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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.

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.

   For each of the experiments we chose the sample size such that training and test images are representative of the variability seen across all developmental time-points.

2. Data exclusions

   Describe any data exclusions.

   No data was excluded from the manuscript.

3. Replication

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

   For all experiments we provide the code and training data to retrain all used models and reproduce the findings.

4. Randomization

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

   For each experiment, the held-out test set was randomly selected from the corpus of data.

5. Blinding

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

   For each experiment, the restoration models were optimized based on a random validation set that had no overlap with the held-out test set on which the final evaluation results were based.

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.	tensorflow (1.4.0), keras (2.0.0), python (3.5), pandas, Fiji/ImageJ, Adobe Illustrator (CS5), spimagine 0.2.5, iMovie (10.1.6), softWoRx Version 6.5.2., Huygens Professional 17.10.0, Andor iQ version 3.4.1, Training and application code is/will be made available on github and csbdeep.bioimagecomputing.com.

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.	No unique materials/reagents were used.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	*For all antibodies, as applicable, provide supplier name, catalog number, clone name, and lot number. Also describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript OR state that no antibodies were used.*

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	- INS-1 cells donated from Claes Wohlheim (Geneva) - HeLa cells, image data taken from Gustafsson, Nat Com, 2016
b. Describe the method of cell line authentication used.	None of the cell lines have been authenticated.
c. Report whether the cell lines were tested for mycoplasma contamination.	INS-1 cells were tested for mycoplasma contamination (negative).
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.	INS-1 cells are not listed in the database.

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.	- Schmidtea mediterranea, RedDot1 staining, asexual, clonal strain CIW4, 3 weeks after amputation - Tribolium castaneum, EFA::nGFP transgenic line, unknown sex (embryos), age between 10-48 hrs - Drosophila melanogaster (projection), Ecad::GFP transgenic line, male and female, between 16 and 26 hours APF (after puparium formation). - Drosophila melanogaster (isotropic restoration), His2Av-mRFP1 line, timelapse of 2-4 hpf. - Danio rerio (isotropic restoration), bactin:eGFP- LAP2B transgenic line, 24 hpf, mixed sex (before sex determination) - Mus musculus liver (isotropic restoration), fixed C57BL/6JOlaHsd mice, 9 weeks old, male - The stable INS-1 cell line (restoration of diffraction limited structures) was donated by Claes Wohlheim (Geneva), and transfected with pEG-hIns-SNAP. The HeLa H2B-mCherry/mEGFP-a-tubulin stable cell line (restoration of diffraction limited structures) was kindly provided by Dr. Buzz Baum, MRC-LMCB, UCL. (doi: 10.1242/jcs.091967).

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.