DIETARY REGIMENS AND METHODS FOR TREATMENT OF COLORECTAL CANCER

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application Number 63/571,720 filed on March 29, 2024, the content of which is incorporated herein by reference in its entirety for all purposes.

BACKGROUND

[0002] Compared to normal cells, many cancer cells have evolved differential metabolic and nutritional demands for survival, proliferation, and metastases. Current therapies for the treatment for cancer or other pathologies can be ineffective due to subject-specific factors. Personalized methods and formulations can be developed for therapy of various diseases, including colorectal cancer.

BRIEF DESCRIPTION OF DRAWINGS

[0003] **FIG. 1** shows an example study schema illustrating the treatment of a subject receiving non-essential amino acid restriction (NEAAR) medical food, short-course radiotherapy, and/or capecitabine and oxaliplatin (CapeOX) chemotherapy.

[0004] **FIG. 2** shows an example study schema illustrating the treatment of a subject receiving NEAAR dietary regimen, short-course radiotherapy, and 5-fluorouracil, leucorovin, and oxaliplatin (FOLFOX) chemotherapy.

SUMMARY

[0005] In some embodiments, disclosed herein is a method of treating a colorectal cancer (*e.g.*, locally advanced rectal cancer, LARC) in a subject in need thereof, the method comprising administering to the subject: a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of at least two amino acids in the subject as compared to baseline and b) a therapeutically effective amount of a radiotherapy. In some embodiments, the method further comprises administering to the subject: c) a therapeutically effective amount of one or more chemotherapeutic agents.

[0006] In some embodiments, disclosed herein is a method of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising administering to the subject: a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of at least two amino acids in the subject as compared to baseline; b) a therapeutically effective amount of a radiotherapy; and c) a therapeutically effective amount of one or more chemotherapeutic agents.

[0007] In some embodiments, disclosed herein is a method of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising administering to the subject: a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of at least two amino acids in the subject as compared to baseline; b) a therapeutically effective amount of a radiotherapy; and c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin, capecitabine, leucovorin, or fluorouracil.

[0008] In some embodiments, disclosed herein is a method of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising administering to the subject: a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of serine, glycine, and proline in the subject as compared to baseline; b) a therapeutically effective amount of a radiotherapy; and c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin and capecitabine (CapeOX), wherein administering the CapeOX comprises intravenously administering oxaliplatin at a dose of about 130 mg/m^2 once on day 1 and orally administering capecitabine at a dose of about 1000 mg/m^2 twice daily on days 1-14.

[0009] In some embodiments, disclosed herein is a method of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising administering to the subject: a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of serine, glycine, and proline in the subject as compared to baseline; b) a therapeutically effective amount of a radiotherapy; and c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin, leucovorin, and fluorouracil (FOLFOX), wherein administering the FOLFOX comprises intravenously administrating fluorouracil at a dose of about 400 mg/m^2, leucovorin at a dose of about 400 mg/m^2, and oxaliplatin at a dose of about 85 mg/m^2 on day 1

and intravenously administrating fluorouracil at a dose of about 1200 mg/m^2 continuously over about 2 days (days 1-2).

[0010] In some embodiments, disclosed herein is use of a therapy (*e.g.*, chemotherapy, radiotherapy, immunotherapy, or surgery) or a therapeutic agent (*e.g.*, a chemotherapeutic agent, a radiotherapeutic agent, or an immunotherapeutic agent) to treat colorectal cancer (*e.g.*, LARC) in a subject in need thereof, wherein the treatment comprises administering a dietary regimen as disclosed herein to the subject.

[0011] In some embodiments, disclosed herein is a therapy (*e.g.*, chemotherapy, radiotherapy, immunotherapy, or surgery) or a therapeutic agent (*e.g.*, a chemotherapeutic agent, a radiotherapeutic agent, or an immunotherapeutic agent) for use in a method of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, wherein the method comprises administering a dietary regimen as disclosed herein to the subject.

[0012] In some embodiments, disclosed herein is use of a therapeutic agent (*e.g.*, a chemotherapeutic agent, radiotherapeutic agent, or an immunotherapeutic agent) in the manufacture of a medicament for the treatment of colorectal cancer (*e.g.*, LARC) in a subject in need thereof, wherein the treatment comprises administering a dietary regiment as disclosed herein to the subject.

DETAILED DESCRIPTION

[0013] The following description sets forth numerous exemplary compounds, methods, uses, and the like. It should be recognized, however, that such description is not intended as a limitation on the scope of the present disclosure, but is instead provided as a description of exemplary embodiments.

[0014] As used herein, the terms "including," "containing," and "comprising" are used in their open, non-limiting sense.

[0015] The articles "a" and "an," as used herein, refer to one or more than one (*i.e.*, to at least one) of the grammatical object of the article. By way of example, "an element" refers to one element or more than one element.

[0016] To provide a more concise description, some of the quantitative expressions given herein are not qualified with the term "about." It is understood that, whether the term "about" is used explicitly or not, every quantity given herein is meant to refer to the actual given value, and it is also meant to refer to the approximation to such given value that would reasonably be

inferred based on the ordinary skill in the art, including equivalents and approximations due to the experimental and/or measurement conditions for such given value. Whenever a yield is given as a percentage, such yield refers to a mass of the entity for which the yield is given with respect to the maximum amount of the same entity that could be obtained under the particular stoichiometric conditions. Concentrations that are given as percentages refer to mass ratios, unless indicated differently.

[0017] When mammalian cells experience amino acid starvation, the cells can undergo a homeostatic response to amino acid shortage. Amino acid deficiency can trigger a general amino acid control pathway that involves shifting resources and energy of cells to expression of membrane transporters, growth hormones, and metabolic enzymes for amino acid homeostasis. Upregulation of membrane transporters can enhance amino acid uptake, and upregulation of metabolic enzymes can enhance amino acid synthesis. The cells can also recycle proteins and organelles to regenerate non-essential amino acids by autophagy. By general amino acid control pathway and autophagy, cells attempt to maintain amino acid homeostasis. Tumor tissues can also overcome amino acid starvation by enhancing angiogenesis to obtain more nutrient supply.

[0018] When homeostasis cannot be achieved upon severe amino acid starvation, cancer cells can inhibit protein synthesis, suppress growth, or undergo programmed cell death. The cell death mechanisms of amino acid starvation can be caspase-dependent apoptosis, autophagic cell death, or ferroptotic cell death. Amino acid transporters, metabolic enzymes, autophagy-associated proteins, and amino acid starvation can be used to control cancer growth.

[0019] Cancer cells can acquire metabolic adaptations that support enhanced rates of growth and proliferation. While the metabolic adaptations can help tune metabolism to support higher anabolic output and bolster antioxidant defenses, the metabolic adaptations can also decrease metabolic flexibility and impose increased dependence on nutrient uptake and de novo nutrient biosynthesis. Cancer cells can have nutrient auxotrophy and have a much higher nutrient demand compared to normal cells. As an adaptation to fulfill the increased nutritional demand, cancer cells can upregulate glucose and amino acid transporters on the cell membrane to obtain more nutrients from circulation. Cancer cells can also rewire metabolic pathways by enhancing glycolysis and glutaminolysis to sustain a higher rate of ATP production or energy supply. Glucose and amino acids are highly demanded nutrients in cancer cells. Cancers' auxotrophy to different amino acids can render the cancer types vulnerable to amino acid-starvation treatments.

[0020] Cancer cells can have high demands for non-essential amino acids, which are precursors for anabolic and antioxidant pathways that support cell survival and proliferation. Controlling the levels of a particular amino acid or a combination of amino acids in the diet of a subject can lead to improved treatment of various diseases, including cancer. Modulation of amino acid levels in a cancer cell can control the production of proteins, metabolites, lipids, and nucleic acids that promote cancer growth and metastasis.

[0021] Cancer cells can adapt their metabolism to support growth and survival, leading to various dependencies and vulnerabilities that could be targeted for therapy. Dietary intake and nutrient metabolism can be critical in supporting human health. The 20 proteinogenic amino acids can be categorized in two subgroups: essential amino acids and non-essential amino acids. An "essential" amino acid cannot be synthesized by the organism and is derived from exogenous sources.

[0022] Controlling specific amino acids cannot be entirely implemented through "normal foods" because any protein-containing food contains the amino acids. Dietary regimens disclosed herein can include two components: 1) a diet, such as a food-based diet that is low in protein; and 2) a dietary product, such as a formulated supplement that administers a mixture of essential and non-essential amino acids excluding particular amino acids. In addition to controlling the supply of specific amino acids, administration of purified amino acids can have unique benefits to systemic protein metabolism in subjects with cancer. Some amino acid forms can be better absorbed in subjects with compromised digestion than other forms.

[0023] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) providing to the subject a diet comprising protein in an amount less than the daily recommended dietary requirement of protein for the subject; and b) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of at least two amino acids, wherein the dietary product is formulated as a powder.

[0024] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising : a) providing to the subject a diet comprising protein in an amount less than the daily recommended dietary requirement of protein for the subject; and b) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of serine and glycine, wherein the dietary product is formulated as a powder.

[0025] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) providing to the subject a diet comprising protein in an amount less than the daily recommended dietary requirement of protein for the subject; and b) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of serine, glycine and proline, wherein the dietary product is formulated as a powder.

[0026] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) providing to the subject a diet comprising protein in an amount less than the daily recommended dietary requirement of protein for the subject; and b) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product does not comprise at least two amino acids, wherein the dietary product is formulated as a powder.

[0027] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) providing to the subject a diet comprising protein in an amount less than the daily recommended dietary requirement of protein for the subject; and b) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product does not comprise serine and glycine, wherein the dietary product is formulated as a powder.

[0028] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) providing to the subject a diet comprising protein in an amount less than the daily recommended dietary requirement of protein for the subject; and b) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product does not comprise serine, glycine and proline, wherein the dietary product is formulated as a powder.

[0029] In some embodiments, the dietary regimen is administered to the subject in combination with radiotherapy. In some embodiments, the dietary regimen is administered to the subject in combination with chemotherapy. In some embodiments, the dietary regiment is administered to the subject in combination with radiotherapy and chemotherapy.

[0030] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering a dietary regimen to the subject to reduce an average plasma level of at least two amino acids in the subject as compared to baseline; b) administering to the subject a therapeutically effective amount of a radiotherapy;

and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0031] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering a dietary regimen to the subject to reduce an average plasma level of serine and glycine in the subject as compared to baseline; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0032] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering a dietary regimen to the subject to reduce an average plasma level of serine, glycine, and proline in the subject as compared to baseline; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0033] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of at least two amino acids.

[0034] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of at least two amino acids; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0035] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of serine and glycine; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0036] Disclosed herein are methods of treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the methods comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product is devoid of serine, glycine, and

proline; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0037] Disclosed herein are pharmaceutical compositions comprising, in unit dosage form: a) a plurality of amino acids, wherein the composition is devoid of at least serine, glycine, and proline; and b) a pharmaceutically acceptable excipient.

[0038] Disclosed herein are methods of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product does not comprise at least two amino acids; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0039] Disclosed herein are methods of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product does not comprise serine and glycine; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

[0040] Disclosed herein are methods of treating a colorectal cancer (*e.g.*, LARC) in a subject in need thereof, the method comprising: a) administering to the subject a therapeutically effective amount of a dietary product, wherein the dietary product does not comprise serine, glycine, and proline; b) administering to the subject a therapeutically effective amount of a radiotherapy; and c) administering to the subject a therapeutically effective amount of one or more chemotherapeutic agents.

Dietary Regimen

[0041] The dietary regimen modulates an amino acid level in a subject by increasing or decreasing an amino acid level in all nutritional intake (*e.g.*, all food and supplements) consumed by the subject. In many embodiments, the dietary regimen comprises 2 components: 1) a diet (*e.g.*, a low-protein food-based diet) that provides most if not all fat and carbohydrates consumed by the subject while providing little or no protein, and 2) a dietary product (*e.g.*, a plurality of amino acids in powder form) that provides some but not necessarily all amino acids

to the subject. In many embodiments, the dietary regimen (*e.g.*, a combination of a diet and a dietary product) provides net levels of one or more amino acids that are below the daily dietary requirement for the amino acids. Also disclosed herein are embodiments wherein the dietary regimen comprises a diet without a dietary product – for example, the diet may be medical or modified food supplemented with amino acids. Further disclosed herein are embodiments wherein the dietary regimen comprises a dietary product without a diet – for example, the dietary product may comprise a plurality of amino acids in addition to fat, carbohydrates, and other nutrients such that the dietary product replaces most if not all food consumed by the subject.

[0042] As used herein, modulating an amino acid level in a subject can comprise increasing or decreasing an amino acid level in a subject. In some embodiments, an amino acid level in a subject or a cell of a subject is increased or decreased by modulating amino acid content in the subject's diet (*e.g.*, in the food consumed by the subject in a day, including meals, snacks, and drinks.)

[0043] In some embodiments, methods comprise administering a dietary regimen to lower an average plasma level of an amino acid in a subject. In some embodiments, the dietary regimen delivers less than a recommended dietary requirement of one or more amino acids (*e.g.*, serine, glycine, proline, or combinations thereof) to a subject. In some embodiments, the dietary regimen comprises a diet (*e.g.*, a food-based diet.) In some embodiments, the dietary regimen comprises a dietary product (*e.g.*, a plurality of amino acids, such as in powder form.) In some embodiments, the dietary regimen comprises a diet (*e.g.*, a food-based diet) and a dietary product (*e.g.*, a plurality of amino acids, such as in powder form.)

[0044] Average plasma levels of a biomarker (*e.g.*, of an amino acid such as serine, glycine, or proline), as used herein, refers to levels of a biomarker as measured from a blood panel. For example, in some embodiments, blood collection for amino acid panels is collected approximately 2 hours (+/- 60 min) after meals. Also, for example, in some embodiments, for baseline average plasma levels of a biomarker (*e.g.*, of an amino acid such as serine, glycine, or proline), two blood collections on different days occur before treatment (*e.g.*, during screening.) In some embodiments, average plasma levels of a biomarker (*e.g.*, of an amino acid such as serine, glycine, or proline) after treatment with a dietary regimen involve blood collection 1-5 days (*i.e.*, 1, 2, 3, 4, or 5 days) after treatment with the dietary regimen.

[0045] Daily recommended dietary requirement, as used herein, refers to the daily dietary intake level (*e.g.*, of protein, carbohydrates, fat, and amino acids) that suffices to meet the nutrient requirements (*e.g.*, protein, carbohydrate, fat, and amino acid requirements) of nearly all (*e.g.*, 95% or more) healthy person of a specific sex and age. For example, recommended dietary intake levels may be recommended dietary allowance (RDA) as determined by the Food and Nutrition Board of the Institute of Medicine. Also for example, recommended dietary intake levels may be daily median intake as recommended by the National Health and Nutrition Examination Survey (NHANES).

[0046] In some embodiments, the dietary regimen is substantially a sole source of calories for the subject. In some embodiments, the dietary regimen is substantially a sole source of amino acids for the subject.

[0047] The term "source" in the phrase "substantially a sole source," as used herein, refers to a provider of nutrition such as a diet, a dietary regimen, or a dietary product as used herein. The phrase "substantially a sole source," as used herein, refers to said source providing almost all if not all of the indicated nutritional component. For example, the phrase "a dietary regimen is substantially a sole source of diet for a subject" indicates the dietary regimen provides almost all, if not all nutrition (macronutrients and micronutrients, providing for all nutritional and caloric needs) taken in by a subject. Also, for example, the phrase "a dietary regimen is substantially a sole source of amino acids for a subject" indicates the dietary regimen provides almost all, if not all of the amino acids taken in by a subject. For example, substantially a sole source may refer to at least 90% of the stated daily intake of the nutritional item originating from the stated source.

[0048] In some embodiments, the dietary regimen changes an average plasma level of at least one amino acid in the subject compared to baseline. In some embodiments, the dietary regimen changes an average plasma level of serine compared to baseline. In some embodiments, the dietary regimen changes an average plasma level of glycine compared to baseline. In some embodiments, the dietary regimen changes an average plasma level of proline compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of at least two amino acids in the subject compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of serine and glycine in the subject compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of serine and proline in the subject compared to baseline. In some embodiments, the dietary regimen changes average

plasma levels of glycine and proline in the subject compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of at least three amino acids in the subject compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of serine, glycine, and proline in the subject compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of at least four amino acids in the subject compared to baseline. In some embodiments, the dietary regimen changes average plasma levels of at least five amino acids in the subject compared to baseline.

[0049] In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 10% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 20% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 30% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 40% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 50% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 60% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 70% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 80% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 90% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 95% compared to baseline. In some embodiments, the dietary regimen increases an average plasma level of at least one amino acid by at least about 99% compared to baseline.

[0050] In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid (*e.g.*, serine, glycine, and/or proline) by at least about 10%, at least 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%,

at least about 80%, at least about 90%, at least about 95%, or by at least about 99% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 10% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 20% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 30% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 40% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 50% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 60% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 70% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 80% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 90% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 95% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of at least one amino acid by at least about 99% compared to baseline.

[0051] In some embodiments, the dietary regimen decreases an average plasma level of serine compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 10% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 20% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 30% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 40% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 50% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 60% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 70% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 80% compared to baseline. In some embodiments, the dietary regimen

decreases an average plasma level of serine by at least about 90% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 95% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of serine by at least about 99% compared to baseline.

[0052] In some embodiments, the dietary regimen decreases an average plasma level of glycine compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 10% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 20% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 30% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 40% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 50% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 60% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 70% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 80% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 90% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 95% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of glycine by at least about 99% compared to baseline.

[0053] In some embodiments, the dietary regimen decreases an average plasma level of proline compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 10% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 20% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 30% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 40% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 50% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 60% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about

70% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 80% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 90% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 95% compared to baseline. In some embodiments, the dietary regimen decreases an average plasma level of proline by at least about 99% compared to baseline.

[0054] In some embodiments, the dietary regimen is administered for 1 to 10 weeks, 1 to 9 weeks, 1 to 8 weeks, 1 to 7 weeks, 1 to 6 weeks, 1 to 5 weeks, 1 to 4 weeks, 1 to 3 weeks, or 1 to 2 weeks. In some embodiments, the dietary regimen is administered for 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, or 10 weeks.

[0055] In some embodiments, the dietary regimen is administered for 1 to 16 months, 1 to 12 months, 1 to 10 months, 1 to 9 months, 1 to 8 months, 1 to 7 months, 1 to 6 months, 1 to 5 months, 1 to 4 months, 1 to 3 months, or 1 to 2 months. In some embodiments, the dietary regimen is administered for 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 13 months, 14 months, 15 months, or 16 months.

[0056] In some embodiments, the dietary regimen is administered at least 4 times per week for 5 weeks. In some embodiments, the dietary regimen is administered at least 6 times per week for 1 week.

[0057] In some embodiments, the dietary regimen is administered 7 times per week. In some embodiments, the dietary regimen is on an intermittent schedule alternating with a habitual diet. For example, in some embodiments, the dietary regimen is administered at least 3 times per week, at least 4 times per week, at least 5 times per week, or at least 6 times per week and the subject consumes a habitual diet on the remaining days of the week. In some embodiments, the dietary regimen is administered 3 times per week. In some embodiments, the dietary regimen is administered 4 times per week. In some embodiments, the dietary regimen is administered 5 times per week. In some embodiments, the dietary regimen is administered 6 times per week.

[0058] Also for example, in some embodiments, the subject consumes the dietary regimen for 5 days of a week and consumes a habitual diet on the remaining 2 days of the week. In some embodiments, the subject consumes a habitual diet for at least 2 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 3 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 4 consecutive days

per week. In some embodiments, the subject consumes a habitual diet for at least 5 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 6 consecutive days per week.

[0059] The term "habitual diet," as used herein, refers to a course of nutritional intake consumed (*e.g.*, all food and drink consumed) by a subject without adherence to the dietary regimen as described herein. For example, a habitual diet may be the food and drink that a subject would normally consume by habit without reference to any particular dietary regimen. Also for example, a habitual diet may be the normal course of nutritional intake the subject consumed before engaging in a dietary regimen as describe herein. A habitual diet may also be a diet recommended by a physician for reasons that may or may not relate to the condition being treated by the dietary regimen. For example, the habitual diet may be a low-glycemic index diet, a low-carbohydrate diet, or a ketogenic diet. The habitual diet may, but does not necessarily, partially adhere to a dietary regimen as describe herein.

[0060] Baseline, as used herein, in some embodiments refers to levels of a biomarker (*e.g.*, of an amino acid such as serine, glycine, or proline within a biological specimen such as blood) before treatment (*e.g.*, taken while consuming habitual diet.) For example, in some embodiments, a blood plasma level of a biomarker at baseline refers to levels of the biomarker before treatment while consuming a habitual diet. For example, for levels of amino acids, two blood collections on different days may be done before treatment while taking a habitual diet (*e.g.*, during screening) to obtain baseline measurements of a given amino acid (*e.g.*, serine, glycine, proline, etc.)

[0061] In some embodiments, an average amino acid level in plasma is increased in a subject by providing the dietary regimen (*e.g.*, a diet and/or a dietary product) comprising the amino acid in an amount greater than the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is increased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 100%, at least about 500%, at least about 1000%, at least about 5000%, or at least about 10000% greater than the daily recommended dietary requirement of the amino acid. In some embodiments, an average

amino acid level in plasma is increased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at least about 20% greater than the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is increased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at least about 50% greater than the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is increased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at least about 75% greater than the daily recommended dietary requirement of the amino acid.

[0062] In some embodiments, an average amino acid level in plasma is decreased in a subject by providing the dietary regimen comprising the amino acid in an amount less than the daily recommended dietary requirement of the amino acid (*e.g.*, serine, glycine, and/or proline). In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 75%, at most about 70%, at most about 65%, at most about 60%, at most about 55%, at most about 50%, at most about 45%, at most about 40%, at most about 35%, at most about 30%, at most about 25%, at most about 20%, at most about 15%, at most about 10%, at most about 5%, at most about 4.5%, at most about 4%, at most about 3.5%, at most about 3%, at most about 2.5%, at most about 2%, at most about 1.5%, at most about 1%, at most about 0.5%, or at most about 0.3% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 75% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 50% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 20% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 10% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen

comprising the amino acid in an amount that is at most about 5% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 1% of the daily recommended dietary requirement of the amino acid. In some embodiments, an average amino acid level in plasma is decreased in the subject by providing the dietary regimen comprising the amino acid in an amount that is at most about 0.5% of the daily recommended dietary requirement of the amino acid.

[0063] In some embodiments, protein levels are modulated in a subject by administering to the subject a diet and/or dietary products with modified levels of protein. In some embodiments, one amino acid level is modulated in the subject or a cell of the subject by administering to the subject a diet and/or dietary products with modified levels of the amino acid. In some embodiments, one or more amino acid levels are modulated in the subject or a cell of the subject by administering to the subject a diet and/or dietary products with modified types of proteins, amino acids, or peptides that contain low levels of specific amino acid levels for the subject's daily food intake.

Diet

[0064] In some embodiments, the dietary regimen comprises administering a diet. In some embodiments, the dietary regimen consists of a diet. In some embodiments, the diet is administered with a therapeutically effective amount of a therapy (*e.g.*, chemotherapy, radiotherapy, immunotherapy, surgery, or combinations thereof) or a therapeutic agent (*e.g.*, chemotherapeutic agent, radiotherapeutic agent, immunotherapeutic agent, or combinations thereof.)

[0065] Diet, as used herein, refers to the nutritional intake consumed by the subject from meals, snacks, and drinks throughout the day. For example, the diet may be a food-based diet that comprises the subject's food and beverages over the course of a day. The diet may also comprise meal replacement products, medical food, or parenteral nutritional intake.

[0066] In some embodiments, the diet comprises about 1200 to about 2600, about 1200 to about 2500, about 1200 to about 2400, about 1200 to about 2300, about 1200 to about 2200, about 1400 to about 2600, about 1400 to about 2500, about 1400 to about 2400, about 1400 to about 2300, about 1400 to about 2200, about 1600 to about 2600, about 1600 to about 2500, about 1600 to about 2400, about 1600 to about 2300, or about 1600 to about 2200 kcals per day.

In some embodiments, the diet comprises about 1200 to about 2600 kcals per day. In some embodiments, the diet comprises about 1600 to about 2400 kcals per day.

[0067] In some embodiments, the diet comprises about 15 to about 45, about 15 to about 40, about 15 to about 35, about 15 to about 30, about 15 to about 20, about 20 to about 45, about 20 to about 40, about 20 to about 35, about 20 to about 30, about 25 to about 45, about 25 to about 40, or about 25 to about 30 kcal per kg of the subject's body weight per day. In some embodiments, the diet comprises about 20 to about 40 kcal per kg of the subject's body weight per day. In some embodiments, the diet comprises about 20 to about 30 kcal per kg of the subject's body weight per day. In some embodiments, the diet comprises about 25 to about 30 kcal per kg of the subject's body weight per day.

[0068] In some embodiments, the diet is low in protein (*i.e.*, in some embodiments, the diet is a low-protein diet.) A typical Western diet has about 20 g of protein per meal, about 10 g of protein per snack, and about 80 g of protein per day. A diet that is low in protein can have less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or less than 5% of the grams of protein normally consumed in a typical Western diet.

[0069] In some embodiments, the diet comprises less than about 50 g, less than about 40 g, less than about 30 g, less than about 20 g, or less than about 10 g of protein per day. In some embodiments, the diet comprises less than about 20 g of protein per day. In some embodiments, the diet comprises about 0 g to about 20 g, about 0 g to about 15 g, about 0 g to about 10 g, about 0 g to about 5 g, about 0 g to about 1 g, about 0.1 g to about 20 g, about 0.1 g to about 15 g, about 0.1 g to about 10 g, about 0.1 g to about 5 g, or about 0.1 g to about 1 g of protein per day. In some embodiments, the diet comprises less than about 20 g, less than about 19 g, less than about 18 g, less than about 17 g, less than about 16 g, less than about 15 g, less than about 14 g, less than about 13 g, less than about 12 g, less than about 11 g, less than about 10 g, less than about 9 g, less than about 8 g, less than about 7 g, less than about 6 g, less than about 5 g, less than about 4 g, less than about 3 g, less than about 2 g, or less than about 1 g of protein per day. In some embodiments, the diet comprises about 20 g, about 19 g, about 18 g, about 17 g, about 16 g, about 15 g, about 14 g, about 13 g, about 12 g, about 11 g, about 10 g, about 9 g, about 8 g, about 7 g, about 6 g, about 5 g, about 4 g, about 3 g, about 2 g, or about 1 g of protein per day.

[0070] In some embodiments, the diet comprises less than about 0.1 g/kg/day, less than about 0.2 g/kg/day, less than about 0.3 g/kg/day, less than about 0.4 g/kg/day, less than about 0.5

g/kg/day, less than about 0.6 g/kg/day, less than about 0.7 g/kg/day, less than about 0.8 g/kg/day, less than about 0.9 g/kg/day, less than about 1.0 g/kg/day, less than about 1.1 g/kg/day, less than about 1.2 g/kg/day, less than about 1.3 g/kg/day, less than about 1.4 g/kg/day, less than about 1.5 g/kg/day, less than about 1.6 g/kg/day, less than about 1.7 g/kg/day, less than about 1.8 g/kg/day, less than about 1.9 g/kg/day, less than about 2.0 g/kg/day, less than about 2.1 g/kg/day, less than about 2.2 g/kg/day, less than about 2.3 g/kg/day, less than about 2.4 g/kg/day, or less than about 2.5 g/kg/day of protein. In some embodiments, the diet comprises less than about 0.2 g/kg/day of protein. In some embodiments, the diet comprises less than about 0.4 g/kg/day of protein. In some embodiments, the diet comprises less than about 0.6 g/kg/day of protein. In some embodiments, the diet comprises less than about 0.8 g/kg/day of protein. In some embodiments, the diet comprises less than about 1.0 g/kg/day of protein. In some embodiments, the diet comprises less than about 1.2 g/kg/day of protein.

[0071] In some embodiments, the diet comprises one or more meals that are low in protein. In some embodiments, the diet comprises less than about 10 g, less than about 9 g, less than about 8 g, less than about 7 g, less than about 6 g, less than about 5 g, less than about 4 g, less than about 3 g, less than about 2 g, less than about 1.8 g, less than about 1.6 g, less than about 1.4 g, less than about 1.2 g, or less than about 1 g of protein per meal. In some embodiments, the diet comprises about 10 g, about 9 g, about 8 g, about 7 g, about 6 g, about 5 g, about 4 g, about 3 g, about 2 g, about 1.8 g, about 1.6 g, about 1.4 g, about 1.2 g, or about 1 g of protein per meal. In some embodiments, the diet comprises about 1 g to about 10 g, about 1 g to about 5 g, or about 5 g to about 10 g of protein per meal.

[0072] In some embodiments, the diet comprises meals comprising less than about 1 g, less than about 2 g, less than about 3 g, less than about 4 g, less than about 5 g, less than about 6 g, less than about 7 g, less than about 8 g, less than about 9 g, or less than about 10 g of protein per meal. In some embodiments, the diet comprises meals comprising less than about 1 g of protein per meal. In some embodiments, the diet comprises meals comprising less than about 2 g of protein per meal. In some embodiments, the diet comprises meals comprising less than about 3 g of protein per meal. In some embodiments, the diet comprises meals comprising less than about 4 g of protein per meal. In some embodiments, the diet comprises meals comprising less than about 5 g of protein per meal.

[0073] In some embodiments, the diet comprises one or more snacks that are low in protein. In some embodiment, the diet comprises about 1 g to about 10 g, about 1 g to about 5 g, about 1 g

to about 4 g, about 1 g to about 3 g, or about 1 g to about 2 g of protein per snack. In some embodiments, the diet comprises snacks comprising less than about 0.1 g, less than about 0.2 g, less than about 0.3 g, less than about 0.4 g, less than about 0.5 g, less than about 0.6 g, less than about 0.7 g, less than about 0.8 g, less than about 0.9 g, less than about 1.0 g, less than about 1.1 g, less than about 1.2 g, less than about 1.3 g, less than about 1.4 g, less than about 1.5 g, less than about 1.6 g, less than about 1.7 g, less than about 1.8 g, less than about 1.9 g, less than about 2.0 g, less than about 2.1 g, less than about 2.2 g, less than about 2.3 g, less than about 2.4 g, or less than about 2.5 g of protein per snack. In some embodiments, the diet comprises snacks comprising less than about 0.6 g of protein per snack. In some embodiments, the diet comprises meals comprising less than about 1.0 g of protein per snack. In some embodiments, the diet comprises meals comprising less than about 1.4 g of protein per snack. In some embodiments, the diet comprises meals comprising less than about 1.8 g of protein per snack. In some embodiments, the diet comprises meals comprising less than about 2.2 g of protein per snack.

[0074] In some embodiments, the diet comprises less than about 15%, less than about 14%, less than about 13%, less than about 12%, less than about 11%, less than about 10%, less than about 9%, less than about 8%, less than about 7%, less than about 6%, less than about 5%, less than about 4%, less than about 3%, less than about 2%, or less than about 1% of daily calories from protein. In some embodiments, the diet comprises less than about 15% of daily calories from protein. In some embodiments, the diet comprises less than about 10% of daily calories from protein. In some embodiments, the diet comprises less than about 5% of daily calories from protein. In some embodiments, the diet comprises less than about 1% of daily calories from protein. In some embodiments, the diet comprises about 0% to about 10%, about 0% to about 8%, about 0% to about 6%, about 0% to about 5%, about 0% to about 4%, about 1% to about 10%, about 1% to about 8%, about 1% to about 6%, about 1% to about 5%, about 1% to about 4%, about 2% to about 10%, about 2% to about 8%, about 2% to about 6%, about 2% to about 5%, or about 2% to about 4% of daily calories from protein.

[0075] In some embodiments, the diet comprises meals, foods, beverages, etc. that are low in or that do not comprise one or more amino acids. In some embodiments, the diet is substantially devoid of one or more amino acids. In some embodiments, the diet is substantially devoid of serine. In some embodiments, the diet is substantially devoid of glycine. In some embodiments, the diet is substantially devoid of proline.

[0076] "Substantially devoid," as used herein, refers to a low amount (*e.g.*, of protein or of an amino acid), such as an amount that is less than about 0.5% or is about 0% of a composition by mass. In some embodiments, substantially devoid refers to an amount far below the recommended daily dietary requirement (*e.g.*, far below the RDA as determined by the Food and Nutrition Board of the Institute of Medicine), such as an amount that is less an about 10%, less than about 5%, less than about 2%, less than about 1%, or less than about 0.1% of the recommended daily dietary requirement. "Substantially devoid" can refer to a trace amount.

[0077] In some embodiments, the diet is substantially devoid of two amino acids. In some embodiments, the diet is substantially devoid of serine and glycine. In some embodiments, the diet is substantially devoid of serine and proline. In some embodiments, the diet is substantially devoid of glycine and proline.

[0078] In some embodiments, the diet is substantially devoid of three amino acids. In some embodiments, the diet is substantially devoid of serine, glycine, and proline.

[0079] "Devoid of," as used herein, is used interchangeably with "does not comprise" or "lacks."

[0080] In some embodiments, the diet provides less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary requirement of serine for the subject's age group: as determined by the Food and Nutrition Board of the Institute of Medicine.

