Reporting Summary

Nature Research 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 Research policies, see our Editorial Policies 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.

Statistics

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

☑ 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
Clinical sample ChIP-seq data. AR ChIP-seq data from normal prostate tissue (n=8) and primary prostate tumor samples (n=8) were merged with samtools (v1.5). Then, the samtools views function was utilized to generate merged files with comparable read numbers. Sample profiles were then plotted with the deepTools plotProfile function as described in the methods section.

Data analysis
ChIP-Seq data analyses used FASTQC v0.11.5, bowtie2 v2.3.2, NACS v2.1.1, deepTools v2.5.7, & Homer v4.10.3. RNA-Seq data analyses used STAR v2.5.2a and DESeq2 v1.12.4 as described in the methods section.

For manuscripts utilizing custom algorithms or software that are not central to the research but 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 Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The datasets generated during the current study have been deposited in public repositories. ChIP-Seq data have been deposited in the NCBI Gene Expression Omnibus (GEO) with the accession code GSE144960. RNA-Seq data have been deposited in the NCBI GEO with the accession code GSE144961. Molecular Signature Database was utilized for pathway analyses. The source data underlying Figs. 1B, 3C-G, 4A-E, 5B-C, 6A, 6C-D, and 7A-B and Supplemental Figs. 3D, 5C, 6D-E, 7B-C, and 7F are provided as a Source Data file.
All experiments were performed in technical triplicate with at least 3 independent biological replicates per condition. Data are displayed as mean ± standard error of the mean (SEM). Statistical significance (p < 0.05) was determined using Student’s t-test, one-way ANOVA, and two-way ANOVA on GraphPad Prism Software as appropriate and indicated in applicable figure legends.

**Life sciences study design**

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

- **Sample size**: All experiments were performed in technical triplicate with at least 3 independent biological replicates per condition. Data are displayed as mean ± standard error of the mean (SEM). Statistical significance (p < 0.05) was determined using Student’s t-test, one-way ANOVA, and two-way ANOVA on GraphPad Prism Software as appropriate and indicated in applicable figure legends.

- **Data exclusions**: No data was excluded from the analyses in this study.

- **Replication**: All experiments in this study were performed at least 3 independent times for biological replicates with at least technical triplicates for each individual biological replicate. The details for each specific experiment are described in the methods section and in each figure legend.

- **Randomization**: For xenograft studies, mice were randomized into the two categories as described in the methods section. For in vitro studies, conditions were randomized into control and experimental conditions as described in each assay.

- **Blinding**: Blinding was not relevant to majority of the assays performed in this study since they were in vitro cell culture and in vivo xenograft studies in which the treatment groups needed to be clear when performing the experiments. For the PDE (patient-derived explant) studies, de-identified tissues was utilized for examination of CRY1 expression levels in non-neoplastic, tumor, and IR treated samples. Investigators were blinded to patient tissue identifiers and were given matched tumor and non-neoplastic tissue to treat accordingly.

**Behavioural & social sciences study design**

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

- **Study description**: N/A

- **Research sample**: N/A

- **Sampling strategy**: N/A

- **Data collection**: N/A

- **Timing**: N/A

- **Data exclusions**: N/A

- **Non-participation**: N/A

- **Randomization**: N/A

**Ecological, evolutionary & environmental sciences study design**

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

- **Study description**: N/A

- **Research sample**: N/A
Field work, collection and transport

Field conditions N/A
Location N/A
Access & import/export N/A
Disturbance N/A

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

| n/a | Involved in the study |
|-----|-----------------------|
|  | Antibodies |
|  | Eukaryotic cell lines |
|  | Palaeontology and archaeology |
|  | Animals and other organisms |
|  | Human research participants |
|  | Clinical data |
|  | Dual use research of concern |

Methods

| n/a | Involved in the study |
|-----|-----------------------|
|  | ChIP-seq |
|  | Flow cytometry |
|  | MRI-based neuroimaging |

Antibodies

Antibodies used

CRY1 (Bethyl A302-614A), ATM (Cell Signaling Technology (CST) 2873), phospho-ATM (Ser1981) (CST 5883S), CHK2 (Bethyl A300-619A), phospho-CHK2 (Thr68) (CST 2661T), MRE11 (CST 8344T), RAD50 (CST 8344T), RAD51 (Abcam ab63801), XRCC3 (Novus NB100-165), and Vinculin (Sigma-Aldrich V9264).

