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Update Information on Drug Metabolism Systems—2009, Part II:

SUMMARY OF INFORMATION ON THE EFFECTS OF DESASES AND ENVIRONMENTAL FACTORS ON HUMAN CYTOCHROME P450 (CYP) ENZYMES AND TRANSPORTERS

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Abstract

The present paper is an update of the data on the effects of diseases and environmental factors on the expression and/or activity of human cytochrome P450 (CYP) enzymes and transporters. The data are presented in tabular form (Tables 1 and 2) and are a continuation of previously published summaries on the effects of drugs and other chemicals on CYP enzymes. The collected information presented here is as stated by the cited author(s), and in cases when several references are cited the latest published information is included. Inconsistent results and conclusions obtained by different authors are highlighted, followed by discussion of the major findings. The searchable database is available as an Excel file, for information about file availability contact the corresponding author.

Keywords

Cytochrome P450s; CYPs; transporters; physiological conditions; illness; environmental condition; demographic factors; expression; activity

Introduction

Cytochrome P450 (CYP) enzymes catalyze a number of metabolic reactions that have profound effects on the biological activities (therapeutic and/or toxic) of xenobiotics, including drugs, and the significance of the human enzymes for drug metabolism has been reviewed before [1-3] and updated in the “Update Information on Drug Metabolism Systems —2009, Part I” [4]. The roles of the transporters which, depending on the site of expression, may enhance or limit absorption or excretion of drugs/chemicals from an organ or tissue and have additional effects on the biological activities of drugs/xenobiotics, are reviewed elsewhere [5,6] and updated in Part I [4]. In addition to a great number of xenobiotics influencing the activity and/or expression of the CYP enzymes and transporters, the effects of diseases and environmental factors are also of interest. These factors can have profound

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effects on the activity and expression and therefore also the final biological activity, efficacy and safety of drugs and other chemicals (Tables 1 and 2). A great number of examples from the literature show that the final effect of a drug/chemical on an organism, whether pharmacological and/or toxicological, depends on regulation of expression and the activity of CYP enzymes and transporters. When these properties are changed by illness or environmental factors, a significant change (e.g. of therapeutic outcome of a drug) might occur. This is of particular interest when diseases such are cancer are considered.

The present summary provides the reader a collection of information on the effects of major disease and environmental factors on function of CYP enzymes and transporters considering also the effects on therapeutic treatment or human health.

Tabular presentation

Data are presented in Tables 1 and 2 and formatted in columns 1 - 9: 1. **CYP/ Transporter**; 2. **Category**; 3. **Subcategory**; 4. **Effectors**; 5. **Model** used; 6. **Method**; 7. **Effect** on particular enzyme or transporter; 8. **Remarks** about effects when stated by the cited authors to additionally characterize the effects. 9. **References**. The data are sorted by Column 1 (**Enzymes/Transporters**), Column 3 (**Subcategory), and** Column 4 **(Effectors)** for an easier approach to the information presented. The tabulated data were obtained either *in vivo* (clinical experiments) or *in vitro* using various models including clinical tissue samples, cell cultures, microsomes, and recombinant systems. References to the Tables 1 and 2 are listed separately at the end of Table 2 and, in addition, PubMed ID numbers (when available) are included to facilitate the ease of location of cited papers.

It is important to emphasize that in some cases the results depend upon the model and/or method used for investigation and contradictory or insufficient results might have been obtained [7]. Such results are designated in the Tables (bold-face font) as **inconsistent results reported**. When effects might influence clinical drug effects, they are designated as having clinically significant pharmacokinetic drug-drug interaction potential. Of the effectors presented in Tables 1 and 2, a great number belong to the effects of cancers on the expression/activity of both transporters and CYP enzymes. Particularly intriguing is interpretation of the results such as “increase” or “decrease” of expression of a particular enzyme/transporter. This is because of the lack of exact limits, diversity of ways of presenting results, and the large numbers of results obtained using immunohistochemistry or immunoblotting which are not always expressed quantitatively and thus making the results difficult to compare with those obtained by other methods. Standardized detection and quantification techniques and methods, e.g. real-time PCR (RT-PCR), can provide more reliable comparisons of experimental results with therapy. In this respect it has been suggested that of the techniques used to analyze drug transporters, flow cytometry is preferred to immunoblots, mRNA blots, and immunocytochemical assays. The use of functional flow cytometric tests (assessing modulator-induced changes in fluorophore retention and/or efflux) has been promoted because these allow evaluation of a protein activity, in contrast to immunochemical or molecular tests [8]. E.g. with P-gp functional analysis is preferred when testing effects of cancers as a more sensitive predictor of

chemoresistance than P-gp expression [9]. This approach should be considered regarding the effects of inflammation and of environmental factors. Detailed analysis of tumor types and expression of CYP enzymes and transporters has identified a variety of tumors with the same pharmacological profile. It was therefore suggested that the anatomical independence of drug pathways promotes efforts to move away from traditional approaches in the selection of cancer therapy (10).

As presented in Tables 1 and 2 (columns **Effects** and **Remarks**) experimental results show that in a number of cases inconsistent results and conclusions have been obtained for the same effectors using different methods and/or models, making it difficult to reach conclusions on the effects of, e.g., tumors and effectors on both CYP and transporter expression and activity. However, some results could link causality with changes of gene expression. For instance, the increases in mRNA and protein expression of glucose transporters (GLUT) were suggested as markers of the aggressive biologic potential of tumors (associated with poor survival of patients). It was suggested that inhibition of up-regulation of these transporters might be a promising tool that would be beneficial in cancer prognosis and therapy. Similarly, increases in expression levels of CYP1B1 and CYP2J2 in tumor cells and tissues (these enzymes otherwise not present or present at very low levels in normal tissues) have been suggested as tumor markers in the diagnosis and prognosis of different malignancies. Although in some cases inconsistent results have been obtained, overexpression and increased functional activity of transporters such as MRPs (in particular MRP1, MRP2, and MRP3), P-gp (MDR1), LRP, and BCRP1 in tumors have been suggested as predictors and to participate in acquired multidrug resistance *in vivo*. On the other hand, enhanced or lowered expression and/or activity of CYP enzymes in some diseases could result in clinically significant drug interaction potential, resulting in unfavorable clinical outcome or increased drug/chemical toxicity. Some examples include increased expression of CYP2E1 in alcoholic healthy subjects and decreased enzyme expression in alcoholic liver disease (ALD), increased CYP2E1 expression in livers of transplant patients, high expression of CYP3A4 enzyme in lymphoid carcinoma (proposed as a useful predictor of poor response to the standard peripheral type lung cancer (PTLC) chemotherapy), and high expression of CYP3A enzymes in osteosarcomas (suggested as a predictor of metastasis and poor prognosis). For detailed comments related to these and other examples refer to the information in Tables 1 and 2 and the references, and for the levels of the CYP enzymes present in different human tissues the readers should consult the results reported elsewhere [11].

In additions to the effectors reported in Table I and Table II there a number of others that might have additional effects on clinical or toxicological outcome influencing the level or the activity of one or more enzymes or transporters. Such effectors are the genetic polymorphism of CYP enzymes and transporters, as well as the effects of drugs/xenobiotics by themselves. The influence of such effectors are not the focus of the present paper, they were reviewed elsewhere [1,2,12]. For instance, some consistent evidence for association between CYP polymorphisms and lung, head and neck, and liver cancers has been reported. Controversial findings suggest that colorectal and prostate cancers may be associated with CYP polymorphisms, whereas no evidence for relevant associations with breast or bladder

cancers has been reported. A summary of the available information related to the association of CYP polymorphisms has been reported [12] with leukemia, lymphomas and diverse types of cancer that were investigated only for some CYP genes, including brain, esophagus, stomach, pancreas, pituitary, cervical epithelium, melanoma, ovarian, kidney, anal, and vulval cancers.

The influence of the drugs themselves can be illustrated by the effect of placitaxel on human colorectal cancer cells (Caco-2). The cells (which are sensititive) were exposed to increasing concentrations of the drug (0-250 nM) during the course of one year, in order to select placitaxel-resistant cells. Subsequently, the sensitivity to placitaxel and the extents of expression of CYP2C8, CYP3A4, and CYP3A5 genes in the original and resistant cells were compared. The results showed that resistant cancer cells displayed a 246-fold increased lethal dose (LD_{50}) to placitaxel compared with the original cancer cells. In addition, a 4.4-fold enhancement of CYP2C8 expression and a 5.6-fold increase of multidrug resistance (MDR)1 expression was observed in resistant cells exposed to placitaxel. When placitaxel was removed from the culture medium, CYP2C8 (but not MDR1) expression, reverted to basal levels and the resistance to placitaxel decreased 3.2-fold. No major changes in the expression levels of CYP3A4 and CYP3A5 were observed. It was concluded that Caco-2 cells are capable of increasing the expression levels of CYP2C8 as a response to long-term exposure to placitaxel. This study provides evidence for a mechanism of acquired resistance to anticancer therapy based on the induction of anticancer-metabolizing enzymes [13]. It is noteworthy to mention that placitaxel has been reported as a selective substrate of CYP2C8 and also CYP3A4, and both enzymes are present in non-tumoral and tumoral tissue samples (thus inactivating the drug). In addition, the enzyme activities when induced or inhibited either in GI tract or in liver might have clinically significant effects on pharmacokinetic properties of the drug (Table 1) (2,13,14).

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Table 1

Effects of selected effectors on expression and activity of cytochrome P450 (CYP) enzymes in humans.

