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Life Sciences Reporting Summary

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Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study. For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

Experimental design

1. Sample size

Describe how sample size was determined.

No sample size calculation was performed since the this is cell line study.

2. Data exclusions

Describe any data exclusions.

One transcript data of a triple repeat was excluded due to obvious abnormal value (less than mean of the triple- 3xSD)

3. Replication

Describe the measures taken to verify the reproducibility of the experimental findings.

The reproducibility of our experimental finding were confirmed by at least three independent repeat experiments.

4. Randomization

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

No randomization was performed as the study are based on cells in different genotype.

5. Blinding

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

The heparan sulfate disaccharide, gene transcript and FGF2 signaling analyses were blind to the investigators. However, the cell surface staining for CD31, VEGFR2, anti-heparan sulfate phage display antibodies and genotyping were not blind to the investigators, because these information were needed essentially to generate the heparan sulfate mutant cell library.

Note: all in vivo studies must report how sample size was determined and 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 *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒	Test values indicating whether an effect is present *Provide confidence intervals or give results of significance tests (e.g. P values) as exact values whenever appropriate and with effect sizes 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 in all relevant figure captions (with explicit mention of central tendency and variation)

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.	Microsoft Excel 2017, Flowjo v8.7 for mac, DSDecodedM (http://skl.scau.edu.cn/dsdecode/), CRISP-ID (http://crispid.gbiomed.kuleuven.be/), CRISPR gRNA design tool (http://tools.genome-engineering.org)

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 third party.	The unique heparan sulfate mouse lung endothelial cell lines were generated in our own laboratory and have been available to researchers in scientific field. To dates, we have shared the cell library with several laboratories world wide.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	The commercial antibodies were widely used and validated in many publications. The anti-heparan sulfate phage display antibodies have been used widely in the heparan sulfate field and validated in many publications too. In our study, we also validated the antibodies are true anti-heapran sulfate antibody using our heparan sulfate-deficient cells. PE-rat anti-mouse VEGFR2 antibody, BD Pharmingen (555308) PE-rat anti-mouse IgG2ak isotype control, BD Pharmingen (553930) CD31 Microbeads, mouse Miltenyibiotec (130-097-418) FITC rat IgG2ak isotype control, eBioscience (11-4321-80) FITC-anti-mouse CD31 antibody, eBioscience (11-0311-82) Anti-heparan aulfate antibody (10E4), amsbio (F58-10E4 clone) Biotin-anti-mouse IgM Monoclonal antibody, eBioscience (13-5790-82) eFluor 450-Streptavidin, eBioscience (48-4317-82) Anti-heparan Sulfate Display Antibodies including EV3C3, AO4B08, HS4C3, RB4EA12 were generated in Dr. Toin H. van Kuppevelt laboratory Biotinylated-anti-VSV-G antibody, Abcam, (Ab34774) Anti-Phospho-p42/p44 MAPK(Erk1/2)(Thr202/Tyr204) antibody ,Cell Signaling Technology (#9101) Anti-p42/p44 MAPK(Erk1/2)(Thr202/Tyr204) antibody, Cell Signaling Technology(#4695) Anti-FGFR1 antibody (clone D8E4) Cell Signaling Technology (#9740) Anti-FGFR2 antibody (clone D4L2V), Cell Signaling Technology (#23328) Anti-beta-actin antibody (clone AC-74), Sigma-Aldrich (# A2228)

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	All the used mouse lung endothelial cell lines were generated in our own laboratory.
b. Describe the method of cell line authentication used.	The mouse lung endothelial cell lines were authenticated by observing cell surface expression of CD31 and VEGFR2 in flowcytomertry (flow cytometry BD LSRII).
c. Report whether the cell lines were tested for mycoplasma contamination.	All our cell lines have 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

11. Description of research animals

Provide all relevant details on animals and/or animal-derived materials used in the study.	All mice in C57BL6 background at 8-10 weeks-old were used including genetically engineered Ext1f/f, Ndst1f/f, Ndst2-/-, Hs2stf/f, Hs6st1f/f, Hs6st2-/-, Sulf1f/f;2f/f mice.

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.

The study did not involve human research participants.