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.
   - No sample-size calculation was performed, as these are proof-of-concept experiments. But for each experiment, 3 or 4 independent biological replicates were used.

2. **Data exclusions**
   - Describe any data exclusions.
   - All the devices used for the experiments were pre-checked to make sure that the permeability is good for further experiments. No data were excluded.

3. **Replication**
   - Describe whether the experimental findings were reliably reproduced.
   - All the devices used for the experiments were pre-checked to make sure that the permeability is good for further experiments. All attempts at replicates were successful.

4. **Randomization**
   - Describe how samples/organisms/participants were allocated into experimental groups.
   - Devices were randomly allocated to each experimental groups. The samples from the sickle-cell patients were grouped on the basis of the ratio of irreversibly sickled red blood cells.

5. **Blinding**
   - Describe whether the investigators were blinded to group allocation during data collection and/or analysis.
   - Investigators were blinded to all clinical information of the patients who donated blood, aside from the primary diagnosis.

   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).
   - 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

Describe the software used to analyze the data in this study.

We used the statistical analysis module in the software Graphpad prism version 5.

Policy information about availability of computer code

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

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 employed in this study are commercially available.

Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

mouse anti-human VE-cadherin (Santa Cruz Biotech, F8, Lot#H2013),
mouse anti-human collagen IV (abcam, col-94, ab6311, Lot#GR199373-2),
rabbit anti-human laminin (abcam, ab11575, Lot#GR202345-2)
mouse monoclonal anti-human E-selectin (ThermoFisher Scientific, CL2/6, MA1-34486),
mouse monoclonal anti-human ICAM-1 (ThermoFisher Scientific, 15.2, MA1-33754),
mouse monoclonal anti-human VCAM-1 (R&D Systems, BBIG-V1, BBA5),
mouse monoclonal anti-human P-selectin (Santa Cruz Biotech, AK4, Lot#A0606)
rabbit polyclonal anti-human MMP2 (abcam, ab37150, lot#GR286050-10)
mouse monoclonal anti-human MMP9 (ThermoFisher Scientific, MA5, MA5-14228, lot#SC2341247)

All these antibodies were validated by published work cited in the Company's website for each antibody.

Eukaryotic cell lines

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

HUVECs and human lung microvascular endothelial cells were purchased from Lonza, and human dermal microvascular endothelial cells were obtained from Thermofisher Scientific. For all these primary cell lines, passages 3-6 were used in the experiments.

b. Describe the method of cell line authentication used.

All the cell lines were authenticated by published work cited in the vendor's website.

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

The cells lines were not tested for mycoplasma contamination.

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.

No commonly misidentified cell lines were used.

Animals and human research participants

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

Description of research animals

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

No animals were used.
12. Description of human research participants

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

Research participants were patients with sickle-cell disease of the Hemoglobin SS genotype, the most common and severe form of sickle-cell disease. Importantly for our studies, blood samples were collected from these patients when they were at clinical baseline and had not received blood transfusions for >1 month. Healthy research participants were randomly selected as controls.