

MDQUEST MultiDrugQuant™ Kit

for MultiDrug Resistance protein function measurement

MDQUEST MultiDrugQuant™ Kit is designed to determine the functional activity of the three clinically most relevant drug efflux proteins: MDR1, MRP1, and BCRP in viable cells by flow cytometry.

Background

Multidrug Resistance (MDR) is associated with the drug-efflux transporter proteins located at physiological barriers. MDR is the principal mechanism by which many cancers develop resistance to chemotherapy or immune suppressant drugs administered in different types of leukemia, cancers, autoimmune diseases and to patients who underwent transplantation. The incidence of MDR in previously untreated cancer cases is approximately 40%, making it the most frequent type of resistance. Conventional anticancer drugs (e.g.: Doxorubicin, Gefitinib, Imatinib, Irinotecan, Methotrexate, Mitoxantrone, Paclitaxel, Tamoxiphen, Topotecan, etc.) are substrates of MDR transporters. Moreover MDR transporters play a distinct role in immune response.

Rationale

Determination of MDR1 (ABCB1), MRP1 (ABCC1), and BCRP (ABCG2) drug-efflux protein function is your tool for

- drug-transporter interaction studies
- drug-drug interactions (ADME)
- drug-efflux modulation
- studying transporter malfunction diseases
- studying hematological malignancies
- studying systemic inflammatory diseases

Features

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

- The kit contains two proprietary assays and measures the three clinically most relevant transporter activities selectively
- Uses highly selective inhibitors and different probe substrates for MDR1/MRP1 and BCRP
- Compatible with cell surface markers
- Contains ready-to-use reagents
- 10 independent MDR1/MRP1 and BCRP measurements could be carried out in triplicates
- Specimen: cell suspension, blood, bone marrow etc.: 6 hours stability before testing
- The first test results can be expected within 90 minutes

Availability

PRODUCT	SIZE	CAT. NO.
MDQUEST MultiDrugQuant™ Kit	10 assays	MDQ0101R

Principle of the test

For quantitative measurement of MDR1 and MRP1 activities in viable cells, MultiDrugQuant™ Kit applies the proprietary Calcein-assay technology. This assay utilizes the fluorogenic dye calcein-acetoxy-methyl ester (calcein-AM), which is a hydrophobic, non-fluorescent compound that readily penetrates the cell membrane. After entering the living cell, calcein AM is rapidly hydrolyzed by endogenous esterases. As a result of the cleavage, a 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: Principle of the test). 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. This difference is normalized to the dye uptake measured in the presence of the inhibitor and the results of the test are expressed in *MDR activity factor* (MAF) values. Thus, the result of the test becomes independent from factors influencing the cellular accumulation of calcein other than the activity of the multidrug transporters. These variables include the differences in cellular properties (membrane composition, intracellular esterase activity, cell size, cell surface, etc.); and 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 inter-laboratory 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 the selective BCRP-inhibitor (Figure: Principle of the test). However, the BCRP-specific reporter substrate is directly fluorescent and does not require cleavage by the intracellular esterases.

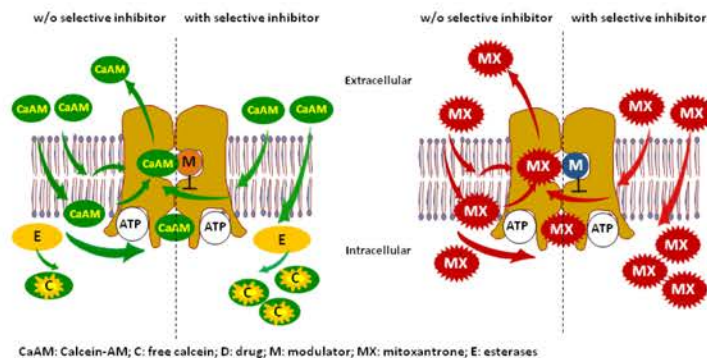
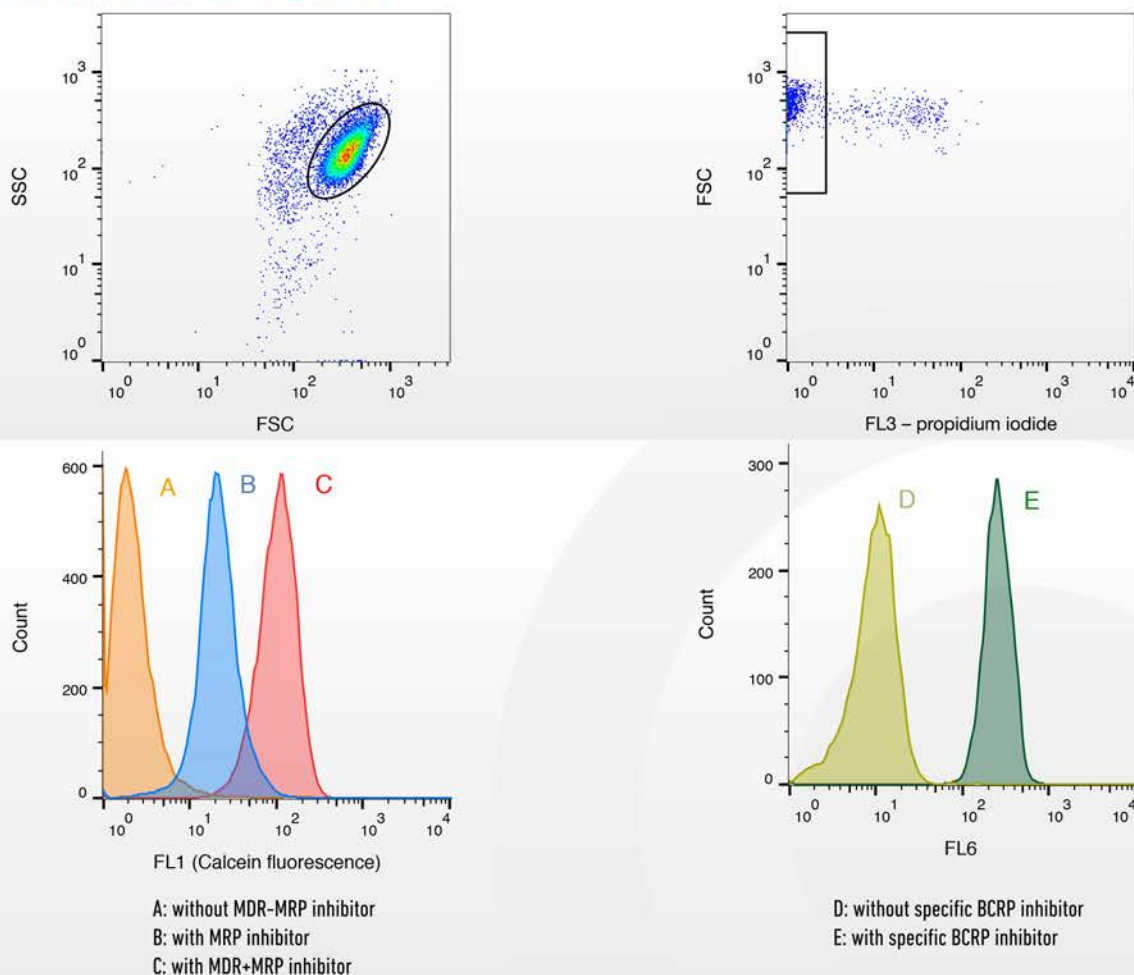


Figure: MDR activities in cultured cells



References

For further information and references check our website at: <http://www.mdquest.hu/products>