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Developing a rugged chiral assay for the biomarker 2-hydroxyglutaric acid for use in routine clinical analysis of plasma samples from oncology studies

Presented by Jennifer Zimmer, PhD

Investigators have shown that one enantiomer of hydroxyglutarate (D-2-HG) is abnormally accumulated in a variety of human cancers, such as glioblastoma, acute myeloid leukemia and cholangiocarcinoma. The isocitrate dehydrogenase (IDH) enzyme normally catalyzes the conversion of isocitrate to alpha-ketoglutarate (α-KG), but in these types of cancer, mutant IDH enzymes acquire an abnormal enzymatic activity which allows them to convert α-KG into D-2-HG. The measurement of D-2-HG levels can be used to monitor tumor burden and effectiveness of cancer treatments meant to inhibit mutant IDH.

We have developed and validated a chiral assay for D-2-HG that allows us to accurately quantify levels of this analyte from plasma samples. This assay employs a surrogate matrix in order to quantify absolute levels in the plasma samples. Because D-2-HG is a very small analyte, derivatization was required in order to separate the enantiomers as well as to increase ionization to achieve the desired lower limit of quantitation.