

CLAIMS:

1. A method for detecting metabolically active bacteria of interest in a sample, the method comprising:

(a) contacting the sample with a carbohydrate-solvatochromic dye conjugate, wherein the sample comprises the metabolically active bacteria of interest in an aqueous environment, and wherein the carbohydrate-solvatochromic dye conjugate comprises:

a carbohydrate moiety configured to facilitate the selective metabolic incorporation of the carbohydrate-solvatochromic dye conjugate into a hydrophobic outer cell membrane of the metabolically active bacteria of interest, and

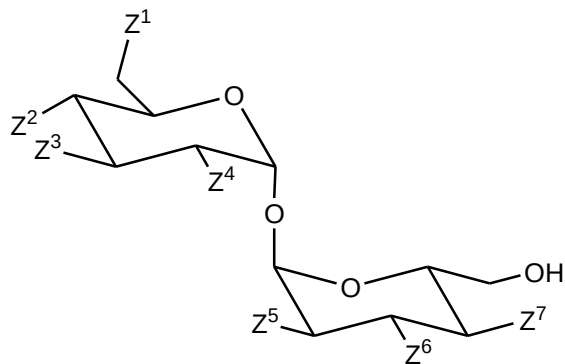
a solvatochromic dye moiety linked to the carbohydrate moiety, the solvatochromic dye moiety having an enhanced spectroscopic signal when incorporated into the hydrophobic outer cell membrane of the metabolically active bacteria of interest, and a lower spectroscopic signal in the aqueous environment;

wherein contacting the sample with the carbohydrate-solvatochromic dye conjugate results in incorporation of one or more molecules of the carbohydrate-solvatochromic dye conjugate into the hydrophobic outer cell membrane of the metabolically active bacteria of interest, with other molecules of the carbohydrate-solvatochromic dye conjugate remaining in the aqueous environment; and

(b) detecting the enhanced spectroscopic signal from the solvatochromic dye moiety of the one or more molecules of the carbohydrate-solvatochromic dye conjugate that have incorporated into the

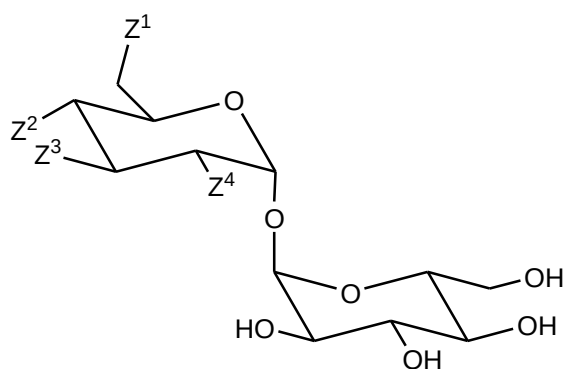
hydrophobic outer cell membrane of the metabolically active bacteria of interest, wherein the enhanced spectroscopic signal indicates the presence of the metabolically active bacteria of interest in the sample, and wherein the molecules of the carbohydrate-solvatochromic dye conjugate remaining in the aqueous environment do not need to be washed away between the steps (a) and (b) in order to detect the enhanced spectroscopic signal over a background spectroscopic signal from the molecules of the carbohydrate-solvatochromic dye conjugate remaining in the aqueous environment.

2. The method of claim 1, wherein the outer cell membrane of the metabolically active bacteria of interest is a mycomembrane rich in hydrophobic mycolates.
3. The method of claim 2, wherein the mycomembrane mycolates include trehalose mycolates.
4. The method of claim 1, wherein the metabolically active bacteria of interest is capable of metabolic uptake of trehalose.
5. The method of claim 1, wherein the metabolically active bacteria of interest metabolically uptakes trehalose with high specificity.
6. The method of claim 1, wherein the metabolically active bacteria of interest are mycobacteria or corynebacteria.
7. The method of claim 1, wherein the carbohydrate-solvatochromic dye conjugate has formula:



wherein one and only one of Z^1 - Z^7 is a linked solvatochromic dye and the rest of Z^1 - Z^7 are OH.

8. The method of claim 7, wherein the carbohydrate-solvatochromic dye conjugate has formula:



wherein one and only one of Z^1 - Z^4 is a linked solvatochromic dye and the rest of Z^1 - Z^4 are OH.