[0081] In some embodiments, the diet provides less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary requirement of glycine for the subject's age group: as determined by the Food and Nutrition Board of the Institute of Medicine.

[0082] In some embodiments, the diet provides less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary requirement of proline for the subject's age group: as determined by the Food and Nutrition Board of the Institute of Medicine.

[0083] In some embodiments, the diet provides less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less

than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary allowance (RDA) of serine. In some embodiments, the diet provides less than 50% of an RDA of serine. In some embodiments, the diet provides less than 45% of an RDA of serine. In some embodiments, the diet provides less than 40% of an RDA of serine. In some embodiments, the diet provides less than 35% of an RDA of serine. In some embodiments, the diet provides less than 30% of an RDA of serine. In some embodiments, the diet provides less than 25% of an RDA of serine. In some embodiments, the diet provides less than 20% of an RDA of serine. In some embodiments, the diet provides less than 15% of an RDA of serine. In some embodiments, the diet provides less than 10% of an RDA of serine. In some embodiments, the diet provides less than 5% of an RDA of serine. In some embodiments, the diet provides less than 1% of an RDA of serine. In some embodiments, the diet provides less than 0.5% of an RDA of serine. In some embodiments, the diet provides less than 0.1% of an RDA of serine. In some embodiments, the RDA of serine is the RDA for the subject's age group as determined by the Food and Nutrition Board of the Institute of Medicine. In some embodiments, the RDA of serine for an adult subject is about 28 mg/kg/day.

[0084] In some embodiments, the diet less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary allowance (RDA) of glycine. In some embodiments, the diet provides less than 50% of an RDA of glycine. In some embodiments, the diet provides less than 45% of an RDA of glycine. In some embodiments, the diet provides less than 40% of an RDA of glycine. In some embodiments, the diet provides less than 35% of an RDA of glycine. In some embodiments, the diet provides less than 30% of an RDA of glycine. In some embodiments, the diet provides less than 25% of an RDA of glycine. In some embodiments, the diet provides less than 20% of an RDA of glycine. In some embodiments, the diet provides less than 15% of an RDA of glycine. In some embodiments, the diet provides less than 10% of an RDA of glycine. In some embodiments, the diet provides less than 5% of an RDA of glycine. In some embodiments, the diet provides less than 1% of an RDA of glycine. In some embodiments, the diet provides less than 0.5% of an RDA of glycine. In some embodiments, the diet provides less than 0.1% of an RDA of glycine. In some embodiments, the RDA of glycine is the RDA for the subject's age group as determined by the Food and Nutrition Board of the Institute of Medicine. In some embodiments, the RDA of glycine for an adult subject is about 50 mg/kg/day.

[0085] In some embodiments, the diet provides less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary allowance (RDA) of proline. In some embodiments, the diet provides less than 50% of an RDA of proline. In some embodiments, the diet provides less than 45% of an RDA of proline. In some embodiments, the diet provides less than 40% of an RDA of proline. In some embodiments, the diet provides less than 35% of an RDA of proline. In some embodiments, the diet provides less than 30% of an RDA of proline. In some embodiments, the diet provides less than 25% of an RDA of proline. In some embodiments, the diet provides less than 20% of an RDA of proline. In some embodiments, the diet provides less than 15% of an RDA of proline. In some embodiments, the diet provides less than 10% of an RDA of proline. In some embodiments, the diet provides less than 5% of an RDA of proline. In some embodiments, the diet provides less than 1% of an RDA of proline. In some embodiments, the diet provides less than 0.5% of an RDA of proline. In some embodiments, the diet provides less than 0.1% of an RDA of proline. In some embodiments, the RDA of proline is the RDA for the subject's age group as determined by the Food and Nutrition Board of the Institute of Medicine. In some embodiments, the RDA of proline for an adult subject is about 55 mg/kg/day.

[0086] In some embodiments, the diet comprises less than about 500 mg/day of serine. In some embodiments, the diet comprises about 0 mg/day, about 10 mg/day or about 50 mg/day to about 200 mg/day, about 300 mg/day, about 400 mg/day or about 500 mg/day of serine. In some embodiments, the diet comprises about 50 mg/day to about 500 mg/day of serine. In some embodiments, the diet comprises about 380 mg/day to about 420 mg/day of serine.

[0087] In some embodiments, the diet comprises less than about 500 mg/day of glycine. In some embodiments, the diet comprises less than about 300 mg/day of glycine. In some embodiments, the diet comprises about 0 mg/day, about 10 mg/day or about 50 mg/day to about 200 mg/day, about 300 mg/day, about 400 mg/day or about 500 mg/day of glycine. In some embodiments, the diet comprises about 50 mg/day to about 500 mg/day of glycine. In some embodiments, the diet comprises about 50 mg/day to about 300 mg/day of glycine. In some embodiments, the diet comprises about 200 mg glycine/day to about 260 mg/day of glycine.

[0088] In some embodiments, the high diet comprises less than about 500 mg/day of proline. In some embodiments, diet comprises about 0 mg/day, about 10 mg/day or about 50 mg/day to about 200 mg/day, about 300 mg/day, about 400 mg/day or about 500 mg/day of proline. In

some embodiments diet comprises about 50 mg/day to about 500 mg/day of proline. In some embodiments, the diet comprises about 380 mg/day to about 450 mg/day of proline.

[0089] In some embodiments, the diet is high in fat (*i.e.*, in some embodiments, the diet is a high-fat diet.) A typical Western diet (of about 2000 kcals per day) has about 16 g of fat per meal, about 7.5 g of fat per snack, and about 63 g of fat per day. A diet that is high in fat can have 200% more, 150% more, 100% more, 80% more, 60% more, 40% more, 20% more, or 10% more grams of fat than is normally consumed in a typical Western diet.

[0090] In some embodiments, the diet comprises more than about 300 g, more than about 250 g, more than about 240 g, more than about 220 g, more than about 200 g, more than about 180 g, more than about 170 g, more than about 150 g, more than about 130 g, more than about 120 g, more than about 100 g, more than about 90 g, more than about 80 g, more than about 70 g, or more than about 60 g of fat per day. In some embodiments, the diet comprises more than about 220 g of fat per day. In some embodiments, the diet comprises more than about 200 g of fat per day. In some embodiments, the diet comprises more than about 170 g of fat per day. In some embodiments, the diet comprises more than about 150 g of fat per day. In some embodiments, the diet comprises more than about 130 g of fat per day. In some embodiments, the diet comprises more than about 120 g of fat per day. In some embodiments, the diet comprises more than about 100 g of fat per day. In some embodiments, the diet comprises more than about 80 g of fat per day. In some embodiments, the diet comprises more than about 70 g of fat per day. In some embodiments, the diet comprises more than about 60 g of fat per day.

[0091] In some embodiments, the diet comprises about 80 g to about 450 g, about 80 g to about 400 g, about 80 g to about 300 g, about 80 g to about 250 g, about 80 g to about 220 g, about 80 g to about 200 g, about 80 g to about 180 g, about 80 g to about 160 g, about 80 g to about 140 g, about 125 g to about 400 g, about 125 g to about 350 g, about 125 g to about 300 g, about 125 g to about 250 g, about 125 g to about 220 g, about 125 g to about 200 g, about 125 g to about 180 g, about 125 g to about 160 g, about 125 g to about 140 g, about 150 g to about 400 g, about 150 g to about 350 g, about 150 g to about 300 g, about 150 g to about 250 g, about 150 g to about 220 g, about 150 g to about 200 g, about 150 g to about 180 g, about 150 g to about 160 g, about 200 g to about 450 g, about 200 g to about 400 g, about 200 g to about 350 g, about 200 g to about 300 g, about 250 g to about 450 g, about 250 g to about 400 g, about 250 g to about 350 g, about 250 g to about 300 g, about 300 g to about 450 g, about 300 g to about 400 g, about 300 g to about 350 g, or about 350 g to about 450 g of fat per day. In some embodiments,

the diet comprises about 80 g to about 450 g of fat per day. In some embodiments, the diet comprises about 80 g to about 250 g of fat per day. In some embodiments, the diet comprises about 150 g to about 200 g of fat per day.

[0092] In some embodiments, the diet comprises about 80 g, about 100 g, about 120 g, about 140 g, about 160 g, about 170 g, about 180 g, about 190 g, about 200 g, about 210 g, about 220 g, about 230 g, about 240 g, about 250 g, about 260 g, about 270 g, about 280 g, about 290 g, about 300 g, about 350 g, about 400 g, or about 450 g of fat per day. In some embodiments the diet comprises about 150 g of fat per day. In some embodiments the diet comprises about 170 g of fat per day. In some embodiments the diet comprises about 200 g of fat per day. In some embodiments the diet comprises about 250 g of fat per day. In some embodiments the diet comprises about 300 g of fat per day.

[0093] In some embodiments, the diet comprises more than about 50%, more than about 60%, more than about 70%, more than about 80%, or more than about 90% of daily calories from fat. In some embodiments, the diet comprises more than about 50% of daily calories from fat. In some embodiments, the diet comprises more than about 60% of daily calories from fat. In some embodiments, the diet comprises more than about 70% of daily calories from fat. In some embodiments, the diet comprises more than about 80% of daily calories from fat. In some embodiments, the diet comprises more than about 90% of daily calories from fat. In some embodiments, the diet comprises about 50% to about 99%, about 50% to about 98%, about 50% to about 95%, about 50% to about 90%, about 50% to about 89%, about 50% to about 85%, about 50% to about 80%, about 60% to about 99%, about 60% to about 98%, about 60% to about 95%, about 60% to about 90%, about 60% to about 89%, about 60% to about 85%, about 60% to about 80%, about 70% to about 99%, about 70% to about 98%, about 70% to about 95%, about 75% to about 90%, about 75% to about 89%, about 75% to about 85%, about 75% to about 80%, about 75% to about 99%, about 75% to about 98%, about 75% to about 95%, about 75% to about 90%, about 75% to about 89%, about 75% to about 85%, about 75% to about 80%, about 80% to about 99%, about 80% to about 98%, about 80% to about 95%, about 80% to about 90%, about 80% to about 89%, or about 80% to about 85% of daily calories from fat. In some embodiments, the diet comprises about 80% to about 95% of daily calories from fat. In some embodiments, the diet comprises about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about

92%, about 93%, about 94%, or about 95% of daily calories from fat. In some embodiments, the diet comprises about 89% of daily calories from fat.

[0094] In some embodiments, the diet is low in carbohydrates (*i.e.*, in some embodiments, the diet is a low-carbohydrate diet or low-carb diet.) A typical Western diet (of about 2000 kcals per day) has about 59 g of carbohydrates per meal, about 28 g of carbohydrates per snack, and about 240 g of carbohydrates per day. A diet that is low in carbohydrates can have less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, or less than 5% of the grams of carbohydrates normally consumed in a Western diet.

[0095] In some embodiments, the diet comprises less than about 170 g, less than about 150 g, less than about 120 g, less than about 100 g, less than about 90 g, less than about 80 g, less than about 70 g, less than about 60 g, less than about 50 g, or less than about 40 g of net carbohydrates per day. In some embodiments, the diet comprises less than about 90 g of carbohydrates per day. In some embodiments, the diet comprises about 10 g to about 90 g, about 10 g to about 80 g, about 10 g to about 70 g, about 10 g to about 60 g, about 10 g to about 50 g, about 10 g to about 40 g, about 10 g to about 30 g, or about 10 g to about 20 g of net carbohydrates per day. In some embodiments, the diet comprises less than about 100 g, less than about 90 g, less than about 80 g, less than about 70 g, less than about 60 g, less than about 50 g, less than about 40 g, less than about 30 g, less than about 20 g, or less than about 10 g of carbohydrates per day. In some embodiments, the diet comprises about 100 g, about 80 g, about 50 g, about 30 g, or about 20 g of carbohydrates per day.

[0096] In some embodiments, the diet comprises less than about 170 g, less than about 150 g, less than about 120 g, less than about 100 g, less than about 80 g, less than about 50 g, less than about 40 g, less than about 30 g, less than about 20 g, or less than about 10 g of carbohydrates per day. In some embodiments, the diet comprises less than about 20 g of carbohydrates per day. In some embodiments, the diet comprises about 0 g to about 20 g, about 0 g to about 15 g, about 0 g to about 10 g, about 0 g to about 5 g, about 0 g to about 1 g, about 0.1 g to about 20 g, about 0.1 g to about 15 g, about 0.1 g to about 10 g, about 0.1 g to about 5 g, or about 0.1 g to about 1 g of carbohydrates per day. In some embodiments, the diet comprises less than about 20 g, less than about 19 g, less than about 18 g, less than about 17 g, less than about 16 g, less than about 15 g, less than about 14 g, less than about 13 g, less than about 12 g, less than about 11 g, less than about 10 g, less than about 9 g, less than about 8 g, less than about 7 g, less than about 6 g, less than about 5 g, less than about 4 g, less than about 3 g, less than about 2 g, or less than about

1 g of carbohydrates per day. In some embodiments, the diet comprises about 20 g, about 19 g, about 18 g, about 17 g, about 16 g, about 15 g, about 14 g, about 13 g, about 12 g, about 11 g, about 10 g, about 9 g, about 8 g, about 7 g, about 6 g, about 5 g, about 4 g, about 3 g, about 2 g, or about 1 g of carbohydrates per day.

[0097] In some embodiments, the diet comprises about 30 g to about 140 g of net carbohydrates per day. In some embodiments, the diet comprises about 30 g to about 120 g, about 30 g to about 100 g, about 30 g to about 90 g, about 50 g to about 140 g, about 50 g to about 120 g, or about 50 g to about 100 g of net carbohydrates per day. In some embodiments, the diet comprises less than about 150 g, less than about 140 g, less than about 130 g, less than about 120 g, less than about 110 g, less than about 100 g, less than about 90 g, less than about 80 g, less than about 70 g, less than about 60 g, less than about 50 g, less than about 40 g, less than about 30 g, or less than about 20 g of net carbohydrates per day. In some embodiments, the diet comprises about 30 g, about 40 g, about 50 g, about 60 g, about 70 g, about 80 g, about 90 g, about 100 g, about 110 g, about 120 g, about 130 g, about 140 g, or about 150 g of net carbohydrates per day. In some embodiments, the diet comprises 3 meals per day, with less than about 20 g of net carbohydrates per meal and with 0 to 10 snacks, wherein the snacks comprise less than about 10 g of net carbohydrates per snack.

[0098] Net carbohydrates (*i.e.*, net carbs) refers to the total amount of fully digestible carbohydrates contained within a diet, food, or meal. Net carbohydrates can be calculated by subtracting the whole amount of fiber and the whole amount of sugar alcohols from the amount of total carbohydrates in a product.

[0099] In some embodiments, the diet comprises less than about 50%, less than about 40%, less than about 30%, less than about 20%, less than about 15%, less than about 12%, less than about 10%, or less than about 5% of daily calories from carbohydrates. In some embodiments, the diet comprises less than about 20% of daily calories from carbohydrates. In some embodiments, the diet comprises less than about 15% of daily calories from carbohydrates. In some embodiments, the diet comprises less than about 12% of daily calories from carbohydrates. In some embodiments, the diet comprises less than about 10% of daily calories from carbohydrates. In some embodiments, the diet comprises less than about 5% of daily calories from carbohydrates. In some embodiments, the diet comprises less than about 5% of daily calories from carbohydrates. In some embodiment, the diet comprises about 1% to about 20%, about 1% to about 15%, about 1% to about 12%, about 1% to about 10%, about 1% to about 8%,

about 3% to about 20%, about 3% to about 15%, about 3% to about 12%, about 3% to about 10%, about 3% to about 8%, about 5% to about 20%, about 5% to about 15%, about 5% to about 12%, about 5% to about 10%, or about 5% to about 8% of daily calories from carbohydrates.

[0100] In some embodiments, the diet has a low glycemic index. In some embodiments, the diet comprises one or more foods with a low glycemic index. Glycemic index (GI) is a measure of how quickly a food elevates blood glucose. GI can be measured by measuring blood glucose levels about 2 hours following ingestion of a food. The GI can be defined as the ratio of the area under the blood glucose response curve after ingestion of a food containing 50 grams of carbohydrate divided by the area under the blood glucose response curve of a reference food containing 50 grams of carbohydrate. Foods can be classified by their GI. High-GI foods can have GI values of at least 70. Medium-GI foods can have GI values of between 56-59. Low-GI foods can have GI values of less than 55. In some embodiments the diet comprises foods with a GI value less than 55, less than 54, less than 53, less than 52, less than 51, less than 50, less than 49, less than 48, less than 47, less than 46, less than 45, less than 44, less than 43, less than 42, less than 41, less than 40, less than 39, less than 38, less than 37, less than 36, less than 35, less than 34, less than 33, less than 32, less than 31, less than 30, less than 29, less than 28, less than 27, less than 26, less than 25, less than 24, less than 23, less than 22, less than 21, less than 20, less than 19, less than 18, less than 17, less than 16, less than 15, less than 14, less than 13, less than 12, less than 11, less than 10, less than 9, less than 8, less than 7, less than 6, less than 5, less than 4, less than 3, less than 2, or less than 1. In some embodiments the diet comprises foods with a GI value less than 55. In some embodiments, the diet is a low-protein diet that comprises foods with a GI value less than 55.

[0101] In some embodiments, the diet is high in fat, low in protein, and low in carbohydrates. (*I.e.*, in some embodiments, the diet is a high-fat, low-carbohydrate, and low-protein diet.) In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 1200 to about 2600 kcals per day. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 1600 to about 2400 kcals per day.

[0102] In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises less than about 0.5 g/kg/day of protein. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 0.1 g/kg/day to about 0.5 g/kg/day of protein. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 0.1 g/kg/day, about 0.2 g/kg/day, about 0.3 g/kg/day, about 0.4 g/kg/day, or about 0.5 g/kg/day of

protein. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 0.2 g/kg/day of protein.

[0103] In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises less than about 500 mg/day of serine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 0 mg/day, about 10 mg/day or about 50 mg/day of serine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 200 mg/day, about 300 mg/day, about 400 mg/day or about 500 mg/day of serine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 50 mg/day to about 500 mg/day of serine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 380 mg/day to about 420 mg/day of serine.

[0104] In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises less than about 500 mg/day of glycine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises less than about 300 mg/day of glycine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 0 mg/day, about 10 mg/day or about 50 mg/day to about 200 mg/day, about 300 mg/day, about 400 mg/day or about 500 mg/day of glycine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 50 mg/day to about 500 mg/day of glycine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 50 mg/day to about 300 mg/day of glycine. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 200 mg glycine/day to about 260 mg/day of glycine.

[0105] In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises less than about 500 mg/day of proline. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 0 mg/day, about 10 mg/day or about 50 mg/day to about 200 mg/day, about 300 mg/day, about 400 mg/day or about 500 mg/day of proline. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 50 mg/day to about 500 mg/day of proline. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 380 mg/day to about 450 mg/day of proline.

[0106] In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 5% to about 25% of carbohydrates by calories, about 0.5% to about 8% of protein by calories, and about 67% to about 93.5% of fat by calories. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 8% to about 20% of carbohydrates by calories, about 1% to about 5% of protein by calories, and about 75% to about 91% of fat by

calories. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 5% to about 12% of carbohydrates by calories, about 1% to about 5% of protein by calories, and about 85% to about 95% of fat by calories. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 9% of carbohydrates by calories, about 2% of protein by calories, and about 89% of fat by calories. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 18% of carbohydrates by calories, about 2% of protein by calories, and about 80% of fat by calories.

[0107] In some embodiments, the dietary regimen comprises about 5% to about 25% of carbohydrates by diet-only calories, about 0.5% to about 8% of protein by diet-only calories, and about 67% to about 93.5% of fat by diet-only calories. In some embodiments, the dietary regimen comprises about 8% to about 20% of carbohydrates by diet-only calories, about 1% to about 5% of protein by diet-only calories, and about 75% to about 91% of fat by diet-only calories. In some embodiments, the dietary regimen comprises about 5% to about 12% of carbohydrates by diet-only calories; about 1% to about 5% of protein by diet-only calories, and about 85% to about 95% of fat by diet-only calories. In some embodiments, the dietary regimen comprises about 9% of carbohydrates by diet-only calories, about 2% of protein by diet-only calories, and about 89% of fat by diet-only calories. In some embodiments, the dietary regimen comprises about 18% of carbohydrates by diet-only calories, about 2% of protein by diet-only calories, and about 80% of fat by diet-only calories.

[0108] Diet-only calories, as used herein with reference to the calories of a dietary regimen, refers to only calories of a diet component of the dietary regimen, and not to calories from a dietary product.

[0109] In some embodiments, the high-fat, low-carbohydrate, and low-protein diet combined with the dietary product comprise 1) about 1200 to about 2600 kcals per day; 2) about 0.8 g/kg/day to about 1.2 g/kg/day of protein; 3) about 380 mg proline/day to about 450 mg proline/day; 4) about 380 mg/serine/day to about 420 mg/serine/day; 5) about 200 mg glycine/day to about 260 mg glycine/day; and 6) about 5% to about 12% of carbohydrates, about 1% to about 5% of protein, and about 85% to about 95% of fat by diet-only calories.

[0110] In some embodiments, the diet is administered orally. In some embodiments, the diet is administered via a tube. In some embodiments, the diet is administered via a nasogastric tube.

[0111] In some embodiments, the diet is administered at least 3 times per week, at least 4 times per week, at least 5 times per week, at least 6 times per week, or 7 times per week. In some

embodiments, the diet is administered 3 times per week. In some embodiments, the diet is administered 4 times per week. In some embodiments, the diet is administered 5 times per week. In some embodiments, the diet is administered 6 times per week. In some embodiments, the diet is administered 7 times per week.

[0112] In some embodiments, the diet is administered for 1 to 10 weeks, 1 to 9 weeks, 1 to 8 weeks, 1 to 7 weeks, 1 to 6 weeks, 1 to 5 weeks, 1 to 4 weeks, 1 to 3 weeks, or 1 to 2 weeks. In some embodiments, the diet regimen is administered for 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, or 10 weeks.

[0113] In some embodiments, the diet is administered at least 4 times per week for 5 weeks. In some embodiments, the diet is administered at least 6 times per week for 1 week.

[0114] In some embodiments, the diet is on an intermittent schedule alternating with a habitual diet. For example, in some embodiments, the subject consumes the diet for 6 days of a week and consumes a habitual diet on the remaining 1 day of the week. In some embodiments, the subject consumes the diet for 5 days of a week and consumes a habitual diet on the remaining 2 days of the week. In some embodiments, the subject consumes the diet for 4 days of a week and consumes a habitual diet on the remaining 3 days of the week. In some embodiments, the subject consumes the diet for 3 days of a week and consumes a habitual diet on the remaining 4 days of the week.

[0115] In some embodiments, the subject consumes a habitual diet for at least 2 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 3 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 4 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 5 consecutive days per week. In some embodiments, the subject consumes a habitual diet for at least 6 consecutive days per week. In some embodiments, the subject consumes a habitual diet for 7 consecutive days per week.

[0116] In some embodiments, the subject consumes the diet for 6 consecutive days of a week and consumes a habitual diet on the remaining 1 day of the week. In some embodiments, the subject consumes the diet for 5 consecutive days of a week and consumes a habitual diet on the remaining 2 days of the week. In some embodiments, the subject consumes the diet for 4 consecutive days of a week and consumes a habitual diet on the remaining 3 days of the week. In some embodiments, the subject consumes the diet for 3 consecutive days of a week and consumes a habitual diet on the remaining 4 days of the week. In some embodiments, the subject

consumes the diet for 2 consecutive days of a week and consumes a habitual diet on the remaining 5 days of the week.

[0117] In some embodiments, in the weeks in which the dietary regimen is given, the dietary regimen is given for at least 3 days of the week. In some embodiments, the dietary regimen is given on an intermittent schedule such that the dietary regimen is given 4 days per week and a habitual diet is given 3 days per week. In some embodiments, the dietary regimen weeks are every week of a month. In some embodiments, the dietary regimen weeks are 3 weeks of a month, with habitual diet for 1 week of the month. In some embodiments, the dietary regimen weeks are 2 weeks of a month, with habitual diet for 2 weeks of the month. In some embodiments, the dietary regimen weeks are 1 week of a month, with habitual diet for 3 weeks of the month.

[0118] The phrase "per day," as used herein with respect to diet, in some embodiments refers to an average daily intake over a week, over a month, or over the course of administering the diet. For example, in some embodiments, the grams of fat per day are an average daily fat intake based on averaging the daily fat intake over a week. In some embodiments, the grams of fat per day are an averaging daily fat intake based on average the daily fat intake over a month. In some embodiments, the grams of fat per day are an average daily fat intake based on averaging the daily fat intake over the course of administering the diet.

Dietary Product

[0119] In some embodiments, the dietary regimen comprises administering a dietary product. In some embodiments, the dietary product is a plurality of amino acids in powder form. In some embodiments, the dietary regimen consists of administering a dietary product. In some embodiments, the dietary product is administered with a therapeutically effective amount of a therapy (*e.g.*, chemotherapy, radiotherapy, immunotherapy, surgery, or combinations thereof) or a therapeutic agent (*e.g.*, chemotherapeutic agent, radiotherapeutic agent, immunotherapeutic agent, or combinations thereof.)

[0120] In some embodiments, the dietary product is substantially a sole source of protein for the subject. In some embodiments, the dietary product is substantially a sole source of amino acids for the subject.

[0121] In some embodiments, the dietary product is substantially devoid of an essential amino acid, a conditionally essential amino acid, a non-essential amino acid, or any combination

thereof. In some embodiments, the dietary product is substantially devoid of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, or valine. In some embodiments, the dietary product is substantially devoid of arginine, cysteine, glutamine, glycine, proline, or tryptophan. In some embodiments, the dietary product is substantially devoid of alanine, aspartic acid, asparagine, glutamic acid, or serine. In some embodiments, the dietary product is substantially devoid of at least one of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, arginine, cysteine, glutamine, glycine, proline, tryptophan, alanine, aspartic acid, asparagine, glutamic acid, or serine.

[0122] In some embodiments, the dietary product is substantially devoid of at least two of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, arginine, cysteine, glutamine, glycine, proline, tryptophan, alanine, aspartic acid, asparagine, glutamic acid, or serine. In some embodiments, the dietary product is substantially devoid of at least three, at least four, or at least five or more of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, arginine, cysteine, glutamine, glycine, proline, tryptophan, alanine, aspartic acid, asparagine, glutamic acid, or serine. In some embodiments, the dietary product is substantially devoid of at least serine and glycine. In some embodiments, the dietary product is substantially devoid of at least serine and proline. In some embodiments, the dietary product is substantially devoid of at least proline and glycine. In some embodiments, the dietary product is substantially devoid of at least serine, glycine, and proline.

[0123] In some embodiments, the dietary products comprises one or more amino acids (*e.g.*, serine, glycine, proline, or combinations thereof) in an amount that is at most about 75%, at most about 70%, at most about 65%, at most about 60%, at most about 55%, at most about 50%, at most about 45%, at most about 40%, at most about 35%, at most about 30%, at most about 25%, at most about 20%, at most about 15%, at most about 10%, at most about 5%, at most about 4.5%, at most about 4%, at most about 3.5%, at most about 3%, at most about 2.5%, at most about 2%, at most about 1.5%, at most about 1%, at most about 0.5%, or at most about 0.3% of the daily recommended dietary requirement of the amino acid. In some embodiments, the dietary product comprises at most about 75% of the daily recommended dietary requirement of amino acids (*e.g.*, serine, glycine, proline, or combinations thereof). In some embodiments, the dietary product comprises at most about 50% of the daily recommended dietary requirement of the amino acids (*e.g.*, serine, glycine, proline, or combinations thereof). In some embodiments, the dietary product comprises at most about 20% of the daily recommended dietary requirement of

the amino acids (*e.g.*, serine, glycine, proline, or combinations thereof) acid. In some embodiments, the dietary product comprises at most about 10% of the daily recommended dietary requirement of the amino acids (*e.g.*, serine, glycine, proline, or combinations thereof). In some embodiments, the dietary product comprises at most about 5% of the daily recommended dietary requirement of the amino acids (*e.g.*, serine, glycine, proline, or combinations thereof). In some embodiments, the dietary product comprises at most about 1% of the daily recommended dietary requirement of the amino acids (*e.g.*, serine, glycine, proline, or combinations thereof). In some embodiments, the dietary product comprises at most about 0.5% of the daily recommended dietary requirement of the amino acids (*e.g.*, serine, glycine, proline, or combinations thereof).

[0124] In some embodiments, the dietary product comprises less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary allowance (RDA) of serine. In some embodiments, the dietary product comprises less than 50% of an RDA of serine. In some embodiments, the dietary product comprises less than 45% of an RDA of serine. In some embodiments, the dietary product comprises less than 40% of an RDA of serine. In some embodiments, the dietary product comprises less than 35% of an RDA of serine. In some embodiments, the dietary product comprises less than 30% of an RDA of serine. In some embodiments, the dietary product comprises less than 25% of an RDA of serine. In some embodiments, the dietary product comprises less than 20% of an RDA of serine. In some embodiments, the dietary product comprises less than 15% of an RDA of serine. In some embodiments, the dietary product comprises less than 10% of an RDA of serine. In some embodiments, the dietary product comprises less than 5% of an RDA of serine. In some embodiments, the dietary product comprises less than 1% of an RDA of serine. In some embodiments, the dietary product comprises less than 0.5% of an RDA of serine. In some embodiments, the dietary product comprises less than 0.1% of an RDA of serine. In some embodiments, the RDA of serine is the RDA for the subject's age group as determined by the Food and Nutrition Board of the Institute of Medicine. In some embodiments, the RDA of serine for an adult subject is about 28 mg/kg/day.

[0125] In some embodiments, the dietary product comprises less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary

allowance (RDA) of glycine. In some embodiments, the dietary product comprises less than 50% of an RDA of glycine. In some embodiments, the dietary product comprises less than 45% of an RDA of glycine. In some embodiments, the dietary product comprises less than 40% of an RDA of glycine. In some embodiments, the dietary product comprises less than 35% of an RDA of glycine. In some embodiments, the dietary product comprises less than 30% of an RDA of glycine. In some embodiments, the dietary product comprises less than 25% of an RDA of glycine. In some embodiments, the dietary product comprises less than 20% of an RDA of glycine. In some embodiments, the dietary product comprises less than 15% of an RDA of glycine. In some embodiments, the dietary product comprises less than 10% of an RDA of glycine. In some embodiments, the dietary product comprises less than 5% of an RDA of glycine. In some embodiments, the dietary product comprises less than 1% of an RDA of glycine. In some embodiments, the dietary product comprises less than 0.5% of an RDA of glycine. In some embodiments, the dietary product comprises less than 0.1% of an RDA of glycine. In some embodiments, the RDA of glycine is the RDA for the subject's age group as determined by the Food and Nutrition Board of the Institute of Medicine. In some embodiments, the RDA of glycine for an adult subject is about 50 mg/kg/day.

[0126] In some embodiments, the dietary product comprises less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 1%, less than 0.5%, or less than 0.1% of a recommended dietary allowance (RDA) of proline. In some embodiments, the dietary product comprises less than 50% of an RDA of proline. In some embodiments, the dietary product comprises less than 45% of an RDA of proline. In some embodiments, the dietary product comprises less than 40% of an RDA of proline. In some embodiments, the dietary product comprises less than 35% of an RDA of proline. In some embodiments, the dietary product comprises less than 30% of an RDA of proline. In some embodiments, the dietary product comprises less than 25% of an RDA of proline. In some embodiments, the dietary product comprises less than 20% of an RDA of proline. In some embodiments, the dietary product comprises less than 15% of an RDA of proline. In some embodiments, the dietary product comprises less than 10% of an RDA of proline. In some embodiments, the dietary product comprises less than 5% of an RDA of proline. In some embodiments, the dietary product comprises less than 1% of an RDA of proline. In some embodiments, the dietary product comprises less than 0.5% of an RDA of proline. In some embodiments, the dietary product comprises less than 0.1% of an RDA of

proline. In some embodiments, the RDA of proline is the RDA for the subject's age group as determined by the Food and Nutrition Board of the Institute of Medicine. In some embodiments, the RDA of proline for an adult subject is about 55 mg/kg/day.

[0127] In some embodiments, the dietary product is devoid of at least 1, 2, 3, 4, 5, 6, 7, or 8 amino acids. In some embodiments, the dietary product is devoid of at least 1 amino acid. In some embodiments, the dietary product is devoid of at least 2 amino acids. In some embodiments, the dietary product is devoid of at least 3 amino acids. In some embodiments, the dietary product is devoid of at least 4 amino acids. In some embodiments, the dietary product is devoid of at least 5 amino acids.

[0128] In some embodiments, the dietary product is devoid of histidine, arginine, alanine, isoleucine, cysteine, aspartic acid, leucine, glutamine, asparagine, lysine, glycine, glutamic acid, methionine, proline, serine, phenylalanine, tyrosine, threonine, tryptophan, or valine. In some embodiments, the dietary product is devoid of at least 1, 2, 3, 4, 5, 6, 7, or 8 of the foregoing amino acids. In some embodiments, the dietary product is devoid of at least 1 of the foregoing amino acids. In some embodiments, the dietary product is devoid of at least 2 of the foregoing amino acids. In some embodiments, the dietary product is devoid of at least 3 of the foregoing amino acids. In some embodiments, the dietary product is devoid of at least 4 of the foregoing amino acids. In some embodiments, the dietary product is devoid of at least 5 of the foregoing amino acids.

