

TECHNOLOGY OFFERS

Diagnosis/Monitoring of Glioblastoma and Acute Myeloid Leukemia by (D)-2-Hydroxyglutarate Test (P-977)

A simple and robust enzymatic assay for the diagnosis and monitoring of IDH1/IDH2/IDH3 dependent diseases

EXECUTIVE SUMMARY

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.



Category

Diagnostics

Indication

Leukemia

Development stage

Clinical proof of concept

Seeking

Licensing

BENEFITS

- 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

TECHNOLOGY BACKGROUND

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, chondrosarcoma and other tumor entities. 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.

DEVELOPMENT STAGE

The test can be used for HTS and was successfully tested using on 96 up to 1536 well format.

APPLICATIONS

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.

INTELLECTUAL PROPERTY

- Priority patent application EP12157663.1
- “Means and Methods for the Determination of (D)-2-Hydroxyglutarate (D2HG)” as well as a PCT application (WO2013127997A1).
- Nationalized as CN104145022B, JP6162729B2, US9487815B2 and EP2820145B1, all granted.

PUBLICATIONS & REFERENCES

- “Detection of 2-hydroxyglutarate in formalin-fixed paraffin-embedded glioma specimens by gas chromatography/mass spectrometry.” in Brain Pathol. 2012 Jan;22(1):26-31 by Sahm F et al.
- “Enzymatic assay for quantitative analysis of (D)-2-hydroxyglutarate.” in Acta Neuropathol. 2012 Dec;124(6):883-91 by Balss J et al.
- “Pan- mutant IDH1 inhibitor BAY 1436032 for effective treatment of IDH1 mutant astrocytoma in vivo.” In Acta Neuropathol. 2017 Jan 25. PMID:28124097 by Stefan Pusch et al.
- “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.

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ABOUT THE DKFZ INNOVATION MANAGEMENT

Working at the interface of research and industry, the Innovation Management of the German Cancer Research Center (DKFZ) helps to get new cancer medications, diagnostic tests, and research instruments onto the market as quickly as possible.

The DKFZ with its more than 3,000 employees is the largest biomedical research institution in Germany. At the Center more than 1,300 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg