Supplementary Materials for

Multi-omics analyses of radiation survivors identify radioprotective microbes and metabolites

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Other Supplementary Material for this manuscript includes the following:
(available at science.sciencemag.org/content/370/6516/eaay9097/suppl/DC1)

Tables S1 to S5 (Excel files)
MDAR Reproducibility Checklist (PDF)

Materials and Methods

Mice

All animal procedures were approved (protocol #17-128/20-054) by the University of North Carolina Chapel Hill (UNC) Institutional Animal Care and Use Committee (IACUC) and were conducted according to US National Institutes of Health Guide for the Care and Use of Laboratory Animals. Animal numbers were empirically determined to optimize numbers necessary for statistical significance based on our previous reports using these models (minimum of three to seven animals per group). Animals were excluded if they exhibited signs of disease not associated with radiation-induced injury (for example, fight wounds and malocclusion). All experiments used littermate controls, or their immediate descendants. Wild-type C57BL/6J mice were obtained from Jackson Laboratory and house-raised at UNC for at least nine generations. Conventionally raised mice were bred and housed in specific-pathogen-free (SPF) conditions, and germ-free (GF) animals were generated and housed in the National Gnotobiotic Rodent Resource Center of North Carolina at Chapel Hill in AAALAC-accredited facilities.

Total body radiation

Total body radiation of mice was performed using an attenuator (X–302) with a ^{137}Cesium gamma-ray irradiating source (Mark I, Model 68-1, J.L. Shepard & Associates, San Fernando, CA). Alternatively, a Gammacell® 40 Exactor ^{137}Cesium source (Serial no. 265, Best Theratronics, Ottawa, Ontario) was also used for gamma-ray irradiation, with dosimetry variation of +/- 0.07 Gy as determined with phantoms by Dr. Ke Sheng, UCLA, Los Angeles, CA. Non-anesthetized mice were placed in ventilated plastic pie cages and exposed to 8.0 Gy-9.2 Gy total body radiation (depending on sex, age, SPF/GF). Following radiation, mice were housed in sterile autoclaved cages and provided standard chow and water *ad libitum* unless otherwise noted. Mice were monitored for changes in body weight and other body parameters through 30 days post radiation unless otherwise noted. A clinical score was determined using a cumulative scoring system (see Supplementary Table S2) based on weight loss, temperature change, physical appearance, posture, mobility, food consumption and hydration (*1*). Last observation carried forward (LOCF) method was used when interpreting the clinical score plots. Immediate indications for euthanasia included: weight loss greater than 25% of starting body weight, unconsciousness, an inability to remain upright, agonal respiration (gasping) or convulsions.

Histopathology

To assess tissue pathology, spleens, femurs, small intestines and colons were collected and fixed in 10% neutral-buffered formalin, paraffin-embedded, and sectioned (4-micron thickness) at the UNC Lineberger Animal Histopathology Core Facility. Prior to paraffin-embedding, femurs underwent an additional decalcification step in ImmunocalTM (StatLab, McKinney, TX). Slides were stained with hematoxylin and eosin (H&E) and semi-quantitatively scored by a board-certified pathologist (N.D.M.), who was blinded to experimental conditions. Histology was performed using an Olympus BX43 microscope with Olympus objective UPlanFL N 20X (na = 0.17). Images were taken with a DP27 camera and CellSens Dimension 1.16 software (Olympus). For all microscopic studies,

evaluation was performed at ambient temperature. Image processing was limited to contrast adjustment and sharpening and was performed using Adobe Photoshop CS4 v11.0.2 (Adobe, San Jose, CA). Histology scores represent the sum of each histological alterations as outlined below.

Spleen scoring system was based on the amount and patterns of extramedullary hematopoiesis (EMH) as described here: (1) atrophy; (2) atrophic white pulp with less than 20% EMH; (3) atrophic white pulp with 20-60% EMH; (4) atrophic white pulp with 60-100% EMH; (5) early white pulp recovery with extensive EMH in red pulp; (6) well-developed white pulp with extensive EMH in red pulp; (7) normal spleen.

Femur scoring system was based on the overall percentage of marrow space occupied by hematopoietic cells as compared to adipocytes and expressed as percent bone marrow cellularity [(marrow space occupied by hematopoietic cells/total marrow space) × ~100%].