[0129] In some embodiments, the dietary product is devoid of an essential amino acid, a conditionally essential amino acid, a non-essential amino acid, or any combination thereof.

[0130] Essential amino acids, as used herein, refers to histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

[0131] Non-essential amino acids, as used herein, refers there the 11 proteinogenic amino acids deemed in the human diet that humans generally have the biochemical ability to synthesize: serine, glycine, alanine, glutamine, glutamic acid, aspartic acid, arginine, cysteine, tyrosine, proline, threonine.

[0132] In some embodiments, the dietary product is devoid of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, or valine. In some embodiments, the dietary product is devoid of arginine, cysteine, glutamine, glycine, proline, or tryptophan. In some embodiments, the dietary product is devoid of alanine, aspartic acid, asparagine, glutamic acid, or serine. In some embodiments, the dietary product is devoid of at least one of histidine,

isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, arginine, cysteine, glutamine, glycine, proline, tryptophan, alanine, aspartic acid, asparagine, glutamic acid, or serine. In some embodiments, the dietary product is devoid of at least two of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, arginine, cysteine, glutamine, glycine, proline, tryptophan, alanine, aspartic acid, asparagine, glutamic acid, or serine. In some embodiments, the dietary product is devoid of at least three, at least four, at least five, or more of histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, arginine, cysteine, glutamine, glycine, proline, tryptophan, alanine, aspartic acid, asparagine, glutamic acid, or serine.

[0133] In some embodiments, the dietary product is devoid of one amino acid. In some embodiments, the dietary product is devoid of serine. In some embodiments, the dietary product is devoid of glycine. In some embodiments, the dietary product is devoid of proline.

[0134] In some embodiments, the dietary product is devoid of two amino acids. In some embodiments, the dietary product is devoid of serine and glycine. In some embodiments, the dietary product is devoid of serine and proline. In some embodiments, the dietary product is devoid of glycine and proline.

[0135] In some embodiments, the dietary product is devoid of three amino acids. In some embodiments, the dietary product is devoid of serine, glycine, and proline.

[0136] The dietary product of the disclosure comprises at least ten amino acids. In some embodiments, the dietary product comprises 10, 11, 12, 13, 14, 15, 16, 17, 18, or 19 amino acids. In some embodiments, the dietary product comprises 10 amino acids. In some embodiments, the dietary product comprises 11 amino acids. In some embodiments, the dietary product comprises 12 amino acids. In some embodiments, the dietary product comprises 13 amino acids. In some embodiments, the dietary product comprises 14 amino acids. In some embodiments, the dietary product comprises 15 amino acids. In some embodiments, the dietary product comprises 16 amino acids. In some embodiments, the dietary product comprises 17 amino acids. In some embodiments, the dietary product comprises 18 amino acids.

[0137] In some embodiments, the dietary product comprises 1, 2, 3, 4, 5, 6, 7, 8, or 9 essential amino acids. In some embodiments, the dietary product comprises 7, 8, or 9 essential amino acids. In some embodiments, the dietary product comprises 8 essential amino acids. In some embodiments, the dietary product comprises 9 essential amino acids.

[0138] In some embodiments, the dietary product comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 non-essential amino acids. In some embodiments, the dietary product comprises 7, 8, 9, 10, or 11 non-essential amino acids. In some embodiments, the dietary product comprises 7 non-essential amino acids. In some embodiments, the dietary product comprises 8 non-essential amino acids. In some embodiments, the dietary product comprises 9 non-essential amino acids. In some embodiments, the dietary product comprises 10 non-essential amino acids.

[0139] In some embodiments, the dietary product comprises essential amino acids and non-essential amino acids. In some embodiments, the dietary product comprises 1, 2, 3, 4, 5, 6, 7, 8, or 9 essential amino acids, and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 non-essential amino acids. In some embodiments, the dietary product comprises 7, 8, or 9 essential amino acids and 6, 7, 8, or 9 non-essential amino acids. In some embodiments, the dietary product comprises 8 or 9 essential amino acids and 8 or 9 non-essential amino acids. In some embodiments, the dietary product comprises 9 essential amino acids and 7 non-essential amino acids. In some embodiments, the dietary product comprises 9 essential amino acids and 8 non-essential amino acids. In some embodiments, the dietary product comprises 9 essential amino acids and 9 non-essential amino acids.

[0140] In some embodiments, the dietary product comprises histidine, isoleucine, leucine, lysine, methionine, cysteine, phenylalanine, tyrosine, threonine, tryptophan, valine, arginine, glutamine, alanine, aspartic acid, asparagine, glutamic acid, proline, taurine, or a combination thereof. In some embodiments, the dietary product comprises histidine, isoleucine, leucine, lysine, methionine, cysteine, phenylalanine, tyrosine, threonine, tryptophan, valine, arginine, glutamine, alanine, aspartic acid, asparagine, glutamic acid, or a combination thereof. In some embodiments, the dietary product comprises L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-cysteine, L-phenylalanine, L-tyrosine, L-threonine, L-tryptophan, L-valine, L-arginine, L-glutamine, L-alanine, L-aspartic acid, L-asparagine, L-glutamic acid, L-proline, or a combination thereof. In some embodiments, the dietary product comprises L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-cysteine, L-phenylalanine, L-tyrosine, L-threonine, L-tryptophan, L-valine, L-arginine, L-glutamine, L-alanine, L-aspartic acid, L-asparagine, L-glutamic acid, or a combination thereof.

[0141] In some embodiments, the dietary product comprises histidine or a salt thereof, such as L-histidine, L-histidine hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 2% to about 10% of the histidine, and salts thereof, by

weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 2% to about 6% of the histidine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0142] As used herein, "by weight of the amino acids, and salts thereof" in reference to the percent mass of a given amino acid, refers to the weight of the given amino acid, and salts of that amino acid, divided by the weight of all amino acids, and salts of all the amino acids, in the dietary product.

[0143] In some embodiments, the dietary product comprises isoleucine or a salt thereof, such as L-isoleucine, L-isoleucine methyl ester hydrochloride, L-isoleucine ethyl ester hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 2% to about 10% of the isoleucine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 2% to about 6% of the isoleucine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0144] In some embodiments, the dietary product comprises leucine or a salt thereof, such as L-leucine, L-leucine methyl ester hydrochloride, L-leucine ethyl ester hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 5% to about 15% of the leucine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 7% to about 10% of the leucine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0145] In some embodiments, the dietary product comprises lysine or a salt thereof, such as L-lysine, L-lysine hydrochloride, L-lysine dihydrochloride, L-lysine monohydrate, L-lysine monohydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 5% to about 15% of the lysine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 8% to about 12% of the lysine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0146] In some embodiments, the dietary product comprises methionine or a salt thereof, such as L-methionine, L-methionine methyl ester hydrochloride, L-methionine hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 1% to about 5% of the methionine, and salts thereof, by weight of the amino acids, and salts thereof, in

the dietary product. In some embodiments, the dietary product comprises between about 1% to about 3% of the methionine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0147] In some embodiments, the dietary product comprises cysteine or a salt thereof, such as L-cysteine, L-cysteine hydrochloride, L-cysteine methyl ester hydrochloride, or L-cysteine ethyl ester hydrochloride, or a combination thereof. In some embodiments, the cysteine or the salt thereof is present as cystine, the homodimeric form of cysteine. Accordingly, in some embodiments, the dietary product comprises L-cysteine, L-cysteine hydrochloride, L-cysteine methyl ester hydrochloride, L-cysteine ethyl ester hydrochloride, L-cystine, or a combination thereof. In some embodiments, the dietary product comprises between about 1% to about 10% of the cysteine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 1% to about 5% of the cysteine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 1% to about 10% of cystine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 1% to about 5% of cystine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0148] In some embodiments, the dietary product comprises phenylalanine or a salt thereof, such as L-phenylalanine, DL-phenylalanine, L-phenylalanine methyl ester hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 5% to about 15% of the phenylalanine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 5% to about 10% of the phenylalanine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0149] In some embodiments, the dietary product comprises tyrosine or a salt thereof, such as L-tyrosine, L-tyrosine hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 1% to about 8% of the tyrosine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 1% to about 5% of the tyrosine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0150] In some embodiments, the dietary product comprises threonine or a salt thereof, such as L-threonine, L-threonine methyl ester hydrochloride, or a combination thereof. In some

embodiments, the dietary product comprises between about 2% to about 10% of the threonine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 4% to about 8% of the threonine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0151] In some embodiments, the dietary product comprises tryptophan or a salt thereof, such as L-tryptophan. In some embodiments, the dietary product comprises between about 1% to about 5% of the tryptophan, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 1% to about 3% of the tryptophan, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0152] In some embodiments, the dietary product comprises valine or a salt thereof, such as L-valine, L-valine methyl ester hydrochloride, L-valine ethyl ester hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 2% to about 10% of the valine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 3% to about 8% of the valine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0153] In some embodiments, the dietary product comprises arginine or a salt thereof, such as L-arginine base, L-arginine hydrochloride, L-arginine-L-glutamate salt, or a combination thereof. In some embodiments, the dietary product comprises between about 5% to about 15% of the arginine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 7% to about 12% of the arginine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0154] In some embodiments, the dietary product comprises glutamine or a salt thereof, such as L-glutamine, L-glutamine hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises between about 1% to about 5% of the glutamine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 2% to about 4% of the glutamine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0155] In some embodiments, the dietary product comprises alanine or a salt thereof, such as L-alanine, β-alanine, or a combination thereof. In some embodiments, the dietary product

comprises between about 3% to about 12% of the alanine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 5% to about 10% of the alanine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0156] In some embodiments, the dietary product comprises aspartic acid or a salt thereof, such as L-aspartic acid, D-aspartic acid, L- or D-aspartic acid potassium salt, L- or D-aspartic acid hydrochloride salt, L- or D-aspartic acid magnesium salt, L- or D-aspartic acid calcium salt, magnesium L-aspartate dihydrate, or a combination thereof. In some embodiments, the dietary product comprises between about 5% to about 15% of the aspartic acid, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 7% to about 13% of the aspartic acid, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0157] In some embodiments, the dietary product comprises asparagine or a salt thereof, such as L-asparagine, L-asparagine hydrate, or a combination thereof. In some embodiments, the dietary product comprises between about 2% to about 10% of the asparagine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 4% to about 8% of the asparagine, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0158] In some embodiments, the dietary product comprises glutamic acid or a salt thereof, such as L-glutamic acid, L-glutamic acid hydrochloride, L-arginine-L-glutamate salt, potassium L-glutamate monohydrate, or a combination thereof. In some embodiments, the dietary product comprises between about 1% to about 6% of the glutamic acid, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 2% to about 5% of the glutamic acid, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 2% to about 10% of the glutamic acid, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 4% to about 9% of the glutamic acid, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0159] In some embodiments, the dietary product comprises proline or a salt thereof, such as L-proline, L-proline hydrochloride, L-proline methyl ester hydrochloride, L-proline ethyl ester hydrochloride, or a combination thereof. In some embodiments, the dietary product comprises

between about 1% to about 6% of the proline, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product. In some embodiments, the dietary product comprises between about 2% to about 5% of the proline, and salts thereof, by weight of the amino acids, and salts thereof, in the dietary product.

[0160] In some embodiments, the dietary product is a pharmaceutical composition comprising, in unit dosage form: a) a plurality of amino acids, wherein the pharmaceutical composition is devoid of at least serine, glycine, and proline; and b) a pharmaceutically acceptable excipient.

[0161] A salt of an amino acid disclosed herein can be a nutritionally acceptable salt. In some embodiments, a nutritionally acceptable salt meets the requirements of its applicable FCC monograph. In some embodiments, a nutritionally acceptable salt meets the requirements of its applicable Joint FAO/WHO Expert Committee on Food Additives (JECFA) reports, monographs, or specifications. In some embodiments, a nutritionally acceptable salt meets the FDA requirements at 21 CFR 172.320.

[0162] In some embodiments, the dietary product comprises a plurality of amino acids in powder form. In some embodiments, the dietary product is reconstituted with water or another liquid solvent prior to administration. In some embodiments, the dietary product comprises a plurality of amino acids in powder form, a zero-calorie sweetener, and one or more natural flavorings.

[0163] The amino acids may be produced by various manufacturing methods. The amino acids may be synthetic products produced by chemical synthesis methods. The amino acids may be produced by microorganism fermentation methods. The amino acids may be products of yeast-based production methods utilizing plant-derived carbohydrates as raw materials. The amino acids may be directly derived from plants.

[0164] In some embodiments, the dietary product comprises a plant-derived powder. In some embodiments, the plant-derived powder comprises a plurality of purified amino acids, a zero-calorie sweetener, and natural flavorings.

[0165] In some embodiments, the dietary product is formulated as a solid. In some embodiments, the dietary product is formulated as a powder. In some embodiments, the dietary product is formulated as a beverage.

[0166] In some embodiments, the dietary product is administered orally. In some embodiments, the dietary product is administered via a tube. In some embodiments, the dietary product is administered via a nasogastric tube.

[0167] In some embodiments, the dietary product is administered at least 1 time, at least 2 times, at least 3 times, at least 4 times, at least 5 times, at least 6 times, at least 7 times, at least 8 times, at least 9 times, or at least 10 times a day. In some embodiments, the dietary product is administered at least 1 time a day. In some embodiments, the dietary product is administered at least 2 times a day. In some embodiments, dietary product is administered at least 3 times a day. In some embodiments, the dietary product is administered at least 4 times a day. In some embodiments, the dietary product is administered at least 5 times a day.

[0168] In some embodiments, the dietary product is administered to a subject throughout a day. In some embodiments, the dietary product is administered to a subject with a meal. In some embodiments, the dietary product is administered to a subject with a snack. In some embodiments, the dietary product is administered to a subject without a meal. In some embodiments, the dietary product is administered to a subject through the day in equal intervals. In some embodiments, a first serving is administered before breakfast, a second serving is administered with breakfast, a third serving is administered with lunch, a fourth and fifth serving is administered with dinner, and a sixth serving is administered before bed. In some embodiments, the dietary product is administered to a subject as a medical food. In some embodiments, a first serving is administered as breakfast, a second serving is administered as lunch, a third serving is administered as a snack, a fourth serving is administered as dinner, a fifth serving is administered as dessert.

[0169] In some embodiments, the dietary product is administered to a subject who is on a diet. In some embodiments, the dietary product is administered to the subject, and the subject is on a diet that is low in protein. In some embodiments, the dietary product is administered to the subject, and the subject is on a low-carbohydrate diet. In some embodiments, the dietary product is administered to the subject, and the subject is on a high-fat, and low-carbohydrate die (*e.g.*, ketogenic type diet). In some embodiments, the dietary product is administered to the subject, and the subject is on a low glycemic-index diet. In some embodiments, the dietary product is administered to the subject, and the subject is on a vegetarian diet. In some embodiments, the dietary product is administered to the subject, and the subject is on a vegan diet. In some embodiments, the dietary product is compatible with a particular diet being consumed by the subject. For example, in some embodiments, the dietary product is low in protein, low in carbohydrates, high in fat, has a low glycemic-index, is vegetarian, or is vegan.

[0170] In some embodiments, the dietary product is administered to a subject who is on a low-protein diet designed to be low in at least one non-essential amino acid. In some embodiments, the dietary product is administered to a subject who is on a low-protein diet designed to be low in serine and glycine. In some embodiments, the dietary product is administered to a subject who is on a low-protein diet designed to be low in serine and proline. In some embodiments, the dietary product is administered to a subject who is on a low-protein diet designed to be low in proline and glycine. In some embodiments, the dietary product is administered to a subject who is on a low-protein diet designed to be low in serine, glycine, and proline. In some embodiments, the dietary product is administered to a subject who is on a low-protein diet designed to be low in serine, glycine, and cysteine. In some embodiments, the dietary product is administered to a subject who is on a low-protein diet with less than about 2 g/day, less than about 1.75 g/day, less than about 1.5 g/day, less than about 1.25 g/day, less than about 1 g/day, less than about 0.75 g/day, or less than about 0.5 g/day of protein. In some embodiments, the dietary product is administered to a subject who is on a low- protein diet with less than about 500 mg/day, less than about 450 mg/day, less than about 400 mg/day, less than about 350 mg/day, less than about 300 mg/day, less than about 250 mg/day, less than about 200 mg/day, less than about 150 mg/day, less than about 100 mg/day, or less than about 50 mg/day of protein.

[0171] In some embodiments, the dietary product is administered in conjunction with other therapies, for example, chemotherapy, radiation, radiotherapeutic agents, surgery, anti-inflammatory agents, immunotherapy, biologicals, and selected vitamins. The other agents can be administered prior to, after, or concomitantly with the dietary product. The other agents can be administered daily. The other agents can be administered at least 1 time, at least 2 times, at least 3 times, at least 4 times, at least 5 times, at least 6 times, at least 7 times, at least 8 times, at least 9 times, or at least 10 times a day. In some embodiments, the dietary product is administered with a chemotherapy. In some embodiments, the dietary product is administered with a radiotherapy or a radiotherapeutic agent. In some embodiments, the dietary product is administered with a vitamin. In some embodiments, the dietary product is administered with a multivitamin. In some embodiments, the vitamin is administered daily. In some embodiments, the multivitamin is administered daily.

[0172] In some embodiments, the dietary product is administered to the subject at least 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 11 times, 12 times, 13 times, 14 times, 15 times, 16 times, 17 times, 18 times, 19 times, 20 times, 21 times, 22

times, 23 times, 24 times, 25 times, 26 times, 27 times, 28 times, 29 times, 30 times, 31 times, 32 times, 33 times, 34 times, 35 times, 36 times, 37 times, 38 times, 39 times, or 40 times per week. In some embodiments, the dietary product is administered at least 4 times per week. In some embodiments, the dietary product is administered at least 6 times per week. In some embodiments, the dietary product is administered at least 10 times per week. In some embodiments, the dietary product is administered at least 15 times per week. In some embodiments, the dietary product is administered at least 18 times per week. In some embodiments, the dietary product is administered at least 21 times per week. In some embodiments, the dietary product is administered at least 24 times per week. In some embodiments, the dietary product is administered at least 28 times per week. In some embodiments, the dietary product is administered at least 35 times per week. In some embodiments, the dietary product is administered at least 42 times per week.

[0173] Amino acids in the dietary products described herein can be administered as any one or more of the following forms: free forms, non-ionic compounds, salts, prodrugs, homodimers, homopolymers, heterodimers, heteropolymers, esters, N-terminal modified forms, or C-terminal modified forms. An amino acid herein can be a pharmaceutically acceptable salt or otherwise acceptable forms thereof for the purposes of use in foods (including medical foods) and dietary supplements. Similarly, diets and dietary products described herein that are devoid of one or more amino acids are devoid of the following forms: free forms, non-ionic compounds, salts, prodrugs, homodimers, homopolymers, heterodimers, heteropolymers, esters, N-terminal modified forms, or C-terminal modified forms. For example, a dietary product that is devoid of or does not comprise cysteine also does not comprise cystine, the homodimeric form of cysteine. Also for example, a dietary product that is devoid of serine does not comprise the free form of serine nor salts of serine. Also for example, a dietary product that is devoid of glycine does not comprise the free form of glycine nor salts of glycine. Also for example, a dietary product that is devoid of glycine does not comprise the free form of glycine nor salts of glycine.

[0174] Pharmaceutically acceptable salt, as used herein, refers to a salt which is generally safe, non-toxic and not biologically or otherwise undesirable, and includes that which is acceptable for veterinary use as well as human pharmaceutical use.

Methods of Use

[0175] The present disclosure provides methods for treating colorectal cancer (*e.g.*, LARC) in a subject in need thereof.

[0176] The terms "treat," "treating," or "treatment," as used herein, refer to any indicia of success in the amelioration of a disorder (such as injury, disease pathology, or condition), including any objective or subjective parameter such as abatement; remission; diminishing of symptoms or making the disorder more tolerable to the subject; slowing or stopping the rate of degeneration, decline, or development; slowing the progression of disorder; making the final point of degeneration less debilitating; improving a subject's physical or mental well-being; or relieving or causing regression of the disorder. The treatment of symptoms, including the amelioration of symptoms, can be based on objective or subjective parameters, which may include the results of a physical examination, a neuropsychiatric exam, and/or a psychiatric evaluation.

[0177] The terms "administered," "administration," or "administering," as used herein, refer to either directly administering a treatment as disclosed herein to a subject, including an animal, in need of treatment by bringing such individual in contact with, or otherwise exposing such individual to, the treatment.

[0178] As used herein, the term "subject" encompasses mammals and non-mammals. Examples of mammals include, but are not limited to, any member of the class Mammalia: humans, non-human primates such as chimpanzees, and other apes and monkey species; farm animals such as cattle, horses, sheep, goats, and swine; domestic animals such as rabbits, dogs, and cats; laboratory animals including rodents, such as rats, mice and guinea pigs, and the like. Examples of non-mammals include, but are not limited to, birds, fish and the like. In one embodiment of the present disclosure, the mammal is a human.

[0179] The term "condition," as used herein, refers to and is used interchangeably with the terms disease, disorder, or illness, unless otherwise indicated.

[0180] In some embodiments, the subject has colorectal cancer (*e.g.*, LARC). In some embodiments, a subject has a solid tumor. In some embodiments, a subject has an adenocarcinoma of the colon or rectum. In some embodiments, a subject has an endometrial adenocarcinoma, *e.g.*, endometrioid adenocarcinoma, serous adenocarcinoma, undifferentiated carcinoma, clear cell adenocarcinoma, mixed epithelial carcinoma, adenocarcinoma not

otherwise specified (N.O.S.), mucinous adenocarcinoma, squamous cell carcinoma, transitional cell carcinoma, or carcinosarcoma. In some embodiments, a subject has an ovarian clear cell or endometrioid carcinoma. In some embodiments, a subject has a colorectal cancer (*e.g.*, LARC) harboring a PIK3CA-activating mutation with or without a PTEN loss-of-function mutation.

[0181] In some embodiments, the methods herein increase overall survival of a subject. In some embodiments, the methods herein increase overall survival of a subject by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95%. In some embodiments, the methods herein increase overall survival of a subject by at least about 10%. In some embodiments, the methods herein increase overall survival of a subject by at least about 20%. In some embodiments, the methods herein increase overall survival of a subject by at least about 30%.

[0182] In some embodiments, the methods herein increase progression-free survival of a subject. In some embodiments, the methods herein increase progression-free survival of a subject by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95%. In some embodiments, the methods herein increase progression-free survival of a subject by at least about 10%. In some embodiments, the methods herein increase progression-free survival of a subject by at least about 20%. In some embodiments, the methods herein increase progression-free survival of a subject by at least about 30%.

[0183] In some embodiments, the subject is directed to reduce use of a medication that may impact proline, serine, and/or glycine levels. In some embodiments, the subject is directed to cease use of a medication that may impact proline, serine, and/or glycine levels. In some embodiments, the methods of treatment described herein are not administered to a subject who must take a medication that impacts proline, serine, and/or glycine levels. Medications that may impact proline, serine, and/or glycine levels include, but are not limited to: collagen, cartilage, hyaluronic acid, probiotics, turmeric with bioperine (or black pepper extract), supplements that contain gelatin as an ingredient, fiber supplements (*e.g.*, Citrucel), MiraLAX (*i.e.*, polyethylene

glycol), lithium, antipsychotic medications such as risperidone (Risperdal-Janssen), aripiprazole (Abilfy-Otsuka), and quetiapine fumarate (Seroquel-AstraZeneca), and Epilepsy drugs (especially divalproex sodium, zonisamide, and topiramate).

Therapeutic Agents

[0184] In some embodiments, a dietary regimen is administered with one or more therapies. Non-limiting examples of therapies include chemotherapy, radiotherapy, immunotherapy, and surgery. In some embodiments, a dietary regimen is administered in combination with, before, or after treatment with a therapy. In some embodiments, a dietary regimen is administered in any order or concurrently with multiple therapies. In some embodiments, the dietary regimen is administered in combination with chemotherapy, radiotherapy, or immunotherapy. In some embodiments, the dietary regimen is administered in combination with chemotherapy and radiotherapy. In some embodiments, the dietary regimen is administered in combination with chemotherapy and immunotherapy. In some embodiments, the dietary regimen is administered in combination with radiotherapy and immunotherapy.

[0185] Various therapies are associated with therapeutics agents, non-limiting examples of which include chemotherapeutic agents, radiotherapeutic agents, and immunotherapeutic agents. The term therapeutically effective amount, as used herein, when used in connection with a therapeutic agent, refers to a sufficient amount of the associated therapeutic agent to provide the desired biological result. Similarly, therapeutically effective amount of a radiotherapy refers to a sufficient application of the therapy (*e.g.*, sufficient application of radiation) to provide the desired biological result. That result can be reduction and/or alleviation of the signs, symptoms, or causes of a disease, or any other desired alteration of a biological system.

[0186] Therapies described herein can be administered before, during, or after the occurrence of a disease or condition, and the timing of administering the therapy can vary. The therapy can be administered to a subject during or as soon after the onset of the symptoms.

[0187] In some embodiments, the methods herein increase a treatment-response rate of a therapy or of a therapeutic agent. In some embodiments, the methods herein increase a treatment-response rate of a therapy or of a therapeutic agent by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%,

at least about 85%, at least about 90%, or at least about 95%. In some embodiments, the methods herein increase a treatment-response rate of a therapy or of a therapeutic agent by at least about 10%. In some embodiments, the methods herein increase a treatment-response rate of a therapy or of a therapeutic agent by at least about 20%. In some embodiments, the methods herein increase a treatment-response rate of a therapy or of a therapeutic agent by at least about 30%.

[0188] In some embodiments, the dietary regimen herein increases the efficacy of a therapy or of a therapeutic agent in a subject compared to a subject treated only with the therapy or the therapeutic agent. In some embodiments, administering a dietary regimen with a therapy or a therapeutic agent increases the efficacy of the therapy or the therapeutic agent in the subject by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95% compared to a subject treated only with the therapy or the therapeutic agent. In some embodiments, administering a dietary regimen with a therapy or a therapeutic agent increases the efficacy of the therapy or the therapeutic agent in a subject by at least about 10% compared to a subject treated only with the therapy or the therapeutic agent. In some embodiments, administering a dietary regimen with a therapy or a therapeutic agent increases the efficacy of the therapy or the therapeutic agent in a subject by at least about 20% compared to a subject treated only with the therapy or the therapeutic agent. In some embodiments, administering a dietary regimen increases the efficacy of the therapy or the therapeutic agent in subject by at least about 30% compared to a subject treated only with the therapy or the therapeutic agent.

[0189] Administering a dietary regimen described herein with a therapeutic agent can facilitate use of a decreased dose of the therapeutic agent to achieve the same outcome compared to a subject treated with the therapeutic agent alone. In some embodiments, administering to a subject a dietary regimen with a therapeutic agent decreases the required dose of the therapeutic agent by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95% compared to a subject treated with the therapeutic agent alone to achieve the same outcome. In some embodiments, administering to a subject a dietary regimen with a therapeutic

agent decreases the required dose of the therapeutic agent by at least about 10% compared to a subject treated with the therapeutic agent alone to achieve the same outcome. In some embodiments, administering to a subject a dietary regimen with a therapeutic agent decreases the required dose of the therapeutic agent by at least about 20% compared to a subject treated with the therapeutic agent alone to achieve the same outcome. In some embodiments, administering to a subject a dietary regimen with a therapeutic agent decreases the required dose of the therapeutic agent by at least about 30% compared to a subject treated with the therapeutic agent alone to achieve the same outcome.

[0190] Administering to a subject a dietary regimen with a therapy or a therapeutic agent can decrease adverse events associated with the therapy or the therapeutic agent compared to a subject treated with the therapy or the therapeutic agent. In some embodiments, administering to a subject a dietary regimen with a therapy or the therapeutic agent decreases adverse events associated with the therapy or the therapeutic agent by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95% compared to a subject treated with therapy or the therapeutic agent alone. In some embodiments, administering to a subject a dietary regimen with a therapy or the therapeutic agent decreases adverse events associated with the therapy or the therapeutic agent by at least about 10% compared to a subject treated with the therapy or the therapeutic agent alone. In some embodiments, administering to a subject a dietary regimen with a therapy or a therapeutic agent decreases adverse events associated with the therapy or the therapeutic agent by at least about 20% compared to a subject treated with the therapy or the therapeutic agent alone. In some embodiments, administering to a subject a dietary regimen with a therapy or a therapeutic agent decreases adverse events associated with the therapy or the therapeutic agent by at least about 30% compared to a subject treated with the therapy or the therapeutic agent alone.

[0191] Multiple therapies and therapeutic agents can be administered in any order or concurrently. If not simultaneously, the first therapy or therapeutic agent can be administered, and following a period of time, the second therapy or therapeutic agent can be administered. In some embodiments, the period of time between administration of the first therapy or therapeutic and the second therapy or therapeutic is 1 day, 2 days, 3 days, 4 days, 5 days, 6, days, 1 week, 2

weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 18 months, 2 years, 3 years, 4 years, or 5 years. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic is 1 day. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic is 2 days. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 3 days. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 4 days. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 5 days. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 6 days. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 1 week. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 2 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 3 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 4 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 5 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 6 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 8 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 12 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 16 weeks. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 5 months. In some embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 6 months. In some

embodiments, the period of time between administration of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 12 months.

[0192] In some embodiments, the first therapy or therapeutic agent can be administered for the duration of a treatment cycle prior to administration of the second therapy or therapeutic agent. In some embodiments, the duration of the treatment cycle is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, 21 days, 22 days, 23 days, 24 days, 25 days, 26 days, 27 days, 28 days, 29 days, 30 days, 31 days, 32 days, 33 days, 34 days, 35 days, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 18 months, 2 years, 3 years, 4 years, or 5 years. In some embodiments, the duration of the treatment cycle is 1 day. In some embodiments, the duration of the treatment cycle is 2 days. In some embodiments, the duration of the treatment cycle is 3 days. In some embodiments, the duration of the treatment cycle is 4 days. In some embodiments, the duration of the treatment cycle is 5 days. In some embodiments, the duration of the treatment cycle is 6 days. In some embodiments, the duration of the treatment cycle is 7 days. In some embodiments, the duration of the treatment cycle is 14 days. In some embodiments, the duration of the treatment cycle is 21 days. In some embodiments, the duration of the treatment cycle is 28 days. In some embodiments, the duration of the treatment cycle is 34 days. In some embodiments, the duration of the treatment cycle is 6 weeks. In some embodiments, the duration of the treatment cycle is 8 weeks. In some embodiments, the duration of the treatment cycle is 12 weeks. In some embodiments, the duration of the treatment cycle is 16 weeks.

[0193] In some embodiments, the first therapy or therapeutic agent can be administered for the duration of a treatment cycle, and following a period of time, the second therapy or therapeutic agent administered. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 1 day, 2 days, 3 days, 4 days, 5 days, 6, days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 18 months, 2 years, 3 years, 4 years, or 5 years. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 1 day. In some embodiments, the period of time following the treatment cycle of the

first therapy or therapeutic agent and the second therapy or therapeutic agent is 2 days. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 3 days. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 4 days. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 5 days. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 6 days. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 1 week. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 2 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 3 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 4 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 5 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 6 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 8 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 12 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 16 weeks. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 5 months. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 6 months. In some embodiments, the period of time following the treatment cycle of the first therapy or therapeutic agent and the second therapy or therapeutic agent is 12 months.

