DIAGNOSIS/MONITORING OF GLIOBLASTOMA & ACUTE MYELOID LEUKEMIA BY (D)-2-HYDROXYGLUTARATE TEST

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HINTERGRUND

Isocitrate dehydrogenase (IDH) enzymes catalyze the oxidative decarboxylation of isocitrate to alpha ketoglutarate. In humans, three IDH isoforms are known, the homodimers IDH1 and IDH2 and the heterotetramer IDH3.

Mutations in genes encoding IDH1 and 2 enzymes have been identified in metabolic disorders, inborn tumor associated disease and numerous tumors. IDH mutations define secondary glioblastoma, diffused astrocytoma, and oligodendrogliomas (100%). IDH mutations occur not only in diffuse gliomas, but also in enchondroma (~80%), chondrosarcoma (~60%), angioimmunoblastic T cell lymphoma (~45%), intrahepatic cholangiocarcinoma (~25%), acute myeloid leukemia (~20%), and other tumor entities (~5%). All mutations lead to a nemorphic enzyme function, now producing (D)-2-hydroxyglutarate (D2HG), which can be used as surrogate marker for all mutations.

The diagnosis of IDH mutations is presently performed by immuno-histological analysis using the IDH1 R132H-specific antibody or sequencing.

As alternative, detection of D2HG in tumor tissue, in paraffin-embedded tissues and in blood/sera can be carried out by individual mass spectrometry analysis.

LÖSUNG

Researchers from DKFZ and University Hospital of Heidelberg developed a test for detecting D2HG in diverse samples by measuring the production of the reduced state of the dye. The technique can be used for diagnosis but in addition monitoring a D2HG-associated disease of a patient.
D2HG was diluted in water, blood serum, and urine to get a standard curve (0-375 pmol = 0-15µM). Samples were prepared according to the protocol in Figure 2 and assayed with the diaphorase/resazurin read-out. In the graph, the relative fluorescence (RFU) is plotted against the D2HG concentration.

**VORTEILE**

- Diagnosis and monitoring of IDH1/IDH2/IDH3 dependent diseases such as: Glioblastomas, astrocytoma, oligodendrogliomas, oligoastrocytoma, acute myeloid leukemia (AML), chondrosarcoma, intrahepatic cholangiocarcinoma, angioimmunoblastic T cell lymphoma
- Simple and robust enzymatic assay; readout in 3 hours; suitable for 96 up to 1536 well format
- Less expensive/time-consuming and high-throughput possible in opposite to established GC-MS test

**ANWENDUNGSBEREICHE**

Development and distribution of a simple and robust enzymatic assays for the specific determination of the D2HG. The readout is available already in about 2 to 3 hours. Moreover, it is suitable for 96-well format and can be even further miniaturized to the 1536-well format, thereby allowing for the parallel analysis (high-throughput) of numerous samples at the same time. Beside an already
granted license for research use only, we now seek a licensee for the DIAGNOSTIC field.

PUBLIKATIONEN & VERWEISE

4. “Pan-mutant-IDH1 inhibitor BAY1436032 is highly effective against human IDH1 mutant acute myeloid leukemia in vivo.” In Leukemia, Jan 2017; doi: 10.1038/leu.2017.46. by A Chaturvedi et al..