Slides of spleen and femur sections were also stained with Ki67 antibody (Cell Signaling, #12202) or cleaved caspase 3 antibody (Cell Signaling, #9661).

Bone marrow stem cells isolation

Bone marrow stem cells were obtained using the magnetic cell sorting (MACS) system (Miltenyi Biotec) according to manufacturer's protocols. Briefly, bone marrow cells were collected from the femur and tibia of mice and then incubated with CD117 MicroBeads (Miltenyi Biotec, #130-091-224) for 15 minutes in the refrigerator (2−8 °C). After washing with buffer, cells were resuspended in 500 µL of buffer and applied to MACS column. Columns were washed with the appropriate buffer and then placed on a suitable collection tube, where magnetically labeled cells were flushed off. The purity of the CD117$^+$cells collected by the MACS was around 90%, and the viability was around 99%. These purified CD117$^+$ cells were used in immunoblotting or ROS detection assay.

Intestinal epithelial cell (IEC) and intestinal intraepithelial lymphocyte (IEL) isolation

Colons were harvested from mice and cut open longitudinally. Feces were removed by swishing the tissue in a 100 cm dish containing ice-cold PBS. Tissues were washed again in a separate dish containing PBS and cut into small pieces. After transferring to 50 mL tubes containing PBS and shaken vigorously by hand, samples were washed with PBS, until no bubbles appeared. Tissue pieces were then transferred into 5 ml Digestion buffer (100 µl DNase (1/50, Sigma, #DN25-1G), 20 µl Collagenase D (1/250, Roche, #11088874103), 100 µl Dispase (1/50, Stemcell, #07913)). Samples were minced well with scissors and transferred into new 50 ml tubes followed by shaking at 37 °C for 30 min. Then, samples were further shaken vigorously for 2 minutes by hand. Homogenates were supplemented with 14 mL complete RPMI and the digestion mixture was passed through a 100 µm cell strainer. Cells were washed with 10 ml complete RPMI and the pellets contained both IEL and IEC, which were used in immunoblot assay.

ROS detection

Intracellular ROS levels in bone marrow stem cells were detected using DCFDA Cellular ROS Detection Assay Kit (abcam, #ab113851) according to manufacturer's protocol. Briefly, cells were washed once in 1X Buffer and then incubated with 25 µM DCFDA for 45 min at 37 °C. Cells were then washed with 1X Buffer and placed in 96-

