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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

Describe how sample size was determined.

All experiments were performed at least in triplicate or where otherwise noted, with a larger sample size. Power calculations for in vivo thrombosis studies suggested a group size of at least 5. Results shown often reflect data summed from multiple experiments with cumulatively larger sample sizes.

2. Data exclusions

Describe any data exclusions.

There were no data exclusions

3. Replication

Describe whether the experimental findings were reliably reproduced.

Replicate experiments were performed for all studies as noted in figure legends, methods, and Source Data. Experimental findings were reliably reproduced.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Mice in all studies were randomized to their particular groups at time of allocation to experimental groups.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Investigators performing quantitative analyses of endpoints (e.g., plasma, urine, or fecal metabolite levels and time to vessel occlusion in in vivo thrombosis assays) were blinded to group allocation with samples labeled by code only. Investigators were not blinded to mouse group allocation during the performance of animal husbandry requirements for experiments.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	Most data was analyzed using R software version 2.15 and Prism 5 (Graphpad Software). 16S microbial data were analyzed using QIIME version 1.9, SUMACLAST version 1.0.00 and PYNAST version 1.2.2 For docking studies, we used Autodock Vina program (version 1) which is a parallel version of Autodock 4 program. To prepare the enzyme and the ligand for docking, we used MGLTools (version 1.5.7rc1) a graphic interface for Autodock program. We built structures for inhibitors (PDB files and Gamess input files) with the Avogadro program (version 1.2.0). Quantum mechanical calculations were performed with the program Gamess US (MacOSX binary "gamess.18Aug2016R1.x"). We specified the level of QM calculation used (HF/6-31G(d)). Enzymatic fecal polymicrobial data was analyzed by Dotmatics Studies Assay data management and analysis software version 5.1.1. A compensation matrix was applied to the data in the Apogee histogram software. Analysis of prothrombotic markers was done in FlowJo 10.4.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	All materials are available from the indicated commercial sources or upon request to the corresponding author

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	All assays included appropriate positive and negative controls as indicated, for assay validation. If applicable, the assays were designed per the manufacturer's instructions. Mouse plasma vWF levels were assessed by using Abcam's (cat# ab208980) vWF A2 (von Willebrand factor A2) in vitro SimpleStep ELISA (Enzyme-Linked Immunosorbent Assay) kit using the manufacturer's instructions. Lot No. GR3197038-1 Annexin V kit: lot no. 7312712: As per manufacturer's instruction 5 ul per test (1:20 dilution not 1:50 as supplementary figure 1 data legend (BD Pharmingen, cat# 556547). FITC-conjugated rat-anti-mouse CD41 (clone MWreg30, BD Biosciences) cat. No. 553848 : citation: https://onlinelibrary.wiley.com/doi/pdf/10.1111j.1538-7836.2008.03188.x For immunoaffinity staining p-selectin analysis, samples were incubated with FITC-CD62p (BD Pharmingen, cat# 561923) at 40ug/ml. http://www.bloodjournal.org/content/122/8/1478/ For Microparticles: Following dilutions were made to titrate abs 1/100, 2/100, 4/100, 8/100 and 16/100 for both abs and based on the titration data on microparticles 8ul was used for Annexin V staining and 5 ul for cd41 staining. PE-CD41 (BD Pharmingen, cat# 558040) and FITC-annexin V (BD Pharmingen, cat# 556547)

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

HK-2 cells (human papillomavirus 16 (HPV-16) transformed, ATCC® CRL-2190™) and HepG2 (human liver hepatocellular carcinoma cell line, ATCC HB-8065™) were purchased from ATCC.

hERG-T-REXTM 293 cells were initially purchased from Invitrogen (Cat No. K1236) and have been maintaining in Pharmaron since then.

b. Describe the method of cell line authentication used.

We identified the authentication of the HK-2 and HepG2 cell lines by the cellular morphology under microscope.

For hERG cells, as the expression of hERG channel requires the extra addition of doxycycline (or tetracycline), the authentication of cells was established on monitoring the induced transmembrane electrical currents under voltage-clamp configuration.

c. Report whether the cell lines were tested for mycoplasma contamination.

Neither of the HK-2 and HepG2 cell lines were listed in the ICLAC database of commonly misidentified cell lines. We have tested the mycoplasma contamination of the cell lines in some early passages and no mycoplasma contamination was detected.

The routine mycoplasma test for hERG-T-REXTM 293 cells is carried out regularly and no contamination was found ever since.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

None of the cell lines were listed in the ICLAC database of commonly misidentified cell lines

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

We used female, wild-type C57BL/6J mice, between 6 to 12 weeks old

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

Human fecal samples were collected from healthy volunteers with no known chronic illnesses, blood borne diseases or active infections. The volunteers had not received antibiotics within two months of donation and provided written informed consent.

Human blood samples for direct inhibitor addition experiments were collected according to protocol and with informed consent. No patient information was collected.