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Corresponding author(s): Florian Erhard, Lars Dölken

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 statistical methods to pre-determine sample size were used. However, in Ribo-seq experiments an n=2 is usually considered to be appropriate to demonstrate the reproducibility of open reading frames identified in a Ribo-seq experiment. The same holds true for the MHC-I peptidome analysis. Accordingly, two biological replicates of ribosome profiling were obtained from primary human fibroblasts (HFF). This includes translation start site profiling using Harringtonin/Lactimidomycin. The analysis of MHC-I peptidomes was based on one previously published and one newly generated data sets. Both showed excellent reproduciblity. Therefore, no additional replicates were performed.

2. Data exclusions

   Describe any data exclusions.

   No data were excluded from the analysis.

3. Replication

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

   All findings could be replicated in at least two independent biological replicates.

4. Randomization

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

   No randomization is required when performing Ribo-seq or MHC-I peptidome analysis without any experimental groups.

5. Blinding

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

   No blinding was possible as the data from uninfected and infected cells differ too substantially from each other not to be recognized thereafte

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.

All new software including source code has been made publicly available on GitHub. Commercially / freely available software that was used in this study include: MaxQuant (version 1.5.8.3), PRICE (version 1.0.1), Rp-Bp (version 1.1.1), ORFRater (downloaded from github 14.2.17), SPECtre (downloaded from github 14.2.17), RibORF (version 0.1), R (version 3.3.2), Bowtie (version 1.0)

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 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).

Antibodies were only used for the preparation of the HLA-I peptidome analysis. The hybridoma producing the pan-HLA class I-specific mAb W6/32 (ATCC HB-95, mouse IgG2a) was obtained from ATCC. Ab production was performed in-house at the Department of Immunology, Tuebingen. This antibody has been used in previous HLA peptidomics studies which are referenced. The lot number of the antibody batch is no longer available.

10. Eukaryotic cell lines

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

Primary human forskin fibroblasts (HFF) were obtained from ATCC.

b. Describe the method of cell line authentication used.

HFF were directly purchased from ATCC at the begin of this study.

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

All cell lines and all virus stocks were continuously tested for mycoplasma by PCR. Touching of tissue culture plates with bare hands was strickly avoided.

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 cross-contaminations reported according to ICLAC for HF99-7.

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.	No animals were used.

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.	This study did not involve human participants.