116 well plate for fluorescent reading at Excitation/Emission settings of 485/535 nm. The
117 average level of ROS in non-radiation naïve group was calculated, and all samples'
118 results were normalized to this average.
119
120 <u>Fecal DNA extraction, 16S rRNA gene sequencing and data analysis</u>
121   Fecal sample preparation and 16S rRNA sequencing were conducted as previously
122 described (*11, 42*). Briefly, fecal samples were collected, snap-frozen and stored at -80°C.
123 DNA was isolated by incubating fecal material at 65 °C for 30 min in Lysing Matrix E
124 tubes (MP Biomedicals, #6913-100) containing 200 mM NaCl, 100 mM Tris, 20 mM
125 EDTA (pH 8.0), SDS and proteinase K (Qiagen). Phenol: Chloroform: Isoamyl alcohol
126 (Invitrogen) was added, and samples were homogenized at 4 °C for 3 min using a bead
127 beater homogenizer followed by a centrifugation at 8000 rpm for 3 min at 4 °C.
128 Supernatants were incubated with Phenol: Chloroform (Invitrogen) for 10 min at room
129 temperature. Samples were then centrifuged at 13,000 rpm for 5 min at 4 °C, and aqueous
130 phases were incubated with isopropanol and 3 M sodium acetate (pH 5.2) at -20 °C
131 overnight. The precipitated DNA was collected by centrifugation at 13000 rpm at 4 °C
132 for 20 min, washed twice with 100% cold ethanol and resuspended in TE buffer. DNA
133 was further purified using a DNeasy Blood and Tissue Kit (Qiagen, #69504) according to
134 the manufacturer's protocol.
135   Fecal DNA samples were amplified by PCR using barcoded primer pairs targeting the
136 V1-V2 or V3-V4 region of the 16S rRNA gene. PCR amplicons were sequenced using
137 the Mi-Seq Illumina sequencer. The resulting bacterial sequence fragments were
138 clustered into Operational Taxonomic Units (OTUs) and aligned to Greengenes microbial
139 gene database with 97% sequence similarity in QIIME (1.8.0). Bacterial taxonomy
140 summarization, rarefaction analyses of microbial diversity, compositional differences
141 (with dissimilarity value indicated by Unweighted UniFrac Distance) were calculated in
142 QIIME as previously described using scripts (including pick_open_reference_otus.py,
143 summarize_taxa.py, alpha_rarefaction.py, jackknifed_beta_diversity.py and
144 make_distance_boxplots.py) (11). PCA plots were generated by QIIME script
145 (make_2d_plots.py). Heatmap was generated based on normalized bacteria abundance
146 using a R function heatmap (a function in R stats). Specifically, we first removed bacteria
147 which have zero or very low abundance (total abundance across samples < 0.000165) in
148 all samples. This reduced the total number of bacteria from 172 to 81. For the remaining
149 81 bacteria, we sorted them by t-test statistics (to test abundance between the elite-
150 survivors and controls). To enhance the contrast, we used by-row (by bacteria)
151 normalized values of relative abundance to generate the heatmap.
152
153 <u>SCFAs detection by GC-MS quantitation</u>
154   Authentic reference standards of acetic acid (AA), propionic acid (PA), and butyric
155 acid (BA) were obtained from Sigma-Aldrich (St. Louis, MO, USA). Stable isotope
156 labelling d4-AA, d2-PA and d2-BA were obtained from CDN Isotopes (Pointe-Claire,
157 Quebec, Canada). HPLC-grade hexane and water were purchased from Thermo Fisher
158 Scientific (Waltham, MA, USA), whereas propyl chloroformate (PCF), pyridine (Py), 1-
159 propanol (PrOH), as well as semiconductor-grade sodium hydroxide (NaOH) and
160 anhydrous sodium sulfate (Na_2SO_4), were purchased from Sigma-Aldrich (St. Louis, MO,
161 USA).

162   Fecal SCFA contents were quantified as described in Zheng *et al.* (*43*) with
163   modifications. For each fecal sample, ~40 mg aliquots were extracted on a TissueLyzer
164   (Qiagen, Hilden, Germany) with 0.005 M NaOH solution containing 50 µg/mL of d4-AA,
165   10 µg/mL of d2-PA, and 10 µg/mL of d2-BA, followed by 20 min centrifugation at
166   13,200 rpm. The supernatant layers were transferred to glass tubes and derivatized by
167   subsequently adding water, PrOH:Py (3:2, v/v) and PCF. Two-minute sonication was
168   then performed, and the propyl derivatives were extracted twice with hexane, combined
169   and transferred to Na_2SO_4-containing autosampler vials for GC-MS quantitation. The
170   instrumental analysis was conducted on an Agilent 7820A GC-5977B MSD system
171   (Santa Clara, CA, USA), where one-microliter extracts were injected under 1:10 split
172   mode, ionized with an electron ionization source, and separated by an Agilent DB-5
173   column (30m x 0.25mm x 0.25 µm) (Santa Clara, CA, USA) with 1 mL/min helium
174   flowing through the column. The temperature program was as follows: initial oven
175   temperature held at 50 ºC for 2 min, ramped to 70 ºC by 10 ºC/min, to 85 ºC by 3 ºC/min,
176   to 110 ºC by 5 ºC/min, to 290 ºC by 30 ºC/min, and finally held at 290 ºC for 8 min. The
177   relative standard deviations of both intra- and inter-day precision of analysis were below
178   10%. Limits of quantitation was determined to be 1 ng on column for AA, 1 ng for PA
179   and 0.1 ng for BA.

