Gene Section
Mini Review

ABCC1 (ATP-binding cassette, sub-family C (CFTR/MRP), member 1)
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Identity
Other names: MRP (multidrug resistance-associated protein)
HGNC (Hugo): ABCC1
Location: 16p13.1
Note: MRP is a gene involved in multidrug resistance, discovered in a multidrug-resistant, P-glycoprotein negative, non small cell lung carcinoma cell line.

DNA/RNA
Description
Spans at least 200 kb and contains 31 exons

Transcription
7 kb mRNA transcript; significant level of variant transcripts due to alternative splicing.

Protein
Description
1531 amino acids, 190 kDa; contains two ATP binding domains and three membrane-spanning helices; member of the ATP-binding cassette proteins (ABC proteins).

Expression
Expressed at a basal level in a wide variety of normal tissues, including epithelial cells and all hematopoietic cell types, which suggests a function common to most cell types; increased expression in various tumor cell type.

Localisation
In normal cells, predominant localisation in the cytoplasm; in tumor cells, predominant in plasma membrane, but also found in endoplasmic reticulum, indicating a probable different function as in normal cells.

Function
Plasma membrane drug-efflux pump; MRP induces a multidrug resistance phenotype (MDR phenotype); overexpression confers tumor cell resistance to a wide variety of hydrophobic drugs: doxorubicin, daunorubicin, vinblastine, vincristine, colchicine, VP16, Rhodamin 123; glutathione is required for the effective expulsion of the chemotherapeutic agents; the mode of action of MRP is very similar to the one of P-glycoprotein, the main protein responsible for the MDR phenotype; however, MRP does not confer resistance to Taxol or m-AMSA, but it is able to transport metallic oxyanions, glutathione and other glutathione conjugates; inhibitors of organic anion transport, such as probenecid, can block MRP activity.

Homology
Structural and/or functional homology with other ABC transporter proteins (CFTR, Pgp, MOAT).

Implicated in
Induced resistance to chemotherapeutic agents
Disease
In a wide variety of solid and hematological tumors.

Oncogenesis
MRP hyperexpression may confer therapeutic resistance in leukemia and solid tumors; however, its relative importance, in comparison with other proteins able to induce the MDR phenotype (P-gp, LRP), is not yet clear; hyperexpression is probably linked to transcriptional activation of the gene and/or increased mRNA stability, and not to gene amplification; increased expression of MRP mRNA and protein is a factor of bad prognosis in neuroblastoma, retinoblastoma, and non small cell lung carcinoma. In haematological malignancies, overexpression is frequent in chronic lymphocytic leukemia and prolymphocytic leukemia, occasional in acute myeloid leukemia and rare in acute lymphoid leukemia, lymphoma, multiple myeloma and myeloproliferative disorders.

References

This article should be referenced as such: