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 statistical analyses were performed to predetermine sample sizes, but our sample sizes are similar to those generally employed in the field.
   Described in the Methods section of the paper.

2. Data exclusions
   Describe any data exclusions.
   
   For guinea-pig cochlear experiments, we interpreted as successful measurements with the following three conditions; first, the EP values exceeded +50 mV; second, voltage drifts observed when the glass microelectrode was pulled back to the perilymph were less than ± 5 mV; and third, the baseline of 'subtraction current' was relatively stable.
   For rat-brain experiments, one rat died during the recording. In three other rats, during drug injection the catheter fell from the tail vein or it was blocked. Moreover, in one rat, the BDD microsensor current was unstable at the outset of the recording because of a problem in the reference electrode.
   In the analyses for LC-MS/MS and in the determination of pharmacokinetics, the data points less than the in vivo LOD were excluded in each experiments using BDD microsensors.
   Described in the Methods section of the paper.

3. Replication
   Describe whether the experimental findings were reliably reproduced.
   
   For each series of the experiments, all attempts at replication were successful.

4. Randomization
   Describe how samples/organisms/participants were allocated into experimental groups.
   
   Randomization of experimental groups were not required to this study.

5. Blinding
   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.
   
   Blinding was not applicable to this study.

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
- [x] 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.

7. Software

Policy information about availability of computer code

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

GraphPad Prism 6 and LabChart 7.2 were used to analyze the data.

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.

8. Materials availability

Policy information about availability of materials

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

N/A

9. Antibodies

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

N/A

10. Eukaryotic cell lines

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

N/A

b. Describe the method of cell line authentication used.

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

N/A
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.

N/A
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.

Male Hartley guinea pigs (230–420 g, 3–5 weeks old) and male Wister rats (90–300 g, 4–7 weeks old) were purchased from Japan SLC Inc. (Hamamatsu, Japan). All animal experimental protocols were approved by the President of Niigata University (Permission Number: #26 Niigata Univ. Res. 96-1 and Number: #26 Niigata Univ. Res. 215-2). The in vivo experiments were carried out under the compliance with the protocol reviewed by the Institutional Animal Care and Use Committee and the Japanese Animal Protection and Management Law. Under the guideline, guinea pigs and rats were housed at the animal facility at the Niigata University School of Medicine. Animals were kept on a 12-h light / 12-h dark cycle and all experiments were performed during the light cycle. Food and water were provided ad libitum. All animal handling and reporting comply with ARRIVE guidelines.

Described in the Methods section of the paper.

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.

N/A