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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	Not applicable
Data analysis	Statistical analyses were performed by using GraphPad Prism 9.2 for Windows. For untargeted metabolomics, data processing was accomplished by using XCMS. Centroided peaks were uploaded to MetaboAnalyst 5.0. Lipid species were annotated by uploading MS/MS spectra into Agilent MassHunter Lipid Annotator 1.0. Raw metabolomics data were analyzed with Qualitative Navigator B.08.00 and Skyline (version 20.1.0.155). RNA-seq reads were aligned to the Genome Reference Consortium Human Build 38 (GRCh38) using STAR2 with Ensembl genes for homo sapiens version 90. Isoform expression levels for *KHK-A* and *KHK-C* were calculated and normalized as Fragments Per Kilobase per Million reads (FPKM) by using Cufflinks with default parameters. Integrative genomics viewer (IGV) was used to visualize and manually inspect sequencing reads from isoform specific exons.

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

Provide your data availability statement here.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Given that a focus of our work is cervical cancer, which exclusively occurs in women, we only considered female sex.
Reporting on race, ethnicity, or other socially relevant groupings	We did not report on race, ethnicity, or other socially relevant groupings in our study.
Population characteristics	All patients had cervical cancer in this cohort and were uniformly treated with curative-intent chemoradiation and clinical data were prospectively collected
Recruitment	Cervical cancer patients were enrolled in a prospective tumor banking study with written informed consent. Self-selection bias is not likely to impact our RNA-seq and overall survival data
Ethics oversight	Washington University Institutional Review Board (IRB). IRB number is 201105374

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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

Life sciences study design

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

Sample size	Sample sizes were based on previous experimental experience in our research group and on previous studies in the literature
Data exclusions	A Grubb's Test was used to determine if outliers were present in the data. It was determined that one data point from the control condition of Figure 1A was an outlier, which was multiple-fold higher than the average of that condition. This single data point was removed.
Replication	Each experimental finding reported was determined by using multiple animals or cell-culture experiments. The data were reproducible.
Randomization	Mice bearing tumors were randomly assigned to different dietary conditions. Zebrafish with resected tumors were randomly assigned to the high-fructose or control conditions. When assessing tumor xenograft outgrowth in mice under two different experimental conditions, initial tumor sizes were assessed to confirm that there were no statistically significant differences in initial tumor sizes between groups.
Blinding	Samples were prepared for metabolomics, analyzed by LC/MS, and the resulting data processed in a blinded fashion

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
☐	☒ Clinical data
☐	☒ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used: anti-ketohexokinase (Santa Cruz; catalog number: sc-377411), anti-ketohexokinase-C (Signalway; catalog number 21709), anti-ketohexokinase-A (Signalway; catalog number: 21708), anti-sorbitol dehydrogenase (Santa Cruz; catalog number: sc-377200), antialdolase B (santa Cruz; catalog number: 393278); anti-beta tubulin (Cell Signaling; catalog number: 2128), anti-lysophosphatidylcholine acyltransferase 1 (Proteintech; catalog number: 16112-1-AP); anti-glyceraldehyde 3-phosphate dehydrogenase (Cell Signaling; catalog number: 3683S); or anti-succinate dehydrogenase (Cell Signaling; catalog number: 5839S)

Validation: All antibodies used in the study had validating data on the antibody on the supplier website. Furthermore, the antibodies have been used in other publications

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s): HeLa cells were obtained from the Tissue Culture Support Center of Washington University in St Louis. CaSki and Siha cells were obtained from the laboratory of Julie Schwarz. E6, E7-expressing TC-1 cells were obtained from the laboratory of TC Wu. BrafV600E-mutant, Pten-deficient mouse melanoma cells were obtained from the laboratory of George Souroullas and were derived from TyCreERT2 Braf V600E/+ PtenF/F genetically engineered C57 BL/6 mouse models. A-498 cells were obtained from the laboratory of James Hsieh. MIA PaCa-2 cells were obtained from the laboratory of William Hawkins. Huh7 cells were obtained from the laboratory of Brian Finck. Z crest C zebrafish melanoma cells were obtained from the laboratory of Charles Kaufman. E0771 (94A001) were obtained from CH3 BioSystems. MCF-7 (HTB-22) and 3T3-L1 (CL-173) cells were obtained from American Type Culture Collection

Authentication: Cell lines from American Tissue Type Collection (ATCC) were authenticated by ATCC

Mycoplasma contamination: Cell lines tested negative for Mycoplasma

Commonly misidentified lines (See ICLAC register): HeLa

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals: Nude mice; Athymic strain (CRL strain code: 490); female, studies were begun when mice were 12-14 weeks old. C57 BL/6J (strain number: 000664) female mice. Studies were begun when mice were 10-14 weeks old.

Wild animals: Not applicable

Reporting on sex: For the use of our cervical cancer and breast cancer models, female mice were the most relevant sex to use. Furthermore, female mice bearing tumors were used in this study as they were protected from insulin resistance and obesity when consuming high amounts of sugar. This allowed us to decouple the effects of insulin resistance and obesity from our observations of sugar-mediated tumor growth enhancement.

Field-collected samples: Not applicable

Ethics oversight: All procedures were approved by the Washington University Institutional Animal Care and Use Committee

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Not applicable; study was not a clinical trial but rather a tumor prognostic study and a validation study of isoforms of KHK and aldolase B in human cervical tumors
Study protocol	The Institutional Review Board (IRB) protocol number is 201105374
Data collection	Data were collected at Washington University School of Medicine
Outcomes	Primary outcomes measured were KHK-A, KHK-C, and aldolase (A, B, and C isoforms) expression. Overall survival and KHK-A expression relative to tumor stage were also measured

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*