[0194] In some embodiments, the first therapy is chemotherapy (*e.g.*, a chemotherapeutic agent) and the second therapy is radiotherapy (*e.g.*, a radiotherapeutic agent). In some

embodiments, the first therapy is radiotherapy and the second therapy is chemotherapy. In some embodiments, radiotherapy is administered for the duration of a treatment cycle and following a period of time, chemotherapy is administered. In some embodiments, the duration of a radiotherapy treatment cycle is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, 21 days, 22 days, 23 days, 24 days, 25 days, 26 days, 27 days, 28 days, 29 days, 30 days, 31 days, 32 days, 33 days, 34 days, 35 days, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, or 12 weeks. In some embodiments, the duration of a radiotherapy treatment cycle is 1 day. In some embodiments, the duration of a radiotherapy treatment cycle is 2 days. In some embodiments, the duration of a radiotherapy treatment cycle is 3 days. In some embodiments, the duration of a radiotherapy treatment cycle is 4 days. In some embodiments, the duration of a radiotherapy treatment cycle is 5 days. In some embodiments, the duration of a radiotherapy treatment cycle is 6 days. In some embodiments, the duration of a radiotherapy treatment cycle is 7 days. In some embodiments, the duration of a radiotherapy treatment cycle is 8 days. In some embodiments, the duration of a radiotherapy treatment cycle is 9 days. In some embodiments, the duration of a radiotherapy treatment cycle is 10 days. In some embodiments, the duration of a radiotherapy treatment cycle is 11 days. In some embodiments, the duration of a radiotherapy treatment cycle is 12 days. In some embodiments, the duration of a radiotherapy treatment cycle is 13 days. In some embodiments, the duration of a radiotherapy treatment cycle is 14 days. In some embodiments, the duration of a radiotherapy treatment cycle is 21 days. In some embodiments, the duration of a radiotherapy treatment cycle is 28 days. In some embodiments, the duration of a radiotherapy treatment cycle is 35 days. In some embodiments, radiotherapy is administered for the duration of a treatment cycle and following a period of time, chemotherapy is administered. In some embodiments, the period of time between radiotherapy and chemotherapy is 1 day, 2 days, 3 days, 4 days, 5 days, 6, days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 18 months, 2 years, 3 years, 4 years, or 5 years. In some embodiments, the period of time between radiotherapy and chemotherapy is 1 day. In some embodiments, the period of time between radiotherapy and chemotherapy is 2 days. In some embodiments, the period of time between radiotherapy and chemotherapy is 3 days. In some embodiments, the period of time between radiotherapy and chemotherapy is 4 days. In

some embodiments, the period of time between radiotherapy and chemotherapy is 5 days. In some embodiments, the period of time between radiotherapy and chemotherapy is 6 days. In some embodiments, the period of time between radiotherapy and chemotherapy is 1 week. In some embodiments, the period of time between radiotherapy and chemotherapy is 2 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 3 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 4 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 5 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 6 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 7 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 8 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 9 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 10 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 11 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 12 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 16 weeks. In some embodiments, the period of time between radiotherapy and chemotherapy is 5 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 6 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 7 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 8 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 9 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 10 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 11 months. In some embodiments, the period of time between radiotherapy and chemotherapy is 1 year. In some embodiments, radiotherapy can be administered for a treatment cycle of 1 week and chemotherapy administered 2 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 1 week and chemotherapy administered 3 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 1 week and chemotherapy administered 4 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 1 week and chemotherapy administered 6 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 1 week and chemotherapy administered 8 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 34 days and chemotherapy administered 2 weeks after. In

some embodiments, radiotherapy can be administered for a treatment cycle of 34 days and chemotherapy administered 3 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 34 days and chemotherapy administered 4 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 34 days and chemotherapy administered 6 weeks after. In some embodiments, radiotherapy can be administered for a treatment cycle of 34 days and chemotherapy administered 8 weeks after.

Radiation Therapy

[0195] Radiation therapy, or radiotherapy, is a therapy using ionizing radiation as a part of cancer treatment to control or kill malignant cells and is normally delivered by a linear accelerator. Ionizing radiation damages the DNA of cancerous tissue, resulting in cellular death. Radiation therapy can be curative in a number of types of cancer if localized to one area of the body. In some embodiments, the dietary regimen is administered in combination with radiotherapy. In some embodiments, radiotherapy comprises administration of a radiotherapeutic agent.

[0196] In some embodiments, radiotherapy is used in combination with a dietary regimen to reduce the likelihood of tumor recurrence after surgery to remove a primary malignant tumor. In some embodiments, the dietary regimen is administered in combination with radiotherapy to treat colorectal cancer (*e.g.*, LARC). In some embodiments, the dietary regiment is administered in combination with radiotherapy to reduce symptoms of a colorectal cancer (*e.g.*, LARC). In some embodiments, the dietary regimen is administered in combination with radiotherapy to slow the growth of a colorectal cancer (*e.g.*, LARC).

[0197] In some embodiments, the radiotherapy is external beam radiation therapy. External beam radiation therapy uses a machine that locally aims radiation at colorectal cancer (*e.g.*, LARC). In some embodiments, the radiotherapy is internal beam radiation therapy. In some embodiments, external beam radiation is used to shrink tumors to treat pain, trouble breathing, or loss of bowel or bladder control. In some embodiments, the external-beam radiation therapy is three-dimensional conformal radiation therapy (3D-CRT). In some embodiments, the external-beam radiation therapy is intensity modulated radiation therapy (IMRT). In some embodiments, the external-beam radiation therapy is proton beam therapy. In some embodiments, the external-beam radiation therapy is image-guided radiation therapy (IGRT). In some embodiments, the external-beam radiation therapy is stereotactic radiation therapy (SRT).

[0198] Internal radiation therapy is a treatment that places a source of radiation in the subject's body. In some embodiments, the source of radiation is a liquid. In some embodiments, the source of radiation is a solid. In some embodiments, the internal radiotherapy uses a permanent implant. In some embodiments, the internal radiotherapy is a temporary internal radiotherapy, for example, a needle, tube, or applicator. In some embodiments, the solid source of radiation is used in brachytherapy. In some embodiments, seeds, ribbons, or capsules containing a radiation source are placed in a subject's body. In some embodiments, the radiotherapy is brachytherapy, where a radioactive source is placed inside or next to an area requiring treatment. In some embodiments, the radiotherapy is total body irradiation (TBI) in preparation for a bone marrow transplant.

[0199] In some embodiments, the radiotherapy is intraoperative radiation therapy (IORT). In some embodiments, the radiotherapy is systemic radiation therapy. In some embodiments, the radiotherapy is radioimmunotherapy. In some embodiments, the radiotherapy uses a radiosensitizer or a radioprotector.

[0200] In some embodiments, shaped radiation beams are aimed from several angles of exposure to intersect at the tumor while sparing normal tissue. In some embodiments, a tumor absorbs a much larger dose of radiation than does a surrounding healthy tissue.

[0201] In some embodiments, a subject or tumor is treated with photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 1 megavoltage (MV), about 2 MV, about 3 MV, about 4 MV, about 5 MV, about 6 MV, about 7 MV, about 8 MV, about 9 MV, about 10 MV, about 11 MV, about 12 MV, about 13 MV, about 14 MV, about 15 MV, about 16 MV, about 17 MV, about 18 MV, about 19 MV, or about 20 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 4 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 5 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 6 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 8 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 10 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 12 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 14 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 16 MV

photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 18 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 20 MV photons from a linear accelerator.

[0202] In some embodiments, a subject or tumor is treated at an amount of about 1 MV to about 6 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 6 MV to about 12 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 6 MV to about 15 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 6 MV to about 18 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 6 MV to about 20 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 12 MV to about 15 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 12 MV to about 20 MV photons from a linear accelerator. In some embodiments, a subject or tumor is treated at an amount of about 15 MV to about 20 MV photons from a linear accelerator.

[0203] In some embodiments, a subject or tumor is treated with about 50 Centigray (cGy), about 100 cGy, about 150 cGy, about 200 cGy, about 250 cGy, about 300 cGy, about 350 cGy, about 400 cGy, about 450 cGy, about 500 cGy, about 550 cGy, about 600 cGy, about 650 cGy, about 700 cGy, about 750 cGy, about 800 cGy, about 850 cGy, about 900 cGy, about 950 cGy, or about 100 cGy. In some embodiments, a subject or tumor is treated with about 500 cGy, about 1000 cGy, about 1500 cGy, about 2000 cGy, about 2500 cGy, about 3000 cGy, about 3500 cGy, about 4000 cGy, about 4500 cGy, about 5000 cGy, about 5500 cGy, about 6000 cGy, about 6500 cGy, about 7000 cGy, about 7500 cGy, about 8000 cGy, about 8500 cGy, about 9000 cGy, about 9500 cGy, or about 10000 cGy of radiation therapy. In some embodiments, a subject or tumor is treated with about 500 cGy of radiation therapy. In some embodiments, a subject or tumor is treated with about 1000 cGy of radiation therapy. In some embodiments, a subject or tumor is treated with about 2000 cGy of radiation therapy. In some embodiments, a subject or tumor is treated with about 2500 cGy of radiation therapy. In some embodiments, a subject or tumor is treated with about 5000 cGy of radiation therapy.

[0204] In some embodiments, a subject or tumor is treated with from about 500 cGy to about 1000 cGy; about 1000 cGy to about 1500 cGy; about 1500 cGy to about 2000 cGy; about 2000 cGy to about 2500 cGy; about 2500 cGy to about 3000 cGy; about 3000 cGy to about 3500 cGy;

about 3500 cGy to about 4000 cGy; about 4000 cGy to about 4500 cGy; about 4500 cGy to about 5000 cGy; about 5000 cGy to about 5500 cGy; about 5500 cGy to about 6000 cGy; about 6000 cGy to about 6500 cGy; about 6500 cGy to about 7000 cGy; about 7000 cGy to about 7500 cGy; about 7500 cGy to about 8000 cGy; about 8500 cGy to about 9000 cGy; about 9000 cGy to about 9500 cGy; or about 9500 cGy to about 10000 cGy. In some embodiments, a subject or tumor is treated with from about 500 cGy to about 1000 cGy. In some embodiments, a subject or tumor is treated with from about 2000 cGy to about 4000 cGy. In some embodiments, a subject or tumor is treated with from about 4000 cGy to about 6000 cGy.

[0205] In some embodiments, one cycle of radiation therapy can comprise the subject or tumor being treated with radiation over a number of days. In some embodiments, the radiation is over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days. In some embodiments, one cycle of radiation therapy can comprise the subject or tumor being treated with radiation over 4 days. In some embodiments, one cycle of radiation therapy can comprise the subject or tumor being treated with radiation over 5 days.

[0206] In some embodiments, one cycle of radiation can comprise administering 1000 cGy over 5 days, for example, 200 cGy a day for 5 days. In some embodiments, one cycle of radiation can comprise administering 1500 cGy over 5 days, for example, 300 cGy a day for 5 days. In some embodiments, one cycle of radiation can comprise administering 2000 cGy over 5 days, for example, 400 cGy a day for 5 days. In some embodiments, one cycle of radiation can comprise administering 2500 cGy over 5 days, for example, 500 cGy a day for 5 days.

[0207] In some embodiments, one cycle of radiation therapy is repeated over a period of time. In some embodiments, a cycle of radiation therapy is repeated for 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, or 16 weeks.

[0208] In some embodiments, a subject or tumor is treated with short-course radiation therapy. In some embodiments, short-course radiation therapy comprises one cycle of administering 500 cGy a day for 5 days.

[0209] In some embodiments, a subject or tumor is treated with long-course radiation therapy. In some embodiments, long-course radiation therapy comprises five cycles of administering 200 cGy a day for 5 days a cycle.

[0210] In some embodiments, a dietary regimen is administered simultaneously with administration of a radiotherapy. In some embodiments, a dietary regimen is administered

simultaneously with a radiotherapy for 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, or 21 days. In some embodiments, a dietary regimen is administered simultaneously with administration of a radiotherapy for 5 days. In some embodiments, a dietary regimen is administered simultaneously with administration of a radiotherapy for 7 days.

[0211] In some embodiments, the dietary regimen is administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days before a subject is treated with radiotherapy. In some embodiments, the dietary regimen is administered 1 day before a subject is treated with radiotherapy. In some embodiments, the dietary regimen is administered 2 days before a subject is treated with radiotherapy. In some embodiments, the dietary regimen is administered 3 days before a subject is treated with radiotherapy. In some embodiments, the dietary regimen is administered 4 days before a subject is treated with radiotherapy.

[0212] In some embodiments, a subject is treated with a dietary regimen and radiotherapy, then goes off treatment before beginning a subsequent treatment cycle with the dietary regimen and radiotherapy. In some embodiments, the length of the treatment period and off-treatment period are identical. In some embodiments, the length of the treatment period and off-treatment period are different. In some embodiments, the length of the treatment period is longer than the off-treatment period. In some embodiments, the length of the treatment period is shorter than the off-treatment period.

[0213] In some embodiments, the length of a treatment period with a dietary regimen and radiotherapy is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days, and the length of off-treatment period is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days. In some embodiments, the length of the treatment period is 5 days, and the length of the off-treatment period is 2 days. In some embodiments, the length of the treatment period is 4 days, and the length of the off-treatment period is 3 days. In some embodiments, the length of the treatment period is 3 days, and the length of the off-treatment period is 4 days. In some embodiments, the length of the treatment period is 2 days, and the length of the off-treatment period is 5 days.

[0214] In some embodiments, a cycle of a treatment period and an off-treatment period is repeated for 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, or 16 weeks.

[0215] In some embodiments, a dietary product and radiotherapy are administered with a low-carbohydrate diet.

[0216] In some embodiments, the subject is be placed on a dietary regimen, which is given one day before starting radiotherapy and on each day that radiotherapy is given, wherein the radiotherapy is a short-course radiotherapy in which the subject is treated with 500 cGy a day for 5 days, wherein the subject returns to a habitual diet after the 5th day of radiotherapy treatment.

[0217] In some embodiments, the subject is placed on a dietary regimen, which is given one day before starting radiotherapy and on each day that radiotherapy is given, wherein the radiotherapy is a long-course radiotherapy in which the subject is treated with 200 cGy a day for 5 days. The subject returns to a habitual diet after the 5th day of radiotherapy treatment for two days before starting an additional round of radiotherapy. Subsequent radiation therapy cycles administer 5 days of an amino-acid depleted diet with 200 cGy of radiation for 5 days, followed by 2 days of a habitual diet. The cycle is repeated as needed (*e.g.*, for 5 cycles).

[0218] In some embodiments, a dietary product and radiotherapy are administered with a high-fat, low-carbohydrate, and low-protein diet. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 1600 to about 2400 kcals/day. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 1g/kg/day of protein. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 420 mg proline/day. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 410 mg/serine/day. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 230 glycine/day. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 9% carbohydrates, 2% protein, and 89% fat of diet-only calories. In some embodiments, the high-fat, low-carbohydrate, and low-protein diet comprises about 1) 1600 to about 2400 kcals/day; 2) about 1g/kg/day of protein; 3) about 420 mg proline/day; 4) about 410 mg/serine/day; 5) about 230 glycine/day; and 6) a diet that is about 9% carbohydrates, 2% protein, and 89% fat of diet-only calories.

[0219] In some embodiments, the diet is on an intermittent schedule alternating with a habitual diet during the period on which the patient is on radiotherapy. For example, in some embodiments, the subject consumes the diet for 6 days of a week and consumes a habitual diet

on the remaining 1 day of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 5 days of a week and consumes a habitual diet on the remaining 2 days of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 4 days of a week and consumes a habitual diet on the remaining 3 days of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 3 days of a week and consumes a habitual diet on the remaining 4 days of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes a habitual diet for at least 2 consecutive days per week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes a habitual diet for at least 3 consecutive days per week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes a habitual diet for at least 4 consecutive days per week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes a habitual diet for at least 5 consecutive days per week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes a habitual diet for at least 6 consecutive days per week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes a habitual diet for 7 consecutive days per week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 6 consecutive days of a week and consumes a habitual diet on the remaining 1 day of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 5 consecutive days of a week and consumes a habitual diet on the remaining 2 days of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 4 consecutive days of a week and consumes a habitual diet on the remaining 3 days of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 3 consecutive days of a week and consumes a habitual diet on the remaining 4 days of the week during the period on which the patient is on radiotherapy. In some embodiments, the subject consumes the diet for 2 consecutive days of a week and consumes a habitual diet on the remaining 5 days of the week during the period on which the patient is on radiotherapy.

Chemotherapy

[0220] In some embodiments, a dietary regimen is used in combination with a chemotherapeutic regimen comprising one or more chemotherapeutic agents. In some embodiments, the chemotherapeutic regimen is administered orally. In some embodiments, the chemotherapeutic agent is administered intravenously. In some embodiments, the chemotherapeutic regimen is administered peritoneally. In some embodiments, the chemotherapeutic regimen is administered via a combination of routes of administration. In some embodiments, the chemotherapeutic regimen is administered intravenously and orally. In some embodiments, the chemotherapeutic regimen is administered orally and peritoneally. In some embodiments, the chemotherapeutic regimen is administered intravenously and peritoneally.

[0221] The chemotherapeutic agent can include one or more of the following categories of anti-cancer agents:

(i) antiproliferative/antineoplastic drugs or combinations thereof, such as alkylating agents (*e.g.*, cisplatin, oxaliplatin, carboplatin, cyclophosphamide, nitrogen mustard, uracil mustard, bendamustine, melphalan, chlorambucil, chlormethine, busulphan, temozolamide, nitrosoureas, ifosamide, melphalan, pipobroman, triethylene-melamine, triethylenethiophoporamine, carmustine, lomustine, streptozotocin, and dacarbazine); antimetabolites (*e.g.*, gemcitabine, antifolates, such as fluoropyrimidines (5-fluorouracil or 5-FU and tegafur), raltitrexed, methotrexate, pemetrexed, cytosine arabinoside, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, pentostatin, and hydroxyurea); antibiotics (*e.g.*, anthracyclines such as adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin, and mithramycin); antimitotic agents (*e.g.*, vinca alkaloids such as vincristine, vinblastine, vindesine, and vinorelbine; taxanes/taxoids such as paclitaxel, nab-paclitaxel, docetaxel, and cabazitaxel; and polo kinase inhibitors); proteasome inhibitors, *e.g.*, carfilzomib and bortezomib; interferon therapy; and topoisomerase inhibitors (*e.g.*, epipodophyllotoxins such as etoposide and teniposide, amsacrine, topotecan, irinotecan, mitoxantrone, and camptothecin); bleomycin, dactinomycin, daunorubicin, doxorubicin, epirubicin, idarubicin, cytarabine (ara-C), paclitaxel (Taxol™), nab-paclitaxel, docetaxel, mithramycin, deoxycoformycin (pentostatin), mitomycin-C, L-asparaginase, interferons (*e.g.*, IFN-alpha), etoposide, teniposide, DNA-demethylating agents (*e.g.*, azacitidine or decitabine);

and histone de-acetylase (HDAC) inhibitors (*e.g.*, vorinostat, MS-275, panobinostat, romidepsin, valproic acid, mocetinostat (MGCD0103), and pracinostat (SB939);

(ii) cytostatic agents such as antiestrogens (*e.g.*, tamoxifen, fulvestrant, toremifene, raloxifene, droloxifene and iodoxyfene), antiandrogens (*e.g.*, bicalutamide, flutamide, nilutamide and cyproterone acetate), LHRH antagonists or LHRH agonists (*e.g.*, goserelin, leuprorelin, and buserelin), progestogens (*e.g.*, megestrol acetate), aromatase inhibitors (*e.g.*, as anastrozole, letrozole, vorazole and exemestane) and inhibitors of 5α-reductase such as finasteride; and navelbene, CPT-II, anastrazole, letrazole, capecitabine, reloxafme, cyclophosphamide, ifosamide, and droloxafine;

(iii) anti-invasion agents, *e.g.*, dasatinib and bosutinib (SKI-606), and metalloproteinase inhibitors, inhibitors of urokinase plasminogen activator receptor function or antibodies to heparanase;

(iv) inhibitors of growth factor function, *e.g.*, growth factor antibodies and growth factor receptor antibodies, *e.g.*, the anti-erbB2 antibody trastuzumab, the anti-EGFR antibody panitumumab, the anti-erbB1 antibody cetuximab, tyrosine kinase inhibitors, *e.g.*, inhibitors of the epidermal growth factor family (*e.g.*, EGFR family tyrosine kinase inhibitors such as gefitinib, erlotinib, canertinib (CI-1033), afatinib, vandetanib, osimertinib, rociletinib, and lapatinib), and antibodies to costimulatory molecules such as CTLA-4, 4-IBB and PD-I, or antibodies to cytokines (IL-10, TGF-beta); inhibitors of the hepatocyte growth factor family; inhibitors of the insulin growth factor family; modulators of protein regulators of cell apoptosis (*e.g.*, Bcl-2 inhibitors); inhibitors of the platelet-derived growth factor family such as imatinib and/or nilotinib (AMN107); inhibitors of serine/threonine kinases (*e.g.*, Ras/Raf signaling inhibitors such as farnesyl transferase inhibitors, sorafenib, tipifarnib, and lonafarnib), inhibitors of cell-signaling through MEK and/or AKT kinases, c-kit inhibitors, Abl kinase inhibitors, PI3K inhibitors, Plt3 kinase inhibitors, CSF-1R kinase inhibitors, IGF receptor, kinase inhibitors; aurora kinase inhibitors and cyclin dependent kinase inhibitors such as CDK2 and/or CDK4 inhibitors; CCR2, CCR4, or CCR6 antagonists; and RAF kinase inhibitors;

(v) antiangiogenic agents such as those that inhibit the effects of VEGF, *e.g.*, the anti-VEGF antibody bevacizumab; thalidomide; lenalidomide; and *e.g.*, a VEGF receptor tyrosine kinase inhibitor such as vandetanib, vatalanib, sunitinib, axitinib, and pazopanib;

(vi) gene therapy approaches, including, *e.g.*, approaches to replace aberrant genes such as aberrant p53 or aberrant BRCA1 or BRCA2;

(vii) immunotherapy approaches, including, *e.g.*, antibody therapy such as alemtuzumab, rituximab, ibritumomab tiuxetan, and ofatumumab; interferons such as interferon α; interleukins such as IL-2 (aldesleukin); interleukin inhibitors, *e.g.*, IRAK4 inhibitors; cancer vaccines including prophylactic and treatment vaccines such as HPV vaccines, *e.g.*, Gardasil®, Cervarix®, Oncophage®, and sipuleucel-T (Provenge®); gp100; dendritic cell-based vaccines (such as Ad.p53 DC); toll-like receptor modulators, *e.g.*, TLR-7 or TLR-9 agonists; PD-1, PD-L1, PD-L2, and CTL4-A modulators (*e.g.*, nivolumab), antibodies and vaccines; indoleamine 2,3-dioxygenase 1 (IDO1) inhibitors (such as indoximod); anti-PD-1 monoclonal antibodies (such as MK-3475 and nivolumab); anti-PDL1 monoclonal antibodies (such as MEDI-4736 and RG-7446); anti-PDL2 monoclonal antibodies; and anti-CTLA-4 antibodies (such as ipilumumab);

(viii) cytotoxic agents, including, *e.g.*, fludaribine (fludara), cladribine, and pentostatin;

(ix) targeted therapies, *e.g.*, PI3K inhibitors, *e.g.*, idelalisib and perifosine; SMAC (second mitochondria-derived activator of caspases) mimetics, also known as inhibitor of apoptosis proteins (IAP) antagonists. These agents act to suppress IAPs, *e.g.*, XIAP, cIAP1, and cIAP2, and thereby re-establish cellular apoptotic pathways. Particular SMAC mimetics include birinapant (TL32711), LCL161 (Novartis), AEG 40730, SM-164, LBW242, ML101, AT-406, GDC-0917, AEG 35156, and HGS1029; and agents which target ubiquitin proteasome system (UPS), *e.g.*, bortezomib, carfilzomib, marizomib (NPI-0052), and MLN9708; and

(x) chimeric antigen receptors, anticancer vaccines, and arginase inhibitors.

[0222] In some embodiments, the dose of the chemotherapy agent is from about 10 mg/m^2 to about 1,000 mg/m^2. In some embodiments, the dose of the chemotherapy agent is from about 10 mg/m^2 to about 50 mg/m^2, from about 10 mg/m^2 to about 100 mg/m^2, from about 10 mg/m^2 to about 200 mg/m^2, from about 10 mg/m^2 to about 300 mg/m^2, from about 10 mg/m^2 to about 400 mg/m^2, from about 10 mg/m^2 to about 500 mg/m^2, from about 10 mg/m^2 to about 600 mg/m^2, from about 10 mg/m^2 to about 700 mg/m^2, from about 10 mg/m^2 to about 800 mg/m^2, from about 10 mg/m^2 to about 900 mg/m^2, from about 10 mg/m^2 to about 1,000 mg/m^2, from about 50 mg/m^2 to about 100 mg/m^2, from about 50 mg/m^2 to about 200 mg/m^2, from about 50 mg/m^2 to about 300 mg/m^2, from about 50 mg/m^2 to about 400 mg/m^2, from about 50 mg/m^2 to about 500 mg/m^2, from about 50 mg/m^2 to about 600 mg/m^2, from about 50 mg/m^2 to about 700 mg/m^2, from about 50 mg/m^2 to about 800 mg/m^2, from about 50 mg/m^2 to about 900 mg/m^2, from about 50 mg/m^2 to about 1,000 mg/m^2, from about 100 mg/m^2 to about 200 mg/m^2, from about

100 mg/m^2 to about 300 mg/m^2, from about 100 mg/m^2 to about 400 mg/m^2, from about 100 mg/m^2 to about 500 mg/m^2, from about 100 mg/m^2 to about 600 mg/m^2, from about 100 mg/m^2 to about 700 mg/m^2, from about 100 mg/m^2 to about 800 mg/m^2, from about 100 mg/m^2 to about 900 mg/m^2, from about 100 mg/m^2 to about 1,000 mg/m^2, from about 200 mg/m^2 to about 300 mg/m^2, from about 200 mg/m^2 to about 400 mg/m^2, from about 200 mg/m^2 to about 500 mg/m^2, from about 200 mg/m^2 to about 600 mg/m^2, from about 200 mg/m^2 to about 700 mg/m^2, from about 200 mg/m^2 to about 800 mg/m^2, from about 200 mg/m^2 to about 900 mg/m^2, from about 200 mg/m^2 to about 1,000 mg/m^2, from about 300 mg/m^2 to about 400 mg/m^2, from about 300 mg/m^2 to about 500 mg/m^2, from about 300 mg/m^2 to about 600 mg/m^2, from about 300 mg/m^2 to about 700 mg/m^2, from about 300 mg/m^2 to about 800 mg/m^2, from about 300 mg/m^2 to about 900 mg/m^2, from about 300 mg/m^2 to about 1,000 mg/m^2, from about 400 mg/m^2 to about 500 mg/m^2, from about 400 mg/m^2 to about 600 mg/m^2, from about 400 mg/m^2 to about 700 mg/m^2, from about 400 mg/m^2 to about 800 mg/m^2, from about 400 mg/m^2 to about 900 mg/m^2, from about 400 mg/m^2 to about 1,000 mg/m^2, from about 500 mg/m^2 to about 600 mg/m^2, from about 500 mg/m^2 to about 700 mg/m^2, from about 500 mg/m^2 to about 800 mg/m^2, from about 500 mg/m^2 to about 900 mg/m^2, from about 500 mg/m^2 to about 1,000 mg/m^2, from about 600 mg/m^2 to about 700 mg/m^2, from about 600 mg/m^2 to about 800 mg/m^2, from about 600 mg/m^2 to about 900 mg/m^2, from about 600 mg/m^2 to about 1,000 mg/m^2, from about 700 mg/m^2 to about 800 mg/m^2, from about 700 mg/m^2 to about 900 mg/m^2, from about 700 mg/m^2 to about 1,000 mg/m^2, from about 800 mg/m^2 to about 900 mg/m^2, from about 800 mg/m^2 to about 1,000 mg/m^2, or about 900 mg/m^2 to about 1,000 mg/m^2. In some embodiments, the dose of the chemotherapy agent is about 10 mg/m^2, about 50 mg/m^2, about 100 mg/m^2, about 200 mg/m^2, about 300 mg/m^2, about 400 mg/m^2, about 500 mg/m^2, about 600 mg/m^2, about 700 mg/m^2, about 800 mg/m^2, about 900 mg/m^2, or about 1,000 mg/m^2. In some embodiments, the dose of the chemotherapy agent is at least about 10 mg/m^2, at least about 50 mg/m^2, at least about 100 mg/m^2, at least about 200 mg/m^2, at least about 300 mg/m^2, at least about 400 mg/m^2, at least about 500 mg/m^2, at least about 600 mg/m^2, at least about 700 mg/m^2, at least about 800 mg/m^2, or at least about 900 mg/m^2. In some embodiments, the dose of the chemotherapy agent is at most about 50 mg/m^2, at most about 100 mg/m^2, at most about 200 mg/m^2, at most about 300 mg/m^2, at most about 400 mg/m^2, at most about 500 mg/m^2, at most about 600 mg/m^2, at most about 700 mg/m^2, at most about 800 mg/m^2, at most about 900 mg/m^2, or at most about 1,000 mg/m^2.

[0223] In some embodiments, the dose of the chemotherapy agent is about 0.1 mg/kg to about 15 mg/kg. In some embodiments, the dose of the chemotherapy agent is about 0.1 mg/kg to about 0.25 mg/kg, about 0.1 mg/kg to about 0.5 mg/kg, about 0.1 mg/kg to about 0.75 mg/kg, about 0.1 mg/kg to about 1 mg/kg, about 0.1 mg/kg to about 3 mg/kg, about 0.1 mg/kg to about 5 mg/kg, about 0.1 mg/kg to about 7 mg/kg, about 0.1 mg/kg to about 9 mg/kg, about 0.1 mg/kg to about 11 mg/kg, about 0.1 mg/kg to about 13 mg/kg, about 0.1 mg/kg to about 15 mg/kg, about 0.25 mg/kg to about 0.5 mg/kg, about 0.25 mg/kg to about 0.75 mg/kg, about 0.25 mg/kg to about 1 mg/kg, about 0.25 mg/kg to about 3 mg/kg, about 0.25 mg/kg to about 5 mg/kg, about 0.25 mg/kg to about 7 mg/kg, about 0.25 mg/kg to about 9 mg/kg, about 0.25 mg/kg to about 11 mg/kg, about 0.25 mg/kg to about 13 mg/kg, about 0.25 mg/kg to about 15 mg/kg, about 0.5 mg/kg to about 0.75 mg/kg, about 0.5 mg/kg to about 1 mg/kg, about 0.5 mg/kg to about 3 mg/kg, about 0.5 mg/kg to about 5 mg/kg, about 0.5 mg/kg to about 7 mg/kg, about 0.5 mg/kg to about 9 mg/kg, about 0.5 mg/kg to about 11 mg/kg, about 0.5 mg/kg to about 13 mg/kg, about 0.5 mg/kg to about 15 mg/kg, about 0.75 mg/kg to about 1 mg/kg, about 0.75 mg/kg to about 3 mg/kg, about 0.75 mg/kg to about 5 mg/kg, about 0.75 mg/kg to about 7 mg/kg, about 0.75 mg/kg to about 9 mg/kg, about 0.75 mg/kg to about 11 mg/kg, about 0.75 mg/kg to about 13 mg/kg, about 0.75 mg/kg to about 15 mg/kg, about 1 mg/kg to about 3 mg/kg, about 1 mg/kg to about 5 mg/kg, about 1 mg/kg to about 7 mg/kg, about 1 mg/kg to about 9 mg/kg, about 1 mg/kg to about 11 mg/kg, about 1 mg/kg to about 13 mg/kg, about 1 mg/kg to about 15 mg/kg, about 3 mg/kg to about 5 mg/kg, about 3 mg/kg to about 7 mg/kg, about 3 mg/kg to about 9 mg/kg, about 3 mg/kg to about 11 mg/kg, about 3 mg/kg to about 13 mg/kg, about 3 mg/kg to about 15 mg/kg, about 5 mg/kg to about 7 mg/kg, about 5 mg/kg to about 9 mg/kg, about 5 mg/kg to about 11 mg/kg, about 5 mg/kg to about 13 mg/kg, about 5 mg/kg to about 15 mg/kg, about 7 mg/kg to about 9 mg/kg, about 7 mg/kg to about 11 mg/kg, about 7 mg/kg to about 13 mg/kg, about 7 mg/kg to about 15 mg/kg, about 9 mg/kg to about 11 mg/kg, about 9 mg/kg to about 13 mg/kg, about 9 mg/kg to about 15 mg/kg, about 11 mg/kg to about 13 mg/kg, about 11 mg/kg to about 15 mg/kg, or about 13 mg/kg to about 15 mg/kg. In some embodiments, the dose of the chemotherapy agent is about 0.1 mg/kg, about 0.25 mg/kg, about 0.5 mg/kg, about 0.75 mg/kg, about 1 mg/kg, about 3 mg/kg, about 5 mg/kg, about 7 mg/kg, about 9 mg/kg, about 11 mg/kg, about 13 mg/kg, or about 15 mg/kg. In some embodiments, the dose of the chemotherapy agent is at least about 0.1 mg/kg, at least about 0.25 mg/kg, at least about 0.5 mg/kg, at least about 0.75 mg/kg, at least about 1 mg/kg, at least about 3 mg/kg, at least about 5 mg/kg, at least about

7 mg/kg, at least about 9 mg/kg, at least about 11 mg/kg, or at least about 13 mg/kg. In some embodiments, the dose of the chemotherapy agent is at most about 0.25 mg/kg, at most about 0.5 mg/kg, at most about 0.75 mg/kg, at most about 1 mg/kg, at most about 3 mg/kg, at most about 5 mg/kg, at most about 7 mg/kg, at most about 9 mg/kg, at most about 11 mg/kg, at most about 13 mg/kg, or at most about 15 mg/kg.

[0224] The therapeutic agents used in the methods of the disclosure can be a single agent or a combination of agents in a regimen. In some embodiments, such combinations include agents that have different mechanisms of action. Such combinations can be administered simultaneously, separately, or sequentially. In some embodiments, a combination chemotherapy regimen provided herein is to be simultaneously administered. In some embodiments, a combination chemotherapy regimen provided herein is to be separately administered. In some embodiments, a combination therapy regimen provided herein is to be sequentially administered.