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181   <u>Untargeted metabolomics</u>

182   LC-MS grade solvents including water, methanol, acetonitrile, and formic acid were
183   purchased from Thermo Fisher Scientific (Waltham, MA, USA). Untargeted
184   metabolomics of mouse feces was performed on a high-resolution accurate mass (HRAM)
185   mass spectrometry-based platform coupling to a cutting-edge integrated
186   chemoinformatics pipeline as modified from a previous publication (*22*). Untargeted
187   metabolomic profiling of mouse feces was conducted on a LC-MS platform. The system
188   consisted of a Vanquish UHPLC and a Thermo Scientific Q-Exactive high resolution
189   /accurate mass spectrometer interfacing with a heated electrospray ionization (HESI)
190   source and a hybrid quadrupole-orbitrap mass analyzer operated at 70,000 mass
191   resolution (Waltham, MA, USA). For each sample, ~25 mg feces was aliquoted, shake-
192   extracted by ice-cold methanol:water (1:1, v/v) and centrifuged at 12,000 rpm for 10 min.
193   The supernatants were dried in a vacuum concentrator (Waltham, MA, USA) and
194   resuspended in acetonitrile:water (2:98, v/v) upon instrumental analysis. Extracts of
195   equivalence to 0.125 mg raw feces were injected and subject to a chromatographic
196   separation using a C18 column (Waters Acquity UPLC HSS T3, 2.1 mm × 100 mm, 1.7
197   µm) (Milford, MA, USA). The mobile phases consisted of 0.1% formic acid in water
198   ("A") and 0.1% formic acid in acetonitrile ("B") and the LC eluents were run at a
199   constant flow rate of 0.4 mL/min under 40 ºC, following the gradient: 2% B, 0-2 min; 2%
200   B to 80% B, 2-11 min; 80% B to 98% B, 11-12 min; 98% B, 12-16 min; 98% B to 2% B,
201   16-16.1 min; 2% B, 16.1-20 min. The HESI ion source conditions were as follows: sheath
202   gas flow rate, 60 L/min; aux gas flow rate, 10 L/min; sweep gas flow rate, 1 L/min; spray
203   voltage, 2.75 kV; capillary temperature, 325 ºC; aux gas heater temperature, 400 ºC.
204   Stringent quality assurance (QA) /quality control (QC) procedures were applied,
205   including timely mass calibration, sample randomization, and intermittent QC injection.

206   All MS1 raw data were processed in XCMS (Scripps, La Jolla, CA) for peak picking,
207 peak alignment, gap filling and sample normalization. Univariate Welch's t-test and
208 multivariate principal component analysis (PCA) were applied to screen for ion features
209 of distinct group differences. For ion features of top 500 largest fold changes or of
210 potential microbial relevance, MS/MS spectral data in fullscan plus parallel reaction
211 monitoring (PRM) hybrid mode were collected and fed to a cutting-edge
212 chemoinformatic pipeline that integrates empirical MS/MS database search and in-silico
213 structural dereplication. Compound identification was implemented in MS-DIAL 2.94
214 and MS-FINDER 3.12, with four analytical metrics (i.e. accurate mass, isotopic
215 abundances, tandem mass spectra and retention time) imported to boost annotation
216 confidence while reducing scoring bias. All identifications were manually curated and
217 validated as available using an in-house metabolomic database established based on
218 authentic chemical standards. Confidence level of annotation was assigned to each
219 structure as required by the Metabolomics Standards Initiative (MSI). For pathway
220 analysis and visualization, MetaboAnalyst 4.0 was used to perform metabolite
221 enrichment analysis (MSEA) and create a heatmap showing a select of 50 annotated
222 structures with largest group difference; a MetaMapp approach was used to compute a
223 metabolomic network clustering by biochemical and chemical relationship that was
224 further visualized in CytoScape 3.7.1.

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Fig. S1.

Gut microbiota from elite-survivors attenuate radiation-induced disease. SPF C57BL/6 mice passively received microbiota exchange via dirty cage sharing followed by a high dose of total body radiation as shown in Fig 1E. Femurs and spleens were obtained from recipients at day 30 post radiation and stained for H&E **(A)**, cleaved caspase 3 **(B)** and Ki67 **(C)**. In (A), white pulp (WP, black dash circles), red pulp (RP, areas between black solid lines), granulopoiesis (yellow dash circle), and megakaryocytes (black arrows) are shown. Bone marrow cellularity and spleen extramedullary hematopoiesis (EMH) scores were quantified (see Method). **(D)** Spleens were collected at day 30 post radiation. Cleaved caspase 3 protein levels were detected by western blot. A.U., arbitrary units. Each lane and symbol represent one mouse. Figures represent or are pooled from two-three independent experiments. Error bars show SEM, **p<0.01, ***p<0.001, **** p<0.0001 determined by Mann-Whitney test (A, D).

