher Scientific,

Waltham, MA, USA). Cells were transfected either with wt or mutant CD11c or CD11b together with CD18 using XFect transfection reagent (Takara Bio Inc, Japan). Transfection efficiency was detected by flow cytometry.

Cell adhesion assays

Cell adhesion assays were performed essentially as described previously[3]. Briefly, complement component iC3b (Merck KGaA, Darmstadt, Germany) was coated onto 96-well MaxiSorp plate (Thermo Fisher Scientific, Waltham, MA, USA) in 6 µg/ml by overnight incubation at 4°C. COS-1 cells transfected either with wt or mutant CD11c or CD11b together with CD18 were suspended to adhesion medium (RPMI 1640 (GIBCO, Thermo Fisher Scientific, Waltham, MA, USA) supplemented with 0,1 % BSA (Sigma-Aldrich, Merck KGaA, Darmstadt, Germany), 40 mM Hepes and 2 mM $MgCl_2$) and added to the plate (1-2 x 10^5 cells per well). Where appropriate, cells were stimulated with 200 nM phorbol dibutyrate (PDBu) (Sigma-Aldrich, Merck KGaA, Darmstadt, Germany) immediately before being added to the plate. Cells were allowed to adhere for 15-20 min at +37°C before gentle washing by floating upside down, and the bound cells were lysed and detected with phosphatase substrate (Sigma-Aldrich, Merck KGaA, Darmstadt, Germany).

Flow cytometry

Expression of integrins was studied with the following antibodies: CD11b-PE, clone ICRF44 (BioLegend, San Diego, California, USA), CD11c-PE-Cy7, clone Bu15 (BioLegend, San Diego, California, USA) and CD18-FITC, clone MEM-48 (Abnova, Taipei, Taiwan). ICRF44 recognizes the CD11b I domain from active and inactive integrin[4], whereas MEM-48 recognizes an epitope in the stalk region involving residues 534-546 in cysteine-rich repeat 3 of the CD18 antigen[5]. Bu15 Ab is suggested to be an antagonist for CD11c, which binds outside of the I domain and divalent cation independently[6]. Data were acquired on a LSRFortessa flow cytometer (BD Biosciences) at the Flow Cytometry Core Facility in the Department of Biosciences, University of Helsinki. Data were analysed using FlowJo software (TreeStar Inc**,** Ashland, OR, USA).

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