[0225] In some embodiments, the chemotherapy agent is capecitabine, or a pharmaceutically acceptable salt thereof. In some embodiments, the dose of capecitabine is from about 500 mg/m^2 to about 1500 mg/m^2, from about 1000 mg/m^2 to about 1500 mg/m^2, from about 1000 mg/m^2 to about 1300 mg/m^2, or about 800 mg/m^2 to about 1200 mg/m^2. In some embodiments, a dietary regimen is administered with a therapeutically effective amount of capecitabine, or a pharmaceutically acceptable salt thereof. In some embodiments, the dose of capecitabine is from about 500 mg/m^2 to about 600 mg/m^2, from about 600 mg/m^2 to about 700 mg/m^2, from about 700 mg/m^2 to about 800 mg/mg^2, from about 800 mg/m^2 to about 900 mg/m^2, from about 900 mg/m^2 to about 1000 mg/m^2, from about 1000 mg/m^2 to about 1100 mg/m^2, from about 1100 mg/m^2 to about 1200 mg/m^2, from about 1200 mg/m^2 to about 1300 mg/m^2, from about 1300 mg/m^2 to about 1400 mg/m^2, from about 1400 mg/m^2 to about 1500 mg/m^2, from about 1500 mg/m^2 to about 1600 mg/m^2, from about 1600 mg/m^2 to about 1700 mg/m^2, from about 1800 mg/m^2 to about 1900 mg/m^2, from about 1900 mg/m^2 to about 2000 mg/m^2, from about 2000 mg/m^2 to about 2100 mg/m^2, from about 2100 mg/m^2 to about 2200 mg/m^2, from about 2200 mg/m^2 to about 2300 mg/m^2, from about 2300 mg/m^2 to about 2400 mg/m^2, or from about 2400 mg/m^2 to about 2500 mg/m^2. In some embodiments, the dose of capecitabine is from about 500 mg/m^2 to about 600 mg/m^2. In some embodiments, the dose of capecitabine is from about 600 mg/m^2 to about 700 mg/m^2. In some embodiments, the dose of capecitabine is from about 800 mg/m^2 to about 900 mg/m^2. In some embodiments, the dose of capecitabine is from about 900 mg/m^2 to about 1000 mg/m^2. In some embodiments, the dose of capecitabine is from about 1000

mg/m^2 to about 1100 mg/m^2. In some embodiments, the dose of capecitabine is from about 1200 mg/m^2 to about 1300 mg/m^2. In some embodiments, the dose of capecitabine is from about 1600 mg/m^2 to about 1700 mg/m^2. In some embodiments, the dose of capecitabine is from about 2500 mg/m^2 to about 2600 mg/m^2. In some embodiments, the dose of capecitabine is about 2500 mg/m^2 capecitabine.

[0226] In some embodiments, a dietary regimen is administered with about 1250 mg/m^2 capecitabine administered orally twice daily on days 1-14 repeated on a 21-day cycle. In some embodiments, a dietary regimen is administered with 2500 mg/m^2 capecitabine. In some embodiments, a dietary regimen is administered with 1250 mg/m^2 capecitabine administered orally twice daily on days 1-14 repeated on a 21-day cycle. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 1 cycle. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 2 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 3 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 4 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 5 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 6 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 7 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 8 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 9 cycles. In some embodiments, a dietary regimen is administered with capecitabine on a repeating 21-day cycle for 10 cycles. In some embodiments, a dietary regimen is administered with a dose of capecitabine typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered with capecitabine repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.)

[0227] In some embodiments, the dose of capecitabine is at least about 500 mg/m^2, at least about 510 mg/m^2, at least about 520 mg/m^2, at least about 530 mg/m^2, at least about 540 mg/m^2, at least about 550 mg/m^2, at least about 560 mg/m^2, at least about 570 mg/m^2, at least about 580

mg/m^2, at least about 590 mg/m^2, at least about 600 mg/m^2, at least about 610 mg/m^2, at least about 620 mg/m^2, at least about 630 mg/m^2, at least about 640 mg/m^2, at least about 650 mg/m^2, at least about 660 mg/m^2, at least about 670 mg/m^2, at least about 680 mg/m^2, at least about 690 mg/m^2, at least about 700 mg/m^2, at least about 710 mg/m^2, at least about 720 mg/m^2, at least about 730 mg/m^2, at least about 740 mg/m^2, at least about 750 mg/m^2, at least about 760 mg/m^2, at least about 770 mg/m^2, at least about 780 mg/m^2, at least about 790 mg/m^2, at least about 800 mg/m^2, at least about 810 mg/m^2, at least about 820 mg/m^2, at least about 830 mg/m^2, at least about 840 mg/m^2, at least about 850 mg/m^2, at least about 860 mg/m^2, at least about 870 mg/m^2, at least about 880 mg/m^2, at least about 890 mg/m^2, at least about 900 mg/m^2, at least about 910 mg/m^2, at least about 920 mg/m^2, at least about 930 mg/m^2, at least about 940 mg/m^2, at least about 950 mg/m^2, at least about 960 mg/m^2, at least about 970 mg/m^2, at least about 980 mg/m^2, at least about 990 mg/m^2, at least about 1000 mg/m^2, at least about 1010 mg/m^2, at least about 1020 mg/m^2, at least about 1030 mg/m^2, at least about 1040 mg/m^2, at least about 1050 mg/m^2, at least about 1060 mg/m^2, at least about 1070 mg/m^2, at least about 1080 mg/m^2, at least about 1090 mg/m^2, at least about 1100 mg/m^2, at least about 1110 mg/m^2, at least about 1120 mg/m^2, at least about 1130 mg/m^2, at least about 1140 mg/m^2, at least about 1150 mg/m^2, at least about 1160 mg/m^2, at least about 1170 mg/m^2, at least about 1180 mg/m^2, at least about 1190 mg/m^2, at least about 1200 mg/m^2, at least about 1210 mg/m^2, at least about 1220 mg/m^2, at least about 1230 mg/m^2, at least about 1240 mg/m^2, at least about 1250 mg/m^2, at least about 1260 mg/m^2, at least about 1270 mg/m^2, at least about 1280 mg/m^2, at least about 1290 mg/m^2, at least about 1300 mg/m^2, at least about 1350 mg/m^2, at least about 1400 mg/m^2, at least about 1450 mg/m^2, or at least about 1500 mg/m^2.

[0228] In some embodiments, the dose of capecitabine is about 500 mg/m^2, about 510 mg/m^2, about 520 mg/m^2, about 530 mg/m^2, about 540 mg/m^2, about 550 mg/m^2, about 560 mg/m^2, about 570 mg/m^2, about 580 mg/m^2, about 590 mg/m^2, about 600 mg/m^2, about 610 mg/m^2, about 620 mg/m^2, about 630 mg/m^2, about 640 mg/m^2, about 650 mg/m^2, about 660 mg/m^2, about 670 mg/m^2, about 680 mg/m^2, about 690 mg/m^2, about 700 mg/m^2, about 710 mg/m^2, about 720 mg/m^2, about 730 mg/m^2, about 740 mg/m^2, about 750 mg/m^2, about 760 mg/m^2, about 770 mg/m^2, about 780 mg/m^2, about 790 mg/m^2, about 800 mg/m^2, about 810 mg/m^2, about 820 mg/m^2, about 830 mg/m^2, about 840 mg/m^2, about 850 mg/m^2, about 860 mg/m^2, about 870 mg/m^2, about 880 mg/m^2, about 890 mg/m^2, about 900 mg/m^2, about 910 mg/m^2, about 920 mg/m^2, about 930 mg/m^2, about 940 mg/m^2, about 950 mg/m^2, about 960 mg/m^2,

about 970 mg/m^2, about 980 mg/m^2, about 990 mg/m^2, about 1000 mg/m^2, about 1010 mg/m^2, about 1020 mg/m^2, about 1030 mg/m^2, about 1040 mg/m^2, about 1050 mg/m^2, about 1060 mg/m^2, about 1070 mg/m^2, about 1080 mg/m^2, about 1090 mg/m^2, about 1100 mg/m^2, about 1110 mg/m^2, about 1120 mg/m^2, about 1130 mg/m^2, about 1140 mg/m^2, about 1150 mg/m^2, about 1160 mg/m^2, about 1170 mg/m^2, about 1180 mg/m^2, about 1190 mg/m^2, about 1200 mg/m^2, about 1210 mg/m^2, about 1220 mg/m^2, about 1230 mg/m^2, about 1240 mg/m^2, about 1250 mg/m^2, about 1260 mg/m^2, about 1270 mg/m^2, about 1280 mg/m^2, about 1290 mg/m^2, about 1300 mg/m^2, about 1350 mg/m^2, about 1400 mg/m^2, about 1450 mg/m^2, or about 1500 mg/m^2. In some embodiments, the dose of capecitabine is about 1000 mg/m^2. In some embodiments, the dose of capecitabine is about 1250 mg/m^2.

[0229] In some embodiments, capecitabine is administered orally for 2 weeks followed by a one week rest period in 3-week cycles. In some embodiments, capecitabine may be administered with water within about 30 minutes after a meal. In some embodiments, the dose of capecitabine may be reduced in subjects with renal impairment. In some embodiments, the dose of capecitabine may be reduced by 25% in subjects with renal impairment.

[0230] In some embodiments, the chemotherapy agent is oxaliplatin, or a pharmaceutically acceptable salt thereof. In some embodiments, the dose of oxaliplatin is from about 50 mg/m^2 to about 100 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 150 mg/m^2, at least about 145 mg/m^2, at least about 140 mg/m^2, at least about 135 mg/m^2, at least about 130 mg/m^2, at least about 125 mg/m^2, at least about 120 mg/m^2, at least about 115 mg/m^2, at least about 110 mg/m^2, at least about 105 mg/m^2, at least about 100 mg/m^2, at least about 95 mg/m^2, at least about 90 mg/m^2, at least about 85 mg/m^2, at least about 80 mg/m^2, at least about 75 mg/m^2, at least about 70 mg/m^2, at least about 65 mg/m^2, at least about 60 mg/m^2, at least about 55 mg/m^2, at least about 50 mg/m^2, at least about 45 mg/m^2, at least about 40 mg/m^2, at least about 35 mg/m^2, at least about 30 mg/m^2, at least about 25 mg/m^2, at least about 20 mg/m^2, at 15 least mg/m^2, at least about 10 mg/m^2, or at least about 5 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 50 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 65 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 80 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 85 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 100 mg/m^2. In some embodiments, the dose of oxaliplatin is at least about 130 mg/m^2. In some embodiments, the dose of capecitabine is about 150 mg/m^2, about 145 mg/m^2, about 140 mg/m^2, about 135 mg/m^2, about 130 mg/m^2, about 125 mg/m^2,

about 120 mg/m^2, about 115 mg/m^2, about 110 mg/m^2, about 105 mg/m^2, about 100 mg/m^2, about 95 mg/m^2, about 90 mg/m^2, about 85 mg/m^2, about 80 mg/m^2, about 75 mg/m^2, about 70 mg/m^2, about 65 mg/m^2, about 60 mg/m^2, about 55 mg/m^2, about 50 mg/m^2, about 45 mg/m^2, about 40 mg/m^2, about 35 mg/m^2, about 30 mg/m^2, about 25 mg/m^2, about 20 mg/m^2, about 15 mg/m^2, about 10 mg/m^2, or about 5 mg/m^2. In some embodiments, the dose of oxaliplatin is about 50 mg/m^2. In some embodiments, the dose of oxaliplatin is about 65 mg/m^2. In some embodiments, the dose of oxaliplatin is about 80 mg/m^2. In some embodiments, the dose of oxaliplatin is about 85 mg/m^2. In some embodiments, the dose of oxaliplatin is about 100 mg/m^2. In some embodiments, the dose of oxaliplatin is about 130 mg/m^2. In some embodiments, the dose of oxaliplatin is from about 0 mg/m^2 to about 10 mg/m^2, from about 10 mg/m^2 to about 20 mg/m^2, from about 20 mg/m^2 to about 30 mg/m^2, from about 30 mg/m^2 to about 40 mg/m^2, from about 40 mg/m^2 to about 50 mg/m^2, from about 50 mg/m^2 to about 60 mg/m^2, from about 60 mg/m^2 to about 70 mg/m^2, from about 70 mg/m^2 to about 80 mg/m^2, from about 80 mg/m^2 to about 90 mg/m^2, from about 90 mg/m^2 to about 100 mg/m^2, from about 100 mg/m^2 to about 110 mg/m^2, from about 110 mg/m^2 to about 120 mg/m^2, from about 120 mg/m^2 to about 130 mg/m^2, from about 130 mg/m^2 to about 140 mg/m^2, or from about 140 mg/m^2 to about 150 mg/m^2. In some embodiments, a dietary regimen is administered with oxaliplatin at a dose from about 50 mg/m^2 to about 60 mg/m^2. In some embodiments, a dietary regimen is administered with oxaliplatin at a dose from about 60 mg/m^2 to about 70 mg/m^2. In some embodiments, a dietary regimen is administered with oxaliplatin at a dose from about 80 mg/m^2 to about 90 mg/m^2. In some embodiments, a dietary regimen is administered with oxaliplatin at a dose from about 100 mg/m^2 to about 110 mg/m^2. In some embodiments, a dietary regimen is administered with oxaliplatin at a dose from about 130 mg/m^2 to about 140 mg/m^2.

[0231] In some embodiments, a dietary regimen is administered with CapeOX, which comprises capecitabine or a pharmaceutically acceptable salt thereof, and oxaliplatin or a pharmaceutically acceptable salt thereof.

[0232] In some embodiments, a dietary regimen is administered with a therapeutically effective amount of capecitabine, or a pharmaceutically acceptable salt thereof, and a therapeutically effective amount of docetaxel, or a pharmaceutically acceptable salt thereof. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel: comprising about 2500 mg/m^2 capecitabine and about 75 mg/m^2 docetaxel. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel comprising

about 75 mg/m^2 docetaxel administered as an intravenous infusion over one hour on day 1, and about 1250 mg/m^2 capecitabine administered orally twice daily on days 1-14 repeated on a 21-day cycle. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel comprising: 2500 mg/m^2 capecitabine and 75 mg/m^2 docetaxel. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel comprising: 75 mg/m^2 docetaxel administered as an intravenous infusion over one hour on day 1, and about 1250 mg/m^2 capecitabine administered orally twice daily on days 1-14 repeated on a 21-day cycle. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 1 cycle. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 2 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 3 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 4 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 5 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 6 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 7 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 8 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 9 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel on a repeating 21-day cycle for 10 cycles. In some embodiments, a dietary regimen is administered with capecitabine and docetaxel comprising a dose of capecitabine and a dose of docetaxel typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered with capecitabine and docetaxel repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.)

[0233] In some embodiments, a dietary regimen is administered with a therapeutically effective amount of CapeOX, which comprises capecitabine or a pharmaceutically acceptable salt thereof, and oxaliplatin or a pharmaceutically acceptable salt thereof. In some embodiments,

a dietary regimen is administered with CapeOX comprising about 130 mg/m^2 oxaliplatin and about 1000 mg/m^2 capecitabine. In some embodiments, a dietary regimen is administered with CapeOX comprising about 130 mg/m^2 oxaliplatin administered as a continuous intravenous infusion over two hours on day 1, and about 1000 mg/m^2 capecitabine administered orally on days 1-14 repeated on a 21-day cycle. In some embodiments, a dietary regimen is administered with CapeOX comprising 130 mg/m^2 oxaliplatin and 1000 mg/m^2 capecitabine. In some embodiments, a dietary regimen is administered with CapeOX comprising 130 mg/m^2 oxaliplatin administered as a continuous intravenous infusion over two hours on Day 1 and 1000 mg/m^2 capecitabine administered orally on days 1-14 repeated on a 21-day cycle. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 1 cycle. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 2 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 3 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 4 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 5 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 6 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 7 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 8 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 9 cycles. In some embodiments, a dietary regimen is administered with CapeOX on a repeating 21-day cycle for 10 cycles. In some embodiments, a dietary regimen is administered with CapeOX comprising dosages of capecitabine and oxaliplatin typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered with CapeOX repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.)

[0234] In some embodiments, the chemotherapy agent is 5-fluorouracil, or a pharmaceutically acceptable salt thereof. In some embodiments, the dose of 5-fluorouracil is at least about 100 mg/m^2, at least about 150 mg/m^2, at least about 200 mg/m^2, at least about 250 mg/m^2, at least about 300 mg/m^2, at least about 350 mg/m^2, at least about 400 mg/m^2, at least about 450 mg/m^2,

at least about 500 mg/m^2, at least about 550 mg/m^2, at least about 600 mg/m^2, at least about 650 mg/m^2, at least about 700 mg/m^2, at least about 750 mg/m^2, at least about 800 mg/m^2, at least about 900 mg/m^2, at least about 1000 mg/m^2, at least about 1100 mg/m^2, at least about 1200 mg/m^2, at least about 1300 mg/m^2, at least about 1400 mg/m^2, at least about 1500 mg/m^2, at least about 1600 mg/m^2, at least about 1700 mg/m^2, at least about 1800 mg/m^2, at least about 1900 mg/m^2, at least about 2000 mg/m^2, at least about 2100 mg/m^2, at least about 2200 mg/m^2, at least about 2300 mg/m^2, at least about 2400 mg/m^2, at least about 2500 mg/m^2, at least about 2600 mg/m^2, at least about 2700 mg/m^2, at least about 2800 mg/m^2, at least about 2900 mg/m^2, or at least about 3000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 250 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 300 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 700 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 800 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 900 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 1000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 1200 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 1600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2700 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2800 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 2900 mg/m^2. In some embodiments, the dose of 5-fluorouracil is at least about 3000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 100 mg/m^2, about 150 mg/m^2, about 200 mg/m^2, about 250 mg/m^2, about 300 mg/m^2, about 350 mg/m^2, about 400 mg/m^2, about 450 mg/m^2, about 500 mg/m^2, about 550 mg/m^2, about 600 mg/m^2, about 650 mg/m^2, about 700 mg/m^2, about 750 mg/m^2, about 800 mg/m^2, about 900 mg/m^2, about 1000 mg/m^2, about 1100 mg/m^2, about 1200 mg/m^2, about 1300 mg/m^2, about 1400 mg/m^2, about 1500 mg/m^2, about 1600 mg/m^2, about 1700 mg/m^2, about 1800 mg/m^2, about 1900 mg/m^2, about 2000 mg/m^2, about 2100 mg/m^2, about 2200 mg/m^2, about 2300 mg/m^2, about 2400 mg/m^2, about 2500 mg/m^2, about 2600 mg/m^2, about 2700 mg/m^2, about 2800 mg/m^2, about 2900

mg/m^2, or about 3000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 250 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 300 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is 700 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 800 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 900 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 1000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 1200 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 1600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2700 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2800 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 2900 mg/m^2. In some embodiments, the dose of 5-fluorouracil is about 3000 mg/m^2.

[0235] In some embodiments, a dietary regimen is administered with a therapeutically effective amount of 5-fluorouracil, or a pharmaceutically acceptable salt thereof. In some embodiments, the dose of 5-fluorouracil is from about 200 mg/m^2 to about 300 mg/m^2, from about 300 mg/m^2 to about 400 mg/m^2, from about 400 mg/m^2 to about 500 mg/m^2, from about 500 mg/m^2 to about 600 mg/m^2, from about 600 mg/m^2 to about 700 mg/m^2, from about 800 mg/m^2 to about 900 mg/m^2, from about 900 mg/m^2 to about 1000 mg/m^2, from about 200 mg/m^2 to about 1000 mg/m^2, from about 1100 mg/m^2 to about 1200 mg/m^2, from about 1200 mg/m^2 to about 1300 mg/m^2, from about 1300 mg/m^2 to about 1400 mg/m^2, from about 1400 mg/m^2 to about 1500 mg/m^2, from about 1500 mg/m^2 to about 1600 mg/m^2, from about 1600 mg/m^2 to about 1700 mg/m^2, from about 1700 mg/m^2 to about 1800 mg/m^2, from about 1800 mg/m^2 to about 1900 mg/m^2, from about 1900 mg/m^2 to about 2000 mg/m^2, from about 2100 mg/m^2 to about 2200 mg/m^2, from about 2300 mg/m^2 to about 2400 mg/m^2, from about 2500 mg/m^2 to about 2600 mg/m^2, from about 2700 mg/m^2 to about 2800 mg/m^2, from about 2800 mg/m^2 to about 2900 mg/m^2, from about 2900 mg/m^2 to about 3000 mg/m^2, from about 2400 mg/m^2 to about 3,000 mg/m^2, from about 3000 mg/m^2 to about 3100 mg/m^2, from about 3100 mg/m^2 to about 3200 mg/m^2 from about 3200 mg/m^2 to about 3300 mg/m^2, from about 3300 mg/m^2 to about 3400 mg/m^2, or from about 2800 mg/m^2 to about 3400 mg/m^2. In some embodiments, the

dose of 5-fluorouracil is from about 200 mg/m^2 to about 1000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 200 mg/m^2 to about 300 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 300 mg/m^2 to about 400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 400 mg/m^2 to about 500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 500 mg/m^2 to about 600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 600 mg/m^2 to about 700 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 700 mg/m^2 to about 800 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 900 mg/m^2 to about 1000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 1000 mg/m^2 to about 1100 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 1100 mg/m^2 to about 1200 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 1200 mg/m^2 to about 1300 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 1300 mg/m^2 to about 1400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 1400 mg/m^2 to about 1500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 1500 mg/m^2 to about 1600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2000 mg/m^2 to about 2100 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2100 mg/m^2 to about 2200 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2200 mg/m^2 to about 2300 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2300 mg/m^2 to about 2400 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2400 mg/m^2 to about 2500 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2500 mg/m^2 to about 2600 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2600 mg/m^2 to about 2700 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2700 mg/m^2 to about 2800 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2800 mg/m^2 to about 2900 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2900 mg/m^2 to about 3000 mg/m^2. In some embodiments, the dose of 5-fluorouracil is from about 2400 mg/m^2 to about 3000 mg/m^2.

[0236] In some embodiments, a dietary regimen is administered with about 2800 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by about 2400 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with about 2900 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-

fluouracil administered as an intravenous bolus on day 1 followed by about 2500 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with about 3000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by about 2600 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with about 3100 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by about 2700 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with about 3200 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by about 2800 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with about 3300 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by about 2900 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with about 3400 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by about 3000 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 2800 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by 2400 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 2900 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by 2500 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 3000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on

day 1 followed by 2600 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 3100 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by 2700 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 3200 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by 2800 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 3300 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by 2900 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 3400 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 400 mg/m^2 5-fluouracil administered as an intravenous bolus on day 1 followed by 3000 mg/m^2 5-fluorouracil administered as a continuous intravenous infusion over 46 hours repeated every 2 weeks. In some embodiments, a dietary regimen is administered with 5-fluorouracil on a repeating 2-week cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with about 3000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with about 500 mg/m^2 5-fluorouracil administered as an intravenous bolus on days 1, 8, 15, 22, 29, and 36 in an 8-week cycle. In some embodiments, a dietary regimen is administered with 3000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with 500 mg/m^2 5-fluorouracil administered as an intravenous bolus on days 1, 8, 15, 22, 29, and 36 in an 8-week cycle. In some embodiments, a dietary regimen is administered with 5-fluorouracil on a repeating 8-week cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with a dose of 5-fluorouracil typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered

with 5-fluorouracil repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.).

[0237] In some embodiments, a dietary regimen is administered with 5-fluoruracil or a pharmaceutically acceptable salt thereof, and cyclophosphamide or a pharmaceutically acceptable salt thereof. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: about 1000 mg/m^2 5-fluorouracil and a therapeutically effective amount of cyclophosphamide. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: about 500 mg/m^2 5-fluorouracil administered intravenously with a therapeutically effective amount of cyclophosphamide on days 1 and 8 repeated on a 28-day cycle. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: 1000 mg/m^2 5-fluorouracil and a therapeutically effective amount of cyclophosphamide. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: 500 mg/m^2 5-fluorouracil administered intravenously with a therapeutically effective amount of cyclophosphamide on days 1 and 8 repeated on a 28-day cycle. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: about 1200 mg/m^2 5-fluorouracil and a therapeutically effective amount of cyclophosphamide. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: about 600 mg/m^2 5-fluorouracil administered intravenously with a therapeutically effective amount of cyclophosphamide on days 1 and 8 repeated on a 28-day cycle. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: 1200 mg/m^2 5-fluorouracil and a therapeutically effective amount of cyclophosphamide. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: 600 mg/m^2 5-fluorouracil administered intravenously with a therapeutically effective amount of cyclophosphamide on days 1 and 8 repeated on a 28-day cycle. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide on a repeating 28-day cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: 500 mg/m^2 5-fluorouracil administered intravenously with a therapeutically effective amount of cyclophosphamide on days 1 and 8 repeated on a 28-day cycle for 6 cycles. In some

embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising: 600 mg/m^2 5-fluorouracil administered intravenously with a therapeutically effective amount of cyclophosphamide on days 1 and 8 repeated on a 28-day cycle for 6 cycles. In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide comprising dosages of 5-fluorouracil and cyclophosphamide typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered with 5-fluorouracil and cyclophosphamide repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.)

[0238] In some embodiments, a dietary regimen is administered with therapeutically effective amounts of 5-fluorouracil, or a pharmaceutically acceptable salt thereof, and therapeutically effective amounts of platinum-based chemotherapeutic agents, or pharmaceutically acceptable salts thereof. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 200 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 300 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 400 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 500 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 600 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 700 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-

fluorouracil and platinum-based chemotherapeutics comprising: about 800 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 900 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: about 1000 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 200 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 300 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 400 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 500 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 600 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 700 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 800 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective

amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 900 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, a dietary regimen is administered with 5-fluorouracil and platinum-based chemotherapeutics comprising: 1000 mg/m^2 5-fluorouracil administered in a continuous intravenous infusion over 24 hours and a therapeutically effective amount of a platinum-based chemotherapeutic agent. In some embodiments, administration of 5-fluorouracial and a platinum-based chemotherapeutic agent is repeated at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, at least 30, at least 31, at least 32, at least 33, at least 34, at least 35, at least 36, at least 37, at least 38, at least 39, or at least 40 times. In some embodiments, a dietary regimen is administered with 5-fluorouracial and a platinum-based chemotherapeutic agent comprising dosages of 5-fluorouracial and a platinum-based chemotherapeutic agent typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered with 5-fluorouracial and a platinum-based chemotherapeutic agent repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.)

[0239] In some embodiments, a dietary regimen is administered with a therapeutically effective amount of 5-fluorouracil, or a pharmaceutically acceptable salt thereof, and leucovorin, or a pharmaceutically acceptable salt thereof. In some embodiments, 5-fluorouracil is administered with leucovorin (folinic acid), or a pharmaceutically acceptable salt thereof.

[0240] In some embodiments, a dietary regimen is administered with 5-fluorouracil and leucovorin comprising: administering about 200 mg/m^2 leucovorin by slow intravenous infusion for a minimum of about 3 minutes followed by about 370 mg/m^2 5-fluorouracil administered by intravenous infusion daily for about 5 days, repeated on 28-day intervals for two courses and then repeated at 28- to 35-day intervals. In some embodiments, a dietary regimen is administered with 5-fluorouracil and leucovorin comprising: administering about 20 mg/m^2 leucovorin by intravenous injection followed by about 425 mg/m^2 5-fluorouracil administered by intravenous infusion daily for about 5 days, repeated on 28-day intervals for two courses and then repeated at 28- to 35-day intervals. In some embodiments, a dietary regimen is administered with 5-

fluorouracil and leucovorin comprising: administering 200 mg/m^2 leucovorin by slow intravenous infusion for a minimum of three minutes followed by 370 mg/m^2 5-fluorouracil administered by intravenous infusion daily for about 5 days, repeated on 28-day intervals for two courses and then repeated at 28- to 35-day intervals. In some embodiments, a dietary regimen is administered with 5-fluorouracil and leucovorin comprising: administering 20 mg/m^2 leucovorin by intravenous injection followed by 425 mg/m^2 5-fluorouracil administered by intravenous infusion daily for about 5 days, repeated on 28-day intervals for two courses and then repeated at 28- to 35-day intervals. In some embodiments, 5-fluorouracil and leucovorin are administered separately to avoid the formation of a precipitate. In some embodiments, a dietary regimen is administered with 5-fluorouracil and leucovorin comprising dosages of 5-fluorouracil and leucovorin typically used in treating colorectal cancer (*e.g.*, LARC.) In some embodiments, a dietary regimen is administered with 5-fluorouracil and leucovorin repeated for a number of cycles typically used in treating colorectal cancer (*e.g.*, LARC.)

[0241] In some embodiments, the dose of 5-fluorouracil is adjusted based on subject tolerance of prior treatment course. In some embodiments, the daily dosage of 5-fluorouracil is reduced by about 20% for subjects who experience moderate hematologic or gastrointestinal toxicity in a prior treatment course. In some embodiments, the daily dosage of 5-fluorouracil is reduced by about 30% for subjects who experience severe hematologic or gastrointestinal toxicity in a prior treatment course. In some embodiments, the daily dosage of 5-fluorouracil is increased by about 10% for subjects who experience no toxicity. In some embodiments, leucovorin dosages are not adjusted for toxicity.

[0242] In some embodiments, the dose of leucovorin is from about 10 mg/m^2 to about 1000 mg/m^2, from about 50 mg/m^2 to about 1000 mg/m^2, from about 50 mg/m^2 to about 500 mg/m^2, or from about 100 mg/m^2 to about 500 mg/m^2. In some embodiments, the dose of leucovorin is about 10 mg/m^2, about 20 mg/m^2, about 30 mg/m^2, about 40 mg/m^2, about 50 mg/m^2, about 60 mg/m^2, about 70 mg/m^2, about 80 mg/m^2, about 90 mg/m^2, about 100 mg/m^2, about 110 mg/m^2, about 120 mg/m^2, about 130 mg/m^2, about 140 mg/m^2, about 150 mg/m^2, about 160 mg/m^2, about 170 mg/m^2, about 180 mg/m^2, about 190 mg/m^2, about 200 mg/m^2, about 210 mg/m^2, about 220 mg/m^2, about 230 mg/m^2, about 240 mg/m^2, about 250 mg/m^2, about 260 mg/m^2, about 270 mg/m^2, about 280 mg/m^2, about 290 mg/m^2, about 300 mg/m^2, about 310 mg/m^2, about 320 mg/m^2, about 330 mg/m^2, about 340 mg/m^2, about 350 mg/m^2, about 360 mg/m^2, about 370 mg/m^2, about 380 mg/m^2, about 390 mg/m^2, about 400 mg/m^2, about 410 mg/m^2,

about 420 mg/m^2, about 430 mg/m^2, about 440 mg/m^2, about 450 mg/m^2, about 460 mg/m^2, about 470 mg/m^2, about 480 mg/m^2, about 490 mg/m^2, or about 500 mg/m^2.

[0243] In some embodiments, a dietary regimen is administered with FOLFIRI, which comprises folinic acid (leucovorin), 5-fluorouracil, and irinotecan

[0244] In some embodiments, a dietary regimen is administered with FOLFOX, which comprises 5-fluorouracil or a pharmaceutically acceptable salt thereof, leucovorin or a pharmaceutically acceptable salt thereof, and oxaliplatin or a pharmaceutically acceptable salt thereof.

[0245] In some embodiments, a dietary regimen is administered with FOLFOX4. In some embodiments, a dietary regimen is administered with FOLFOX4 comprising about 400 mg/m^2 leucovorin, about 85 mg/m^2 oxaliplatin, and about 2000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with FOLFOX4 comprising about 200 mg/m^2 leucovorin and about 85 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours, about 400 mg/m^2 5-fluorouracil administered as a bolus, followed by about 600 mg/m^2 5-fluorouracil administered as a 22-hour continuous infusion on day 1, and about 200 mg/m^2 leucovorin administered as a continuous infusion over 2 hours, about 400 mg/m^2 5-fluorouracil administered as a bolus, followed by about 600 mg/m^2 5-fluorouracil administered as a 22-hour continuous infusion on day 2, administered every 2 weeks. In some embodiments, a dietary regimen is administered with FOLFOX4 comprising 400 mg/m^2 leucovorin, 85 mg/m^2 oxaliplatin, and 2000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with FOLFOX4 comprising 200 mg/m^2 leucovorin and 85 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours, 400 mg/m^2 5-fluorouracil administered as a bolus, followed by 600 mg/m^2 5-fluorouracil administered as a 22-hour continuous infusion on day 1; and 200 mg/m^2 leucovorin administered as a continuous infusion over 2 hours, 400 mg/m^2 5-fluorouracil administered as a bolus, followed by 600 mg/m^2 5-fluorouracil administered as a 22-hour continuous infusion on day 2, administered every 2 weeks.

[0246] In some embodiments, a dietary regimen is administered with modified FOLFOX4 (mFOLFOX4). In some embodiments, a dietary regimen is administered with mFOLFOX4 comprising about 200 mg/m^2 leucovorin, about 85 mg/m^2 oxaliplatin, and about 2000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with mFOLFOX4 comprising about 200 mg/m^2 leucovorin and about 85 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and about 400 mg/m^2 5-fluorouracil administered as a bolus,

followed by about 1600 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks. In some embodiments, a dietary regimen is administered with mFOLFOX4 comprising 200 mg/m^2 leucovorin, about 85 mg/m^2 oxaliplatin, and 2000 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with mFOLFOX4 comprising 200 mg/m^2 leucovorin and 85 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and 400 mg/m^2 5-fluorouracil administered as a bolus, followed by 1600 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks.