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1A	Illness	Cancer	Bone carcinoma	clinical osteosarcoma biopsies samples of primary tumors	immunohistochemistry	expressed in tumor tissue		[285]
CYP1A	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, normal colon, colonic adenoma, and colon carcinoma biopsies	immunohistochemistry	expressed in tumor, not expressed in normal tissue	suggested as specific marker of colonic neoplasia	[263,270,296]
CYP1A	Illness	Cancer	Esophagea 1 carcinoma	esophageal squamous-cell carcinoma, SCC, adenocarcinoma, clinical samples, microsomes from human esophagus with and without tumor tissue	immunoblotting, immunohistochemistry	increase of protein level in tumor tissue compared to samples without tumor, also not present in non-neoplastic samples		[274,275,296]
CYP1A	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples	immunoblotting	expressed in tumor, not expressed in normal stomach tissue		[276]
CYP1A	Illness	Cancer	Leukemia	L1210 leukemia cell lines	immunoblotting	expressed in sensitive and BCNU resistant lines		[279]
CYP1A	Illness	Cancer	Liver carcinoma	clinical tumor and normal liver tissue samples, hepatocellular carcinomas (HCC)	immunohistochemistry	variable expression of protein in primary malignant liver tumors		[273]
CYP1A	Illness	Cancer	Prostate carcinoma	clinical prostate tissue samples	immunoblotting	expression of protein in prostate epithelium and in prostate tumor cells		[277,296]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1A	Illness	Cancer	Soft tissue carcinoma	soft tissue sarcomas, clinical samples	immunoblotting	expression of mRNA in tumor and control tissues		[284]
CYP1A	Food	Dietary habit	Char grilled meat diet	small intestine specimens, enzyme activity	RT-PCR, Western immunoblotting, hepatic enzyme activity	increase of mRNA and protein expression in liver and small intestine		[305]
CYP1A1	Illness	Cancer	Brain carcinoma	medulloblastoma UW228-3 cell line, microsomal proteins	Western immunoblotting, immunohistochemistry, RT-PCR, 7-Ethoxyresorufin de-ethylation O-	not expressed in untreated cells, expressed in Resveratrol and beta-NF treated cells		[256,300,301]
CYP1A1	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples, immortalized non-tumor- and tumor-derived cell lines, T47D and MDA-MB-231 cells	RT-PCR, Western immunoblotting immunohistochemistry, Northern blotting	**Inconsistent results reported** - mRNA and protein present in tumor and normal tissues samples, decrease of mRNA expression in tumor as compared with morphologically normal adjacent tissues samples, higher amplification occurred in normal tissues of same individuals, very low level of mRNA in both tumor and normal tissues samples, also protein not expressed, in cells	**no consistent associations** between breast cancer and CYP1A1 polymorphisms were found, absence of a major association of CYP1A1 with breast cancer	[34,40,66,69,70,245,246,250,251,296,310,425]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						present only after present only after induction with an AhR agonist		
CYP1A1	Illness	Cancer	Colorectal carcinoma	clinical tissue samples	enzyme activity assay	activity present in tumor tissue	**Conflicting results reported on** association of colorectal cancer with CYP1A1 polymorphism	[296,425]
CYP1A1	Illness	Cancer	Esophageal carcinoma	esophagectomy specimens, Barrett's esophagus, esophageal squamous mucosa, and normal tissue	RT-PCR	expression of mRNA in tumor tissue, weak expression of mRNA in some normal tissues	significant, although weak, association of the CYP1A1*2C allele with esophageal cancer in smokers	[307,425]
CYP1A1	Illness	Cancer	Lung carcinoma	non-small cell lung cancer tissue, tumor and no tumor lung tissue samples, A549 adenocarcinoma cell line, bronchioloalveolar carcinomas	RT-PCR, Northern hybridization, Western immunoblotting, immunohistochemistry	expression of mRNA and protein, lower expression of CYP1A protein in tumors	proposed as markers for the determination of quality of lung cancer, neither CYP1A1 MspI nor CYP1A1 Ile462Val was associated with lung cancer susceptibility, secondary role of CYP1A1 polymorphism and lung cancer risk proposed	[37,38,39,263,267,282,289,296,337,389,425]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1A1	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in tumor and control tissues		[41]
CYP1A1	Illness	Cancer	Prostate carcinoma	clinical prostate and normal tissues samples	RT-PCR	expression of mRNA in tumor tissue, benign prostatic hyperplasia (BPH), in prostate cancer cell lines, and normal tissues	weak association of CYP1A1*2C alleles with increased risk reported	[291,387,425]
CYP1A1	Environmental condition	Cellular osmolality	Hypertonic environment	human primary hepatocytes in hypertonic media	cDNA microarray and RT-PCR	increase of mRNA expression		[43]
CYP1A1	Environmental condition	Cigarette smoke exposure	Cigarette smoke	lung tissue samples, bronchial epithelial cells, adenocarcinoma, bronchoalveolar cancer	RT-PCR, immunohistochemistry, immunoblotting	increase of mRNA and protein expression, and activity in lung of smokers, not expressed in non-smokers	pulmonary expression appears to be associated with lung cancer risk, no clear association between polymorphism and enzyme inducibility	[11,39,308,309,333,334,335,336,389,425]
CYP1A1	Environmental condition	Oxidative stress	Reactive oxygen species, hydrogen peroxide	human hepatoma cell line HepG2, transfected	Northern blotting, Western immunoblotting	decrease of mRNA expression, decrease of induced mRNA expression	intracellular H_2O_2 released during the catalytic cycle	[46,47,48,49]
CYP1A1	Physiological condition	Stress	Shear stress	human umbilical vein endothelial cells (HUVECs), human aortic endothelial cells (HAECs)	RT-PCR, Western immunoblotting, Northern blotting	increase of mRNA, protein expression and activity, mRNA expressed and protein not detected under static conditions		[388,390]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1A2	Demographic factor	Age	Adults, aged 18–46 (median 27) years	blood samples, human liver microsomes (HLM)	Alosetron pharmacokinetics, 7-Ethoxyresorufin de-ethylation O- in HLM	decrease of metabolic clearance ratio with age, decrease or no statistical difference in activity as a function of age in HLM		[10,11]
CYP1A2	Demographic factor	Age	Children under three years old	clinical urine samples	Theophylline metabolites urinary ratios	decrease of activity		[238]
CYP1A2	Illness	Cancer	Esophagea 1 carcinoma	Esophagectomy specimens, Barrett's esophagus, esophageal squamous mucosa, and normal tissue	Western immunoblotting, immunohistochemistry, RT-PCR	expression of mRNA and protein		[307]
CYP1A2	Illness	Cancer	Prostate carcinoma	clinical prostate and normal tissues samples	RT-PCR	expression of mRNA in tumor tissue, benign prostatic hyperplasia (BPH), in prostate cancer cell lines, and normal tissues		[291,292 ,296,387]
CYP1A2	Illness	Cancer	Testicular carcinoma	urine samples	Caffeine metabolic ratio (AFMU, 1X , 1 U)/17 U	decrease of activity		[55]
CYP1A2	Environmental condition	Cellular osmolality	Hypertonic environment	human primary hepatocytes in hypertonic media	cDNA microarray and RT-PCR	decrease of mRNA expression		[43]
CYP1A2	Environmental condition	Cigarette smoke exposure	Cigarette smoke	human liver samples, human liver microsomes (HLM), urine samples	Western immunoblotting, immunohistochemistry, 7-Ethoxyresorufin de-ethylation O-, Caffeine metabolic ratio (AFMU, 1X , 1	increase of expression and activity in liver of smokers	positive correlation was found with liver CYP1A2 protein	[7,8,12,13,309,333]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
					U)/17 U,			
CYP1A2	Therapeutic condition	Contraceptives	Contraceptives	urine samples	Caffeine metabolic ratio (AFMU, 1× , 1 U)/17 U	decrease of activity		[12,13]
CYP1A2	Food	Dietary habit	Broccoli	urine samples	Caffeine metabolic ratio (AFMU, 1× , 1 U)/17 U	increase of activity		[12,232]
CYP1A2	Food	Dietary habit	Kwashiorkor, malnutrition	African population, children, plasma samples	Caffeine metabolic index	decrease of activity, Paraxanthine Cmax and Paraxanthine/ Caffeine plasma ratio was significantly lower in kwashiorkor patients than in healthy control		[223]
CYP1A2	Demographic factor	Ethnicity	Hispanic	human liver microsomes (HLM)	7-Ethoxyresorufin de-ethylation O-	decrease of activity, half of the average activity of those from Caucasians and African Americans		[11]
CYP1A2	Physiological condition	Exercise	Physical exercise	urine samples	Caffeine metabolic ratio (AFMU, 1× , 1 U)/17 U	increase of activity		[12]
CYP1A2	Demographic factor	Gender	Male, Female	blood samples, human liver microsomes (HLM), urine samples	Alosetron pharmacokinetics, 7-Ethoxyresorufin de-ethylation O-, Caffeine metabolic ratio (AFMU, 1× , 1 U)/17U	increase of activity in non-induced males comparing to non-induced females in clinical studies and in HLM		[10,11,13]
CYP1A2	Illness	Heart failure	Congestive heart failure	clinical urine samples	Caffeine metabolic index	decrease of activity		[240,241]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1A2	Illness	Infection	Influenza virus epidemic	young children	Theophylline metabolism	decrease of activity		[235]
CYP1A2	Illness	Infection	Plasmodium falciparum malaria	African population, adults and children, plasma and saliva samples	Caffeine metabolic index	decrease of activity, Paraxanthine Cmax and Paraxanthine/Caffeine plasma ratio was significantly lower in malaria patients than in healthy control		[222,223]
CYP1A2	Illness	Liver disease	Liver disease, not specified	liver disease severity was categorized by use of the Child-Pugh score, plasma and urine samples from volunteers	Caffeine metabolic index	decrease of activity		[51]
CYP1A2	Physiological condition	Pregnancy	Pregnancy	saliva samples	Caffeine metabolic ratio (AFMU, 1× , 1U)/17U, Caffeine clearance	decrease of activity		[12,53]
CYP1A2	Medicine	Vaccine	Virus vaccination	clinical urine samples	Theophylline clearance	decrease of activity	clearance depression after vaccination	[239]
CYP1B1	Illness	Cancer	Bladder carcinoma	clinical tumor and normal tissue samples, transitional cell carcinoma	immunoblotting, immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]
CYP1B1	Illness	Cancer	Bone carcinoma	clinical osteosarcoma biopsies samples of primary tumors	immunohistochemistry	expressed in tumor tissue	high expression frequency found	[285]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1B1	Illness	Cancer	Brain carcinoma	clinical tissue samples, glial cell tumors, astrocytoma, medulloblastoma UW228-3 cell line, microsomal proteins	Western immunoblotting, immunohistochemistry, RT-PCR, 7-Ethoxyresorufin de-ethylation O-	expressed in tumor tissue, not expressed in normal tissue	increased CYP1B1 expression in glial tumors was associated with decreased patient survival time, suggested as prognostic biomarker of human medulloblastomas, DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[244,249,256,257,296,300,301]
CYP1B1	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples, immortalized non-tumor- and tumor-derived cell lines, T47D and MDA-MB-231 cells	RT-PCR, Western immunoblotting, immunohistochemistry, Northern blotting	**Inconsistent results reported** - mRNA and protein present in tumor and in adjacent normal tissues samples, high overexpression in tumor cells, also no qualitative differences in expression at mRNA level between tumor and surrounding normal tissues samples, lower expression in tumor than in adjacent no tumor	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy, presence of CYP1B1 in cells decreases their sensitivity to the cytotoxic effects of a specific anticancer drug, no clea association between	[34,35,40,69,70,75,246,249,250,251,257,258,263,296,4

