

5 CLAIMS

What is claimed is:

- 10 1. [3-¹³C]acetoacetate, wherein at least 0.1%, more preferably at least 1%, and most preferably at least 10% of said [3-¹³C]acetoacetate is hyperpolarized .
2. Composition comprising the [3-¹³C]acetoacetate of claim 1.
- 15 3. Method of preparing the [3-¹³C]acetoacetate of claim 1 or the composition of claim 2, wherein the method comprises the steps of :
- (a) chemically synthesizing [3-¹³C]acetoacetate or a composition comprising [3-¹³C]acetoacetate; and
- (b) hyperpolarizing said [3-¹³C]acetoacetate or said composition.
- 20 4. The method of claim 3, wherein [3-¹³C]acetoacetate is prepared from [3-¹³C]ethyl acetoacetate.
5. The method of claim 4, wherein the chemical synthesis of [3-¹³C]acetoacetate involves the saponification of [3-¹³C]ethyl acetoacetate.
- 25 6. The method of any one of claims 3-5, wherein the chemical synthesis of [3-¹³C]acetoacetate comprises reacting [3-¹³C]ethyl acetoacetate and a base, preferably an alkali hydroxide, more preferably lithium hydroxide, under conditions allowing said reaction.
- 30 7. The method of any one of claims 3-6, wherein the synthesized [3-¹³C]acetoacetate is hyperpolarized using Dynamic Nuclear Polarization (DNP).
8. Method of determining the spatial and temporal distribution and metabolism of [3-¹³C]acetoacetate and/or its metabolites in a cell or a subject, wherein the method comprises the
- 35 steps of:
- (a) administering the [3-¹³C]acetoacetate of claim 1 or the composition of claim 2 to the cell or subject; and
- (b) determining the distribution and metabolism of hyperpolarized [3-¹³C]acetoacetate and/or its metabolites in the cell or subject by magnetic resonance imaging (MRI), magnetic resonance
- 40 spectroscopy (MRS), and/or magnetic resonance spectroscopic imaging (MRSI).

- 5 9. The method of claim 8, wherein the cell or subject is a cell culture, an ex vivo tissue, a human, or an animal.
- 10 10. The method of claim 8 or 9, wherein the metabolites of [3-¹³C]acetoacetate are selected from the group consisting of [5-¹³C]glutamate, [1-¹³C]citrate, [1-¹³C]acetylcarnitine, and [3-¹³C]beta-hydroxybutyrate.
- 15 11. The method of any one of claims 8-10, wherein the magnetic resonance signals from hyperpolarized [3-¹³C]acetoacetate and its metabolites are used to study the in vivo metabolism of acetoacetate and/or other ketone bodies.
- 20 12. The method of any one of claims 8-11, wherein the magnetic resonance signals from hyperpolarized [3-¹³C]acetoacetate and its metabolites are used to quantify specific physiological functions of the cell or subject in healthy (e.g. starvation) and/or diseased conditions.
- 25 13. The method of any one of claims 8-12, wherein the magnetic resonance signals from hyperpolarized [3-¹³C]acetoacetate and its metabolites are used to diagnose a condition, disease, or disorder associated with the metabolism of acetoacetate and/or other ketone bodies
- 30 14. The method of claim 13, wherein the condition, disease, or disorder is a cancer, diabetes, cardiovascular disease, or neurodegenerative disease.
15. Method of diagnosing a condition, disease, or disorder associated with the metabolism of acetoacetate and/or other ketone bodies in a subject, said method comprising analyzing the magnetic resonance signals obtainable by the method of any one of claims 8-14.
- 35 16. The method of claim 15, wherein the condition, disease, or disorder is a cancer, diabetes, cardiovascular disease, or neurodegenerative disease.
18. Use of the [3-¹³C]acetoacetate of claim 1 or the composition of claim 2 in MRI, MRS, and/or MRSI.
- 40 19. Use of the [3-¹³C]acetoacetate of claim 1 or the composition of claim 2 in the diagnosis of a condition, disease, or disorder associated with the metabolism of acetoacetate and/or other ketone bodies.