[0247] In some embodiments, a dietary regimen is administered with FOLFOX6. In some embodiments, a dietary regimen is administered with FOLFOX6 comprising about 400 mg/m^2 leucovorin, about 100 mg/m^2 oxaliplatin, and about 2800 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with FOLFOX6 comprising about 400 mg/m^2 leucovorin and about 100 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and about 400 mg/m^2 5-fluorouracil administered as a bolus, followed by about 2400 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks. In some embodiments, a dietary regimen is administered with FOLFOX6 comprising 400 mg/m^2 leucovorin, 100 mg/m^2 oxaliplatin, and 2800 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with FOLFOX6 comprising 400 mg/m^2 leucovorin and 100 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and 400 mg/m^2 5-fluorouracil administered as a bolus, followed by 2400 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks.

[0248] In some embodiments, a dietary regimen is administered with modified FOLFOX6 (mFOLFOX6). In some embodiments, a dietary regimen is administered with mFOLFOX6 comprising about 400 mg/m^2 leucovorin, about 85 mg/m^2 oxaliplatin, and about 2800 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with mFOLFOX6 comprising about 400 mg/m^2 leucovorin and about 85 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and about 400 mg/m^2 5-fluorouracil administered as a bolus, followed by about 2400 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks. In some embodiments, a dietary regimen is administered with mFOLFOX6 comprising 400 mg/m^2 leucovorin, 85 mg/m^2 oxaliplatin, and 2800 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with mFOLFOX6 comprising 400 mg/m^2 leucovorin and 85 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and 400

mg/m^2 5-fluorouracil administered as a bolus, followed by 2400 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks.

[0249] In some embodiments, a dietary regimen is administered with FOLFOX7. In some embodiments, a dietary regimen is administered with FOLFOX7 comprising about 400 mg/m^2 leucovorin, about 130 mg/m^2 oxaliplatin, and about 2400 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with FOLFOX7 comprising about 400 mg/m^2 leucovorin and about 130 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and about 2400 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks. In some embodiments, a dietary regimen is administered with FOLFOX7 comprising 400 mg/m^2 leucovorin, 130 mg/m^2 oxaliplatin, and 2400 mg/m^2 5-fluorouracil. In some embodiments, a dietary regimen is administered with FOLFOX7 comprising 400 mg/m^2 leucovorin and 130 mg/m^2 oxaliplatin administered as a continuous infusion over 2 hours and 2400 mg/m^2 5-fluorouracil administered as a 46-hour continuous infusion every 2 weeks.

[0250] In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 1 cycle, 2 cycles, 3 cycles, 4 cycles, 5 cycles, 6 cycles, 7 cycles, 8 cycles, 9 cycles, 10 cycles, 11 cycles, 12 cycles, 13 cycles, 14 cycles, 15 cycles, 16 cycles, 17 cycles, 18 cycles, 19 cycles, or 20 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 1 cycle. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 2 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 3 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 4 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 5 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 6 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 7 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 8 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 9 cycles. In some embodiments, a dietary regimen is administered with a FOLFOX regimen on 14-day cycle for 10 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 1 cycle. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 2 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 3 cycles. In some

embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 4 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 5 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 6 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 7 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 8 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 9 cycles. In some embodiments, a dietary regimen is administered with mFOLFOX6 on a 14-day cycle for 10 cycles. In some embodiments, a dietary regimen is administered with FOLFOX comprising dosages of fluorouracil, leucovorin, and oxaliplatin typically used in treating colorectal cancer (*e.g.*, LARC.)

[0251] In some embodiments, a dietary regimen is administered simultaneously with administration of a chemotherapy. In some embodiments, a dietary regimen is administered simultaneously with a chemotherapy for 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, or 21 days. In some embodiments, a dietary regimen is administered simultaneously with administration of a chemotherapy for 5 days. In some embodiments, a dietary regimen is administered simultaneously with administration of a chemotherapy for 7 days.

[0252] In some embodiments, the dietary regimen is administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days before a subject is treated with chemotherapy. In some embodiments, the dietary regimen is administered 1 day before a subject is treated with chemotherapy. In some embodiments, the dietary regimen is administered 2 days before a subject is treated with chemotherapy. In some embodiments, the dietary regimen is administered 3 days before a subject is treated with chemotherapy. In some embodiments, the dietary regimen is administered 4 days before a subject is treated with chemotherapy.

[0253] In some embodiments, a subject is treated with a dietary regimen and chemotherapy, then goes off treatment with the dietary regimen before beginning a subsequent treatment cycle with the dietary regimen and chemotherapy. In some embodiments, a subject is treated with a dietary regimen and chemotherapy, then goes off treatment before beginning a subsequent treatment cycle with the dietary regimen and chemotherapy. In some embodiments, a subject is

treated with a dietary regimen and chemotherapy, then goes off treatment with the chemotherapy before beginning a subsequent treatment cycle with the dietary regimen and chemotherapy. In some embodiments, the length of the treatment period and off-treatment period are identical. In some embodiments, the length of the treatment period and off-treatment period are different. In some embodiments, the length of the treatment period is longer than the off-treatment period. In some embodiments, the length of the treatment period is shorter than the off-treatment period.

[0254] In some embodiments, the length of a treatment period with the dietary regimen and chemotherapy is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days, and the length of off-treatment period is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days. In some embodiments, the length of the treatment period is 5 days, and the length of the off-treatment period is 2 days. In some embodiments, the length of the treatment period is 4 days, and the length of the off-treatment period is 3 days. In some embodiments, the length of the treatment period is 3 days, and the length of the off-treatment period is 4 days. In some embodiments, the length of the treatment period is 2 days, and the length of the off-treatment period is 5 days.

[0255] In some embodiments, a cycle of a treatment period and an off-treatment period is repeated for 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, or 16 weeks.

[0256] In some embodiments, the subject is treated with chemotherapy after the radiotherapy (*e.g.*, after a short-course radiotherapy or a long-course radiotherapy). In some embodiments, the subject is placed on a cycled diet (*i.e.*, alternating between a dietary regimen and a habitual diet) throughout the chemotherapy. For example, in some embodiments, the subject is administered a chemotherapy course comprising administration of CapeOX and the subject is given a dietary regimen at least 3 days a week for 5 to 7 weeks and is given a habitual diet for a week between the weeks in which a dietary regimen is given. The subject returns to a habitual diet for 1 week before starting an additional round of 5 to 7 weeks in which a dietary regimen is given. A CapeOX chemotherapy course is given with two weeks in between each week in which CapeOX is given. The diet cycle and the CapeOX cycle are repeated as needed (*e.g.*, for 5 diet cycles and for 6 chemotherapy cycles.) In some embodiments, in the weeks in which the dietary regimen is given, the dietary regimen is given for at least 3 days of the week. In some embodiments, the dietary regimen is given on an intermittent schedule such that the dietary regimen is given 4

days per week and a habitual diet is given 3 days per week. These schedules can be varied such that. In some embodiments, the dietary regimen weeks are every week of a months. In some embodiments, the dietary regimen weeks are 3 weeks of a month, with habitual diet for 1 week of the month. In some embodiments, the dietary regimen weeks are 2 weeks of a month, with habitual diet for 2 weeks of the month. In some embodiments, the dietary regimen weeks are 1 week of a month, with habitual diet for 3 weeks of the month.

[0257] Also for example, in some embodiments, a chemotherapy course comprising administration of FOLFOX is administered to the subject, wherein the subject is given a dietary regimen at least 3 days a week for 5 to 7 weeks and is given a habitual diet between the weeks in which a dietary regimen is given. The subject returns to a normal, habitual diet for 1 week before starting an additional round of 5 to 7 weeks in which a dietary regimen is given. A FOLFOX chemotherapy course is given with one week in between each week in which FOLFOX is given. The diet cycle and the FOLFOX cycle are repeated as needed (*e.g.*, for 4 diet cycles and for 8 chemotherapy cycles.) In some embodiments, in the weeks in which the dietary regimen is given, the dietary regimen is given for at least 3 days of the week. In some embodiments, the dietary regimen is given on an intermittent schedule such that the dietary regimen is given 4 days per week and a habitual diet is given 3 days per week. These schedules can be varied such that. In some embodiments, the dietary regimen weeks are every week of a months. In some embodiments, the dietary regimen weeks are 3 weeks of a month, with habitual diet for 1 week of the month. In some embodiments, the dietary regimen weeks are 2 weeks of a month, with habitual diet for 2 weeks of the month. In some embodiments, the dietary regimen weeks are 1 week of a month, with habitual diet for 3 weeks of the month.

[0258] In some embodiments, the dietary regimen is on an intermittent schedule alternating with a habitual diet during the period on which the patient is on chemotherapy. For example, in some embodiments, the subject consumes the dietary regimen for 6 days of a week and consumes a habitual diet on the remaining 1 day of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the dietary regimen for 5 days of a week and consumes a habitual diet on the remaining 2 days of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the dietary regimen for 4 days of a week and consumes a habitual diet on the remaining 3 days of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the dietary regimen for 3 days of a week and consumes a habitual diet on the

remaining 4 days of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes a habitual diet for at least 2 days per week during the period on which the patient is on chemotherapy and consume a habitual diet on the remaining 5 days of the week during the period on which the patient is on chemotherapy.

[0259] In some embodiments, the subject consumes a habitual diet for at least 3 consecutive days per week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes a habitual diet for at least 4 consecutive days per week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes a habitual diet for at least 5 consecutive days per week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes a habitual diet for at least 6 consecutive days per week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes a habitual diet for 7 consecutive days per week during the period on which the patient is on chemotherapy.

[0260] In some embodiments, the subject consumes the dietary regimen for 6 consecutive days of a week and consumes a habitual diet on the remaining 1 day of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the dietary regimen for 5 consecutive days of a week and consumes a habitual diet on the remaining 2 days of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the diet for 4 consecutive days of a week and consumes a habitual diet on the remaining 3 days of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the diet for 3 consecutive days of a week and consumes a habitual diet on the remaining 4 days of the week during the period on which the patient is on chemotherapy. In some embodiments, the subject consumes the diet for 2 consecutive days of a week and consumes a habitual diet on the remaining 5 days of the week during the period on which the patient is on chemotherapy.

Surgery

[0261] In some embodiments, a dietary regimen is used in combination with surgery. In some embodiments, surgery can follow administration of at least one other therapeutic agent. In some embodiments, surgery can precede administration of at least one other therapeutic agent.

[0262] In some embodiments, the surgery is curative surgery, wherein the malignant tissue is removed from the body of a subject. In some embodiments, the malignant tissue is a tumor. In some embodiments, the malignant tissue is a growth. In some embodiments, the curative surgery is total mesorectal excision (TME). In some embodiments, the curative surgery is transanal-total mesorectal excision (TaTME). In some embodiments, the surgery is preventive surgery, wherein precancerous tissue is removed from the body of the subject. In some embodiments, the preventive surgery is polyp removal. In some embodiments, the surgery is diagnostic surgery. In some embodiments, the diagnostic surgery is a biopsy. In some embodiments, the biopsy is of malignant tissue. In some embodiments, the biopsy is of non-malignant tissue. In some embodiments, the biopsy is of precancerous tissue. In some embodiments, the surgery is staging surgery, wherein the extent of the condition in the body of a subject is uncovered. In some embodiments, the staging surgery is laparoscopy. In some embodiments, the surgery is debulking surgery, wherein a portion of the malignant tissue is removed. In some embodiments, the surgery is palliative surgery. In some embodiments, the surgery is supportive surgery. In some embodiments, the supportive surgery facilitates administration of other therapeutic agents. In some embodiments, the supportive surgery is catheter insertion. In some embodiments, the supportive surgery is insertion of a central venous catheter. In some embodiments, the surgery is restorative surgery.

Exemplary Embodiments

[0263] Embodiment I-1. A method of treating colorectal cancer in a subject in need thereof, the method comprising administering to the subject:

a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of at least two amino acids in the subject as compared to baseline; and

b) a therapeutically effective amount of a radiotherapy.

[0264] Embodiment I-2. The method of embodiment I-1, wherein the at least two amino acids comprise serine and glycine, serine and proline, or glycine and proline.

[0265] Embodiment I-3. The method of embodiments I-1 and 2, wherein the dietary regimen reduces an average plasma level of at least three amino acids.

[0266] Embodiment I-4. The method of embodiment I-3, wherein the at least three amino acids comprise serine, glycine, and proline.

[0267] Embodiment I-5. The method of embodiments I-1 to 4, wherein the dietary regimen reduces an average plasma level of serine in the subject by at least about 20% as compared to baseline, reduces an average plasma level of glycine in the subject by at least about 20% as compared to baseline, reduces an average plasma level of proline in the subject by at least about 20% as compared to baseline, or a combination thereof.

[0268] Embodiment I-6. The method of embodiments I-1 to 5, wherein the dietary regimen comprises less than about 500 mg/day of proline, less than about 500 mg/day of serine, less than about 500 mg/day of glycine, or a combination thereof.

[0269] Embodiment I-7. The method of embodiments I-1 to 6, wherein the dietary regimen comprises less than 25% of an RDA of serine for the subject's age group, less than 25% of an RDA of glycine for the subject's age group, less than 25% of an RDA of proline for the subject's age group, or a combination thereof.

[0270] Embodiment I-8. The method of embodiments I-1 to 7, wherein the dietary regimen comprises less than 20% of an RDA of serine for the subject's age group, less than 20% of an RDA of glycine for the subject's age group, less than 20% of an RDA of proline for the subject's age group, or a combination thereof.

[0271] Embodiment I-9. The method of embodiments I-7 and 8, wherein the RDA of serine for an adult subject is about 28 mg/kg/day, the RDA of glycine for an adult subject is about 50 mg/kg/day, and the RDA of proline for an adult subject is about 55 mg/kg/day.

[0272] Embodiment I-10. The method of embodiments I-1 to 9, wherein the dietary regimen is substantially devoid of serine, substantially devoid of glycine, substantially devoid of proline, or a combination thereof.

[0273] Embodiment I-11. The method of embodiments I-1 to 10, wherein the dietary regimen comprises about 8% to about 20% of carbohydrates from diet-only kcals, about 1% to about 5% of protein from diet-only kcals, and about 75% to about 91% of fat from diet-only kcals.

[0274] Embodiment I-12. The method of embodiments I-1 to 10, wherein the dietary regimen comprises about 9% of carbohydrates from diet-only kcals, about 2% of protein from diet-only kcals, and about 89% of fat from diet-only kcals.

[0275] Embodiment I-13. The method of embodiments I-1 to 10, wherein the dietary regimen comprises about 18% of carbohydrates from diet-only kcals, about 2% of protein from diet-only kcals, and about 80% of fat from diet-only kcals.

[0276] Embodiment I-14. The method of embodiments I-1 to 13, wherein the dietary regimen is substantially a sole source of calories for the subject.

[0277] Embodiment I-15. The method of embodiments I-1 to 14, wherein the dietary regimen comprises administration of a dietary product to the subject.

[0278] Embodiment I-16. The method of embodiment I to 15, wherein the dietary product comprises a plurality of amino acids, optionally wherein the plurality of amino acids is a powder that is reconstituted with water prior to administration to the subject.

[0279] Embodiment I-17. The method of any embodiments I-15 and 16, wherein the dietary product comprises histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

[0280] Embodiment I-18. The method of embodiments I-15 to 17, wherein the dietary product comprises one or more of cysteine, cystine, arginine, tyrosine, alanine, aspartic acid, asparagine, glutamic acid, glutamine, and taurine.

[0281] Embodiment I-19. The method of embodiments I-15 to 18, wherein the dietary product is devoid of serine, glycine, or proline.

[0282] Embodiment I-20. The method of embodiments I-15 to 19, wherein the dietary product is devoid of serine and glycine, serine and proline, or glycine and proline.

[0283] Embodiment I-21. The method of embodiments I-15 to 20, wherein the dietary product is devoid of serine, glycine, and proline.

[0284] Embodiment I-22. The method of embodiments I-15 to 21, wherein the dietary product is substantially a sole source of amino acids for the subject.

[0285] Embodiment I-23. The method of embodiments I-1 to 22, wherein the dietary regimen comprises administration of a diet to the subject.

[0286] Embodiment I-24. The method of embodiment I-23, wherein the diet comprises less than about 500 mg/day of proline, less than about 500 mg/day of serine, less than about 500 mg/day of glycine, or a combination thereof.

[0287] Embodiment I-25. The method of embodiments I-23 and 24, wherein the diet comprises less than 25% of an RDA of serine for the subject's age group, less than 25% of an RDA of glycine for the subject's age group, less than 25% of an RDA of proline for the subject's age group, or a combination thereof.

[0288] Embodiment I-26. The method of embodiments I-23 to 25, wherein the diet comprises less than 20% of an RDA of serine for the subject's age group, less than 20% of an RDA of

glycine for the subject's age group, less than 20% of an RDA of proline for the subject's age group, or a combination thereof.

[0289] Embodiment I-27. The method of embodiments I-25 and 26, wherein the RDA of serine for an adult subject is about 28 mg/kg/day, the RDA of glycine for an adult subject is about 50 mg/kg/day, and the RDA of proline for an adult subject is about 55 mg/kg/day.

[0290] Embodiment I-28. The method of embodiments I-23 to 27, wherein the diet comprises about 1200 kcals/day to about 2600 kcals/day.

[0291] Embodiment I-29. The method of embodiments I-23 to 28, wherein the diet comprises about 0.8 g/kg/day to about 1.2 g/kg/day of protein.

[0292] Embodiment I-30. The method of embodiments I-23 to 29, wherein the diet is a high-fat, low-carbohydrate, low-protein diet.

[0293] Embodiment I-31. The method of embodiments I-23 to 30, wherein the diet comprises about 8% to about 20% of carbohydrates by calories, about 1% to about 5% of protein by calories, and about 75% to about 91% of fat by calories.

[0294] Embodiment I-32. The method of embodiments I-23 to 30, wherein the diet comprises about 9% of carbohydrates by calories, about 2% of protein by calories, and about 89% of fat by calories.

[0295] Embodiment I-33. The method of embodiments I-23 to 30, wherein the diet comprises about 18% of carbohydrates by calories, about 2% of protein by calories, and about 80% of fat by calories.

[0296] Embodiment I-34. The method of embodiments I-23 to 33, wherein the diet is substantially a sole source of carbohydrates for the subject.

[0297] Embodiment I-35. The method of embodiments I-23 to 34, wherein the diet is substantially a sole source of fat for the subject.

[0298] Embodiment I-36. The method of embodiments I-23 to 35, wherein the diet is a low glycemic index diet.

[0299] Embodiment I-37. The method of embodiments I-1 to 36, wherein the dietary regimen is administered at least 4 times per week, at least 5 times per week, or at least 6 times per week.

[0300] Embodiment I-38. The method of embodiment I-37, wherein the dietary regime is administered at least 4 times per week for 5 weeks or at least 6 times per week for 1 week.

[0301] Embodiment I-39. The method of embodiments I-1 to 38, wherein the radiotherapy is administered 5 days per week.

[0302] Embodiment I-40. The method of embodiments I-1 to 39, wherein the radiotherapy is administered once per day.

[0303] Embodiment I-41. The method of embodiments I-1 to 40, wherein the radiotherapy is administered at an amount of about 6 MV to about 15 MV photons from a linear accelerator in 5 daily fractions.

[0304] Embodiment I-42. The method of embodiments I-1 to 40, wherein the radiotherapy is administered at an amount of about 6 MV photons from a linear accelerator in 5 daily fractions.

[0305] Embodiment I-43. The method of embodiments I-1 to 42, wherein the radiotherapy is a short-course radiation therapy.

[0306] Embodiment I-44. The method of embodiment I-43, wherein the short-course radiotherapy comprises administering about 500 cGy per day.

[0307] Embodiment I-45. The method of embodiment I-43, wherein the short-course radiotherapy comprises administering about 2500 cGy in 5 daily fractions.

[0308] Embodiment I-46. The method of embodiments I-1 to 42, wherein the radiotherapy is a long-course radiotherapy.

[0309] Embodiment I-47. The method of embodiment I-46, wherein the long-course radiotherapy comprises administering about 200 cGy per day.

[0310] Embodiment I-48. The method of embodiment I-46, wherein the long-course radiotherapy comprises administering about 1000 cGy in 5 daily fractions, optionally every week for 3 weeks, 4 weeks, or 5 weeks.

[0311] Embodiment I-49. The method of embodiments I-1 to 48, further comprising administering:

c) a therapeutically effective amount of one or more chemotherapeutic agents.

[0312] Embodiment I-50. The method of embodiment I-49, wherein administering the one or more chemotherapeutic agents is oral or intravenous.

[0313] Embodiment I-51. The method of any embodiments I-49 and 50, wherein the one or more chemotherapeutic agents comprise oxaliplatin, capecitabine, leucovorin, fluorouracil, or a combination thereof.

[0314] Embodiment I-52. The method of embodiment I-51, wherein the oxaliplatin is intravenously administered at a dose of about 85 mg/m^2 or about 130 mg/m^2, optionally over about 2 hours.

[0315] Embodiment I-53. The method of embodiments I-51 and 52, wherein the capecitabine is orally administered at a dose of about 1000 mg/m^2.

[0316] Embodiment I-54. The method of embodiments I-51 to 53, wherein the one or more chemotherapeutic agents comprise oxaliplatin and capecitabine (CapeOX), optionally wherein administering the CapeOX comprises intravenously administering oxaliplatin once on day 1 and orally administering capecitabine twice daily on days 1-14.

[0317] Embodiment I-55. The method of embodiment I-54, wherein administering the CapeOX comprises intravenously administering oxaliplatin at a dose of about 130 mg/m^2 once on day 1 and orally administering capecitabine at a dose of about 1000 mg/m^2 twice daily on days 1-14.

[0318] Embodiment I-56. The method of embodiments I-54 and 55, wherein administering the CapeOX is repeated on a 21-day cycle, optionally for a total of 18 weeks (6 cycles).

[0319] Embodiment I-57. The method of embodiments I-51 to 56, wherein the leucovorin is administered at a dose of about 400 mg/m^2, optionally over about 2 hours.

[0320] Embodiment I-58. The method of embodiment I-57, wherein the leucovorin is leucovorin calcium.

[0321] Embodiment I-59. The method of embodiments I-51 to 58, wherein the fluorouracil is administered at a dose of about 400 mg/m^2, about 1200 mg/m^2, or about 2400 mg/m^2.

[0322] Embodiment I-60. The method of embodiment I-59, wherein the fluorouracil is administered over about 2 hours.

[0323] Embodiment I-61. The method of embodiment I-59, wherein the fluorouracil is administered over about 2 days.

[0324] Embodiment I-62. The method of embodiments I-51 to 61, wherein the one or more chemotherapeutic agents comprise oxaliplatin, leucovorin, and fluorouracil (FOLFOX).

[0325] Embodiment I-63. The method of embodiment I-62, wherein administering the FOLFOX comprises a FOLFOX4 regimen, a FOLFOX6 regimen, a modified FOLFOX6 (mFOLFOX6) regimen, or a FOLFOX7 regimen.

[0326] Embodiment I-64. The method of embodiments I-62 and 63, wherein administering the FOLFOX comprises intravenously administrating fluorouracil, leucovorin, and oxaliplatin on day 1 and intravenously administrating fluorouracil continuously over 46-48 hours (days 1-2).

[0327] Embodiment I-65. The method of embodiments I-62 to 64, wherein administering the FOLFOX comprises intravenously administrating fluorouracil at a dose of about 400 mg/m^2, leucovorin at a dose of about 400 mg/m^2, and oxaliplatin at a dose of about 85 mg/m^2 on day 1

and intravenously administrating fluorouracil at a dose of about 1200 mg/m^2 continuously over about 2 days (days 1-2).

[0328] Embodiment I-66. The method of embodiments I-62 to 65, wherein administering the FOLFOX is repeated on a 14-day cycle, optionally for a total of 16 weeks (8 cycles).

[0329] Embodiment I-67. The method of embodiments I-1 to 66, wherein administering the dietary regimen is before administering the radiotherapy.

[0330] Embodiment I-68. The method of embodiments I-1 to 67, wherein administering the dietary regimen is at least 24 hours prior to administering the radiotherapy and continued throughout administering the radiotherapy.

[0331] Embodiment I-69. The method of embodiments I-1 to 68, wherein administering the dietary regimen is on an intermittent schedule alternating with a habitual diet.

[0332] Embodiment I-70. The method of embodiment I-69, wherein the habitual diet is consumed by the subject for at least two consecutive days per week.

[0333] Embodiment I-71. The method of embodiments I-49 to 70, wherein administering the dietary regimen is before administering the one or more chemotherapeutic agents.

[0334] Embodiment I-72. The method of embodiments I-49 to 71, wherein administering the dietary regimen is at least 24 hours prior to administering the one or more chemotherapeutic agents and on the day of administering the one or more chemotherapeutic agents.

[0335] Embodiment I-73. The method of embodiments I-49 to 72, wherein administering the radiotherapy is before administering the one or more chemotherapeutic agents.

[0336] Embodiment I-74. The method of embodiments I-1 to 73, further comprising providing a surgical intervention to the subject.

[0337] Embodiment I-75. The method of embodiment I-74, wherein the surgical intervention is total mesorectal excision (TME).

[0338] Embodiment I-76. The method of embodiments I-1 to 75, wherein the colorectal cancer is rectal cancer.

[0339] Embodiment I-77. The method of embodiment I-76, wherein the cancer is locally advanced rectal cancer (LARC).

[0340] Embodiment I-78. A method of treating colorectal cancer in a subject in need thereof, the method comprising administering to the subject:

a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of serine, glycine, and proline in the subject as compared to baseline;

b) a therapeutically effective amount of a radiotherapy; and

c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin and capecitabine (CapeOX), wherein administering the CapeOX comprises intravenously administering oxaliplatin at a dose of about 130 mg/m^2 once on day 1 and orally administering capecitabine at a dose of about 1000 mg/m^2 twice daily on days 1-14.

[0341] Embodiment I-79. A method of treating colorectal cancer in a subject in need thereof, the method comprising administering to the subject:

a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of serine, glycine, and proline in the subject as compared to baseline;

b) a therapeutically effective amount of a radiotherapy; and

c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin, leucovorin, and fluorouracil (FOLFOX), wherein administering the FOLFOX comprises intravenously administrating fluorouracil at a dose of about 400 mg/m^2, leucovorin at a dose of about 400 mg/m^2, and oxaliplatin at a dose of about 85 mg/m^2 on day 1 and intravenously administrating fluorouracil at a dose of about 1200 mg/m^2 continuously over about 2 days (days 1-2).

EXAMPLES

EXAMPLE 1: Dietary product devoid of serine, glycine, and proline.

[0342] A dietary product devoid of serine, glycine, and proline is prepared and contains 0.8 g/kg/day of amino acids. **TABLE 1A-1E** show the components and amounts of example compositions. In some embodiments, the dietary product comprises the formulation of **TABLE 1A**. In some embodiments, the dietary product comprises the formulation of **TABLE 1B**. In some embodiments, the dietary product comprises the formulation of **TABLE 1C**. In some embodiments, the dietary product comprises the formulation of **TABLE 1D**. In some embodiments, the dietary product comprises the formulation of **TABLE 1E**.

[0343] A dietary product is administered to a subject in conjunction with a low-protein, low-carbohydrate, high-fat diet. The low-protein, low-carbohydrate, high-fat diet comprises about 9% carbohydrates, 2% protein, and 89% fat by kcal. The low-protein, low-carbohydrate, high-fat diet with dietary product results in a daily dietary intake of: 1) 1600-2400 kcals/day; 2) about 1g/kg/day of protein; 3) about 420 mg proline/day; 4) about 410 mg/serine/day; 5) about 230 glycine/day; and 6) a diet that is about 9% carbohydrates, 2% protein, and 89% fat of diet-only kcals.

TABLE 1A

Amino Acids	Chemical Name	Milligrams (mg)
1	L-Histidine	445.00
2	L-Isoleucine	600.00
3	L-Leucine	1,150.00
4	L-Lysine Monohydrate	995.00
5	L-Methionine	300.00
6	L-Phenylalanine	750.00
7	L-Threonine	600.00
8	L-Tryptophan	220.00
9	L-Valine	600.00
10	L-Cystine	138.00
11	L-Tyrosine	330.00
12	L-Glutamine	300.00
13	L-Arginine Base	246.00
14	L-Alanine	600.00
15	L-Aspartic Acid	508.70
16	L-Asparagine Hydrate	600.00
17	L-Arginine-L-Glutamate Salt	1,300.00
18	**L-Serine**	**0.00**
19	**Glycine**	**0.00**
20	**L-Proline**	**0.00**
21	Taurine	50.00
Total Amino Acids		9,732.70
Other Materials		
22	L-Aspartic Acid Potassium Salt	380.00
23	L-Aspartic Acid Magnesium Salt	211.00
Total Materials		10,323.70

TABLE 1B

Amino Acids	Chemical Name	Milligrams (mg)
1	L-Histidine	350.00
2	L-Isoleucine	724.60
3	L-Leucine	900.30
4	L-Lysine Monohydrate	1000.00
5	L-Methionine	300.00
6	L-Phenylalanine	756.20
7	L-Threonine	608.00
8	L-Tryptophan	250.00
9	L-Valine	600.00
10	L-Cystine	100.70
11	L-Tyrosine	400.00
12	L-Glutamine	200.00
13	L-Arginine Base	260.00
14	L-Alanine	620.00
15	L-Aspartic Acid	400.00
16	L-Asparagine Hydrate	600.00
17	L-Arginine-L-Glutamate Salt	1,600.00
18	**L-Serine**	**0.00**
19	**Glycine**	**0.00**
20	**L-Proline**	**0.00**
21	Taurine	100.00
Total Amino Acids		9,769.80
Other Materials		
22	L-Aspartic Acid Potassium Salt	600.00
Total Materials		10,369.80

TABLE 1C

Amino Acids	Chemical Name	Milligrams (mg)
1	L-Histidine	300.00
2	L-Isoleucine	600.00
3	L-Leucine	850.00
4	L-Lysine Monohydrate	695.00
5	L-Methionine	300.00

Amino Acids	Chemical Name	Milligrams (mg)
6	L-Phenylalanine	750.00
7	L-Threonine	632.00
8	L-Tryptophan	160.00
9	L-Valine	450.00
10	L-Cystine	100.00
11	L-Tyrosine	330.00
12	L-Glutamine	300.00
13	L-Arginine Base	178.00
14	L-Alanine	600.00
15	L-Aspartic Acid	508.70
16	L-Asparagine Hydrate	350.00
17	L-Arginine-L-Glutamate Salt	1,300.00
18	**L-Serine**	**0.00**
19	**Glycine**	**0.00**
20	**L-Proline**	**0.00**
Total Amino Acids		8,403.70
Total Materials		8,403.70

TABLE 1D

Amino Acids	Chemical Name	Milligrams (mg)
1	L-Histidine	300.00
2	L-Isoleucine	600.00
3	L-Leucine	1,375.00
4	L-Lysine Monohydrate	995.00
5	L-Methionine	100.00
6	L-Phenylalanine	500.00
7	L-Threonine	450.00
8	L-Tryptophan	220.00
9	L-Valine	620.00
10	L-Cystine	138.00
11	L-Tyrosine	150.00
12	L-Glutamine	300.00
13	L-Arginine Base	143.00
14	L-Alanine	600.00
15	L-Aspartic Acid	508.70

Amino Acids	Chemical Name	Milligrams (mg)
16	L-Asparagine Hydrate	600.00
17	L-Arginine-L-Glutamate Salt	1,300.00
18	**L-Serine**	**0.00**
19	**Glycine**	**20.00**
20	**L-Proline**	**10.00**
21	Taurine	15.00
Total Amino Acids		8,944.70
Other Materials		
23	L-Aspartic Acid Magnesium Salt	105.00
Total Materials		9,049.70

TABLE 1E

Amino Acids	Chemical Name	Milligrams (mg)
1	L-Histidine	445.00
2	L-Isoleucine	600.00
3	L-Leucine	1,150.30
4	L-Lysine Monohydrate	995.00
5	L-Methionine	50.00
6	L-Phenylalanine	750.00
7	L-Threonine	450.00
8	L-Tryptophan	220.00
9	L-Valine	800.00
10	L-Cystine	138.00
11	L-Tyrosine	330.00
12	L-Glutamine	150.00
13	L-Arginine Base	246.00
14	L-Alanine	640.00
15	L-Aspartic Acid	130.00
16	L-Asparagine Hydrate	600.00
17	L-Arginine-L-Glutamate Salt	1,600.00
18	**L-Serine**	**0.00**
19	**Glycine**	**0.00**
20	**L-Proline**	**50.00**
Total Amino Acids		9,344.30

Amino Acids	Chemical Name	Milligrams (mg)
Total Materials		9,334.30

EXAMPLE 2: Use of radiotherapy to treat a cancer.

[0344] A first subject with a colorectal cancer is treated with a short-course of radiotherapy to treat the colorectal cancer. The first subject is placed on a diet substantially devoid of serine, glycine, and proline 2 days before starting radiotherapy treatment (*i.e.*, day -2). The amino acid-depleted diet is administered for a total of 10 days, starting 2 days before treatment through 4 days post-treatment (*i.e.*, day -2 through day 8). The first subject is treated with 500 cGy a day for 5 days. The first subject returns to a normal, habitual diet after day 8, or 4 days post-radiation treatment. If the first subject is treated with chemotherapy after the radiotherapy, the first subject is placed on a cycled diet throughout the chemotherapy. The cycle diet places the first subject on an alternating 5-day amino acid-depleted diet (*e.g.*, Monday-Friday) followed by a 2-day habitual diet (*e.g.*, Saturday, Sunday) throughout the chemotherapy treatment period. **TABLE 2** shows a short-course radiotherapy to treat a colorectal cancer.