Fig. S2

Fecal microbiota transplant protects against radiation-induced injury and death. (A)
Illustration of FMT experiment in SPF C57BL/6 mice. **(B)** Survival rates and **(C)** clinical scores
were monitored for 30 days post total body radiation. Fractions indicate the number of mice that
survived to the end of the experiment. Figures represent pooled data from three independent
experiments. **(D)** Mice were euthanized at day 12 post radiation. Femurs and spleens were
stained for H&E and quantified for bone marrow cellularity and spleen extramedullary
hematopoiesis (EMH) scores. Focal hematopoiesis (yellow arrows and area within yellow solid
lines) and lymphocyte depleted follicles (area within black dashed lines) are shown. Each symbol
represents one mouse. Error bars show SEM, **p<0.01, ***p<0.001 determined by log-rank
(Mantel Cox) test (B) and Mann-Whitney test for area under the curve (AUC) (C).

Fig. S3

Bacteria strains that were reduced in elite-survivors do not show any radioprotection. SPF C57BL/6 mice received antibiotics treatment followed by *Staphylococcus aureus*，*Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Lachnospiraceae* (Lachno, a mixture of 23 individual strains in the family *Lachnospiraceae*) or media control (BHI) administration twice a week for eight weeks. A high dose of total body radiation was conducted. **(A)** Survival rates and **(B)** clinical scores were monitored for 30 days post radiation. Fractions indicate the number of mice that survived to the end of the experiment. Figures represent pooled data from three independent experiments. Each symbol represents one mouse. Error bars show SEM, *p<0.05, ***p<0.001 determined by log-rank (Mantel Cox) test (A) and Mann-Whitney test for area under the curve (AUC) (B).

Fig. S4

***Lachnospiraceae* does not promote tumor growth nor does it interfere with the efficacy of radiotherapy. (A)** Illustration of *Lachnospiraceae* administration in tumor models. SPF C57BL/6 mice received antibiotics treatment followed by *Lachnospiraceae* (Lachno) or media control (BHI) administration twice a week for eight weeks. Then, melanoma cell line (B16) or lymphoma cell line (EL4) were subcutaneously injected into recipients' abdomen. **(B-C)** Tumor volumes were monitored and calculated by length*length*width/2. **(D)** Illustration of *Lachnospiraceae* administration in tumor radiotherapy models. SPF mice received antibiotics treatment followed by *Lachnospiraceae* (Lachno) or media control (BHI) administration twice a week for eight weeks. Then, melanoma cell line (B16) was subcutaneously injected into recipients' abdomen. Ten days later, tumor site localized radiation (10 Gy) was conducted. **(E)** Survival rate and **(F)** Tumor volumes (length*length*width/2) were monitored. **(G)** Tumor growth in each individual mouse was shown. Figures represent or are pooled from two-three independent experiments. Each symbol represents one mouse. Error bars show SEM, n.s. not significant, **$p<0.01$ determined by log-rank (Mantel Cox) test (E) and Mann-Whitney test for area under the curve (AUC) (F).

Fig. S5

Short chain fatty acid levels are increased in elite-survivors or ES-Recipients as detected by GC-MS. Acetate, butyrate, propionate and total SCFAs levels in the fecal materials were determined by Mass Spectrometry from **(A)** controls (n=6) and elite-survivors (n=8-12) groups or from **(B)** recipient groups of dirty cage sharing experiment (Ctrl-Recip, n=7; ES-Recip, n=8) described in Fig. 2A. Fecal samples were collected from two independent experiments. Each symbol represents one mouse. Error bars show SEM, n.s., not significant, $*p<0.05$, determined by Mann-Whitney test.