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						tissues samples, also no or very low expression in normal tissue and cells and protein not detectable in normal tissues samples	breast cancer and *CYP1B1* polymorphism	
CYP1B1	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples, adenocarcinoma, primary colorectal cancer, lymph node metastasis	Western immunoblotting, immunohistochemistry	**Inconsistent results reported** - expressed in tumor tissue, not expressed in normal tissue, also expressed at low levels in normal colonic epithelia and in blood vessels within the colon, higher expression in tumor	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy, also expression in colon tumors does not correlate with tumor stage or degree of lymph node invasion	[249,253,255,257,263,296,339]
CYP1B1	Illness	Cancer	Connective tissue carcinoma	clinical tissue samples, sarcoma	immunoblotting, immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1B1	Illness	Cancer	Esophagea 1 carcinoma	clinical tissue samples, squamous carcinoma, esophagectomy specimens, Barrett's esophagus, and normal tissue	RT-PCR, Western immunoblotting, immunohistochemistry	expression of mRNA and protein in tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257 ,296,307]
CYP1B1	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples, adenocarcinoma	immunoblotting, immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]
CYP1B1	Illness	Cancer	Kidney carcinoma	clinical tissue samples, clear cell and transitional cell carcinoma	immunoblotting, immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]
CYP1B1	Illness	Cancer	Lung carcinoma	clinical tissue samples, squamous carcinoma, adenocarcinoma, non-small cell lung cancer, tumor and non-tumor lung tissue samples, A549 adenocarcinoma cell line, bronchoalveolar cancer	RT-PCR, Western immunoblotting, immunohistochemistry	increase of mRNA and protein expression in tumor tissue, expressed in microsomes and cytoplasm of smooth muscle cells, not expressed in pneumocytes of normal tissue	DNA-based vector encoding CYP1B1 DNA proposed as widely applicable cancer immunotherapy, overexpression considered to be aggressive biomarker for non-small cell	[249,257 ,282,283 ,289,296 ,337,389]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							lung cancer, CYP1B1 Leu432Val was associated with lung cancer susceptibility, CYP1B1 expression was not dependent on cigarette smoking in lung adenocarcinoma	
CYP1B1	Illness	Cancer	Lymphoid carcinoma	clinical tissue samples, non-Hodgkin's lymphoma	immunoblotting, immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]
CYP1B1	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues, higher expression in NPC tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[41,257]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1B1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, adenocarcinoma, primary epithelial ovarian cancer, primary and metastatic ovarian cancer	immunoblotting, immunohistochemistry	highly expressed in primary tumor tissue, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy, positive correlation with prostate cancer risk reported	[249,252,257,260,425]
CYP1B1	Illness	Cancer	Prostate carcinoma	clinical prostate tissue samples and prostate cancer cell lines	RT-PCR, Western immunoblotting, immunohistochemistry	increase of expression of mRNA and protein comparing to control tissue samples, present in benign prostatic hyperplasia (BPH), and normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy, positive association with prostate cancer risk reported	[68,257,291,292,296,387,425]
CYP1B1	Illness	Cancer	Skin carcinoma	clinical tissue samples, squamous carcinoma	immunoblotting, immunohistochemistry	expressed in tumor, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP1B1	Illness	Cancer	Testicular carcinoma	clinical tissue samples, malignant germ cell tumor	immunoblotting, immunohistochemistry	expressed in tumor, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]
CYP1B1	Illness	Cancer	Uterus carcinoma	clinical tissue samples, adenocarcinoma, malignant mixed Mullerian tumor	immunoblotting, immunohistochemistry	expressed in tumor, not expressed in normal tissue	DNA-based vector encoding CYP1B1 DNA proposed for widely applicable cancer immunotherapy	[249,257]
CYP1B1	Environmental condition	Cigarette smoke exposure	Cigarette smoke	lung tissue samples, bronchial epithelial cells, bronchoalveolar cancer	RT-PCR, immunohistochemistry, immunoblotting	increase of expression of mRNA and protein in smokers		[11,309, 335,336, 389]
CYP1B1	Physiological condition	Stress	Shear stress	human umbilical vein endothelial cells (HUVECs), human aortic endothelial cells (HAECs)	RT-PCR, Western immunoblotting, Northern blotting	increase of mRNA, protein expression and activity, mRNA and protein expressed under static conditions		[388,390]
CYP2A,2B	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian tissue	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue, high expression in metastatic ovarian tissue	negative or low or moderate expression compared to high expression associated with poor survival	[252]
CYP2A,2B	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer, lymph node metastasis	immunoblotting, immunohistochemistry	low expression in tumor tissue	correlation between expression in primary	[253]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							tumors and corresponding lymph node metastases	
CYP2A6	Demographic factor	Age	Adults aged less then 20 till over 60 years	human liver microsomes (HLM)	Coumarin hydroxylation C7-	increase of activity with age		[11]
CYP2A6	Environmental condition	Cadmium exposure	Cadmium	urine samples	7-Hydroxycoumarin, Umbelliferone urine excretion	increase of activity in men and women, increase of expression proposed		[25,26,27]
CYP2A6	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, breast reduction sample microsomes	RT-PCR, Western immunoblotting	mRNA not present in tumor and normal tissues samples, mRNA, protein and activity detected in reduction samples		[69,70]
CYP2A6	Illness	Cancer	Colorectal carcinoma	clinical tumor tissue samples, adenoma, adenocarcinoma and adjacent mucosa	immunohistochemistry, in situ hybridization	increased expression of mRNA and protein in adenocarcinoma, very low or no protein detected in normal mucosa	suggested that may have important roles in human colorectal tumorigenesis and progression, risk for colorectal cancer increased in parallel with CYP2A6 enzyme activity.	[69,70,407,420]
CYP2A6	Illness	Cancer	Lung carcinoma	clinical tumor tissue samples, non-small cell lung cancer tissue, squamous cell carcinoma, lung adenocarcinoma	RT-PCR, Northern blotting, immunohistochemistry, in situ hybridization (ISH)	expression of mRNA and protein	proposed as markers for the determination of quality of lung cancer, no	[37,237,413]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							association was observed between CYP2A6 genotype and risk of lung cancer	
CYP2A6	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP2A6	Illness	Cancer	Prostate carcinoma	clinical prostate and normal tissues samples	RT-PCR	expression of mRNA in tumor and normal tissues		[306]
CYP2A6	Demographic factor	Ethnicity	Hispanic	human liver microsomes (HLM)	Coumarin hydroxylation C7-	increase of activity, twice of the average activity of those from Caucasians and African Americans		[11]
CYP2A6	Environmental condition	Lead exposure	Lead	urine samples	7-Hydroxycoumarin, Umbelliferone urine excretion	decrease of activity in men due to decrease of expression proposed, not observed in women		[26,27]
CYP2A6	Illness	Liver disease	Alcoholic liver disease (ALD)	liver biopsy samples	immunohistochemistry, Western immunoblotting	increase of protein level		[225]
CYP2A6	Illness	Liver disease	Steatosis, nonalcoholic fatty liver (NAFL)	liver biopsy samples	immunohistochemistry, Western immunoblotting	increase of protein level		[225]
CYP2A7	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR	mRNA not present in tumor and normal tissue samples		[69]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2A13	Illness	Cancer	Breast carcinoma	clinical samples, breast tissue and tumors	RT-PCR	mRNA not present in tumor and normal tissues samples		[69]
CYP2A13	Illness	Cancer	Lung carcinoma	lung adenocarcinoma tissue, normal tissue and tissue lung carcinoma samples	RT-PCR, immunohistochemistry, immunoblotting	expression of mRNA in tumor tissue, low or no expression of protein in tumor tissue, expressed in the epithelial cells of human bronchus and trachea of normal tissue	high efficiency in the metabolic activation of tobacco carcinogen NNK, CYP2A13 genotype is associated with reduced risk of lung adenocarcinoma	[237,259]
CYP2A13	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP2B6	Demographic factor	Age	Adults aged less then 20 to over 60 years	human liver microsomes (HLM)	Mephenytoin (S)-demethylation N- (Nirvanol formation)	decrease of activity with age		[11]
CYP2B6	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples	RT-PCR, Western immunoblotting	**Inconsistent results reported** - decrease of protein expression in tumor as compared with morphologically normal adjacent tissues samples, also no qualitative differences in expression at mRNA level between tumor and surrounding normal tissues		[66,69,70]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2B6	Illness	Cancer	Esophageal carcinoma	esophageal squamous-cell carcinoma, SCC, clinical samples, microsomes from human esophagus with and without tumorous tissue	immunoblotting	expression of protein in tumor tissue		[275]
CYP2B6	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP2B6	Demographic factor	Ethnicity	Hispanic	human liver microsomes (HLM)	Mephenytoin (S)-demethylation N- (Nirvanol formation)	increase of activity, twice the average activity of those from Caucasians and African Americans		[11]
CYP2B7	Illness	Cancer	Lung carcinoma	non-small cell lung cancer tissue samples	RT-PCR, immunohistochemistry	decrease of expression of mRNA in tumor tissue, expressed in normal tissue		[263,264,296]
CYP2C	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples	RT-PCR, Western immunoblotting, immunohistochemistry	very low expression, mRNA and protein present in tumor and normal tissues samples, no qualitative differences in expression of mRNA between tumor and surrounding normal tissue		[35,69,70,296,310]
CYP2C	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer, lymph node metastasis	immunoblotting, immunohistochemistry	low expression in tumor tissue	correlation between expression in primary tumors and corresponding lymph node	[253]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							metastases	
CYP2C	Illness	Cancer	Esophageal carcinoma	esophageal squamous-cell carcinoma, SCC, carcinoma endoscopy tissue samples, esophagectomy specimens, Barrett's esophagus, esophageal squamous mucosa	RT-PCR	expression of mRNA and protein in tumor and normal tissue, expression of mRNA significantly lower in tumor tissue		[31,307]
CYP2C	Illness	Cancer	Lung carcinoma	A549 adenocarcinoma cell line	Northern blotting, RT-PCR, immunohystochemistry	expression of mRNA in tumor cells, protein expressed in normal cells		[296,337]
CYP2C	Illness	Cancer	Prostate carcinoma	clinical prostate tissue samples	immunoblotting, immunohistochemistry	expression of protein in prostate epithelium and in prostate tumor cells		[277,296]
CYP2C	Illness	Cancer	Silvary gland carcinoma	clinical samples, pleomorphic adenoma	immunoblotting, immunohistochemistry	expression of protein		[324]
CYP2C8	Demographic factor	Age	Adults aged less then 20 till over 60 years	human liver microsomes (HLM)	Placitaxel hydroxylation C6alpha-	no statistically significant difference of activity with age		[11]
CYP2C8	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples, microsomes	RT-PCR, Western immunoblotting	very low expression		[35,40,67]
CYP2C8	Illness	Cancer	Colorectal carcinoma	normal tissue and adenomatous colonic tissue endoscopy samples, Human colorectal cancer cells (Caco-2)	RT-PCR, Western immunoblotting, 6alpha- i 3′-*p*-paclitaxel hydroxylation	expression of CYP mRNA similar among adenomatous colonic and normal tissues, decrease of protein level in normal tissue of patients with adenomas comparing to		[65,423]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						biopsies obtained biopsies obtained from disease-free controls		
CYP2C8	Illness	Cancer	Esophageal carcinoma	esophageal squamous-cell carcinoma, SCC, carcinoma endoscopy tissue samples	Western immunoblotting	increase of protein level in normal tissue of esophageal SCC patients compared to controls		[31]
CYP2C8	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP2C8	Demographic factor	Ethnicity	Hispanic	human liver microsomes (HLM)	Hydroxylation C6alpha-(taxane ring)	increase of activity, twice the average activity of those from Caucasians and African Americans		[11]
CYP2C8	Physiological condition	Hypoxia	Decreased oxygen pressure	human umbilical vein endothelial cells (HUVECs)	RT-PCR, Western immunoblotting, RT-PCR, 11,12-EET and 11,12-Dihydroxyeicosatrienoic acid (11,12-DHET) formation	increase of mRNA expression, protein level, and activity		[56]
CYP2C8,19	Environmental condition	Cadmium exposure	Cadmium	human liver samples, human liver microsomes (HLM)	Western immunoblotting, liver histopathology	decrease of protein levels associated with liver pathology after Cd exposure in vivo		[7]
CYP2C9	Demographic factor	Age	Adults aged less then 20 till over 60 years	human liver microsomes (HLM)	Diclofenac hydroxylation C4′-	no statistically significant difference of activity with age		[11]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2C9	Physiological condition	Ambient osmolality	Hypertonic environment	human primary hepatocytes in hypertonic media	RT-PCR	no change in mRNA expression reported		[43]
CYP2C9	Environmental condition	Cadmium exposure	Cadmium	human liver samples, human liver microsomes (HLM)	Western immunoblotting	elevated levels of protein associated with cadmium accumulation		[7]
CYP2C9	Illness	Cancer	Brain carcinoma	clinical tissue samples, glioma, ependymoma, lymphoma-metastases	RT-PCR, immunohistochemistry	expressed in tumor and normal tissues		[296,299]
CYP2C9	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples, microsomes	RT-PCR, Western immunoblotting	very low expression		[35,40,67]
CYP2C9	Illness	Cancer	Carcinoma, not specified	plasma and urine samples	Tolbutamide urine metabolite ratios, oral clearance	no difference in activity in people with and without cancer		[229]
CYP2C9	Illness	Cancer	Colorectal carcinoma	healthy vountiers and tumor colonic tissue endoscopy biopsies and/or surgical resection samples	RT-PCR and restriction mapping	expression of CYP mRNA in both tumorand normal tissues	**Inconsitent results obtained** on polymorphism as a risk factors	[426]
CYP2C9	Illness	Cancer	Esophageal carcinoma	esophagectomy specimens, esophageal squamous-cell carcinoma, SCC, adenocarcinoma, Barrett's esophagus, esophageal squamous mucosa, and normal tissue	RT-PCR, Western immunoblotting, immunohistochemistry	expression of mRNA and protein in tumor tissue, not expressed in normal tissue samples		[274,307]
CYP2C9	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2C9	Demographic factor	Ethnicity	Japanese	blood samples, unbound oral clearance	genotyping, Warfarin (S)-unbound concentrations, Warfarin (S)-C7-hydroxy urinary excretion rates	genotype dependent unbound oral clearance in Japanese, gene-dose effect of defective CYP2C9 alleles on the *in vivo* CYP2C9 activity is evident in Japanese patients but not in Caucasian patients		[230]
CYP2C9	Physiological condition	Hypoxia	Decreased oxygen pressure	human umbilical vein endothelial cells (HUVECs)	RT-PCR, Western immunoblotting, RT-PCR, 11,12-EET and 11,12-Dihydroxyeicosatrienoic acid (11,12-DHET) formation	increase of mRNA expression, protein level, and activity		[56]
CYP2C19	Demographic factor	Age	Adults aged less then 20 to over 60 years	human liver microsomes (HLM)	Mephenytoin (S)-hydroxylation C4′-	decrease of activity with age		[11]
CYP2C19	Illness	Cancer	Advanced metastatic cancer	blood samples	Omeprazole C5-pyridinyl methyl hydroxylation index	decrease of activity		[241,242]
CYP2C19	Illness	Cancer	Hepatic carcinoma	clinical cancer tissue samples, hepatocarcinoma cell lines	RT-PCR, Western immunoblotting	expression of protein in tumor and normal tissues, increase of expression of mRNA in tumor comparing to normal tissues		[298]
CYP2C19	Illness	Cancer	Prostate carcinoma	clinical prostate and normal tissues samples	RT-PCR	expression of mRNA in tumor and normal	no association of the	[291,292 ,296,425]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						tissues	CYP2C19* 2 allele and prostate cancer observed	
CYP2C19	Therapeutic condition	Contraceptives	Contraceptives	urine samples	Mephenytoin (S)-hydroxylation C4′-, the S/R-ratio ,	decrease of activity in females		[23]
CYP2C19	Demographic factor	Ethnicity	Oriental extensive metabolizers (EMs)	blood samples, oral clearance	Omeprazole hydroxylation C5-pyridinyl methyl	decrease of clearance comparing to Caucasian EMs		[21]
CYP2C19	Demographic factor	Gender	Male, Female	human liver microsomes (HLM), urine and blood samples,	Mephenytoin (S)-hydroxylation C4′-, ratio of micromoles of (S)-Mephenytoin dose to micromoles of 4′-OH-M excreted in urine and the S/R-ratio	**Inconsistent results reported** - increase of activity in females, other results show opposite or no differences		[11,22]
CYP2C19	Illness	Heart failure	Congestive heart failure	clinical blood and urine samples	Mephenytoin metabolism	decrease of activity		[240,241]
CYP2C19	Illness	Liver disease	Liver disease, not specified	liver disease severity was categorized by use of the Child-Pugh score, plasma and urine samples from volunteers	Mephenytoin metabolic index and disposition	decrease of activity, decrease of plasma clearance		[51,52]
CYP2D6	Demographic factor	Age	Adults	human liver microsomes (HLM), hepatocytes,	Dextromethorphan demethylation N-	decrease of activity with age in HLM, no significant differences in hepatocytes		[11]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2D6	Illness	Cancer	Bladder carcinoma	clinical tumor and normal tissue samples, human bladder microsomes	RT-PCR, Western immunoblotting, immunochemistry	expression of mRNA in tumor tissue		[304]
CYP2D6	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples	RT-PCR, Western immunoblotting	**Inconsistent results reported** - mRNA and protein present in tumor and normal tissues samples, no qualitative differences at mRNA level between tumor and surrounding normal tissue samples, also no expression reported		[34,40,69, 70]
CYP2D6	Illness	Cancer	Lung carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR, immunohistochemistry	very low or no expression of mRNA or protein in tumor and normal tissue	modest association of polymorphism as a risk factor	[281,425]
CYP2D6	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41
CYP2D6	Illness	Cancer	Prostate carcinoma	clinical prostate and normal tissues samples	RT-PCR, Dextromethorphan demethylation N-	expression of mRNA and activity in tumor and normal tissues		[291,292 ,295,296]
CYP2D6	Environmental condition	Cellular osmolality	Hypertonic environment	human primary hepatocytes in hypertonic media	cDNA microarray and RT-PCR	decrease of mRNA expression		[43]
CYP2D6	Demographic factor	Ethnicity	Black extensive metabolizers (EMs)	blood samples, oral clearance	Debrisoquine/Sparteine hydroxylation	decrease of mean activity comparing to		[20]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						Caucasian EMs		
CYP2D6	Demographic factor	Ethnicity	Oriental extensive metabolizers (EMs)	blood samples, oral clearance	Debrisoquine/Sparteine hydroxylation	decrease of mean activity comparing to Caucasian EMs		[20]