TABLE 2

Day number	Day of week	Radiotherapy dose	Diet
-3	Fri	0 cGy	Habitual
-2	Sat	0 cGy	AA depleted Day 1
-1	Sun	0 cGy	AA depleted Day 2
0	Mon	500 cGy	AA depleted Day 3
1	Tue	500 cGy	AA depleted Day 4
2	Wed	500 cGy	AA depleted Day 5
3	Thu	500 cGy	AA depleted Day 6
4	Fri	500 cGy	AA depleted Day 7
5	Sat	0 cGy	AA depleted Day 8
6	Sun	0 cGy	AA depleted Day 9
7	Mon	0 cGy	AA depleted Day 10
8	Tue	0 cGy	Habitual
Chemotherapy	Ongoing	n/a	Cycle 5 days of AA depleted diet + 2 days habitual diet throughout Chemotherapy treatment

[0345] A second subject with a colorectal cancer is treated with a long-course of radiotherapy to treat the colorectal cancer. The second subject is placed on a diet substantially devoid of

serine, glycine, and proline 2 days before starting radiotherapy treatment (*i.e.*, day -2). The amino acid-depleted diet is administered for a total of 7 days, starting 2 days before treatment through the course of treatment (*i.e.*, day -2 through day 4). The second subject is treated with 200 cGy a day for 5 days. The second subject returns to a normal, habitual diet for two days before starting an additional round of radiotherapy. Subsequent radiation therapy cycles administer 5 days of an amino-acid depleted diet with 200 cGy of radiation for 5 days, followed by 2 days of a habitual diet. The cycle is repeated as needed.

[0346] If the second subject is treated with chemotherapy after the radiotherapy, the second subject is placed on a cycled diet throughout the chemotherapy. The cycle diet places the second subject on an alternating 5-day amino acid-depleted diet (*e.g.*, Monday-Friday) followed by a 2-day habitual diet (*e.g.*, Saturday, Sunday) throughout the chemotherapy treatment period.

TABLE 3 shows a long-course radiotherapy treatment to treat a colorectal cancer.

TABLE 3

Day number	Day of week	Radiotherapy dose	Diet
-3	Fri	0 cGy	Habitual
-2	Sat	0 cGy	AA depleted Day 1
-1	Sun	0 cGy	AA depleted Day 2
0	Mon	200 cGy	AA depleted Day 3
1	Tue	200 cGy	AA depleted Day 4
2	Wed	200 cGy	AA depleted Day 5
3	Thu	200 cGy	AA depleted Day 6
4	Fri	200 cGy	AA depleted Day 7
5	Sat	0 cGy	Habitual
6	Sun	0 cGy	Habitual
7	Mon	200 cGy	AA depleted Day 1
8	Tue	200 cGy	AA depleted Day 2
9	Wed	200 cGy	AA depleted Day 3
10	Thu	200 cGy	AA depleted Day 4
11	Fri	200 cGy	AA depleted Day 5
12	Sat	0 cGy	Habitual
13	Sun	0 cGy	Habitual
14	Mon	200 cGy	AA depleted Day 1
15	Tue	200 cGy	AA depleted Day 2
16	Wed	200 cGy	AA depleted Day 3
17	Thu	200 cGy	AA depleted Day 4
18	Fri	200 cGy	AA depleted Day 5
19	Sat	0 cGy	Habitual
20	Sun	0 cGy	Habitual
21	Mon	200 cGy	AA depleted Day 1
22	Tue	200 cGy	AA depleted Day 2
23	Wed	200 cGy	AA depleted Day 3

Day number	Day of week	Radiotherapy dose	Diet
24	Thu	200 cGy	AA depleted Day 4
25	Fri	200 cGy	AA depleted Day 5
26	Sat	0 cGy	Habitual
27	Sun	0 cGy	Habitual
28	Mon	200 cGy	AA depleted Day 1
29	Tue	200 cGy	AA depleted Day 2
30	Wed	200 cGy	AA depleted Day 3
31	Thu	200 cGy	AA depleted Day 4
32	Fri	200 cGy	AA depleted Day 5
33	Sat	0 cGy	Habitual
34	Sun	0 cGy	Habitual
Chemotherapy	Ongoing	n/a	Cycle 5 days of AA depleted diet + 2 days habitual diet throughout Chemotherapy treatment

EXAMPLE 3: Clinical trial to evaluate dietary regimen for treatment of Locally Advanced Rectal Cancer (LARC) in a subject when combined with radiotherapy and chemotherapy.

[0347] A non-randomized, single-arm phase IIa study is performed to assess the clinical efficacy and feasibility of a dietary regimen disclosed herein on treating LARC when combined with total neoadjuvant therapy (TNT) comprising radiotherapy and chemotherapy. A maximum of 25 subjects with LARC are recruited to participate in the study. Subjects entered in the trial are administered non-essential amino acid restriction (NEAAR) dietary regimen. NEAAR dietary regimen can comprise two elements: 1) standardized meals with minimal protein to provide a protein intake of up to about 1 g/kg/day, and 2) a plant-derived powder formulation comprising a plurality of powdered purified amino acids to be reconstituted with water that administers all proteinogenic essential and non-essential amino acids except for proline, serine, and glycine (which can be reduced or eliminated). Subjects will also take a multivitamin.

[0348] LARC can be treated with TNT. TNT consists of either long-course chemoradiation therapy (LCCRT) or short-course radiation therapy (SCRT) and followed by chemotherapy and total mesorectal excision (TME)-based surgery. This intensive multimodality treatment can achieve local tumor control in over 90% of subjects. However, the combination of pelvic radiotherapy and radical surgery can result in high morbidity and long-term sequelae that impair subject quality of life (QoL).

[0349] Subjects who achieve complete tumor regression (or clinical complete response, cCR) to TNT can present a dilemma for the thoughtful surgeon as the pre-operative discussion must include the very real possibility that the specimen would not contain cancer. Subjects' refusal of radical surgery coupled with surgeons' desire to balance oncologic outcomes with QoL provide motive to re-evaluate the clinical utility of radical and life-changing surgery often requiring temporary or permanent colostomy. Interest in avoiding surgery can be an oncologically-safe and cost-effective strategy to improve subject quality of life.

[0350] Tumors can have a significantly higher need for nutrients than most healthy tissues to fuel growth and defend against the effects of radical oxygen species induced by chemotherapy and radiotherapy. Cancer cells can mitigate the effects of chemotherapy and radiotherapy by engaging antioxidant responses to neutralize ROS, and by repairing damaged DNA. These defense mechanisms, which prevent cancer cell death and directly promote chemo- and radio-resistance, can be largely dependent on metabolic processes: the synthesis of nucleotides to repair DNA and the synthesis/turnover of antioxidant glutathione (GSH) require glucose and amino acid metabolism. As serine (Ser) and glycine (Gly) are essential precursors for the synthesis of nucleotides and GSH in the majority of colorectal tumors, combining Ser and Gly restriction with chemotherapy and radiotherapy can be a potentially-effective therapy.

[0351] Subjects enrolled in this study will consume the NEAAR dietary regimen during SCRT, starting at least one day prior to the initiation of radiotherapy. Subjects are planned to meet weekly with Registered Dieticians (RD) who assist in monitoring study diet compliance and tolerability. The RDs may make nutrition recommendations and will be reported to the site study team via email. Any potential AE reported to the RD will be communicated to the site study team via email for the site study team to follow-up on with the subjects directly and recorded as appropriate.

[0352] **NEAAR dietary regimen**: Participants are encouraged to consume at least 2 days of NEAAR dietary regimen during the screening period.

[0353] *NEAAR dietary regimen during SCRT*: NEAAR dietary regimen is started at least 24 hours prior to initiation of SCRT and continued through the final day of SCRT. Participants may be on the NEAAR dietary regimen for up to 6 consecutive days. SCRT can be started on any day, at the discretion of the radiation oncologist, though Monday is preferred to complete treatment in a single week. After completing SCRT subjects will continue the NEAAR dietary regimen food during the break between SCRT and chemotherapy.

[0354] *NEAAR dietary regimen during TNT*: Participants will consume the NEAAR dietary regimen on an intermittent schedule alternating with habitual diet, where habitual diet is consumed on at least two consecutive days per week. The schedule includes at least 24 hours on the NEAAR dietary regimen before chemotherapy administration, and on the day of chemotherapy administration. Subjects will continue to consume the NEAAR dietary regimen on weeks where no chemotherapy treatment is administered.

[0355] The RD may adjust the NEAAR dietary regimen intermittent schedule during the participant's participation. There are planned weeks where participants will consume habitual diet for the entire week. Schedule changes will be fully discussed with the participant and number of times the schedule is adjusted will be kept to a minimum. All changes in the NEAAR dietary regimen will be recorded by the RD.

[0356] Registered Dietitian (RD) Support: Participants will have ongoing communication with the study dietitian on a scheduled and as needed basis to provide general nutrition guidance around a participant's experience with the NEAAR dietary regimen. The RD may make nutrition-recommendations to participants and recommend over-the-counter (OTC) supplements that are compliant with the NEAAR dietary regimen. When absolutely necessary, the RD may provide recommendations for off-shelf food items that are compliant with the NEAAR dietary regimen (such as long-term unexpected delivery interruptions, travel, events, or if symptoms are interfering with a participant's ability to eat the NEAAR dietary regimen for short periods of time).

[0357] The SCRT plus chemotherapy regimens used in this trial represent standard-of-care for treatment of subjects with LARC. Initiation of consolidation chemotherapy should occur within 4 weeks (± 14 days) post-SCRT completion. Subjects receiving CapeOX will have oxaliplatin administered intravenously on day 1 and capecitabine orally twice daily on days 1-14. This regimen will be repeated on a 21-day cycle for a total of 18 weeks (6 cycles). Subjects receiving FOLFOX will follow the mFOLFOX6 regimen. This regimen entails intravenous administration of 5-FU, leucovorin, and oxaliplatin on day 1, and 5-FU continuous infusion over 46-48 hours (days 1-2) of each cycle, every other week. This regimen will be repeated on a 14-day cycle for a total of 16 weeks (8 cycles).

[0358] **SCRT**: SCRT is delivered with 6 MV to 15 MV photons from a linear accelerator in 5 daily fractions. 3D-conformation radiotherapy (3D-CRT) or intensity modulated radiation (IMRT) can be used depending on the clinical scenario. The treatment planning system has a

record and verification record of each treatment time and dose delivered. Linear accelerators with a minimum energy of 6MV will be used. 3D-CRT using a 3- or 4-field plan or a multiple-field technique using intensity modulated radiotherapy (IMRT) is acceptable. Radiation will be delivered 5 business days/week, once per day, at 500 cGy/day. Daily image guidance to ensure accurate targeting of the tumor and at-risk lymph node regions is recommended, but not required. Radiation is preferably started on a Monday, but this is at the discretion of the radiation oncologist.

[0359] Uninterrupted treatment is planned. Acute side effects of radiation usually do not present until 7-10 days after the completion of SCRT. Treatment interruptions and modifications should be made at the discretion of the treating physician. The following are recommendations provided as a guide: The treating physician should consider holding SCRT in subjects with Grade 3 or higher non-hematologic, except for Grade 3 diarrhea unless persisting for more than 7 days despite provision of appropriate care such as anti-diarrheal medications, or Grade 4 hematologic adverse events attributable to SCRT. If SCRT is held it is recommended to wait until the toxicity resolves to less than Grade 2 before resuming.

[0360] **Capecitabine**: Capecitabine is an oral prodrug of 5-FU. 5-FU is a fluoropyrimidine antimetabolite considered to act primarily as an inhibitor of thymidylate synthase. Capecitabine is supplied as biconvex, oblong film-coated 500 mg tablets and stored tightly closed at 25 degrees C (77 degrees F). Capecitabine is stable for brief periods at 15 to 30 degrees C (59 to 86 degrees F). Tablets should be taken orally within 30 minutes after meals to improve absorption.

[0361] Capecitabine is commercially-available as a multisource product. For this study, locally-obtained commercial supplies of Capecitabine will be used.

[0362] **Oxaliplatin**: Oxaliplatin is an organoplatinum complex in which the platinum atom is complexed with 1,2-diaminocyclohexane with an oxalate ligand as a leaving group. Platinum content is 48.1% to 50.1%. Oxaliplatin-lyophilized powder is reconstituted by adding 10 mL (for the 50 mg vials) or 20 mL (for the 100 mg vials) of water for injection, or dextrose 5% in water, which yields a 5 mg/mL solution. This solution is further diluted for infusion with 250 mL to 500 mL dextrose 5% in water. The reconstitution or final dilution is generally not performed with a sodium chloride solution. Oxaliplatin is also available as a solution for injection 50 mg/10 mL (10 mL), 100 mg/20 mL (20 mL), and 200 mg/40 mL (40 mL). Needles, syringes, catheters, or intravenous administration sets containing aluminum should not be used with oxaliplatin. As with other platinum compounds, contact with aluminum may result in a black precipitate.

Oxaliplatin will be administered by intravenous infusion over 120 minutes or according to standard institutional guidelines. Infusion time may be prolonged (up to 6 hours) in subjects experiencing pharyngolaryngeal dysesthesia. Intact vials should be stored at room temperature. Reconstituted solutions are stable for 24 hours under refrigeration. Solution further diluted in DSW is stable for 6 hours at room temperature or 24 hours under refrigeration. Oxaliplatin is commercially-available as a multisource product. For this study, locally-obtained commercial supplies of oxaliplatin will be used.

[0363] **Fluorouracil (5-FU)**: 5-FU is a fluoropyrimidine antimetabolite considered to act primarily as an inhibitor of thymidylate synthase. 5-FU is supplied as a colorless-to-faint yellow solution in 10-mL single use vials. Each 10 mL solution contains 500 mg 5-FU, with pH adjusted to approximately 9.2 with sodium hydroxide. 5-FU vials may be stored at room temperature but should be protected from light. 5-FU is administered directly as an IV bolus injection and as a continuous infusion. No dilution is required. 5-FU is commercially available as a multisource product. For this study, locally obtained commercial supplies of 5-FU will be used.

[0364] **Leucovorin**: Leucovorin is a mixture of diastereoisomers of 5-formyl derivative of tetrahydrofolic acid. The active component is the (-)-L-isomer known as Citrovorum. Leucovorin is useful as an antidote to drugs which act as folic acid antagonists. Leucovorin may be reconstituted with bacteriostatic water for injection (BWO) or with sterile water for injection. Solutions should be further diluted in DSW, 0.9% NaCl or Ringers solution for infusion over 2 hours. Leucovorin will be administered as a 400 mg/m^2 IV infusion over 2 hours post-oxaliplatin administration or according to standard institutional guidelines. Leucovorin may also be administered concurrently with oxaliplatin, via same infusion lines or according to standard institutional guidelines. Intact vials should be stored at room temperature and protected from light. Solutions reconstituted with BWI are stable for at least 7 days at room temperature. Leucovorin is commercially-available as a multisource product. For this study, locally-obtained commercial supplies of leucovorin will be used.

[0365] **Consolidation Chemotherapy**: Initiation of consolidation CTX should occur within 4 weeks post-SCRT completion ±14 days. The CapeOX and FOLFOX regimens used in this clinical trial represent standard-of-care for treatment of subjects with LARC. In effort to prevent adverse events, all participants are recommended to be treated with anti-emetics and supportive agents.

[0366] *CapeOX*: Oxaliplatin will be delivered at 130 mg/m^2 IV over two hours Day 1 or according to standard institutional guidelines and capecitabine at 1000 mg/ m^2 BID PO on Days 1-14. Capecitabine dose will be rounded up or down in increments of 500 mg for each dose. They will be repeated on a 21-day cycle, for a total of 18 weeks/6 cycles (maximum total cumulative oxaliplatin dose 520 mg/m^2).

[0367] *FOLFOX*: There are several variations of the basic FOLFOX regimen. The specific version of the FOLFOX regimen that will be used in this trial is modified, or mFOLFOX6. This entails administration of 5-FU and leucovorin all on day 1 and administration of 85 mg/m^2 of oxaliplatin. Instead of referring to the regimen as mFOLFOX6, we refer to this more simply as FOLFOX.

[0368] Participants will receive 8 cycles of FOLFOX, administered every other week, FOLFOX will be initiated on Day 1 of each cycle. Participants will receive oxaliplatin 85 mg/m^2 IV (over 120 minutes or according to standard institutional guidelines), leucovorin 400 mg/m^2 IV (over 120 minutes or according to standard institutional guidelines), 5-FU 400 mg m^2 IVP, and 5-FU 1200 mg/2/day continuous infusion over 2 days (total dose of 2400 mg/m^2 over 46-48 hours) for a total of 16 weeks/8 cycles.

[0369] Treatment Evaluation during TNT: Subjects undergo clinical response at Week 4 (± 14 days) and clinical and molecular response assessment 8 ± 2 weeks following SCRT-TNT. Completion of SCRT is defined as the last day of radiation therapy and completion of TNT is defined as the last day of capecitabine for CapeOX or the 5-FU disconnect date for FOLFOX.

1. Subjects present with histologically-confirmed diagnosis of adenocarcinoma of the rectum.
2. Subjects present with rectal cancer clinical stage II (cT3-4, N-) or stage III (cT any, N+) based on MRI.
3. Subjects are eligible for total mesorectal excision (TME).
4. Subjects with no evidence for distant metastasis.
5. Subjects with no prior pelvic radiation therapy.
6. Subjects with no prior chemotherapy.
7. Subjects who are 18 years of age or older.
8. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2.

9. Women with childbearing potential (WOCBP) who are negative for pregnancy test (urine or blood) and who agree to use effective contraceptive methods from trial screening and throughout the study.

[0370] Subjects are excluded from the study if any of the following criteria apply:

1. Subjects are unable to undergo MRI.
2. Subjects are receiving other anticancer or experimental therapy.
3. Women who are pregnant or breast feeding.
4. Subjects have any other concurrent medical or psychiatric condition or disease which in the investigator's judgment, would make them inappropriate candidates for entry into the study.
5. Subjects have a body mass index (BMI) <18.5 kg/m^2 or >40 kg/m^2 or, serious or refractive cachexia or anorexia that, in the investigator's opinion, realistically prohibits subjects from having energy or appetite sufficient to reliably engage in a strict medical food regimen for an extended time. (BMI <20 and ≥18.5 is excluded if any of the following are true: ≥5% weight loss in the last month; or ≥7.5% weight loss in the last 3 months; or eating <75% of estimated energy requirements in the last month; or consuming <75% of the subject's usual caloric intake in the last month).
6. Subjects have insulin-dependent diabetes.
7. Subjects who must take medications that impact proline, serine, glycine levels (refer to **TABLE 4** for a list of commonly known medications that can impact proline, serine, and glycine levels).
8. Inability or unwillingness to comply with study and/or follow-up procedures, or medical food modifications described in the protocol.
9. Subjects with a condition (including gallbladder disease and/or fatty acid oxidation disorders) where high-fat or fatty food is contraindicated.
10. Presence of any condition (*e.g.*, persistent diarrhea) that renders the subject unable to satisfactorily chew, swallow, digest, or tolerate the majority of foods and liquids of the NEAAR dietary regimen.
11. Taking or needs to take any protein or amino acid containing nutritional supplements (*e.g.*, Ensure®).
12. History of confirmed food allergy.

13. Subjects have active wound or skin graft that would require a significant increase in protein requirements for skin integrity and healing.

TABLE 4

Medication or Supplement Name
Collagen
Cartilage
Hyaluronic acid
Probiotics
Turmeric with bioperine (or black pepper extract)
Supplements that contain gelatin as an ingredient
Liquid medications (over-the-counter or prescribed) will be avoided, given that they are often formulated with flavoring and/or sweetening agents
Fiber supplements (*e.g.*, Citrucel) should be avoided. MiraLAX (*i.e.*, polyethylene glycol) is recommended if required.
Lithium (may cause lithium blood levels to rise as result of water loss during transition)
Antipsychotic medications such as risperidone (Risperdal-Janssen), aripiprazole (Abilfy-Otsuka), and quetiapine fumarate (Seroquel-AstraZeneca)
Epilepsy drugs, especially divalproex sodium, zonisamide, and topiramate.

[0371] *Study Procedure*: Each subject's plasma proline, serine, and glycine concentrations and metabolic health are tracked over time. Subjects are administered a standardized dietary regimen comprising medical food and a dietary product disclosed herein, where the dietary regimen includes all essential/non-essential amino acids and nutrients except for proline, serine, and glycine. The standardized dietary regimen can be referred to as NEAAR dietary regimen. Subjects are treated with total neoadjuvant therapy comprising short-course radiotherapy followed by consolidative chemotherapy per standard-of-care. Subjects consume the NEAAR dietary regimen at least 24 hours prior to and throughout administration of radiotherapy. Refer to **TABLE 2** for a short-course radiotherapy treatment plan. For example, radiotherapy is administered on a Monday, NEAAR dietary regimen is consumed Sunday, Monday, Tuesday, Wednesday, Thursday, and Friday. Following administration of short-course radiotherapy, subjects consume the NEAAR dietary regimen for 5 consecutive days out of 7 days each week. Following radiotherapy, subjects consume NEAAR dietary regimen for approximately 3 weeks prior to administration of chemotherapeutic regimens per standard-of-care. The

chemotherapeutic regimens are either capecitabine and oxaliplatin (CapeOX) administered on a 21-day cycle for 6 cycles.

[0372] Refer to **FIG. 1** for an example CapeOX trial schema; 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) are administered on a 14-day cycle for 8 cycles. Subjects are administered the NEAAR dietary regimen for at least 24 hours prior to short course radiotherapy (SCRT). Administration of the NEAAR dietary regimen continues for 8 months. NEAAR dietary regimen administration is intermittent over this period; *e.g.*, NEAAR is given on 6 consecutive days per week with one day per week on habitual diet during SCRT phase, and then NEAAR is given on 2-5 consecutive days per week with 5-2 days per week on habitual diet during chemotherapy phase

[0373] Refer to **FIG. 2** for an example FOLFOX trial schema. Subjects are administered the NEAAR dietary regimen for at least 24 hours prior to short course radiotherapy (SCRT). Administration of the NEAAR dietary regimen continues for 8 months. NEAAR dietary regimen administration is intermittent over this period; *e.g.*, NEAAR is given on 6 consecutive days per week with one day per week on habitual diet during SCRT phase, and then NEAAR is given on 2-5 consecutive days per week with 5-2 days per week on habitual diet during chemotherapy phase

[0374] The 5 consecutive days of NEAAR dietary regimen consumption include 1 day before chemotherapy administration and during chemotherapy administration. For example, if either CapeOX or FOLFOX are administered Tuesday and Wednesday, NEAAR dietary regimen is consumed Monday, Tuesday, Wednesday, Thursday, Friday and subjects eat their habitual food on Saturday and Sunday. In addition to the 2 days of habitual diet each week, subjects are allowed to consume habitual diet for the entire week on planned weeks in consultation with registered dieticians.

[0375] On days of habitual diet there are no specific prescribed limits or strict guidelines about what a subject can and cannot eat; subjects are encouraged to eat a 'balanced diet' comprising protein, carbohydrates, and fat. On days of habitual diet, subjects complete a daily Food Quality and Quantity Questionnaire. Allowing subjects to consume habitual food on 2 out of 7 days and during scheduled weeks encourages full compliance during the 5 out of 7 days with the NEAAR dietary regimen, because subjects can look forward to having a regular "break" from the NEAAR dietary regimen.

[0376] One mechanism of treatment by the NEAAR dietary regimen is that it can make a tumor more sensitive to other therapies. Consequently, the NEAAR dietary regimen is administered prior, during, and after radiotherapy and chemotherapy. The maximum potential management of a subject's disease is mechanistically predicted to be greatest on days before, during, and just after radiotherapy or chemotherapy are administered. Metabolic adaptation (of systemic and / or tumor metabolism) to the NEAAR dietary regimen is minimized by the intermittent schedule, which produces a greater benefit on disease management than giving the NEAAR dietary regimen in a constant fashion.

[0377] *Assessment of Subjects and Efficacy*: Efficacy is monitored through a combination of diagnostic modalities, including endoscopy; MRI of the rectum or pelvis; digital rectal examination; CT scans of the chest, abdomen, and pelvis; and cancer specific biomarkers over the study's time-points. A full physical examination includes, at a minimum, assessments of the gross neuro, heart, lungs, abdomen, and extremities. Height (initial screening only) and weight are measured and recorded at each visit. During study visits the subject is asked if he or she has been compliant with the NEAAR dietary regimen protocol and the subject's answers are recorded. Compliance is further assessed by the subject's Food Quality and Quantity questionnaire and via the subject's amino acid-level assessments. Investigators document and review laboratory results to assess any abnormal results, which are reported as either clinically significant (CS) or not CS (NCS). Laboratory abnormalities are not automatically regarded as an adverse event (AE) unless accompanied by signs or symptoms related to the abnormal lab. The schedule of activities for FOLFOX administration is provided in **TABLE 5**.

TABLE 5

Visit Name	**Screening**	**Intervention Period**					
		V1	**V2**	**V3-10**	**V11**	**V12**	**V13**
Study Visit Day	Day -45 to Day -1	Day 1 (±1 day)	Week 4 (±14 days)	Weeks 5, 6, 8, 10, 12, 16, 19, 23	Week 26 (± 14 days)	Week 32	Week 36 (± 14 days)
Informed consent	X						
Inclusion & exclusion criteria	X						
Demography	X						
Medical History	X						
Prior & Concomitant Medication	X	X					
Full physical examination including height[a] & weight	X	X	X		X		X
Rectal examination	X		X		X		X
Vital Signs	X	X	X		X		X
ECOG Performance	X	X	X		X		X
ECG	X						
Blood collection for CBC, CMP, and magnesium	X	X	X		X		X
Blood collection for lipid panel	X		X		X		X
Blood collection for amino acid panel[b]	X	X[b]	X	X	X	X	X
Blood collection for circulating tumor markers	X	X	X (monthly)				
Pregnancy test (WOCBP only)	X						
CT CAP ± PET[c]	X				X		X
MRI Rectum or Pelvis[d]	X				X		X
Endoscopy	X		X		X		X
Biopsy			X		X		X
Signatera ctDNA	X				X		X
Altera tumor molecular profiling	X						
Tumor tissue enzyme expression (central lab)	X		X (When additional tumor tissue is available including surgical specimen, if performed)				
Tumor tissue RNA & DNA sequencing	X						
NEAAR dietary regimen	X	X	X	X	X	X	X
Short-course radiation therapy		X (5 days)					
FOLFOX Chemotherapy Start[e]			X				
Adverse Events		X					

Visit Name	Screening	Intervention Period					
		V1	V2	V3-10	V11	V12	V13
Study Visit Day	Day -45 to Day -1	Day 1 (±1 day)	Week 4 (±14 days)	Weeks 5, 6, 8, 10, 12, 16, 19, 23	Week 26 (± 14 days)	Week 32	Week 36 (± 14 days)
Virtual visit with a RD	X	X (as scheduled by RD, including exit visit at study completion or discontinuation)					
Food Quality & Quantity Questionnaires via the App	X	X	X	X	X	X	X
Weekly Body Weight via the App		X	X	X	X	X	X

[a] Height at screening visit only
[b] Blood collection for amino acid panel collected approximately 2 hours (+/- 30 min) after meals. Two blood collections on different days should occur during screening to obtain baseline measurement. Blood collections throughout the study should occur on day 2 or 3 of NEAAR dietary regimen days.
[c] CT CAP does not have to be repeated prior to Visit 1 if existing CT had been performed < 4 weeks prior to Visit 1; CT CAP to be repeated approximately every 12 weeks after start of chemotherapy.
[d] Baseline MRI will be a rectum and pelvic MRI and does not have to be repeated if an existing pelvic MRI has been performed < 4 weeks prior to Visit 1. Subsequent MRIs will be rectal MRIs.
[e] FOLFOX (D1 fol/5-FU/OX IV; D2: fol/5-FU IV; D3-D14: rest) is 8 cycles, and each cycle is 14 days.

[0378] The subject answers questionnaires both on- and off-site. The body composition questionnaire is completed at baseline and weekly by the subject and comprises of entering the subject's weight and body fat percentage after using a provided scale as instructed. The subject answers a daily questionnaire on food quality, quantity, and taste of each meal consumed on both NEAAR dietary regimen and habitual food days. The subject answers a monthly questionnaire on his or her general quality of life, including general well-being, physical activity, social activities, emotional state, and symptoms of fatigue and appetite. The Eastern Cooperative Oncology Group (ECOG) Performance Status scale is used to assess disease progression and how it affects activities of daily living at each site visit. The scale is a Grade from 0 meaning fully active to 5 for deceased. Cancer biomarkers and tumor biopsy are collected at select site visits, and amino acid profiles are collected at each site visit.

[0379] *Adverse Events*: Subjects are carefully monitored for adverse events (AEs) from the time of consent through Study Discontinuation. The investigator is responsible for identifying, documenting, and recording events that meet the definition of an AE or serious adverse event (SAE) and are responsible for following all AEs, including AEs that are serious, considered related to the NEAAR dietary regimen or study procedures, or that caused the subject to discontinue. AEs are assessed in terms of seriousness, severity, expectedness, relationship to the NEAAR dietary regimen (causality), and outcome. Disease progression is not characterized an AE or SAE unless the investigator feels that the progression was clearly unusual for rectal

cancer in quantitative or qualitative aspects. The AE reporting period will start with the first day of NEAAR dietary regimen consumption and will end 30 days after consumption of the last meal. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 will be utilized for toxicity evaluation.

[0380] An AE is any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention related. AEs are further defined as those untoward signs or symptoms that are not otherwise related to the subject's underlying medical conditions, comorbid condition present at the time of enrollment, or commonly-known side effects from any concomitant therapeutics.

[0381] An adverse event is classified as serious (SAE) if the AE results in any of the following:

- Death.
- Life-threatening.
- Subject was at substantial risk of dying at the time of the AE or use or continued use of the NEAAR dietary regimen might have resulted in death.
- If the AE resulted in admission to hospital or prolonged a hospitalization. Emergency room visits that do not result in admission to hospital are not considered serious unless the event met one of the other criteria for seriousness. Planned hospitalization for a pre-existing condition without serious deterioration in health is not considered an SAE.
- If the AE resulted in a substantial disruption of a person's ability to conduct normal life functions, *i.e.*, the AE resulted in significant, persistent, or permanent change, impairment, damage or disruption in the subject's body function/structure, physical activities, and/or QOL.
- Congenital Anomaly/Birth Defect - if it is suspected that exposure to the NEAAR dietary regimen prior to conception or during pregnancy may have resulted in an adverse outcome in the child.

[0382] Other events (Important Medical Events) are considered serious when the event does not fit the other outcomes, but the event may jeopardize the subject and may require medical or surgical intervention (treatment) to prevent one of the other outcomes. Examples include allergic bronchospasm (a serious problem with breathing) requiring treatment in an emergency room, serious blood dyscrasias (blood disorders), or seizures/convulsions that do not result in hospitalization. The development of drug dependence or drug abuse is also an example of

important medical events. Disease progression is not considered an AE or SAE unless the Investigator feels that the progression was clearly unusual for colorectal cancer in quantitative or qualitative aspects.

[0383] Treatment interruptions and modifications should be made at the discretion of the treating physician. The following dose reduction and modification tables (**TABLES 6-8**) should be used as a guide. If the treating physician feels that it is feasible to continue treatment without interruption, and/or use a modification other than what is indicated below, and without putting the participant at undue risk, then the treating physician may proceed with treatment as planned.

TABLE 6

Dose reductions for oxaliplatin, leucovorin, and 5-FU				
Drug	**Dose level 0*** **(mg/m^2)**	**Dose level -1** **(mg/m^2)**	**Dose level -2** **(mg/m^2)**	**Dose level -3** **(mg/m^2)**
Oxaliplatin	85	65	50	0
Leucovorin	400	320	260	260
5-FU bolus	400	320	260	260
5-FU infusion	1200	900	720	720

*Dose level 0 refers to the starting dose

[0384] **TABLE 7** describes those modifications to be used for Day 1 of a new cycle of FOLFOX therapy and are suggested guidelines for treatment modifications. All dose modifications in a new cycle are based upon the most severe toxicity observed in the previous cycle. Any modifications to treatment should be made at the discretion of the treating physician.

TABLE 7

Dose modifications for oxaliplatin, leucovorin, and 5-FU			
Toxicity: CTCAE grade	**Oxaliplatin**	**5-FU**	**Leucovorin**
Neutropenia or thrombocytopenia			
Grade 2	Hold to resolution to ≤ grade 1. Resume at same dose.	Hold to resolution to ≤ grade 1. Resume at same dose.	Hold to resolution to ≤ grade 1. Resume at same dose.
Grade 3 or 4	Hold to resolution to ≤ grade 1. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 1. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 1. Resume at same dose.
Neutropenic fever or infection			
Any grade	Hold to resolution to ≤ grade 1. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 1. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 1. Resume at same dose.

