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Life Sciences Reporting Summary

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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 in vitro experiments, at least three independent experiments were performed. For in vivo animal studies, sample size was not predetermined, and the experiments were performed using five biological replicates and in duplicate, and the results pooled.

2. Data exclusions

   Describe any data exclusions.

   Two mice with tail-vein injections of Caco2 cells were unintentionally culled.

3. Replication

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

   All attempts at data reroducibility were successful.

4. Randomization

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

   Animals were randomly assigned to different experimental groups.

5. Blinding

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

   For in vivo imaging experiments of the animals, researchers were not blinded to the group allocation.

   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.	Data analysis was performed using either GraphPad Prism 6 or R statistical software. Mass spectrometry data were analyzed by MaxQuant. Flow cytometry data were analyzed using software Summit 5.2. Microarray data were analyzed using GeneSpring.

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.	Microarray data are available in Gene Expression Omnibus under accession number for the study: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?token=sdmluyaqplgvtuz&acc=GSE76180 Mass spectrometry data are available upon request.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	Cleaved Caspase 3 antibody was purchased from Cell Signaling Technologies (#9661). The dilution was 1: 100.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Human colorectal cancer cell lines (HT-29, Caco2 and SW480) were acquired from the University of North Carolina Lineberger Comprehensive Cancer Center Tissue Culture Facility. The luciferase-expressing cell line, HT-29-luc2, was purchased from Caliper Life Sciences (Hopkinton, MA). CRC119 was obtained from Dr. David Hsu from Duke University.
b. Describe the method of cell line authentication used.	Cell lines were authenticated using short tandem repeat DNA profiling.
c. Report whether the cell lines were tested for mycoplasma contamination.	The cells were tested and found to be negative for mycoplasma contamination.
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 commonly misidentified cell lines were used in this study.

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.	Female Nu/Nu mice, 8–10 weeks old, were purchased from the Animal Studies Core at University of North Carolina at Chapel Hill. Male Sprague-Dawley rats, 250–300 gr, were purchased from Charles River.

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.	No human participants were involved in this study.

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Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

☒ 1. The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ 2. 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).

☒ 3. All plots are contour plots with outliers or pseudocolor plots.

☒ 4. A numerical value for number of cells or percentage (with statistics) is provided.

Methodological details

5. Describe the sample preparation.	For proliferation assays, CRC cells grown on plastic, collagen, Matrigel, liver biomatrix, or lung biomatrix (100 ug/cm2) were incubated with 10 µM 5-ethynyl-2′-deoxyuridine (EdU) for 4 hours. Cells were then washed with PBS, processed into single cells using TrypLE, and stained for EdU using a Click-iT Plus EdU Assay for Flow Cytometry kit (Thermofisher Scientific) according to the manufacturer's instructions. Cells were then washed in PBS containing 10% FBS three times and submitted for flow-cytometric analysis. For apoptosis assays, CRC cells grown on plastic, collagen, Matrigel, liver biomatrix, or lung biomatrix (100 ug/cm2) were collected, processed into single cells, and fixed in 4% paraformaldehyde for 10 minutes at room temperature. Cell suspensions were blocked over night in Dako block (Agilent Technologies). Cells were then resuspended and stained with primary conjugated Cleaved Caspase 3 (Cell Signaling Technologies) (1:100) for 2 hours at room temperature. Cells were then washed with PBS containing 10% FBS three times and submitted for flow cytometric analysis.
6. Identify the instrument used for data collection.	All flow cytometric analysis was done using a Beckman Coulter CyAn ADP.
7. Describe the software used to collect and analyze the flow cytometry data.	All data were analyzed using software Summit 5.2.
8. Describe the abundance of the relevant cell populations within post-sort fractions.	The abundance of our relevant cell population was 100%, as these represent pure CRC cell cultures.
9. Describe the gating strategy used.	CRC cells were distinguished from cellular debris based on scatter profiles and Sytox positivity (a florescent nuclear stain applied to cells after fixation). Cells were defined as events that fell withing gates applied to FSC (larea) vs SSC (area) and FSC (lin) vs FSC (area) plots, as well as within a gate selecting for Sytox positive events. Events meeting these criteria were then applied to plots of EdU vs FSC or Cleaved Caspase 3 vs FSC to assess proliferation and apoptosis, respectively, in independent experiments.

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