9. The method of claim 8, wherein the linked solvatochromic dye is selected from 4-DMAP, 4-DMN, 6-DMN, Nile Red, 3-HC, 3-MC, PRODAN, Anthradan, and NBD ~~and derivatives thereof~~.
10. The method of claim 1, wherein the sample is a biological sample selected from the group of: sputum, blood, serum, plasma, urine, bronchoalveolar lavage fluid, buccal swab (e.g., cheek swab), or tissue samples.

11. The method of claim 1, wherein the sample is an environmental sample.
12. The method of claim 11, wherein the sample is taken from an environment selected from the group of: air, water, or inanimate surface.
13. The method of claim 10, wherein the biological sample is a sample from a subject suspected of having, or at risk of infection with the bacteria of interest.
14. The method of claim 13, wherein the biological sample is a sample from a subject suspected of having, or at risk of infection with *Mycobacterium tuberculosis*.
15. The method of claim 1, wherein the metabolically active bacteria of interest is present inside a eukaryotic cell.
16. A method for determining bacteria drug or treatment plan sensitivity comprising:
 - (a) obtaining a sample of a bacteria of interest;
 - (b) splitting the sample into a plurality of samples, wherein each of the plurality of samples comprises the bacteria of interest in an aqueous environment;
 - (c) treating each of the plurality of samples with a drug cocktail or treatment plan to produce a plurality of treated samples;
 - (d) contacting each of the plurality of treated samples with a carbohydrate-solvatochromic dye conjugate that comprises:

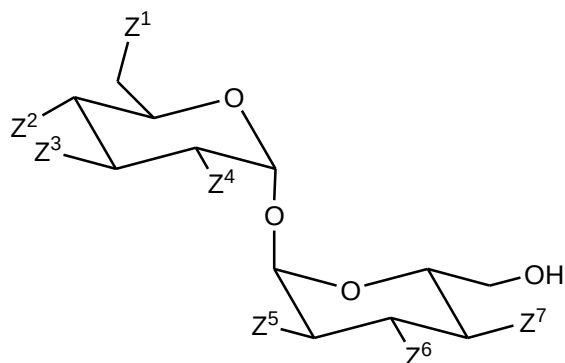
a carbohydrate moiety configured to facilitate the selective metabolic uptake of the carbohydrate-solvatochromic dye conjugate into a hydrophobic outer cell membrane of the bacteria of interest, and

a solvatochromic dye linked to the carbohydrate moiety, the solvatochromic dye moiety having an enhanced spectroscopic signal when incorporated into the hydrophobic outer cell membrane of the bacteria of interest, and a lower spectroscopic signal in the aqueous environment;

wherein contacting each of the plurality of treated samples with the carbohydrate-solvatochromic dye conjugate results in the incorporation of one or more molecules of the carbohydrate-solvatochromic dye conjugate into the hydrophobic outer cell membrane of the bacteria of interest, with the other molecules of the carbohydrate-solvatochromic dye conjugate remaining in the aqueous environment; and

- (e) for each of the plurality of treated samples, detecting the enhanced spectroscopic signal from the solvatochromic dye moiety of the one or more molecules of the carbohydrate-solvatochromic dye conjugate that have incorporated into the hydrophobic outer cell membrane of the bacteria of interest, wherein the enhanced spectroscopic signal indicates the persistence of the bacteria of interest which remain metabolically active in the treated sample, and wherein the molecules of the carbohydrate-solvatochromic dye conjugate remaining in the aqueous environment do not need to be washed away between the steps (d) and (e) in order to detect the enhanced spectroscopic signal over a background spectroscopic signal from the molecules of the carbohydrate-solvatochromic dye conjugate remaining in the aqueous environment.

17. The method of claim 16, wherein the bacteria of interest is selected from the group of: *Mycobacterium tuberculosis*, *Mycobacterium leprae*, or *Corynebacterium diphtheriae*.
18. The method of claim 16, wherein the carbohydrate-solvatochromic dye conjugate has formula:



wherein one and only one of Z¹-Z⁷ is a linked solvatochromic dye and the rest of Z¹-Z⁷ are OH.

19. The method of claim 16, wherein the sample is selected from the group of: sputum, blood, serum, plasma, urine, bronchoalveolar lavage fluid, and buccal swab.