SOLVO MDQ Kit™

Multi Drug Resistance Protein function measurement

Novelty

SOLVO MDQ Kit™ is the first biomarker-based detection kit for the detection of Multi Drug Resistance (MDR) protein function by flow cytometry. It is designed to determine the functional activity of the three clinically most relevant drug efflux proteins, namely MDR1, MRP1 and BCRP.

Background

MDR is associated with drug-efflux transporter proteins located at physiological barriers. MDR is the principal mechanism by which many cancer develops resistance to chemotherapy or immunosuppressant drugs administered in different type of leukemia, cancers, autoimmune diseases and to patients who underwent transplantation. Conventional anticancer drugs (e.g.: doxorubicin, gefitinib, imatinib, irinotecan, methotrexate, mitoxanthrone, paclitaxel, tamoxiphen, topotecan, etc.) are substrates of MDR transporters. Moreover, MDR transporters play distinct role in immune response.

Clinical relevance

- The incidence of MDR in previously untreated cancer cases is approximately 40 %
- MDR protein function is an independent negative prognostic biomarker in AML
- MDR protein function can be correlated with disease activity in autoimmune diseases
- MDR protein activity can be correlated with treatment response to DMARDs and TNF inhibitors
- MDR protein activity determination is a safe measurement for patients on highly demanding cytotoxic or immunsuppressant drugs
- Allows therapy selection based on selective cell sensitivity results
- Allows patients profiling and stratification by detection of MDRs in clinical trials.

Features

The SOLVO MDQ Kit™ is designed to maximize the benefits of flow cytometry. Literature data suggest that the functional determination of MDR provides fast and more accurate results for the clinical lab than other methods, such as quantifying the expressions of the transporters at mRNA or protein level.

- Contains ready-to-use reagents
- Uses highly selective inhibitors and different probe substrates for MDR1/MRP1 and BCRP
- Compatible with cell surface markers
- Enough for 10 independent activity measurements in triplicates
- The reagents work on every popular cell analyzer

Availability

PRODUCT	SIZE	CAT. NO.
SOLVO MDQ Kit™ CE IVD	10 assays	MDQ101D

Principle of the test

For quantitative measurement of MDR1 and MRP1 activities in viable cells, SOLVO MDQ Kit™ applies the proprietary Calcein-assay technology. This assay utilizes the fluorogenic dye calcein-acetoxymethyl ester (calcein-AM) which is a hydrophobic, non-fluorescent compound that readily penetrates the cell membrane. After entering the living cell, calcein-AM rapidly hydrolyzed by endogenous esterases. As a result of cleavage, highly fluorescent free acid derivative of the dye is formed which becomes trapped in the cytoplasm due to its hydrophilic character. Since calcein-AM is an excellent substrate of both MDR1 and MRP1, the activity of these efflux transporters results in a lower cellular accumulation of the fluorescent calcein (***Figure 1***).

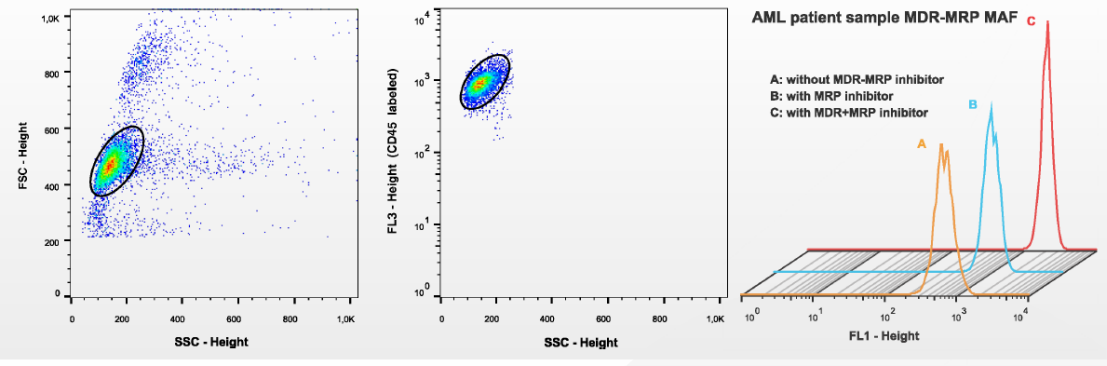

Figure 1. *MDR1 and MRP1 activities on CD45$^+$ cells from acute myeloid leukemia (AML) patients*

Addition of selective inhibitors of MDR1 and MRP1 in excess blocks the dye extrusion activity of the relevant transporter and increases calcein accumulation in the cells. Activities of MDR1 and MRP1 transporters are reflected by the difference between the amount of calcein accumulated in the presence or absence of the selective inhibitors. The difference is normalized to dye uptake measured in the presence of the inhibitor and the results of the expressed MDR activity factor (MAF) values. Thus the result of test becomes independent from factors influencing the cellular accumulation of calcein other than the activity of multidrug transporters. These variables include the differences in cellular properties (membrane composition, intracellular esterase activity, cell size, cell surface, etc.) and the methodological differences (e.g. use of different equipment, amplification and individual variables). Since the influence of these factors is diminished by the simple normalization approach mentioned above, the intra-and interlaboratory comparison of MAF values is possible.

BCRP activity is measured using a similar principle: intracellular accumulation of the fluorescent BCRP-specific reporter substrate is measured in the presence and absence of selective BCRP inhibitor. However, the BCRP-specific reporter substrate is directly fluorescent and does not require cleavage by intracellular esterases (***Figure 2***).

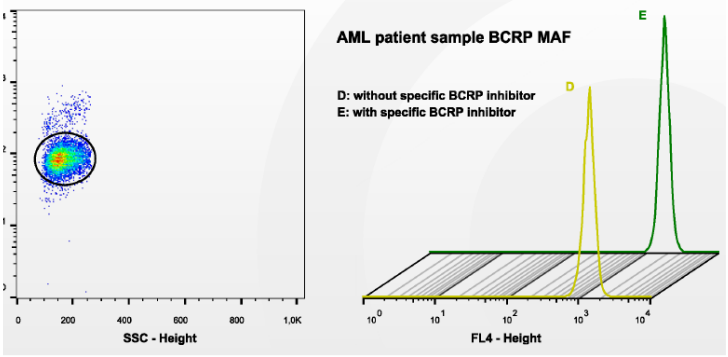

Figure 2. *BCRP activities on CD45$^+$ cells from acute myeloid leukemia (AML) patients*

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