Fig. S6

The efficiency of *Lachnospiraceae* radioprotection depends on SCFA production. (A-B) 23 individual strains in the family *Lachnospiraceae* were cultured separately and the SCFAs levels in the culture medium were detected by mass spectrometry. Three strains (No. 8, 9, 21) that produced low levels of SCFAs were referred to as Lachno-SCFA low producer; while three strains (No. 2, 14, 20) that produced high levels of SCFAs were referred to as Lachno-SCFA high producer. Although strain No. 7 and 10 produced high levels of SCFAs, we didn't choose them because they grew extremely slowly in vitro. **(B)** The butyrate and propionate production from these two groups are shown. **(C)** Illustration of Lachno-SCFA low/high producer treatment in SPF C57BL/6 mice. **(D)** Survival rates and **(E)** clinical scores were monitored for 30 days post total body radiation. Error bars show SEM, *p<0.05, ****p<0.0001 determined by log-rank (Mantel Cox) test (D) and Mann-Whitney test for area under the curve (AUC) (E).

Fig. S7

Radiation-induced DNA damage is attenuated by SCFAs treatment. SPF C57BL/6 mice received 200 mM acetate-, butyrate- or propionate-containing drinking water for eight weeks followed by a high dose of total body radiation. Primary intestinal epithelial cell (IEC) and intestinal intraepithelial lymphocyte (IEL) were isolated from indicated groups (N: naïve; B: butyrate; P: propionate; C: control) at 24h post radiation. Phosphorylated and total p53 and 53BP1 were detected by western blot.

Fig. S8

Metabolic alterations between age-matched controls and elite-survivors by untargeted metabolomics. Metabolite profiles were measured in fecal samples from controls and elite-survivors at day 290 post total body radiation. **(A)** Hierarchical clustering heatmap representing 50 highly changed metabolites of distinct group patterns are shown. **(B)** Relative abundance of selected tryptophan metabolites. Each symbol represents one mouse. Error bars show SEM, *p<0.05, **p<0.01 determined by Student's t test.

Table S1.

Bacterial taxa list in heatmap analysis compared between elite-survivors and age-matched controls. (separate file)

Table S2.

Clinical score parameters for radiation induced sickness. (separate file)

Table S3.

Leukemia patients' information. (separate file)

Table S4.

A list of metabolites assayed and analyzed with significant difference between age- matched controls and elite-survivors (Wech's t-test, P<0.05, fold change>1.2). (separate file)

Table S5.

A list of 141 unique metabolites that showed difference between age-matched controls and elite-survivors, detailing correlations between metabolomics data and community metabolic potential scores and potential taxonomic contributors. (separate file)

A H&E

B Cleaved caspase 3

C Ki67

D

A

Controls
(Ctrl-Donors)

Feces → Ctrl-Recipient
SPF

4 weeks   FMT

Elite-survivors
(ES-Donors)

Feces → ES-Recipient
SPF

Radiation

B

Survival rate %

Days post radiation

C

Clinical score

Days post radiation

1/19

7/29

**

Ctrl-Recip (n=19)

ES-Recip (n=29)

D

	Ctrl-Recip	ES-Recip
Bone marrow	1mm / 200 μm	1mm / 200 μm
Spleen	1mm / 200 μm	1mm / 200 μm

Bone marrow cellularity %

Ctrl-Recip   ES-Recip

EMH score

Ctrl-Recip   ES-Recip

A

B

BHI (n=33)
Lachnospiraceae (n=18)
Staphylococcus aureus (n=20)
Staphylococcus saprophyticus (n=18)
Streptococcus agalactiae (n=20)

A

Abx | Lachnospiraceae / BHI (twice a week) | Tumor

Day -1 | Weeks | 8

SPF mice (Recipients)

B B16

Tumor volume (mm3)

Days post tumor injection

- BHI-Recip (n=11)
- Lachno-Recip (n=13)

C EL4

Tumor volume (mm3)

Days post tumor injection

- BHI-Recip (n=12)
- Lachno-Recip (n=13)

D

Abx | Lachnospiraceae / BHI (twice a week) | Tumor | 10 Gy localized radiation

Day -1 | Weeks | 8 | 10 days post tumor injection

SPF mice (Recipients)

- BHI-Recip (n=7)
- Lachno-Recip (n=9)

Tumor localized radiation
- BHI-Recip (n=10)
- Lachno-Recip (n=9)

E

Survival rate %

Days post tumor injection

n.s.

n.s.