CYP2D6	Demographic factor	Gender	Male, Female	human liver microsomes (HLM)	Dextromethorphan demethylation N-	no significant difference in activity or higher activity in male HLM, decrease of activity when investigated as ratio *in vivo* in EMs		[11]
CYP2D6	Illness	Infection	Human immunodeficiency virus, HIV, positive patients	blood samples	Dextromethorphan demethylation N-, RT-PCR	changes may occur in HIV-positive patients such that their CYP2D6 activity approaches that of PMs, despite having an EM genotype		[221]
CYP2D6	Illness	Liver disease	Liver disease, not specified	liver disease severity was categorized by use of the Child-Pugh score, plasma and urine samples from volunteers	Debrisoquine metabolic index and disposition	decrease of recovery ratio, no effect on disposition		[51,52]
CYP2D6	Physiological condition	Pregnancy	Pregnancy	urine samples	Dextromethorphan/Dextrorphan urinary ratio	increase of activity in EM		[53,54]
CYP2E1	Demographic factor	Age	Adults aged less then 20 to over 60 years	human liver samples, human liver microsomes (HLM), hepatocytes	protein level determination, Chlorzoxazone hydroxylation C6-	decrease of activity in HLM, negative association between age and protein content, no significant differences in activity in		[8,11,16]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						hepatocytes		
CYP2E1	Environmental condition	Cadmium exposure	Cadmium	liver autopsy samples, human liver microsomes (HLM)	Western immunoblotting	increase of protein expression with increased Cd accumulation		[28]
CYP2E1	Illness	Cancer	Brain carcinoma	clinical tissue samples, glioma, acoustic neuroma	RT-PCR, immunohistochemistry	expressed in tumor and normal tissue samples		[296,300]
CYP2E1	Illness	Cancer	Breast carcinoma	tumor and normal tissue samples, clinical samples	RT-PCR, Western immunoblotting, immunohistochemistry	**Inconsistent results reported-** expression of mRNA and protein in tumor and normal tissue samples with no qualitative differences, increase of expression with an invasive lobular type of tumor, also no expression, or decrease of protein expression in tumor tissue as compared with morphologically normal adjacent tissue reported	potential role as a breast cancer prognosis marker suggested	[35,40,66, 69,70, 296]
CYP2E1	Illness	Cancer	Colorectal carcinoma	normal tissue and adenomatous colonic tissue endoscopy samples	RT-PCR, Western immunoblotting	expression of CYP mRNA was similar among normal and adenomatous colonic tissues		[65]
CYP2E1	Illness	Cancer	Esophageal carcinoma	esophageal squamous-cell carcinoma, SCC, carcinoma endoscopy tissue samples, esophagectomy specimens, Barrett′s esophagus, esophageal squamous mucosa	RT-PCR, Western immunoblotting, immunohistochemistry	expression of mRNA and protein in tumor and in normal tissue, expression of protein was significantly		[31,307]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						lower in control tissue		
CYP2E1	Illness	Cancer	Lung carcinoma	non-small cell lung cancer tissue, primary pulmonary adenocarcinomas and squamous cell carcinoma and surrounding normal bronchial tissue, A549 adenocarcinoma cell line	RT-PCR, immunohistochemistry, Northern blotting	mRNA expression in adenocarcinoma, protein expressed in tumor and normal bronchial tissue, mRNA expressed in tumor cells	proposed as marker for the determination of quality of lung cancer	[37,280, 296,309, 332,337]
CYP2E1	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non cancerous nasopharynx tissues		[41]
CYP2E1	Environmental condition	Cellular osmolality	Hypertonic environment	human primary hepatocytes in hypertonic media	cDNA microarray and RT-PCR, Nitrophenol hydroxylation	increase of mRNA expression, protein level and activity		[43]
CYP2E1	Illness	Diabetes	Diabetes, type I	blood plasma samples, urine samples, peripheral blood mononuclear cells	Chlorzoxazone hydroxylation C6-, AUC, RT-PCR	increase of mRNA expression, no difference in oral clearance		[60]
CYP2E1	Illness	Diabetes	Diabetes, type II	blood plasma samples, urine samples, peripheral blood mononuclear cells	Chlorzoxazone hydroxylation C6-, AUC, RT-PCR	increase of mRNA expression and activity, increase of oral clearance		[6,59]
CYP2E1	Food	Dietary habit	Fasting, Dietary sugar restriction	blood plasma samples	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio, AUC	decrease of oral clearance and lower hydroxylation activity		[14,19]
CYP2E1	Food	Dietary habit	High dietary sugar	blood plasma samples	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio, AUC	decrease of activity		[14]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2E1	Food	Dietary habit	Moderate alcohol consumption	serum samples, peripheral lymphocytes	Chlorzoxazone oral clearance, RT-PCR	Chlorzoxazone clearance was significantly higher in alcoholics than in nonalcoholic, mRNA levels were not significantly different between the groups	**clinically significant interaction potential** - no correlation was observed between lymphocyte CYP mRNA and *in vivo* CYP activity	[16,218]
CYP2E1	Demographic factor	Gender	Male, Female	blood samples, hepatocytes, human liver microsomes (HLM)	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio, activity	decrease of 6-OH/ Chlorzoxazone ratio in women comparing to men, no difference in activity in hepatocytes or HLM		[10,11]
CYP2E1	Illness	Inflammation	Inflammatory liver disease	liver biopsy samples	RT-PCR	decrease of mRNA level		[294]
CYP2E1	Illness	Liver disease	Alcoholic liver disease (ALD)	blood mononuclear cells, blood plasma samples, lymphocyte microsomes, human liver samples	RT-PCR, Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio, Western immunoblotting immunohistochemistry, protein level determination	increase of mRNA expression, protein level, hydroxylation activity and drug clearance in alcoholic healthy subjects, decrease of activity with progression and severity of ALD	**clinically significant drug interaction potential** - monitoring CYP2E1 mRNA expression in mononuclear cells suggested as useful predictor of alcohol-mediated alterations in hepatic activity in heavy alcohol consumption, no	[6,8,16,215, 216,217, 218,224, 225]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							correlation in moderate alcohol consumption	
CYP2E1	Illness	Liver disease	Liver disease, not specified	liver disease severity was categorized by use of the Child-Pugh score, plasma and urine samples from volunteers	Debrisoquine metabolic index	decrease of metabolic ratio		[51]
CYP2E1	Illness	Liver disease	Nonalcoholic steatohepatitis (NASH)	blood plasma samples, liver biopsy samples, human liver microsomes (HLM), peripheral lymphocytes	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio, immunohistochemistry, Western immunoblotting, RT-PCR, Nitrophenol hydroxylation	increase of mRNA expression protein level and activity, increase of oral clearance	suggested as reliable indicator of liver injury	[18,219, 220,224, 226,227, 228,248]
CYP2E1	Illness	Liver disease	Steatosis in chronic hepatitis C	liver biopsy samples	RT-PCR	increase of mRNA expression		[213]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2E1	Illness	Liver disease	Steatosis, nonalcoholic fatty liver (NAFL)	blood plasma samples, liver biopsy samples, human liver microsomes (HLM), peripheral lymphocytes	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio, immunohistochemistry, Western immunoblotting, RT-PCR	**Inconsistent results reported** - increase of oral clearance, increase of protein level and activity, also no increase in protein level and activity observed, higher levels of mRNA could be observed in the steatotic/normal biopsy samples as compared with the inflammation samples		[219,220,225,226,227,228,294]
CYP2E1	Illness	Obesity	Morbid obesity	blood plasma samples, urine samples	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio	increase of oral clearance and activity	**clinically significant pharmacokinetic drug-drug interaction potential**	[18,19,59,215,219,243]
CYP2E1	Environmental condition	Oxidative stress	Reactive oxygen species, hydrogen peroxide	human hepatoma cell line HepG2, transfected, HepG2 microsomal fraction	Northern blotting, Western immunoblotting	decrease of mRNA expression and labilization of protein, repression of ROS-producing system	intracellular H_2O_2 production resulting from CYP2E1 activity can repress the expression of CYP1A1, CYP1A1 activity represses the CYP2E1 gene promoter	[49]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2E1	Therapeutic condition	Transplantation	Liver transplantation	blood plasma samples	Chlorzoxazone hydroxylation C6-, metabolite/substrate ratio	increase of activity in liver of transplant patients	**clinically significant pharmacokinetic drug-drug interaction potential** -	[17]
CYP2F1	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR	mRNA not present in tumor and normal tissue samples		[69]
CYP2F1	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer, lymph node metastasis	immunoblotting, immunohistochemistry	low expression in tumor tissue	correlation between expression in primary tumors and corresponding lymph node metastases	[253]
CYP2F1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue		[252]
CYP2J2	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissues samples, cancer cell lines	immunohistochemistry, immunoblotting, RT-PCR	expression of mRNA and protein in tumor tissues and cells not expressed in adjacent normal tissue	potential biomarker and target for therapy of human cancers	[338]
CYP2J2	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissues samples, colon adenocarcinoma, cancer cell lines	immunohistochemistry, immunoblotting, RT-PCR	expression of mRNA and protein in tumor tissues and cells not expressed in adjacent normal tissue	potential biomarker and target for therapy of human cancers	[338]
CYP2J2	Illness	Cancer	Esophageal carcinoma	clinical tumor and normal tissues samples, esophageal adenocarcinoma, cancer cell lines	immunohistochemistry, immunoblotting, RT-PCR	expression of mRNA and protein in tumor tissues and cells not expressed in adjacent normal tissue	potential biomarker and target for therapy of human cancers	[338]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2J2	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples, cancer cell lines	immunohistochemistry, immunoblotting, RT-PCR	expression of mRNA and protein in tumor tissues and cells, not expressed in adjacent normal tissue	potential biomarker and target for therapy of human cancers	[338]
CYP2J2	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissues samples, cancer cell lines	immunohistochemistry, immunoblotting, RT-PCR	expression of mRNA and protein in tumor tissues and cells not expressed in adjacent normal tissue	potential biomarker and target for therapy of human cancers	[338]
CYP2J2	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissues samples, small cell lung cancer tissue samples, pulmonary squamous-cell carcinoma, pulmonary adenocarcinoma, cancer cell lines	immunohistochemistry, immunoblotting, RT-PCR	expression of mRNA and protein in tumor tissues and cells not expressed in adjacent normal tissue	potential biomarker and target for therapy of human cancers	[338]
CYP2J2	Physiological condition	Hypoxia	Decreased oxygen pressure	human hepatoma cell line HepG2, transfected	RT-PCR, Western immunoblotting	decrease of mRNA and protein expression		[57,58]
CYP2R1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue		[252]
CYP2S1	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer, lymph node metastasis	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue, high expression in normal colon, high expression in metastatic ovarian tissue	correlation between expression and tumor stage found, high expression associated with poor prognosis	[253,288]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2S1	Illness	Cancer	Lung carcinoma	clinical tissue samples, squamous cell carcinomas	immunoblotting, immunohistochemistry	**Inconsistent results reported** - high expression or only weak expression in lung squamous cell carcinomas tumor tissue, in adenocarcinoma expression was undetectable, high expression in the respiratory epithelium of the bronchus normal tissue		[288]
CYP2S1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian tissue	immunoblotting, immunohistochemistry	high expression in primary tumor tissue, no or very low expression in normal tissue, high expression in metastatic ovarian tissue		[252,288]
CYP2S1	Illness	Cancer	Uterus carcinoma	clinical tissue samples, squamous cell carcinoma of the uterine cervix	immunoblotting, immunohistochemistry	high expression in the squamous cell carcinoma of the uterine cervix, expressed in normal tissue		[288]
CYP2S1	Physiological condition	Hypoxia	Decreased oxygen pressure	human umbilical vein endothelial cells (HUVECs), human hepatocellular carcinoma cell line HepG2	RT-PCR, Western immunoblotting, RT-PCR, 11,12-EET and 11,12-Dihydroxyeicosatrienoic acid	increase of mRNA expression, protein level, and activity		[56,286]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
					(11,12-DHET) formation			
CYP2U1	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer	immunoblotting, immunohistochemistry	increase of expression in tumor comparing to normal tissue	correlation between expression and tumor stage reported	[253]
CYP2U1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting immunohistochemistry	high increase of expression in primary tumor tissue comparing to normal tissue		[252]
CYP2W1	Illness	Cancer	Adrenal carcinoma	tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	mRNA and protein expressed in tumor samples, not expressed in normal tissue		[311]
CYP2W1	Illness	Cancer	Bladder carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	low expression of mRNA and protein		[311]
CYP2W1	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	low expression of mRNA and protein		[311]
CYP2W1	Illness	Cancer	Colorectal carcinoma	tumor and normal tissue samples, human colon carcinoma cell lines, immunohistochemistry	RT-PCR, Northern blotting, Western immunoblotting	high expression of mRNA and low to high expression of protein in tumor samples, low or no expression in normal tissue	suggested as an independent prognostic factor for overall survival, high expression was associated with a worse clinical outcome	[311,312,382]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP2W1	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	higher expression in tumor samples then in normal tissue		[311]
CYP2W1	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	low expression of mRNA and protein		[311]
CYP2W1	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	expression in tumor samples, not expressed in normal tissue		[311]
CYP2W1	Illness	Cancer	Pancreatic carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	low expression of mRNA and protein		[311]
CYP2W1	Illness	Cancer	Thyroid carcinoma	clinical tumor and normal tissue samples	RT-PCR, Northern blotting, Western immunoblotting	low expression of mRNA and protein		[311]
CYP3A	Demographic factor	Age	Adults, aged 20 to 83 years	human plasma samples, human liver microsomes (HLM), hepatocytes	Triazolam pharmacokinetics, Erythromycin demethylation N-, Testosterone hydroxylation C6beta-	**Inconsistent results reported-** decrease of clearance with increasing age in men, age had no significant effect on clearance of Triazolam in women, activity unaffected by age reported for Erythromycin N-demethylation, no significant differences in hepatocytes for Testosterone hydroxylation		[8,9,11,15]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						C6beta-		
CYP3A	Illness	Cancer	Bone carcinoma	clinical osteosarcoma biopsies samples of primary tumors	immunohistochemistry	expressed in tumor tissue, higher expression in primary biopsies of patients who developed distant metastatic disease	suggested that high expression may predict metastasis and poor prognosis in osteosarcomas	[285]
CYP3A	Illness	Cancer	Breast and other carcinoma	clinical samples, tumor and normal tissue samples, blood samples	RT-PCR, Erythromycin breath test, Docetaxel or Vinorelbine clearance, immunohistochemistry	mRNA present in tumor and normal tissue samples, decrease of activity		[70,233, 241,291]
CYP3A	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, normal colon, colonic adenoma, and colon carcinoma biopsies, colonal cancer and healthy tissue microsomes	immunohistochemistry, Western immunoblotting, immunohistochemistry, nifedipine oxidase and 3′-*P*-hydroxypaclitaxel activity	expressed in healthy and tumor samples, low expression in normal tissue samples	suggested as specific marker of colonic neoplasia	[263,269 ,270,296 ,424]
CYP3A	Illness	Cancer	Esophageal carcinoma	esophageal squamous-cell carcinoma, SCC, adenocarcinoma, clinical samples	immunoblotting immunohistochemistry	expression of protein in tumor, not expressed in normal tissue samples, MRNA expressed in normal tissue		[274,275 ,296]
CYP3A	Illness	Cancer	Gastric carcinoma	clinical stomach tissue samples	immunoblotting	expressed in tumor, not expressed in normal tissue samples		[276]
CYP3A	Illness	Cancer	Liver carcinoma	clinical tumor and normal liver tissue samples, hepatocellular carcinomas (HCC)	immunohistochemistry	decreased or variable expression of protein in primary malignant liver		[271,272 ,273]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						tumors compared tumors compared to normal tissue samples, decrease or no expression in metastasis, decrease of activity		
CYP3A	Illness	Cancer	Lung carcinoma	non-small cell lung cancer tissue samples, blood samples	RT-PCR, Erythromycin breath test, immunohistochemistry	expression of mRNA and protein in adenocarcinoma and normal tissue samples, decrease of activity in tumor tissue samples	proposed as markers for the determination of quality of lung cancer	[37,233, 263,265, 266,296]
CYP3A	Illness	Cancer	Prostate carcinoma	clinical prostate tissue samples	immunoblotting, Dextromethorphan demethylation O-	expression of mRNA and activity in tumor and normal tissue samples		[277,295 ,296]
CYP3A	Illness	Cancer	Soft tissue carcinoma	soft tissue sarcomas, clinical samples	immunoblotting	expression of mRNA in tumor and normal tissue samples		[284]
CYP3A	Environmental condition	Cigarette smoke exposure	Cigarette smoke	lung tissue samples, bronchoalveolar macrophages	RT-PCR, immunoblotting	decrease of mRNA and protein in expression of smokers	high level of CYP3A in smokers or non-smokers associated with DNA-adduct formation	[336]
CYP3A	Food	Dietary habit	Moderate alcohol consumption	clinical samples, serum samples, peripheral lymphocytes, RT-PCR	Midazolam intravenous and oral clearances	oral availability of Midazolam significantly lower in alcoholics than in the nonalcoholic, systemic and oral	no correlation was observed between lymphocyte mRNA and *in vivo* activity	[218]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						clearance of Midazolam was not altered, mRNA levels were not significantly different between the groups		
CYP3A	Demographic factor	Gender	Male, Female	human plasma samples, human liver microsomes (HLM)	Triazolam pharmacokinetics, Erythromycin demethylation N-	no apparent gender differences in Triazolam pharmacokinetics observed, increase of activity in females comparing to males in Erythromycin demethylation N-		[9,15]
CYP3A	Illness	Infection	HBV chronic infection	human liver samples, human liver microsomes (HLM)	Western immunoblotting, activity measured in microsomes	decrease of expression and activity		[29]
CYP3A	Illness	Inflammation	Cancer patients exhibiting clinical and laboratory features of an inflammatory response	human and animal studies	*in vivo* and *in vitro* mechanistic studies	decrease of expression		[234]
CYP3A	Illness	Inflammation	Inflammatory bowel disease, Crohn′s disease	clinical samples, duodenal biopsies	RT-PCR	increase of mRNA expression		[61]
