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ProductInformation

MONOCLONAL ANTI-P-GLYCOPROTEIN (MDR)
CLONE F4
Mouse Ascites Fluid

Product No. **P 7965**

Product Description

Monoclonal Anti-P-Glycoprotein (MDR) (mouse IgG1 isotype) is derived from the F4 hybridoma produced by the fusion of mouse myeloma cells and splenocytes from BALB/c mice. A mixture of human and hamster drug-resistant whole cells and crude plasma membranes was used as the immunogen.[1] The isotype is determined using Sigma ImmunoType™ Kit (Product Code ISO-1) and by a double diffusion immunoassay using Mouse Monoclonal Antibody Isotyping Reagents (Product Code ISO-2).

Monoclonal Anti-P-Glycoprotein (MDR) recognizes an epitope located in the amino terminal half of P-glycoprotein (Pgp), at the third extracellular loop of the molecule. The epitope is resistant to formalin fixation and periodate oxidation.[1] The product detects human MDR1 P-glycoprotein, but does not appear to recognize human MDR3 product[1], mouse mdr1a, mdr1b or the mdr3 P-glycoprotein.[2] It may be used in immunoblotting[1,2] immunoprecipitation,[1,2] immunocytochemistry,[1] immunohistochemistry,[1] cellular ELISA[1], flow cytometry and cell surface RIA.[1] Cross- reactivity has been observed with human[1,2] and hamster[1] P-glycoprotein.

Multidrug resistance (MDR) in humans is a unique phenomenon, leading to the failure of chemotherapy which is a significant problem in the treatment of neoplastic disease.[3-5] Despite exhibiting initial sensitivity to a particular chemotherapeutic regimen, some tumors become progressively unresponsive to the same or different antitumor drugs i.e., they acquire resistance. Other tumors appear to be insensitive to therapy from the outset and may be described as being intrinsically resistant. In the case of MDR, the resistance to one drug is associated with resistance to a whole panel of cytostatic drugs, like vincristine, doxorubicin, tenoposide and many others. The major cancers involved with MDR are leukemias, lymphomas, myelomas and breast and ovarian cancer. In addition, colon and renal tumors are relatively refractory to chemotherapy. MDR is commonly associated with an overexpression of the human multidrug resistance gene *mdr*, which encodes an energy-dependent transmembrane protein, also known as P-glycoprotein (170-180 kDa). P-glycoprotein is absent from most normal tissues, but is present in the proximal tubule of kidney, the adrenal medulla, the pancreas, the colon and the biliary ducts. One biological function of P-glycoprotein is to transport some chemotherapeutic agents out of cells, thereby conferring a drug resistant phenotype to cancer cells expressing P-glycoprotein. The protein appears to cause multidrug resistance via an ATP-dependent drug-efflux mechanism, which prevents the intracellular accumulation of drugs to an effective cytotoxic concentration. P-glycoprotein is encoded by a small family of genes. Two human genes (*mdr1, mdr3*), three mouse genes (*mdr1, mdr2, mdr3*), and three hamster genes (*pgp1, pgp2, pgp3)* have been identified and cloned. The human *mdr* genes show 80% nucleotide homology. Human *mdr3* and mouse *mdr3* are similar. In human only the *mdr1*-encoded P-glycoprotein is biologically active in multidrug resistant cells, and serves as a membrane efflux to pump the drugs out of the cells. Genetic and molecular biological investigation has revealed that *mdr1*- encoded prototype P-glycoprotein consists of twelve transmembrane domains and two cytoplasmic ATP binding sites, with two highly symmetrical peptide halves. Although P-glycoprotein is usually found in the membrane, there is some evidence that soluble forms of the protein may bind chemotherapeutics cytoplasmically and chaperone them to the cell surface for expulsion as well. Extracellular fluids obtained from cancer patients, such as malignant ascites and serum, were found to contain soluble P-glycoprotein, whereas those from normal healthy individuals were found not to express any detectable level of P-glycoprotein.[2] Thus, it would be desirable to have an effective simple procedure for screening tumors for the expression of P-glycoprotein before deciding the best course of treatment.

P-glycoprotein can be studied using a wide variety of methods: Northern blotting, Southern blotting, immunoblotting, polymerase chain reaction, *in situ* hybridization, immunohistochemistry, flow cytometry, labeled drug (doxorubicin, cytochalasin) accumulation, and MTT test-cell viability. All of these methods require tumor tissue specimens and are based upon the fact that P-glycoprotein is a plasma membrane bound component. Immunological techniques permit the identification, isolation and characterization of the *mdr1* gene-encoded P-glycoprotein.[6] Screening for P-glycoprotein expression with antibodies may be the more reliable indicator, since the presence of mRNA transcript may not necessarily reflect the level of protein within the cell.

Monoclonal Anti-P-Glycoprotein (MDR) may be used for the localization of P-glycoprotein using various immunochemical assays including immunocyto- chemistry,[1] immunohistochemistry,[1] immunoblotting,[1,2] immunoprecipitation, ELISA,[1] flow cytometry and cell surface RIA.[1,2]

Reagents
The product is provided as ascites fluid with 0.1% sodium azide as a preservative.

Precautions and Disclaimer
Due to the sodium azide content a material safety sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution. Consult the MSDS for information regarding hazardous and safe handling practices.

Product Profile
A minimum working dilution of at least 1:500 is determined by immunoperoxidase labeling of formalin-fixed, paraffin-embedded human kidney section.

In order to obtain best results, it is recommended that each user determine the optimal working dilution for individual applications by titration assay.

Storage
For continuous use, store at 2-8 °C for up to one month. For extended storage freeze in working aliquots. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is not recommended. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use.

References

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