F B16

Tumor volume (mm³)

Days post tumor injection

n.s.

**

n.s.

n.s.

G

BHI-Recip
No radiation

Tumor volume (mm³)

Days post tumor injection

BHI-Recip
Localized radiation

Tumor volume (mm³)

Days post tumor injection

Lachno-Recip
No radiation

Tumor volume (mm³)

Days post tumor injection

Lachno-Recip
Localized radiation

Tumor volume (mm³)

Days post tumor injection

A Age-matched controls vs. elite-survivors

Acetate — n.s. — Controls vs. Elite-survivors (µg/g)

Butyrate — n.s. — Controls vs. Elite-survivors (µg/g)

Propionate — n.s. — Controls vs. Elite-survivors (µg/g)

SCFAs — n.s. — Controls vs. Elite-survivors (µg/g)

B Dirty cage sharing expt.

Acetate — n.s. — Ctrl-Recip vs. ES-Recip (µg/g)

Butyrate — 0.054 — Ctrl-Recip vs. ES-Recip (µg/g)

Propionate — * — Ctrl-Recip vs. ES-Recip (µg/g)

SCFAs — * — Ctrl-Recip vs. ES-Recip (µg/g)

A

Butyrate

Propionate

B

Butyrate+Propionate

Lachno-SCFA low producer

Lachno-SCFA high producer

C

Abx

Lachno strains / BHI (twice a week)

Radiation

Day -1   0   2   4   6   8   Weeks

SPF mice (Recipients)

D

Survival rate %

Days post radiation

E

Clinical score

Days post radiation

Lachno-SCFA low producer (n=7)

Lachno-SCFA high producer (n=8)

Radiation

N (n=5)   B (n=5)   P (n=4)   C (n=4)

IEC & IEL

IB: p-p53

IB: p53

IB: p-53BP1

IB: 53BP1

IB: α-β-actin

A

Controls (n=4)
Elite-survivors (n=10)

5-Hydroxy-L-tryptophan
1-Pyrroline-5-carboxylic acid
Crocusatin H
PubChem CID 3235868
(+)-Pulchellamine G
PubChem CID 54632148
Puqienine B
Doxazosin
Indole-3-acetaldehyde
O-Phosphoethanolamine
Melatonin
Alanyl-leucine
PubChem CID 5362595
Leu-Gly-Pro
PubChem CID 71655
L-Kynurenine
5-(2-Hydroxyethyl)-4-methylthiazole
Paulomycin E
Stigmasterol
Rishitin
Lumacaftor
PubChem CID 53297441
PubChem CID 2952440
Pyrethrolone
Suberic acid
1-Hydroxyprevitamin D3 diacetate
2-Aminomuconic acid semialdehyde
Hexadecasphing-4-enine
(-)-Naucleofficine A
PubChem CID 54633770
[1-(2,5-Dihydroxyphenyl)-3-phenylpropoxy]sulfonic acid
Kynurenic acid
1-Nitro-3,5-dinitroso-1,3,5-triazinane
Flucloxacillin
4-(2-Aminophenyl)-2,4-dioxobutanoic acid
Epicoccin B
Dicloxacillin
3-(4-Hydroxyphenyl)-2-(sulfooxy)propanoic acid
Clusiparalicoline C
6α-Hydroxyundulatine
Salviandulin E
Indolelactic acid
Indole
(+)-(S)-Carvone
keto-3-Deoxy-D-manno-octulosonate
3-Hydroxyindolin-2-one
Dolichotheline
γ-Aminobutyryl-lysine
α-Linolenic acid
N-(1-Adamantyl)-N'-(4-Guanidinobenzyl)Urea

B

1H-Indole-3-carboxaldehyde — **

Kynurenic acid — **

4-(2-Amino-3-hydroxyphenyl)-2,4-dioxobutanoic acid — **

Xanthurenic acid — **

2-Aminomuconic acid semialdehyd — 0.053

Indolelactic acid — 0.075

Indole — 0.188

5-Hydroxyindoleacetic acid — *

N'-Formylkynurenine — *

Controls
Elite-survivors

L-Kynurenine — **

Indoleacetaldehyde — **

5-Hydroxy-L-tryptophan — *

Melatonin — **

References and Notes

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