CYP3A	Illness	Liver disease	Alcoholic liver disease (ALD)	liver biopsy samples	immunohistochemistry, Western immunoblotting	increase of protein level		[225]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A	Illness	Liver disease	Nonalcoholic steatohepatitis (NASH)	clinical samples, liver biopsy samples	immunohistochemistry	decrease of protein level		[224]
CYP3A	Physiological condition	Pregnancy	Pregnancy	clinical samples, urine samples	Dextromethorphan/3-Hydroxymorphinan urinary ratio	increase of activity		[53]
CYP3A4	Demographic factor	Age	Adults aged less then 20 to over 60 years	clinical samples, human liver samples, human liver microsomes (HLM)	RT-PCR, Western immunoblotting	increase of liver mRNA expression, positive correlation was found between the liver protein level and subject age		[2,5,7,11]
CYP3A4	Demographic factor	Age	Children, 1 to 17 years	clinical samples, duodenal biopsies samples	RT-PCR	decrease of mRNA expression, expression was high in the first year of life and decreased with age to reach lower values in older children (17 years)		[62]
CYP3A4	Physiological condition	Ambient osmolality	Hypertonic environment	clinical samples, human-intestinal C2bbe1 cells, primary human colon epithelia, human colon carcinoma-derived cell line, and human hepatoma cell line HepG2, human primary hepatocytes in hypertonic media	RT-PCR	increase of mRNA expression and protein level		[43,44]
CYP3A4	Physiological condition	Ambient osmolality	Hypotonic environment	clinical samples, human-intestinal C2bbe1 cells, primary human colon epithelia and human colon carcinoma-derived cell	RT-PCR	decrease of mRNA expression and protein level		[44]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				line, and human hepatoma cell line HepG2				
CYP3A4	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples, blood samples	RT-PCR, Western immunoblotting, erythromycin breath test, immunohistochemistry	**Inconsistent results obtained** - decrease of mRNA, protein expression and activity in tumor tissue, also no expression of protein, very low expression mRNA or not present in tumor and normal tissue samples, protein expressed in tumor and normal tissue samples, increased expression in tumors		[34,35,40, 66,69, 233,263, 291,310]
CYP3A4	Illness	Cancer	Colorectal carcinoma	clinical samples, adenomatous colonic and normal tissue endoscopy samples, primary colorectal cancer, lymph node metastasis, tumor microsomes, Human colorectal cancer cells (Caco-2)	RT-PCR, Western immunoblotting	expression of CYP mRNA similar among normal and adenomatous colonic tissues, decrease of protein level in tumor and normal tissue samples of patients with adenomas comparing to biopsies obtained from disease-free controls, high expression in normal colon	correlation between expression and tumor stage reported	[65,253, 263,268, 296,423]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A4	Illness	Cancer	Engelbreth-Holm-Swarm (EHS) sarcoma	Engelbreth-Holm-Swarm sarcoma cells in transgenic mouse model incorporating human CYP3A4, liver tissue samples	RT-PCR and Taqman technology, Midazolam sleep test, proteins were visualized by enhanced chemiluminescence and quantified using densitometric analysis	decrease of mRNA expression, protein and activity in tumor-bearing transgenic mice	down-regulation of hepatic human transgene proposed	[30]
CYP3A4	Illness	Cancer	Esophageal carcinoma	clinical samples, esophageal squamous-cell carcinoma (SCC) carcinoma endoscopy tissue samples, esophagectomy specimens, Barrett′s esophagus, esophageal squamous mucosa	RT-PCR, Western immunoblotting, immunohistochemistry	mRNA expression and protein level was significantly lower in malignant tissue than in normal tissue		[31,307]
CYP3A4	Illness	Cancer	Gastric carcinoma	clinical samples, foveolar epithelium of the human stomach with intestinal metaplasia	immunoblotting immunohistochemistry, RT-PCR	expressed in foveolar epithelium with intestinal metaplasia, not detected in foveolar epithelium without intestinal metaplasia		[293]
CYP3A4	Illness	Cancer	Large intestine tumor	clinical samples, tumor and normal tissue samples	RT-PCR, Western immunoblotting	no difference in mRNA and protein expression between normal and tumor tissue		[63]
CYP3A4	Illness	Cancer	Lung carcinoma	clinical tissue samples	RT-PCR, immunohistochemistry	expression of mRNA in tumor tissue, expression of protein in normal tissue		[296]
CYP3A4	Illness	Cancer	Lymphoid carcinoma	clinical primary tumors tissue samples, 44 T-cell lymphomas	immunoblotting immunohistochemistry	high expression in tumor tissue	high tumor expression could be useful to	[287]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							predict poor response to the standard PTCL chemotherapy	
CYP3A4	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP3A4	Illness	Cancer	Ovarian carcinoma and normal tissue	clinical tissue samples, primary epithelial ovarian cancer	immunoblotting, immunohistochemistry	expressed in normal tissue		[252]
CYP3A4	Illness	Cancer	Renal carcinoma	clinical samples, renal cell carcinoma and normal tissue samples	immunohistochemistry, immunoblotting, RT-PCR	expressed mRNA and protein in renal cell cancer and in normal tissue samples		[261]
CYP3A4	Demographic factor	Ethnicity	Japanese	clinical samples, liver samples	RT-PCR	increase of mRNA expression comparing to Caucasians	ethnic differences in the expression levels of adult liver CYP3A mRNAs between Japanese and Caucasians obtained	[64]
CYP3A4	Demographic factor	Gender	Male, Female	clinical samples, human liver and human endometrial samples, human liver microsomes (HLM), cryopreserved human hepatocytes	RT-PCR, Western immunoblotting, Verapamil N-dealkylation, Testosterone hydroxylation C6beta-	decrease of hepatic mRNA and protein levels in younger females comparing to younger males, decrease of mRNA expression in premenopausal women comparing to	**no clinically significant pharmacokinetic drug-**drug interaction potential	[2,3,11]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						men, no difference in expression of mRNA in postmenopausal women comparing to men, down-regulation of mRNA expression in females by estrogen suggested, increase of mRNA expression and of activity in females group comparing to males when age influence of females has not been considered		
CYP3A4	Therapeutic condition	Hypothermia	Temperature decrease	blood samples	Midazolam pharmacokinetics	decrease of activity		[42]
CYP3A4	Illness	Inflammation	Inflammation after elective surgery	breath test	carbon-14 [^{14}C]Erythromycin demethylation	decrease of activity with acute inflammation	clinically significant drug-drug interaction potential	[4]
CYP3A4	Illness	Inflammation	Inflammatory bowel disease, Crohn′s disease	clinical samples, duodenal biopsies	RT-PCR	increase of mRNA expression		[61]
CYP3A4	Illness	Obesity	Morbid obesity	clinical studies	pharmacokinetic studies	decrease of activity	clinically significant pharmacokinetic drug-drug interaction potential	[243]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A4	Physiological condition	Oxidative stress	Reactive oxygen species, hydrogen peroxide	human erythroleukemic cell line, K562	RT-PCR, Western immunoblotting	increase of mRNA and protein expression	oxidative stress may affect GST and/or CYP expression in human blood cells, which may alter the metabolism of drugs and xenobiotics	[50]
CYP3A5	Demographic factor	Age	Adults	clinical samples, human liver samples	RT-PCR	**Inconsistent results reported** - increase of liver mRNA expression, also no difference observed with age		[2,5]
CYP3A5	Demographic factor	Age	Children, 1 to 17 years	clinical samples, duodenal biopsies samples	RT-PCR	decrease of mRNA expression with age without reaching statistical significance		[62]
CYP3A5	Physiological condition	Ambient osmolality	Hypertonic environment	human-intestinal C2bbe1 cells, primary human colon epithelia and colon carcinoma-derived cell line, and human hepatoma cell line HepG2	RT-PCR	increase of mRNA expression and protein level		[44]
CYP3A5	Physiological condition	Ambient osmolality	Hypotonic environment	human-intestinal C2bbe1 cells, primary human colon epithelia and colon carcinoma-derived cell line, and human hepatoma cell line HepG2	RT-PCR	decrease of mRNA expression and protein level		[44]
CYP3A5	Illness	Cancer	Brain carcinoma	clinical tissue samples, meningeomas, medulloblastoma grade IV	RT-PCR	expressed in some of tumor tissue samples		[296,299]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A5	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR, Western immunoblotting	**Inconsistent results reported-** expression of mRNA in tumor and normal tissue samples, also no expression reported		[34,69]
CYP3A5	Illness	Cancer	Colorectal carcinoma	clinical samples, normal tissue and adenomatous colonic tissue endoscopy samples, primary colorectal cancer, Human colorectal cancer cells (Caco-2)	RT-PCR, Western immunoblotting, immunohistochemistry	increase of mRNA expression in adenomatous colonic tissues, decrease of protein level in normal tissue of patients with adenomas comparing to biopsies obtained from disease-free controls	correlation between expression and tumor stage reported	[65,253, 423]
CYP3A5	Illness	Cancer	Esophageal carcinoma	clinical samples, esophageal squamous-cell carcinoma, SCC, carcinoma endoscopy tissue samples	RT-PCR, Western immunoblotting	increase of mRNA expression and protein in tumor comparing to normal tissue		[31]
CYP3A5	Illness	Cancer	Large intestine tumor	clinical tumor tissue samples	RT-PCR, Western immunoblotting	no difference in mRNA and protein expression between normal and tumor tissue		[63]
CYP3A5	Illness	Cancer	Lung carcinoma	clinical samples, non-small cell lung cancer tissue samples, A549 adenocarcinoma cell line	RT-PCR, immunohistochemistry, Northern blotting	expression of mRNA and protein in tumor and normal tissue		[263,265 ,266,296 ,309,337]
CYP3A5	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non cancerous nasopharynx tissues		[41]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A5	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting, immunohistochemistry	high increase of expression in primary tumor tissue comparing to normal tissue		[252]
CYP3A5	Illness	Cancer	Prostate carcinoma	clinical prostate tissue samples, microsomal fractions	RT-PCR, Western immunoblotting, immunohistochemistry, testosterone hydroxylation 6beta-, progesterone hydroxylation 6beta-	**Inconsistent results reported-** expression of mRNA and protein in tumor and normal tissues, high expression and activity in normal tissue, also not expressed or decreased expression of mRNA and protein in tumor tissue		[231,291,292,296,297,306]
CYP3A5	Illness	Cancer	Renal carcinoma	clinical samples, renal cell carcinoma and normal tissue samples	immunohistochemistry, immunoblotting, RT-PCR	expressed mRNA and protein in renal cell cancer and in normal tissue samples		[261]
CYP3A5	Environmental condition	Cigarette smoke exposure	Cigarette smoke	clinical samples, lung tissue samples, bronchoalveolar macrophages	RT-PCR, immunoblotting	expression of mRNA and protein in smokers and non-smokers	proposed that CYP3A5 may be an important determinant in the activation of procarcinogens present in cigarette smoke, and may contribute to the total burden of ultimate PAH carcinogens in human lung	[336]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A5	Demographic factor	Ethnicity	Japanese	clinical samples, liver samples	RT-PCR	increase of mRNA expression comparing to Caucasians	ethnic differences in the expression levels of adult liver CYP3A mRNAs between Japanese and Caucasians obtained	[64]
CYP3A5	Illness	Inflammation	Inflammatory bowel disease, Crohn′s disease	clinical samples, duodenal biopsies	RT-PCR	increase of mRNA expression		[61]
CYP3A7	Demographic factor	Age	Adults,	clinical samples, human liver samples	RT-PCR	increase of liver mRNA expression with age		[2]
CYP3A7	Demographic factor	Age	Children, 1 to 17 years	clinical samples, duodenal biopsies samples	RT-PCR	no statistical relation with age in mRNA expression		[62]
CYP3A7	Physiological condition	Ambient osmolality	Hypertonic environment	clinical samples, human-intestinal C2bbe1 cells, primary human colon epithelia and human colon carcinoma-derived cell line, and human hepatoma cell line HepG2	RT-PCR	increase of mRNA expression and protein		[44]
CYP3A7	Physiological condition	Ambient osmolality	Hypotonic environment	clinical samples, human-intestinal C2bbe1 cells, primary human colon epithelia and colon carcinoma-derived cell line, and human hepatoma cell line HepG2	RT-PCR	decrease of mRNA expression and protein level		[44]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP3A7	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR	expressed mRNA and protein in tumor and normal tissue samples		[69]
CYP3A7	Illness	Cancer	Large intestine tumor	clinical samples, tumor tissue	RT-PCR, Western immunoblotting	no difference in mRNA and protein expression between normal and tumor tissue		[63]
CYP3A7	Illness	Cancer	Lung carcinoma	clinical samples, lung cancer and normal tissue samples, A549 adenocarcinoma cell line	RT-PCR, immunohistochemistry, Northern blotting	low or no mRNA expression of in tumor tissue and cells, expression in normal tissue,		[266,337]
CYP3A7	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP3A7	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian tissue	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue high expression in metastatic ovarian tissue		[252]
CYP3A7	Illness	Cancer	Renal carcinoma	clinical samples, renal cell carcinoma and normal tissue samples	immunohistochemistry, immunoblotting, RT-PCR	expressed mRNA and protein in renal cell cancer and in normal tissue samples		[261]
CYP3A7	Demographic factor	Ethnicity	Japanese	clinical samples, liver samples	RT-PCR	increase of mRNA expression comparing to Caucasians	ethnic differences in the expression levels of adult liver CYP3A mRNAs	[64]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							between Japanese and Caucasians obtained	
CYP3A43	Demographic factor	Age	Adults	clinical samples, human liver samples	RT-PCR	increase of liver mRNA expression with age		[2,5]
CYP3A43	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer	immunoblotting, immunohistochemistry	low expression, increase of expression comparing to normal tissue	correlation between expression and tumor stage reported	[253]
CYP3A43	Demographic factor	Gender	Male, Female	clinical samples, human liver and human endometrial samples	RT-PCR	decrease of mRNA expression in premenopausal women, down-regulation of mRNA expression in females by estrogen suggested, no difference in hepatic mRNA levels	**no clinically significant pharmacokinetic drug-drug interaction potential**	[2]
CYP3F1	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non cancerous nasopharynx tissues		[41]
CYP4A11	Demographic factor	Age	Adults aged less then 20 to over 60 years	clinical samples, liver and kidney cortex autopsy samples, human liver microsomes (HLM)	Lauric acid hydroxylation C12- (omega -)	increase of activity with age		[11]
CYP4A11	Environmental condition	Cadmium exposure	Cadmium	clinical samples, kidney cortex and liver autopsy samples, human kidney microsomes, human liver microsomes (HLM)	Western immunoblotting	liver protein levels were positively correlated with tissue Cd content while in contrast kidney protein abundance was		[1,24]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						inversely correlated with kidney Cd burden		
CYP4A11	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR	expressed mRNA and protein in tumor and normal tissue samples		[70]
CYP4A11	Illness	Liver disease	Chronic hepatitis	clinical samples, liver autopsy samples, human liver microsomes (HLM)	Western immunoblotting	decrease of protein level		[24]
CYP4A11	Illness	Liver disease	Fatty liver	clinical samples, liver autopsy samples, human liver microsomes (HLM)	Western immunoblotting	decrease of protein level		[24]
CYP4B1	Illness	Cancer	Bladder carcinoma	clinical samples, tumor and normal tissue samples, human bladder microsomes	RT-PCR, Western immunoblotting, immunochemistry, 2-aminofluorene activation	increase of expression of mRNA, protein and activity in patients with tumor compared to no tumor patients	suggested that high expression increases the risk of bladder tumor	[304]
CYP4B1	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissue samples	RT-PCR	mRNA present in tumor and normal tissues samples, no qualitative differences expression at mRNA level between tumor and surrounding normal breast tissue samples		[69]
CYP4B1	Illness	Cancer	Lung carcinoma	clinical samples, non-small cell lung cancer tissue samples	RT-PCR, immunohistochemistry	decrease of mRNA expression in tumor tissue, expressed in normal tissue		[263,264,296]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CYP4B1	Illness	Cancer	Nasopharyngeal carcinoma (NPC)	NPC and non-cancerous nasopharynx tissue samples	RT-PCR	mRNA present in NPC and non-cancerous nasopharynx tissues		[41]
CYP4B1	Illness	Cancer	Prostate carcinoma	clinical prostate and normal tissues samples	RT-PCR	expression of mRNA in tumor and normal tissues		[291,292,306]
CYP4F2	Environmental condition	Cadmium exposure	Cadmium (Cd)	clinical samples, kidney cortex autopsy samples, human kidney microsomes	Western immunoblotting	increase of protein expression with increased Cd accumulation		[28]
CYP4V2	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer, lymph node metastasis	immunoblotting, immunohistochemistry	low or no expression in tumor tissue	correlation between expression in primary tumors and corresponding lymph node metastases	[253]
CYP4X1	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer	immunoblotting, immunohistochemistry	low expression but increase of expression comparing to normal tissue	correlation between expression and tumor stage reported	[253]
CYP4Z1	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples	RT-PCR, immunoblotting	low expression in normal colon, increase of mRNA and protein expression in tumor tissue samples, expressed in normal breast tissues		[247]
CYP4Z1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue	negative or low or moderate expression compared to high expression	[252]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							associated with poor survival	
CYP5A1 (Thromboxane A2, TXA(2), synthase)	Illness	Cancer	Colorectal carcinoma	clinical samples, colorectal cancer tissue and its accompanying normal mucosa, human colonic cancer cell lines	RT-PCR, Western immunoblotting	increase of mRNA and protein expression		[32]
CYP5A1 (Thromboxane A2, TXA(2), synthase)	Illness	Cancer	Papillary thyroid carcinoma	clinical samples, carcinoma and adjacent normal tissue, human papillary thyroid cell line TPC-1	RT-PCR	increase of mRNA expression		[71,74]
CYP5A1 (Thromboxane A2, TXA(2), synthase)	Illness	Cancer	Pituitary adenomas and carcinomas	clinical samples, tumor and normal pituitaries	immunohistochemistry, RT-PCR	increase of expression		[73]
CYP5A1 (Thromboxane A2, TXA(2), synthase)	Illness	Cancer	Prostate carcinoma	clinical samples, prostate cancer cells and normal prostate epithelial cells	RT-PCR, Western immunoblotting	increase of mRNA and protein expression, low expression in normal cells		[72]
CYP7B1	Illness	Cancer	Colorectal carcinoma	clinical cancer tissue samples	RT-PCR, Western immunoblotting	increase of mRNA and protein expression		[33]
CYP7B1	Illness	Cancer	Prostate carcinoma	clinical prostate tissue samples and prostate cancer cell lines	RT-PCR, Western immunoblotting	increase of mRNA and protein expression in prostatic intraepithelial neoplasia (PIN) and adenocarcinomas		[33]
CYP11A1	Illness	Cancer	Breast carcinoma	clinical samples, tumor and normal tissues samples	RT-PCR	mRNA present in tumor and normal tissues samples, no qualitative		[69]

