

## Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

### Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement
- A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- 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 all covariates tested
- A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- For null hypothesis testing, the test statistic (e.g.  $F$ ,  $t$ ,  $r$ ) with confidence intervals, effect sizes, degrees of freedom and  $P$  value noted  
*Give  $P$  values as exact values whenever suitable.*
- For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- Estimates of effect sizes (e.g. Cohen's  $d$ , Pearson's  $r$ ), indicating how they were calculated

*Our web collection on [statistics for biologists](#) contains articles on many of the points above.*

### Software and code

Policy information about [availability of computer code](#)

Data collection

Data analysis

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

### Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Data supporting the findings of this study are available within the paper and its Supplementary Information files. Cryo-EM density maps have been deposited in the Electron Microscopy Data Bank (EMDB) under the accession codes EMD-19618 (hDH), EMD-19625 (MCM5 AG DH), EMD-19619 (hSH), EMD-19620 (hMO\*), EMD-19621 (locally refined ORC of hMO\*), EMD-19622 (composite map of the globally refined hMO\* and the locally refined ORC map), EMD-19623 (hOCCM), EMD-19624 (hOC1M). Atomic coordinates have been deposited in the Protein Data Bank (PDB) with the accession codes 8S09 (hDH), 8S0A (hSH), 8S0B (MCM-ORC6 of hMO\*, which was modelled using the globally refined hMO\* map), 8S0C (ORC1-5 of hMO\*, which was modelled using the locally refined map of ORC), 8S0D (composite model of MCM-ORC6 and ORC1-5 docked into the composite map), 8S0E (hOCCM), 8S0F (hOC1M).

## Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

Life sciences       Behavioural & social sciences       Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Negative stain EM experiments were used to determine the nucleotide and protein dependency of the human MCM loading reaction. To obtain 2D classes of different reaction intermediates, we usually collected 60-150 micrographs per condition.  To yield high-resolution structures of hDH and hSH in the cryo-EM experiment, ~3.6 K micrographs were collected from a single grid. High-resolution structures of hOCCM, hOC1M and hMO* were obtained from ~31.6 K micrographs, which were collected from a single grid.  No statistical methods were used to predetermine sample size. Sample size was chosen to obtain interpretable negative stain 2D averages and cryo-EM volumes of resolution appropriate for atomic model building.
Data exclusions	Negative stain and cryo-EM micrographs with poor staining, ice contamination or without graphene oxide, respectively, were excluded. Picked particles that did not align to a distinct class in 2D and 3D (cryo-EM only) were excluded from further analysis.
Replication	The different complexes identified in this study were visualised in multiple experiments (both negative stain and cryo-EM). All findings from nuclease footprinting assays were reproducible. Please refer to statistics and reproducibility section of the manuscript.
Randomization	For 3D reconstructions independent halves of the dataset were used to compute Fourier Shell Correlation.
Blinding	Blinding is not relevant for single particle reconstruction, because reference free models are used.

## Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

### Materials & experimental systems

### Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Sf9 cells were purchased from Thermo Fisher (12659017). RPE-1 and U2-OS cells were obtained from the Crick Cell Services science technology platform.
Authentication	None of the cell lines were authenticated.
Mycoplasma contamination	All cell lines were tested negative for mycoplasma contamination.
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	No commonly misidentified cell lines were used in this study.