

| Biomarker <u>Species</u> | Tracer substrate (route) | Bio fluid/Tissue Marker isotope/ratios | Validation Publication date | Translation to clinic Sponsor |
|--|---|--|---|---|
| <u>Serine oxidation/glycine cleavage</u> <i>In vitro, animals, human cells</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.P.) | <i>Cells, SOG pathway fingerprint</i> | <i>In vitro, animals, humans</i> <i>October, 2013</i> | Plasma marker for alternate ATP synthesis <i>Academic, Pharmaceutical</i> |
| <u>Regulation/Activation of AMP-activated protein kinase</u> <i>In vitro, Mice</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.P.) [U- ¹³ C ₁₆]-palmitate (P.O.) | <i>Plasma, liver, muscle, adipose</i> <i>Glucose/lactate cross-labeling via malate shuttling (¹³C-M₂)</i> | <i>In vitro and animals</i> <i>April, 2013</i> | Plasma marker for liver, muscle and adipose <i>Academic, Pharmaceutical</i> |
| <u>miR-1 and miR-206 regulation by NRF2 in tumorigenesis</u> <i>Mice</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.P.) | <i>Tumors, organs</i> <i>Ribose/glutamine cross-labeling via direct glucose oxidation/pyruvate carboxylase (¹³C-M₁)</i> | <i>In vitro and animals</i> <i>July, 2013</i> | Oncoisotopomer marker/biopsies <i>Academic</i> |
| <u>Metformin's mechanism/efficacy marker for FAS control in cancer</u> <i>In vitro human cell lines</i> | [1,2- ¹³ C ₂]-D-glucose (media) | <i>Tumor cells</i> <i>Palmitate cross-labeling via FAS in the presence of cholesterol (¹³C-M₄/M₂)</i> | <i>In vitro</i> <i>July, 2013</i> | Oncoisotopomer marker/biopsies <i>Foundation</i> |
| <u>Hepatic de novo lipo-sterol synthesis</u> <i>Human-infants</i> | [1,2- ¹³ C ₂]-acetate (P.O., I.V.) | <i>Plasma</i> <i>Palmitate, stearate, cholesterol cross-labeling from acetate (¹³C-M₄/M₂)</i> | <i>Human</i> <i>June, 2013</i> | Feeding benefits and adrenal enzyme deficiency <i>Academic</i> |
| <u>SiD CLAMP</u> <i>Mice</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.V.) | <i>Plasma</i> <i>Glucose cross-labeling via all gluconeogenic mechanisms and hepatic release (¹³C-M₁₋₆)</i> | <i>In vivo, preclinical</i> <i>April, 2013</i> | Glucose production/insulin sensitivity without infusion of glucose/insulin <i>Academic, Pharmaceutical</i> |
| <u>Precursor product isotope matching (PRISMOMATCH)</u> <i>In vitro human cell lines</i> | Low enrichment or natural variations in isotope content | <i>Plasma, tissues</i> <i>Protein, product turnover</i> | <i>In vitro (isolated/sorted cells), animals</i> <i>July, 2013</i> | Real-time turnover/captured proteins <i>Hirshberg conspiracy to diagnose pancreatic cancer</i> |
| <u>Glucagon and Glucagon-Like Peptide 1 Receptor targeting</u> <i>Obese rats</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.V.) | <i>Plasma, liver, muscle, adipose</i> <i>Glucose, lactate, glutamine cross-labeling via gluconeogenesis, TCA cycle or futile cycles (¹³C-ΣM)</i> | <i>In vivo</i> <i>July, 2011</i> | Tissue specific drug effect and efficacy markers <i>Pharmaceutical</i> |
| <u>Liver/kidney toxicity markers</u> <i>Rats</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.V.) | <i>Plasma, liver, brain, kidneys</i> <i>Glucose, lactate, glutamine, fatty acid cross-labeling via gluconeogenesis, citrate shuttling, fatty acid transport (¹³C-ΣM)</i> | <i>In vivo</i> <i>September, 2009</i> | Targeted Tracer Fate Associations among multiple plasma products <i>Government (USA)</i> |
| <u>Liver cell/mitochondria toxicity markers</u> <i>Primary hepatocytes</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.V.) | <i>Culture media, hepatocytes</i> <i>Glucose, lactate, glutamine, fatty acid cross-labeling via TCA cycle metabolism, citrate shuttling, fatty acid synthesis (¹³C-ΣM)</i> | <i>In vitro</i> <i>November, 2011</i> | Targeted Tracer Fate Associations among multiple plasma products <i>Government (USA)</i> |
| <u>Targeted drug resistance in leukemia</u> <i>- Human, cultured cells (clinical samples)</i> | [U- ¹³ C ₆]-D-glucose (P.O., I.V.) | <i>Culture media, clinical samples of CML cells</i> <i>Glucose, lactate, glutamine cross-labeling and drug dosing (¹³C-ΣM)</i> | <i>In vitro</i> <i>April, 2009</i> | Targeted Tracer Fate Associations and drug dosing <i>Pharmaceutical</i> |
| <u>Plasma markers of pancreatic cancer</u> <i>Rats</i> | [1,2- ¹³ C ₂]-D-glucose (P.O., I.V.) | <i>Plasma, tumors, pancreas, liver</i> <i>Glucose, lactate, glutamine cross-labeling and tumor size (¹³C-M_n)</i> | <i>Plasma, biopsy</i> <i>November, 2005</i> | Altered hepatic glucose production <i>Hirshberg conspiracy to diagnose pancreatic cancer</i> |