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CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						differences in CYP expression at mRNA level between tumor and surrounding normal breast tissues samples		
CYP19A1 (Aromatase)	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples	RT-PCR	mRNA and protein present in tumor and control tissues, in the course of the disease a switch of promoter occurs and results in higher expression levels, also high incidence of no expression reported in postmenopausal women	patients with expression of tumor aromatase (CYP19) had a better prognosis than patients with no expression of this transcript	[70,236, 385]
CYP19 (Aromatase)	Illness	Cancer	Gastric carcinoma	clinical tumor and adjacent no tumor tissue samples, intestinal-type and diffuse-type adenocarcinomas, gastric cancer cell lines	immunohistochemistry, RT-PCR, Western immunoblotting	expression of mRNA in gastric cancer cell lines, expression of mRNA and protein in cancer and in no tumor mucosa tissue		[383]
CYP19 (Aromatase)	Illness	Cancer	Lung carcinoma	clinical tumor tissue samples, non-small cell lung cancer tissue	RT-PCR	expression of mRNA in tumor tissue		[36]
CYP19 (Aromatase)	Illness	Cancer	Ovarian carcinoma	clinical tumor and no tumor tissue samples, ovarian epithelial cancer cell lines, ovarian epithelial cancers	immunohistochemistry, RT-PCR, Western immunoblotting	decreased expression of mRNA, protein and activity in some ovarian epithelial cancer cells and tissues comparing to normal ovarian epithelial tissues	no significant differences in aromatase expression were observed according to the tumor histotype (endometrio	[384]