Validation

The antibodies listed above are all commercially available and were used at 1:1000 dilution per manufacturer's instructions and protocols. Bethyl, Cell Signaling Technology, Abcam, Novus, and Sigma-Aldrich validated their antibodies and the description can be found on their websites for specific antibodies listed above. Additionally, the commercially available antibodies used in this study were produced by immunizing animals with recombinant human CRY1, ATM, pATM, CHK2, pCHK2, MRE11, RAD50, RAD51, XRCC3, or Vinculin.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s) C4-2, 22Rv1, and LNCaP cells were purchased from ATCC.
C4-2, 22Rv1, and LNCaP cells were purchased from ATCC and authenticated directly by ATCC using their morphology, karyotyping, and PCR based approaches to confirm the identity of human cell lines. All cell lines utilized in this study (i.e. C4-2, 22Rv1, and LNCaP cells and their inducible shCON and shCRY1 lines) were all tested for mycoplasma upon thawing of cells. All tests were negative for myco contamination.

Cells were authenticated directly by ATCC. No commonly misidentified lines were used in this study.
Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No  Yes
☐ Public health  ☐ National security
☐ Crops and/or livestock  ☐ Ecosystems
☐ Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No  Yes
☐ Demonstrate how to render a vaccine ineffective
☐ Confer resistance to therapeutically useful antibiotics or antiviral agents
☐ Enhance the virulence of a pathogen or render a nonpathogen virulent
☐ Increase transmissibility of a pathogen
☐ Alter the host range of a pathogen
☐ Enable evasion of diagnostic/detection modalities
☐ Enable the weaponization of a biological agent or toxin
☐ Any other potentially harmful combination of experiments and agents

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE144962 with token ivwzacmcbixxaz

Files in database submission

ChIP-Seq – Veh IP and Input for CRY1 in C4-2 cells. RNA-Seq – shCON and shCRY1 in C4-2 cells.

GSE144960 and GSE144961

Genome browser session

(e.g. UCSC)

Methodology

Replicates

Two biological replicates for Veh condition for CRY1 IP in C4-2 cells with corresponding input.

Sequencing depth

FASTQ files were assessed for quality using FASTQC v0 11 5. Reads were aligned to the human genome reference version hg19 using bowtie2 v2.3.2. Click or tap here to enter text. with default parameters.

Antibodies

CRY1 antibody previously used for ChIP-Seq in human U2OS cells in Hoffmann, J. et al. Non-circadian expression masking clock-driven weak transcription rhythms in U2OS cells. PloS one 9, e102238 (2014).

Peak calling parameters

Peak calling was performed using MACS2 v2.1.172 with combined replicates, utilizing a q < 0.05 cutoff.

Data quality

FDR > 1.5 and q < 0.05 was used for the peak calling cutoff as described in the methods section in detail.

Software

The ChIP-Seq libraries were constructed using the Swift BioSciences ACCEL-NGS 2S Plus DNA Library kit with approximately 10 ng of ChIP DNA. NextSeq 500 sequencer from illumina was utilized to sequence samples. ChIP-Seq binding heatmaps and profiles were generated using deepTools v2.5.7. Peak annotation and motif analysis performed using Homer v4 10 314 using the parameters indicated.
## Flow Cytometry

### Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

| Sample preparation | All C4-2 and 22Rv1 derived cells were plated at equal densities in hormone-proficient media. |
|-------------------|-------------------------------------------------------------------------------------------------|
| Instrument        | Millipore Guava flow cytometry machine                                                        |
| Software          | Analysis was performed using InCyte software (Guava) for cell-cycle profile with BrdU incorporation and PI (propidium iodide). |
| Cell population abundance | Once all treatments were completed, cells were incubated with BrdU (1:1000) for 2 hrs prior to harvesting. At least 10,000 events per sample were assessed. |
| Gating strategy   | Gating was established to measure G0, G1, S, and G2/M phases and calculate percent of population in each phase with BrdU and PI incorporation. |

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

### Magnetic Resonance Imaging

#### Experimental design

| Design type        | N/A |
|--------------------|-----|
| Design specifications | N/A |
| Behavioral performance measures | N/A |

#### Acquisition

| Imaging type(s) | N/A |
|-----------------|-----|
| Field strength  | N/A |
| Sequence & imaging parameters | N/A |
| Area of acquisition | N/A |
| Diffusion MRI   | Used |
|                  | Not used |

#### Preprocessing

| Preprocessing software | N/A |
|------------------------|-----|
| Normalization          | N/A |
| Normalization template | N/A |
| Noise and artifact removal | N/A |
### Statistical modeling & inference

| Model type and settings | N/A |
|-------------------------|-----|
| Effect(s) tested        | N/A |

Specify type of analysis:  
- [ ] Whole brain  
- [ ] ROI-based  
- [ ] Both

Statistic type for inference  
(See Eklund et al. 2016)
  
| Correction | N/A |
|------------|-----|

**Models & analysis**

n/a involved in the study  
- [ ] Functional and/or effective connectivity  
- [ ] Graph analysis  
- [ ] Multivariate modeling or predictive analysis

Functional and/or effective connectivity  
N/A

Graph analysis  
N/A

Multivariate modeling and predictive analysis  
N/A

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