Dose modifications for oxaliplatin, leucovorin, and 5-FU			
Toxicity: CTCAE grade	**Oxaliplatin**	**5-FU**	**Leucovorin**
Diarrhea			
Grade 3 or 4	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at same dose.
Mucositis			
Grade 2	No modification	No modification	No modification
Grade 3	No modification	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.
Grade 4	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.
Vomiting			
Grade 0-2	No modification	No modification	No modification
Grade 3	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at same dose.	Hold to resolution to ≤ grade 2. Resume at same dose.
Grade 4	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at same dose.
Pulmonary			
Cough, dyspnea, hypoxia, pneumonitis, or pulmonary infiltrates ≥ grade 3	Hold oxaliplatin until interstitial lung disease is ruled out. Resume at same dose.	No modification	No modification
Other non-hematologic toxicities			
Grade 0-2	No modification	No modification	No modification
Grade 3-4	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at dose decreased by 1 level.	Hold to resolution to ≤ grade 2. Resume at same dose.

[0385] **TABLE 8** describes those modifications to be used for Day 1 of a new cycle of CapeOX therapy and are suggested guidelines for treatment modifications. All dose modifications in a new cycle are based on the most severe toxicity observed in the previous cycle. Any modifications to treatment should be made at the discretion of the treating physician.

TABLE 8

Dose reductions for oxaliplatin and capecitabine				
Drug	**Dose level 0*** **(mg/m^2)**	**Dose level -1** **(mg/m^2)**	**Dose level -2** **(mg/m^2)**	**Dose level -3** **(mg/m^2)**

Oxaliplatin	130	100	80	65
Capecitabine	1000	800	640	510

*Dose level 0 refers to the starting dose.

[0386] *Study Schedule: Pre-trial Visit* – 45 days to 1 day prior to expected Day 1 of radiotherapy administration (Initial Screening): Subjects are screened for eligibility and considered enrolled when informed consent is signed. The following study procedures for standard-of-care evaluations should be performed within 45 days of the expected administration of radiotherapy, unless otherwise indicated:

- Informed Consent
- Confirmation of eligibility (review and confirmation of inclusion/exclusion criteria)
- Recording of demographics; medical history; and record of medications, both prior and concurrent
- Full physical examination, including height and weight
- Vital signs
- Rectal examination
- ECOG assessment
- ECG
- Laboratory collection for: CBC w/diff, CMP, Urinalysis, Serum hCG for women of childbearing potential (any premenopausal female capable of becoming pregnant) must have a negative pregnancy test, Lipid Panel, circulating tumor markers including CEA, and Magnesium
- Blood draw for Amino Acids (Proline, Glycine, Serine) preferably 2-3 hours after the subject's last habitual meal
- Eligible subjects proceed as follows: subject returns to the site for a second blood draw for Amino Acids (Proline, Glycine, Serine), 2-3 hours after the subject's habitual breakfast or lunch
- CT of the chest, abdomen, and pelvis with or without PET
- MRI of the rectum or the pelvis
- Endoscopy
- Biopsy, signatera ctDNA and tumor molecular profiling. Tumor enzyme expression performed at central laboratory, and tumor RNA & DNA sequencing

- A smart scale is provided to the subject and the subject receives a call from a registered dietician. During this call, the dietician: reviews the subject's dietary preferences, instructs the subject on how to operate his or her smart scale, instructs the subject on use of a HIPAA-compliant App (the "App"), and gives specific medical food instructions. The App allows the subject to communicate with the registered dietitian regarding any nutrition-related concerns that may interfere with his or her ability to comply with the NEAAR dietary regimen. The subject is provided with study supplies prior to his or her first dose of radiotherapy. The subject ingests the NEAAR dietary regimen for at least 1 day prior to the administration of radiotherapy

[0387] *First Visit* – Day 1: The subject receives his or her first dose of radiotherapy. In addition to radiotherapy administration, the following procedures will occur during this visit:

- Full physical exam
- Vital signs and weight
- Recording of prior and concomitant medication.
- ECOG assessment
- Laboratory collection for: CBC w/diff, CMP, Urinalysis, blood, or urine hCG for women of childbearing potential, Lipid Panel, Magnesium
- Blood draw for Amino Acids (Proline, Glycine, Serine): the timing of this blood draw is dependent on when the subject's last NEAAR dietary regimen was ingested and preferably should occur 2-3 hours after a NEAAR dietary regimen consumption
- Assessment of NEAAR dietary regimen tolerability and compliance
- Adverse Event Assessment
- Recording of body weekly via the HIPPA-compliant App

[0388] *Second Visit* – Clinical Response Assessment Week 4 –3 weeks after completion of radiotherapy. The subject receives his or her 1st dose of chemotherapy. If the chemotherapy is held, the study visit still proceeds. The following procedures occur during this visit:

- Full physical exam
- Vital signs and weight
- Rectal examination
- ECOG assessment
- Laboratory collection for (before chemotherapy if applicable): CBC w/diff, CMP, and lipid panel

- Blood draw for Amino Acids (Proline, Glycine, Serine): the timing of this blood draw is dependent on when the subject's last NEAAR dietary regimen was and preferably should occur 2-3 hours after a NEAAR dietary regimen consumption
- Endoscopy
- Biopsy, signatera ctDNA and tumor molecular profiling. Tumor enzyme expression performed at central laboratory if additional tumor tissue is available
- Assessment of NEAAR dietary regimen tolerability and compliance
- Adverse Event Assessment
- Virtual visit with registered dietician
- Recording of weekly body weight via the HIPPA-compliant App

[0389] *Third – Tenth Visits* – For subjects receiving CapeOX, visits three through ten occur at weeks 5, 6, 8, 10, 13, 17, 19, and 23. For subjects receiving FOLFOX, visits three through ten occur at weeks 5, 6, 8, 10, 12, 16, 19, 23. During these visits, the following procedures will occur:

- Blood draw for Amino Acids (Proline, Glycine, Serine): the timing of this blood draw is dependent on when the subject's last NEAAR dietary regimen was and preferably should occur 2-3 hours after a NEAAR dietary regimen consumption
- Laboratory collection for circulating tumor markers will occur monthly throughout the duration of the study
- Assessment of NEAAR dietary regimen tolerability and compliance
- Adverse Event Assessment
- Virtual visit with registered dietician
- Recording of weekly body weight via the HIPPA-compliant App

[0390] *Eleventh Visit* – Clinical response 8 weeks after completion of chemotherapy regimen. For subjects receiving CapeOX, the eleventh visit occurs at Week 28. For subjects receiving FOLFOX, the eleventh visit occurs at Week 26. The clinical response of each subject will be assessed. The following procedures will occur:

- Full physical exam
- Vital signs and weight
- Rectal examination
- ECOG assessment

- Laboratory collection (before chemotherapy if applicable) for: CBC w/diff, CMP. Laboratory collection for circulating tumor markers (monthly)
- Blood draw for Amino Acids (Proline, Glycine, Serine): the timing of this blood draw is dependent on when the subject's last NEAAR dietary regimen was and preferably occurs 2-3 hours after a NEAAR dietary regimen consumption
- CT of the chest, abdomen, and pelvis with or without PET, contrast preferred but not required
- MRI of the rectum or pelvis
- Endoscopy
- Biopsy, and Signatera ctDNA. Tumor enzyme expression performed at central laboratory if additional tumor tissue is available
- Assessment of NEAAR dietary regimen tolerability and compliance
- Adverse Event Assessment
- Virtual visit with registered dietician
- Recording of weekly body weight via the HIPPA-compliant App

Subjects with an incomplete response or no response will proceed with standard-of-care TME. Subjects with a near complete response may undergo a repeat assessment 10 weeks-post prior assessment. Subjects with a clinical complete response will be considered as having completed the study

[0391] *Twelfth Visit* – For subjects receiving CapeOX, the twelfth visit occurs at Week 32. For subjects receiving FOLFOX, the twelfth visit occurs at Week 34. During the visit, the following procedures will occur:

- Blood draw for Amino Acids (Proline, Glycine, Serine): the timing of this blood draw is dependent on when the subject's last NEAAR dietary regimen was and preferably occurs 2-3 hours after a NEAAR dietary regimen consumption
- Adverse Event Assessment
- Virtual visit with registered dietician
- Recording of weekly body weight via the HIPPA-compliant App

[0392] *Final Visit* – For subjects receiving CapeOX, the final visit occurs at the latest at Week 38. For subjects receiving FOLFOX, the final visit occurs at the latest at Week 36. The Final Study Visit takes place at a study site after the subject has completed or discontinued the NEAAR dietary regimen and the following final safety assessments are performed:

- Full physical exam
- Vital signs and weight
- Rectal examination
- ECOG assessment
- Laboratory collection (before chemotherapy if applicable) for: CBC w/diff, CMP. Laboratory collection for circulating tumor markers (monthly)
- Blood draw for Amino Acids (Proline, Glycine, Serine): the timing of this blood draw is dependent on when the subject's last NEAAR dietary regimen was and preferably occurs 2-3 hours after a NEAAR dietary regimen consumption
- CT of the chest, abdomen, and pelvis with or without PET
- MRI of the rectum or pelvis
- Endoscopy
- Biopsy. Tumor enzyme expression performed at central laboratory if additional tumor tissue is available
- Assessment of NEAAR dietary regimen tolerability and compliance
- Adverse Event Assessment
- Virtual visit with registered dietician
- Recording of weekly body weight via the HIPPA-compliant app
- Study Discontinuation

[0393] Primary objective: The primary objective is to assess safety, tolerability, and compliance with NEAAR dietary regimen during standard-of-care SCRT-TNT.

[0394] Secondary objectives:

- To evaluate the clinical complete response rate 8 weeks post SCRT-TNT with NEAAR dietary regimen
- To characterize pharmacodynamics of circulating serine, glycine, and proline following NEAAR dietary regimen consumption
- To evaluate the clinical complete response at week 4 post SCRT with NEAAR dietary regimen
- To evaluate molecular ctDNA response at week 4 post SCRT with NEAAR dietary regimen and 8 weeks post SCRT-TNT with NEAAR dietary regimen

[0395] Exploratory objectives:

- To assess genetic determinants of response to SCRT-TNT with NEAAR dietary regimen based on tumor tissue at baseline
- To define metabolic enzyme expression in the tumor at baseline and during NEAAR dietary regimen consumption
- To assess tumor heterogeneity, tumor immune microenvironment, and transcriptional programs activated or repressed in response to NEAAR and TNT
- To assess medical food palatability

[0396] Primary endpoint: The primary endpoint is rate of CTCAE v5.0 non-hematological Grade 3 or higher diarrhea.

[0397] Secondary endpoints:

- Proportion of clinical complete response 8 weeks post SCRT-TNT with NEAAR dietary regimen defined by the Memorial Sloan Kettering (MSK) Regression Schema
- Absolute and relative change from baseline of circulating serine, glycine, and proline
- Proportion of clinical complete response at Week 4-post SCRT with NEAAR dietary regimen
- Descriptive

[0398] Exploratory endpoints:

- Comparison of gene mutation as predictors of disease management with NEAAR dietary regimen
- Comparison of gene expression as predictors of disease management with NEAAAR medical food
- Evaluation of available on-treatment biopsy
- Subject-reported measure via HIPPA-compliant App

[0399] Clinical response will be assessed using the MSK Regression schema in **TABLE 9**. Clinical response at Week 4-post SCRT (Visit 2) will be assessed omitting MRI measurements, while clinical response at Week 8-post TNT (Visit 11) will be assessed with MRI measurements included.

TABLE 9

MSK Regression Schema			
	Clinical Complete Response	**Near Complete Response**	**Incomplete / No Response**
Endoscopy	• Flat, white scar • Telangiectasia • No ulcer • No nodularity	• Irregular mucosa • Superficial ulceration • Mild persisting erythema of the scar	• Visible tumor

MSK Regression Schema			
	Clinical Complete Response	**Near Complete Response**	**Incomplete / No Response**
Digital Rectal Exam	• Normal^	• Smooth induration or minor mucosal irregularity^	• Palpable tumor nodules^
MRI-T2WI	• Normal appearing rectal wall OR • Only fibrosis (dark T2 signal) and no intermediate signal intensity at the site of tumor* AND • No suspicious lymph nodes (Table 6)	• Predominantly fibrosis at the site of tumor* with punctate areas of T2 intermediate signal AND/OR • No suspicious or borderline enlarged lymph nodes (Table 6)	• Predominantly residual tumor with T2 intermediate signal and no or minimal fibrosis at the site of tumor* AND/OR • Suspicious lymph nodes (Table 6) AND/OR • Mucin at the site of tumor***
MRI-DW	• No restricted diffusion** at the site of tumor*	• Punctate areas of restricted diffusion** at the site of tumor*	• Restricted diffusion** at the site of tumor*

EXAMPLE 4: Use of radiotherapy and chemotherapy to treat a colorectal cancer.

[0400] Further to the radiotherapy and chemotherapy courses described in **Example 2**, **Example 4** presents additional example radiotherapy courses (short-course and long-course) and chemotherapy courses.

[0401] For example, the subject is placed on a NEAAR dietary regimen as described herein, which is given one day before starting radiotherapy and on each day that radiotherapy is given. The subject is treated with 500 cGy a day for 5 days. The subject returns to a normal, habitual diet after the 5th day of radiotherapy treatment. **TABLE 10** shows an example short-course radiotherapy regimen.

TABLE 10: Short-Course Radiotherapy

Day number	Diet	Radiotherapy dose
Day 1	Habitual	
Day 2	Habitual	
Day 3	NEAAR	
Day 4	NEAAR	500 cGy
Day 5	NEAAR	500 cGy
Day 6	NEAAR	500 cGy
Day 7	NEAAR	500 cGy
Day 8	NEAAR	500 cGy
Day 9	Habitual	

Day number	Diet	Radiotherapy dose
Day 10	Habitual	
Day 11	Habitual	
Day 12	Habitual	
Day 13	Habitual	
Day 14	Habitual	
Day 15	Habitual	

[0402] Also for example, the subject is placed on a NEAAR dietary regimen as described herein, which is given one day before starting radiotherapy and on each day that radiotherapy is given. The subject is treated with 200 cGy a day for 5 days. The subject returns to a normal, habitual diet after the 5th day of radiotherapy treatment for two days before starting an additional round of radiotherapy. Subsequent radiation therapy cycles are administered within 5 days of an amino-acid depleted diet with 200 cGy of radiation for 5 days, followed by 2 days of a habitual diet. The cycle is repeated as needed (*e.g.*, for 5 cycles, as shown in **TABLE 11**.) **TABLE 11** shows an example long-course radiotherapy regimen.

TABLE 11: Long/Standard-Course Radiotherapy

Day number	Diet	Radiotherapy dose
Day 1	Habitual	
Day 2	Habitual	
Day 3	Habitual	
Day 4	NEAAR	200 cGy
Day 5	NEAAR	200 cGy
Day 6	NEAAR	200 cGy
Day 7	NEAAR	200 cGy
Day 8	NEAAR	200 cGy
Day 9	Habitual	
Day 10	Habitual	
Day 11	NEAAR	200 cGy
Day 12	NEAAR	200 cGy
Day 13	NEAAR	200 cGy
Day 14	NEAAR	200 cGy
Day 15	NEAAR	200 cGy
Day 16	Habitual	
Day 17	Habitual	
Day 18	NEAAR	200 cGy
Day 19	NEAAR	200 cGy

Day number	Diet	Radiotherapy dose
Day 20	NEAAR	200 cGy
Day 21	NEAAR	200 cGy
Day 22	NEAAR	200 cGy
Day 23	Habitual	
Day 24	Habitual	
Day 25	NEAAR	200 cGy
Day 26	NEAAR	200 cGy
Day 27	NEAAR	200 cGy
Day 28	NEAAR	200 cGy
Day 29	NEAAR	200 cGy
Day 30	Habitual	
Day 31	Habitual	
Day 32	NEAAR	200 cGy
Day 33	NEAAR	200 cGy
Day 34	NEAAR	200 cGy
Day 35	NEAAR	200 cGy
Day 36	NEAAR	200 cGy
Day 37	Habitual	
Day 38	Habitual	
Day 39	Habitual	

[0403] If the subject is treated with chemotherapy after the radiotherapy (short-course or long-course), the subject is placed on a cycled diet throughout the chemotherapy. Example Chemotherapy Courses are shown in **TABLE 12**:

TABLE 12: Examples Chemotherapy Courses

Post-Radiation Week	EX: Chemo = CapeOX		EX: Chemo = FOLFOX	
	Radio/Chemo	**Diet**	**Radio/Chemo**	**Diet**
Pre-Radiation		Habitual		Habitual
N/A	Radiation (long or short-course)	NEAAR	Radiation (long or short-course)	NEAAR
1		Habitual		Habitual
2		Habitual		Habitual
3	C1D1	NEAAR	C1D1	NEAAR
4		NEAAR		NEAAR

Post-Radiation Week	EX: Chemo = CapeOX		EX: Chemo = FOLFOX	
	Radio/Chemo	**Diet**	**Radio/Chemo**	**Diet**
5		NEAAR	C2D1	NEAAR
6	C2D1	NEAAR		NEAAR
7		NEAAR	C3D1	NEAAR
8		Habitual		NEAAR
9	C3D1	NEAAR	C4D1	NEAAR
10		NEAAR		Habitual
11		NEAAR	C5D1	NEAAR
12	C4D1	NEAAR		NEAAR
13		NEAAR	C6D1	NEAAR
14		NEAAR		NEAAR
15	C5D1	NEAAR	C7D1	NEAAR
16		Habitual		NEAAR
17		NEAAR	C8D1	NEAAR
18	C6D1	NEAAR		Habitual
19		NEAAR		NEAAR
20		NEAAR		NEAAR
21		NEAAR		NEAAR
22		NEAAR		NEAAR
23		NEAAR		NEAAR
24		Habitual		NEAAR
25		NEAAR		NEAAR
26		NEAAR		Habitual
27		NEAAR		NEAAR
28		NEAAR		NEAAR
29		NEAAR		NEAAR
30		NEAAR		NEAAR
31		NEAAR		NEAAR
32		Habitual		NEAAR
33		NEAAR		NEAAR
34		NEAAR		Habitual
35		NEAAR		NEAAR
36		NEAAR		
37		NEAAR		

NEAAR = week in which NEAAR dietary regimen is given for at least 3 days/week
Habitual = week in which NEAAR dietary regimen is not given

Post-Radiation Week	EX: Chemo = CapeOX		EX: Chemo = FOLFOX	
	Radio/Chemo	**Diet**	**Radio/Chemo**	**Diet**

[0404] For example, in an example chemotherapy course comprising administration of CapeOX, the subject is given a NEAAR dietary regimen at least 3 days a week for 5 to 7 weeks and is given a habitual diet for a week between the weeks in which a NEAAR dietary regimen is given. The subject returns to a normal, habitual diet for 1 week before starting an additional round of 5 to 7 weeks in which a NEAAR dietary regimen is given. A CapeOX chemotherapy course is given with two weeks in between each week in which CapeOX is given. The diet cycle and the CapeOX cycle are repeated as needed (*e.g.*, for 5 diet cycles and for 6 chemotherapy cycles, as is shown in the example CapeOX chemotherapy course in **TABLE 12**).

[0405] Also for example, in an example chemotherapy course comprising administration of FOLFOX, the subject is given a NEAAR dietary regimen at least 3 days a week for 5 to 7 weeks and is given a habitual diet between the weeks in which a NEAAR dietary regimen is given. The subject returns to a normal, habitual diet for 1 week before starting an additional round of 5 to 7 weeks in which a NEAAR dietary regimen is given. A FOLFOX chemotherapy course is given with one week in between each week in which FOLFOX is given. The diet cycle and the FOLFOX cycle are repeated as needed (*e.g.*, for 4 diet cycles and for 8 chemotherapy cycles, as is shown in the example FOLFOX chemotherapy course in **TABLE 12**).

[0406] In the weeks in which the NEAAR dietary regimen is given, the NEAAR dietary regimen is given for at least 3 days of the week. In some examples, the NEAAR dietary regimen is given on an intermittent schedule where NEAAR dietary regimen is given 4 days per week and a habitual diet is given 3 days per week.

[0407] These schedules can be varied such that the NEAAR dietary regimen weeks are every week of a month; such that NEAAR dietary regimen weeks are 3 weeks of a month, with habitual diet for 1 week of the month; such that NEAAR dietary regimen weeks are 2 weeks of a month, with habitual diet for 2 weeks of the month; or such that NEAAR dietary regimen weeks are 1 week of a month, with habitual diet for 3 weeks of the month.

Equivalents

[0408] While the present disclosure has been described in conjunction with the specific embodiments set forth above, many alternatives, modifications and other variations thereof will be apparent to those of ordinary skill in the art. All such alternatives, modifications and variations are intended to fall within the spirit and scope of the present disclosure.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of treating colorectal cancer in a subject in need thereof, the method comprising administering to the subject:

a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of at least two amino acids in the subject as compared to baseline; and

b) a therapeutically effective amount of a radiotherapy.

2. The method of claim 1, wherein the at least two amino acids comprise serine and glycine, serine and proline, or glycine and proline.

3. The method of claim 1 or 2, wherein the dietary regimen reduces an average plasma level of at least three amino acids.

4. The method of claim 3, wherein the at least three amino acids comprise serine, glycine, and proline.

5. The method of any one of claims 1-4, wherein the dietary regimen reduces an average plasma level of serine in the subject by at least about 20% as compared to baseline, reduces an average plasma level of glycine in the subject by at least about 20% as compared to baseline, reduces an average plasma level of proline in the subject by at least about 20% as compared to baseline, or a combination thereof.

6. The method of any one of claims 1-5, wherein the dietary regimen comprises less than about 500 mg/day of proline, less than about 500 mg/day of serine, less than about 500 mg/day of glycine, or a combination thereof.

7. The method of any one of claims 1-6, wherein the dietary regimen comprises less than 25% of an RDA of serine for the subject's age group, less than 25% of an RDA of glycine for the subject's age group, less than 25% of an RDA of proline for the subject's age group, or a combination thereof.

8. The method of any one of claims 1-7, wherein the dietary regimen comprises less than 20% of an RDA of serine for the subject's age group, less than 20% of an RDA of glycine for the subject's age group, less than 20% of an RDA of proline for the subject's age group, or a combination thereof.

9. The method of claim 7 or 8, wherein the RDA of serine for an adult subject is about 28 mg/kg/day, the RDA of glycine for an adult subject is about 50 mg/kg/day, and the RDA of proline for an adult subject is about 55 mg/kg/day.

10. The method of any one of claims 1-9, wherein the dietary regimen is substantially devoid of serine, substantially devoid of glycine, substantially devoid of proline, or a combination thereof.

11. The method of any one of claims 1-10, wherein the dietary regimen comprises about 8% to about 20% of carbohydrates from diet-only kcals, about 1% to about 5% of protein from diet-only kcals, and about 75% to about 91% of fat from diet-only kcals.

12. The method of any one of claims 1-10, wherein the dietary regimen comprises about 9% of carbohydrates from diet-only kcals, about 2% of protein from diet-only kcals, and about 89% of fat from diet-only kcals.

13. The method of any one of claims 1-10, wherein the dietary regimen comprises about 18% of carbohydrates from diet-only kcals, about 2% of protein from diet-only kcals, and about 80% of fat from diet-only kcals.

14. The method of any one of claims 1-13, wherein the dietary regimen is substantially a sole source of calories for the subject.

15. The method of any one of claims 1-14, wherein the dietary regimen comprises administration of a dietary product to the subject.

16. The method of claim 15, wherein the dietary product comprises a plurality of amino acids, optionally wherein the plurality of amino acids is a powder that is reconstituted with water prior to administration to the subject.

17. The method of any claim 15 or 16, wherein the dietary product comprises histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

18. The method of any one of claims 15-17, wherein the dietary product comprises one or more of cysteine, cystine, arginine, tyrosine, alanine, aspartic acid, asparagine, glutamic acid, glutamine, and taurine.

19. The method of any one of claims 15-18, wherein the dietary product is devoid of serine, glycine, or proline.

20. The method of any one of claims 15-19, wherein the dietary product is devoid of serine and glycine, serine and proline, or glycine and proline.

21. The method of any one of claims 15-20, wherein the dietary product is devoid of serine, glycine, and proline.

22. The method of any one of claims 15-21, wherein the dietary product is substantially a sole source of amino acids for the subject.

23. The method of any one of claims 1-22, wherein the dietary regimen comprises administration of a diet to the subject.

24. The method of claim 23, wherein the diet comprises less than about 500 mg/day of proline, less than about 500 mg/day of serine, less than about 500 mg/day of glycine, or a combination thereof.

25. The method of claim 23 or 24, wherein the diet comprises less than 25% of an RDA of serine for the subject's age group, less than 25% of an RDA of glycine for the subject's age group, less than 25% of an RDA of proline for the subject's age group, or a combination thereof.

26. The method of any one of claims 23-25, wherein the diet comprises less than 20% of an RDA of serine for the subject's age group, less than 20% of an RDA of glycine for the subject's age group, less than 20% of an RDA of proline for the subject's age group, or a combination thereof.

27. The method of claim 25 or 26, wherein the RDA of serine for an adult subject is about 28 mg/kg/day, the RDA of glycine for an adult subject is about 50 mg/kg/day, and the RDA of proline for an adult subject is about 55 mg/kg/day.

28. The method of any one of claims 23-27, wherein the diet comprises about 1200 kcals/day to about 2600 kcals/day.

29. The method of any one of claims 23-28, wherein the diet comprises about 0.8 g/kg/day to about 1.2 g/kg/day of protein.

30. The method of any one of claims 23-29, wherein the diet is a high-fat, low-carbohydrate, low-protein diet.

31. The method of any one of claims 23-30, wherein the diet comprises about 8% to about 20% of carbohydrates by calories, about 1% to about 5% of protein by calories, and about 75% to about 91% of fat by calories.

32. The method of any one of claims 23-30, wherein the diet comprises about 9% of carbohydrates by calories, about 2% of protein by calories, and about 89% of fat by calories.

33. The method of any one of claims 23-30, wherein the diet comprises about 18% of carbohydrates by calories, about 2% of protein by calories, and about 80% of fat by calories.

34. The method of any one of claims 23-33, wherein the diet is substantially a sole source of carbohydrates for the subject.

35. The method of any one of claims 23-34, wherein the diet is substantially a sole source of fat for the subject.

36. The method of any one of claims 23-35, wherein the diet is a low glycemic index diet.

37. The method of any one of claims 1-36, wherein the dietary regimen is administered at least 4 times per week, at least 5 times per week, or at least 6 times per week.

38. The method of claim 37, wherein the dietary regime is administered at least 4 times per week for 5 weeks or at least 6 times per week for 1 week.

39. The method of any one of claims 1-38, wherein the radiotherapy is administered 5 days per week.

40. The method of any one of claims 1-39, wherein the radiotherapy is administered once per day.

41. The method of any one of claims 1-40, wherein the radiotherapy is administered at an amount of about 6 MV to about 15 MV photons from a linear accelerator in 5 daily fractions.

42. The method of any one of claims 1-40, wherein the radiotherapy is administered at an amount of about 6 MV photons from a linear accelerator in 5 daily fractions.

43. The method of any one of claims 1-42, wherein the radiotherapy is a short-course radiation therapy.

44. The method of claim 43, wherein the short-course radiotherapy comprises administering about 500 cGy per day.

45. The method of claim 43, wherein the short-course radiotherapy comprises administering about 2500 cGy in 5 daily fractions.

46. The method of any one of claims 1-42, wherein the radiotherapy is a long-course radiotherapy.

47. The method of claim 46, wherein the long-course radiotherapy comprises administering about 200 cGy per day.

48. The method of claim 46, wherein the long-course radiotherapy comprises administering about 1000 cGy in 5 daily fractions, optionally every week for 3 weeks, 4 weeks, or 5 weeks.

49. The method of any one of claims 1-48, further comprising administering:

c) a therapeutically effective amount of one or more chemotherapeutic agents.

50. The method of claim 49, wherein administering the one or more chemotherapeutic agents is oral or intravenous.

51. The method of any claim 49 or 50, wherein the one or more chemotherapeutic agents comprise oxaliplatin, capecitabine, leucovorin, fluorouracil, or a combination thereof.

52. The method of claim 51, wherein the oxaliplatin is intravenously administered at a dose of about 85 mg/m^2 or about 130 mg/m^2, optionally over about 2 hours.

53. The method of claim 51 or 52, wherein the capecitabine is orally administered at a dose of about 1000 mg/m^2.

54. The method of any one of claims 51-53, wherein the one or more chemotherapeutic agents comprise oxaliplatin and capecitabine (CapeOX), optionally wherein administering the CapeOX comprises intravenously administering oxaliplatin once on day 1 and orally administering capecitabine twice daily on days 1-14.

55. The method of claim 54, wherein administering the CapeOX comprises intravenously administering oxaliplatin at a dose of about 130 mg/m^2 once on day 1 and orally administering capecitabine at a dose of about 1000 mg/m^2 twice daily on days 1-14.

56. The method of claim 54 or 55, wherein administering the CapeOX is repeated on a 21-day cycle, optionally for a total of 18 weeks (6 cycles).

57. The method of any one of claims 51-56, wherein the leucovorin is administered at a dose of about 400 mg/m^2, optionally over about 2 hours.

58. The method of claim 57, wherein the leucovorin is leucovorin calcium.

59. The method of any one of claims 51-58, wherein the fluorouracil is administered at a dose of about 400 mg/m^2, about 1200 mg/m^2, or about 2400 mg/m^2.

60. The method of claim 59, wherein the fluorouracil is administered over about 2 hours.

61. The method of claim 59, wherein the fluorouracil is administered over about 2 days.

62. The method of any one of claims 51-61, wherein the one or more chemotherapeutic agents comprise oxaliplatin, leucovorin, and fluorouracil (FOLFOX).

63. The method of claim 62, wherein administering the FOLFOX comprises a FOLFOX4 regimen, a FOLFOX6 regimen, a modified FOLFOX6 (mFOLFOX6) regimen, or a FOLFOX7 regimen.

64. The method of claim 62 or 63, wherein administering the FOLFOX comprises intravenously administrating fluorouracil, leucovorin, and oxaliplatin on day 1 and intravenously administrating fluorouracil continuously over 46-48 hours (days 1-2).

65. The method of any one of claims 62-64, wherein administering the FOLFOX comprises intravenously administrating fluorouracil at a dose of about 400 mg/m^2, leucovorin at a dose of about 400 mg/m^2, and oxaliplatin at a dose of about 85 mg/m^2 on day 1 and intravenously administrating fluorouracil at a dose of about 1200 mg/m^2 continuously over about 2 days (days 1-2).

66. The method of any one of claims 62-65, wherein administering the FOLFOX is repeated on a 14-day cycle, optionally for a total of 16 weeks (8 cycles).

67. The method of any one of claims 1-66, wherein administering the dietary regimen is before administering the radiotherapy.

68. The method of any one of claims 1-67, wherein administering the dietary regimen is at least 24 hours prior to administering the radiotherapy and continued throughout administering the radiotherapy.

69. The method of any one of claims 1-68, wherein administering the dietary regimen is on an intermittent schedule alternating with a habitual diet.

70. The method of claim 69, wherein the habitual diet is consumed by the subject for at least two consecutive days per week.

71. The method of any one of claims 49-70, wherein administering the dietary regimen is before administering the one or more chemotherapeutic agents.

72. The method of any one of claims 49-71, wherein administering the dietary regimen is at least 24 hours prior to administering the one or more chemotherapeutic agents and on the day of administering the one or more chemotherapeutic agents.

73. The method of any one of claims 49-72, wherein administering the radiotherapy is before administering the one or more chemotherapeutic agents.

74. The method of any one of claims 1-73, further comprising providing a surgical intervention to the subject.

75. The method of claim 74, wherein the surgical intervention is total mesorectal excision (TME).

76. The method of any one of claims 1-75, wherein the colorectal cancer is rectal cancer.

77. The method of claim 76, wherein the cancer is locally advanced rectal cancer (LARC).

78. A method of treating colorectal cancer in a subject in need thereof, the method comprising administering to the subject:

a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of serine, glycine, and proline in the subject as compared to baseline;

b) a therapeutically effective amount of a radiotherapy; and

c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin and capecitabine (CapeOX), wherein administering the CapeOX comprises intravenously administering oxaliplatin at a dose of about 130 mg/m^2 once on day 1 and orally administering capecitabine at a dose of about 1000 mg/m^2 twice daily on days 1-14.

79. A method of treating colorectal cancer in a subject in need thereof, the method comprising administering to the subject:

a) a therapeutically effective amount of a dietary regimen, wherein the dietary regimen reduces an average plasma level of serine, glycine, and proline in the subject as compared to baseline;

b) a therapeutically effective amount of a radiotherapy; and

c) a therapeutically effective amount of one or more chemotherapeutic agents, wherein the one or more chemotherapeutic agents comprise oxaliplatin, leucovorin, and fluorouracil (FOLFOX), wherein administering the FOLFOX comprises intravenously administrating fluorouracil at a dose of about 400 mg/m^2, leucovorin at a dose of about 400 mg/m^2, and oxaliplatin at a dose of about 85 mg/m^2 on day 1 and intravenously administrating fluorouracil at a dose of about 1200 mg/m^2 continuously over about 2 days (days 1-2).