CYP	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							id, mucinous, serous papillary and undifferentiated histotype), grade or stage	
CYP24A1	Illness	Cancer	Lung carcinoma	non-small cell lung cancer tissue samples	RT-PCR	mRNA expression in tumor tissue		[36]
CYP26A1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting, immunohistochemistry	high increase of expression in primary tumor tissue comparing to normal tissue		[252]
CYP39	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer, lymph node metastasis	immunoblotting, immunohistochemistry	low expression in tumor tissue	correlation between expression in primary tumors and corresponding lymph node metastases	[253]
CYP51A1	Illness	Cancer	Colorectal carcinoma	clinical tissue samples, primary colorectal cancer	immunoblotting, immunohistochemistry	increase of expression comparing to normal tissue	high expression associated with poor prognosis	[253]
CYP51A1	Illness	Cancer	Ovarian carcinoma	clinical tissue samples, primary epithelial ovarian cancer and metastatic ovarian cancer	immunoblotting, immunohistochemistry	increase of expression in primary tumor tissue comparing to normal tissue		[252]
total CYP	Illness	Liver disease	Postoperative septic liver failure	clinical samples, survivors and no survivors	Aminopyrine breath test	decrease of activity	suggested as clinically useful tool for predicting the outcome in the early stages of sepsis	[214]

