systems is a system called the ABC transporters. As reviewed by Elliott and Al-Hajj (76) the human genome encodes nearly 50 ABC transporters. Of these transporters, those used for multi-drug transport are listed below.

In the following list of drug transporters, the alternate names are disclosed, for example ABCC1 is the same protein as MRP1:

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MRP1/ABCC1;MRP2/ABCC2;MRP3/ABCC3;MRP4/ABCC4;MRP5/ABCC5;MRP6/ABCC6;MRP7/
ABCC10; MRP8/ABCC11; and MRP9/ABCC12.77
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According to various publications (78,79) the transporter known as ABCC1 may confer resistance to doxorubicin, daunorubicin, vincristine, etoposide, epirubicin, chlorambucil, methotrexate (80,81) melphalan, and paclitaxel; ABCC2 may confer resistance to doxorubicin, etoposide, methotrexate, irinotecan (SN-38), vincristine, vinblastine, camptothecin, paclitaxel, docetaxel, etoposide, and cisplatin; and ABCC4 may confer resistance to rubitecan and irinotecan.

b. Biology of cross-resistance

Cross-resistance refers to the situation where treating a patient with a first drug confers changes in the physiology of the tumor that reduce efficacy of a second, unrelated drug that may be administered at a later time (82).

Cross-resistance can result from the situation where the first drug induces expression of one of the ABC transporters, and where this particular ABC transporter pumps the first drug out of the tumor cell, and also pumps a second drug out of the tumor cell, for example a second drug administered at some later time in a clinical trial.

In making clinical decisions on the administration of different sequences of drugs, caution should be used when faced with a publication stating that a first drug induces resistance to a second drug, by way of stimulating the activity of a drug transporter, in the situation where the first drug is hydrophobic and the second drug is lipophilic, or where the first drug is large, and the second drug is small (83). In other words, skepticism should be exercised when faced with descriptions that take these particular fact patterns.

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