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A company of the LifeScience Foundation

REFERENCE NUMBER TO 15-00502

Predicting the therapeutic effect of compositions containing BH3 mimetics

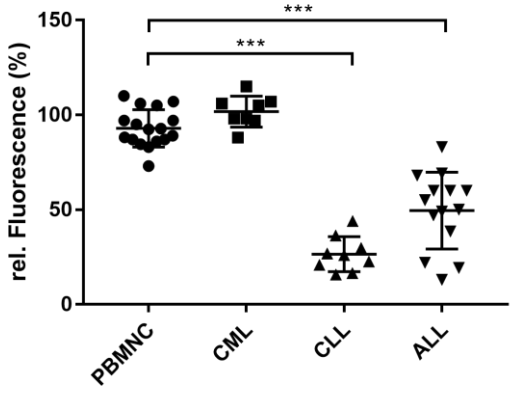
Keywords: Cancer, Leukemia, BH3 Mimetics, In vitro Diagnostics, Drug Discovery, Companion Diagnostics, FACS, MOMP

INVENTION NOVELTY

BH3 mimetics are a novel class of therapeutics for improved cancer therapy, with a focus on treatment of leukemic diseases such as acute lymphoblastic leukemia (ALL), chronic lymphatic leukemia (CLL) or acute myeloid leukemia (AML) which demonstrated to be remarkably effective. MHH's proprietary *in vitro* assay is a reliable tool for the extraordinary fast assessment of an individual´s response to a BH3 mimetic therapy. Patients who are diagnosed to suffer from leukemia require fast, safe and efficient treatment. Noteworthy, test results will be obtained within a maximum of three hours. The easy-to-use assay is based on fluorescence detection of the mitochondria transmembrane potential and utilizes isolated blood cells as patient-specific material.

VALUE PROPOSITION

Patients respond individually to BH3 mimetics and therefore treatment may at worst lead to adverse effects in already critically ill leukemia patients. There is a strong need for a fast and precise assessment of an individual´s response to a BH3 mimetic before starting an intervention and during an ongoing treatment. Furthermore, the assay is well suited to assess the efficacy of combinational treatments and for the application in drug discovery.



Response to treatment with venetoclax in primary ALL and CLL cells (at initial diagnosis) while primary healthy and CML cells show no induction of apoptosis.

TECHNOLOGY DESCRIPTION

In order to analyze the therapeutic efficacy of a single or multiple BH3 mimetics or combinations of pharmaceutical substances with a single or multiple BH3 mimetics, isolated mononuclear cells are treated with the respective substances and are stained with a fluorescent dye sensitive to the transmembrane mitochondrial potential. The fluorescence in viable cells can be quantified using fluorescence activated cell sorting (FACS) indicating mitochondrial outer membrane permeabilization (MOMP) and apoptosis induction. A comparison of MOMP induction in tumor and non-tumor cells enables the determination of adverse side effects of therapeutic treatments.

COMMERCIAL OPPORTUNITY

In-licensing or collaboration for further development is possible.

DEVELOPMENT STATUS

Initial proof-of-concept studies have been performed at Hannover Medical School.

PATENT SITUATION

Patents have been granted in Europe (EP 3607325B1, national validation in DE, CH, FR, GB) and USA (US 11,333,660 B2) with priority of 2017.

FURTHER READING

Scherr et al., Optimized induction of mitochondrial apoptosis for chemotherapy-free treatment of BCR-ABL+acute lymphoblastic leukemia, Leukemia 2019, DOI: 10.1038/s41375-018-0315-6

Kirchhoff et al., Venetoclax and dexamethasone synergize with inotuzumab ozogamicin–induced DNA damage signaling in B-lineage ALL. Blood 2021, 137, 2657–2661. DOI: 10.1182/blood.2020008544

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Last updated June 2023