Gabapentin for the treatment of Glioblastoma or astrocytic brain tumors (P-957)

Key facts
- Second indication for Gabapentin in the field of cancer therapy
- Identification of branched-chain-aminotransferase-1 (BCAT1) as a direct target for neoplasia treatment

Background
Malignant human glioblastomas account for the largest number of human malignant brain tumors. The treatment of gliomas includes neurosurgical techniques (resection or stereotactic procedures), radiation therapy and chemotherapy. Up to know these therapies only achieve a very limited prolongation of lifespan of patients so that new strategies like targeting the angiogenesis in glioblastomas are tried.

Technology
Researchers from the DKFZ now verified that the well-known Gabapentin, normally used in the treatment of epilepsy, effectively inhibits cell proliferation of the humane glioma/astrocytoma cell lines HS683 and U87-MG as shown in Figure 1. Thus inhibiting the biological activity of branched-chain-aminotransferase-1 (BCAT1) or its expression (as shown in Figure 2) offers a new method of treating neoplasia.

Advantages
- Gabapentin has well-established pharmacokinetics and pharmacodynamics
- Since glioblastoma/astrocytoma are rare diseases Gabapentin can attain “orphan drug status”

Development Stage
The efficacy of Gabapentin was shown in in-vitro studies using different glioma cell lines. Subsequently animal studies are in preparation to demonstrate in preclinical studies (in vivo) with animals the new application of Gabapentin for the treatment of glioblastoma or astrocytoma.

Inventors
The invention was jointly conceived by Bernhard Radlwimmer, Sebastian Barbus, Martje Tönjes and Peter Lichter of the division molecular genetics (B060).

Intellectual Property
A priority patent application EP 11 000 720.0 “Inhibitors of branched-chain-aminotransferase-1 (BCAT1) for the treatment of neoplasia” have been filed January 28, 2011 at the EPA.

Further Information
No other public information is currently available, but further information (speaking with the inventor) is available under a signed Confidential Disclosure Agreement (CDA).

DKFZ Contact:
For further information please contact:

Dr. Frieder Kern
Deutsches Krebsforschungszentrum
Technology Transfer Office T010
Email: F.Kern@dkfz.de
Tel.: +49-(0)6221-42-2952
Fax: +49-(0)6221-42-2956
Fig. 1: Cell proliferation was assayed using Click-iT® EdU detecting/quantitating newly synthesized DNA.

Click-iT EdU Assay after Gabapentin treatment for 24h (Inhib.#3)

<table>
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<th>Condition</th>
<th>Alexa488/EdU Counts [%]</th>
<th>EdU-negative</th>
<th>EdU-positive</th>
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Fig. 2: Cell proliferation after BCAT1 knock-down.