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Table 2

Effects of selected effectors on expression and activity of transporters in humans

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
ABCA1, ABC1	Illness	Endothelial cell dysfunction	Uremic plasma	clinical samples, human coronary arterial endothelial cells	RT-PCR, microarray	decrease of mRNA expression		[208]
ABCA1, ABC1	Physiological condition	Oxidative stress	Reactive oxygen species	CuSO(4) generated, J774 macrophages, normal human skin fibroblast and Tangier fibroblasts	Western immunoblotting, cholesterol and phospholipids efflux	increase of activity		[204]
ABCB11, BSEP	Illness	Liver disease	Cholecyst cholesterol lithiasis	clinical samples, liver tissue samples	RT-PCR, Western immunoblotting	increase of mRNA and protein expression		[90]
ABCG1, ABC8	Illness	Endothelial cell dysfunction	Uremic plasma	clinical samples, human coronary arterial endothelial cells	RT-PCR, microarray	decrease of mRNA expression		[208]
ABCG2, MXR, BCRP1, ABCP	Illness	Cancer	Bladder carcinoma	clinical tumor tissue samples	immunohistochemistry	high protein expression	no prognostic impact	[401]
ABCG2, MXR, BCRP1, ABCP	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, primary breast cancers, MCF7 and BT20 breast cancer cell lines	RT-PCR, immunohistochemistry, Northern blotting	low expression of mRNA in tumor samples, protein detected in normal duct cells but not in tumor cells, mRNA and protein	**Inconsistent results reported** - suggested that may play a role in anthracycline resistance, reported not to relate to the relapse or prognosis in patients treated with doxorubicin-	[344,398,422]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						expressed at higher level in MCF7 and BT20 breast cancer cell lines then in tumor samples	based chemotherapy , also no indication that elevated expression in breast carcinomas confers resistance to anthracyclines, high tumor malignancy grade was associated with a decreased mRNA expression, survival and disease-free survival were not significantly associated with BCRP mRNA expression	
ABCG2, MXR, BCRP1, ABCP	Illness	Cancer	Leukemia	clinical tumor tissue samples, acute lymphocytic (lymphoblastic) leukemia (ALL), adult acute myeloid leukemia (AML), bone marrow samples	RT-PCR, immunoblotting	increase of mRNA expression, functional assay, expression of protein in PC13 2-2 and HL60/MRP cell lines	**Inconsistent results reported** - suggested to be involved in chemoresistance, coexpression of MDR1/BCRP in AML patients was associated with a lower complete response (CR) rate and with worse event-free and overall survival, suggested as a prognostic factor in AML patients, might contribute to drug resistance in B-lineage ALL, also no association between BCRP overexpression and unfavorable outcome in ALL patients reported	[345,357,377,411,412]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
ABCG2, MXR, BCRP1, ABCP	Illness	Cancer	Liver carcinoma	clinical tumor tissue samples, hepatocellular carcinoma (HCC) , HepG2 cell line	RT-PCR, immunohistochemistry	expression of mRNA as in normal tissue	could be up-regulated by anti-cancer agents *in vitro*	[396,397]
ABCG2, MXR, BCRP1, ABCP	Illness	Cancer	Lymphoid carcinoma	clinical tumor tissue samples, T/NK-cell lymphomas	immunohistochemistry	expression of protein		[399]
ABCG2, MXR, BCRP1, ABCP	Physiological condition	Hypoxia	Decreased oxygen pressure	Saos-2, JAR, OCI-AML3 cells	RT-PCR, Hoechst 33342 efflux	increase of mRNA, protein expression and activity	suggested that increase of expression could lead to increased chemotherapeutic resistance to compounds that are BCRP substrates	[188]
ABCG2, MXR, BCRP1, ABCP	Illness	Liver disease	Acetaminophen overdoses	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of protein level		[205]
ABCG2, MXR, BCRP1, ABCP	Illness	Liver disease	Primary biliary cirrhosis	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression and protein level		[205]
AE2, SLC4A2	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, hepatocellular carcinoma (HCC) and paired	RT-PCR, Western immunoblotting	increase of mRNA and protein expression		[86]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				adjacent normal liver tissue samples				
ASCT1, SATT, SLC1A4	Illness	Cancer	Esophageal carcinoma	clinical tumor tissue samples, esophageal carcinomas tissue samples, squamous cell carcinoma, adenocarcinoma	immunohistochemistry	increase of mRNA expression in adenocarcinomas comparing to squamous cell carcinomas		[104]
ASCT2, AAAT, SLC1A5	Illness	Infection	Legionella pneumophila infection	clinical samples, Mono Mac 6 cells, human isolate from a patient with severe Legionella pneumonia	RT-PCR, Western immunoblotting	increase of mRNA expression		[194]
ASCT2, AAAT, SLC1A5	Illness	Ischemia	Restriction in blood supply	ischemic injured Caco-2 cell lines	RT-PCR, Western immunoblotting, Glutamine transport	decrease of mRNA expression, protein level and activity		[192]
ATA1, SNAT1, NAT2, SAT1, SLC38A1	Nutritional condition	Amino acid depletion	Neutral amino acids depletion	BeWo choriocarcinoma cell line	RT-PCR, Northern blotting, Western immunoblotting, immunocytochemistry, radiolabeled amino acids uptake, N-(methylamino)isobutyric acid (MeAIB) transcellular transport	no effect in BeWo cells, or decrease of mRNA expression after long-term incubation		[195,199]

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Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
ATA1, SNAT1, NAT2, SAT1, SLC38A1	Illness	Cancer	Liver carcinoma	HepG2, HLF, HuH7 and JHH4 cell lines, surgical pre-malignant cirrhotic livers, hepatocellular carcinoma (HCC) and non-cancerous liver tissue samples	RT-PCR, immunohistochemistry	increase of mRNA expression and protein level compared to non-cancerous liver cells		[96]
ATA1, SNAT1, NAT2, SAT1, SLC38A1	Physiological condition	Hypoxia	Decreased oxygen pressure	cultured term human trophoblasts, gas mixture	Northern blotting, Alanine uptake	decrease of expression and activity		[185]
ATA2, SNAT2, SAT2, SLC38A2	Nutritional condition	Amino acid depletion	Neutral amino acids depletion	BeWo choriocarcinoma cell line, HepG2 human hepatoma cells, HeLa and C6 cells	RT-PCR, Northern blotting, Western immunoblotting, immunocytochemistry radiolabeled amino acids uptake, MeAIB transcellular transport	increase of mRNA, protein expression and activity after long-term incubation		[196,197,198,199]
ATA2, SNAT2, SAT2, SLC38A2	Illness	Cancer	Liver carcinoma	HepG2, HLF, HuH7 and JHH4 cell lines, surgical pre-malignant cirrhotic livers, hepatocellular carcinoma and non-cancerous liver tissue samples	RT-PCR, immunohistochemistry	increase of mRNA expression and protein level compared to non-cancerous liver cells		[96]
ATA2, SNAT2, SAT2, SLC38A	Physiological condition	Hypoxia	Decreased oxygen pressure	cultured term human trophoblasts, gas mixture	Northern blotting, Alanine uptake	decrease of expression and activity		[185]

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Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
2								
ATB0,+, SLC6A14	Illness	Cancer	Cervical carcinoma	clinical tumor and normal tissue samples, normal ectocervical mucosa and cervical squamous cell carcinoma	RT-PCR, immunohistochemistry, immunofluorescence	increase of mRNA expression and protein level		[85]
ATB0,+, SLC6A14	Illness	Cancer	Colorectal carcinoma	clinical tumor tissue samples, carcinoma and control tissue from colectomy samples, liver tissue, lymph node metastases	RT-PCR, Western immunoblotting	increase of mRNA and protein expression		[84]
BGT1, SLC6A12	Physiological condition	Cellular osmolality	Hypertonic environment	HaCaT keratinocytes, primary normal human keratinocytes, hyperosmotic exposure	RT-PCR, osmolyte uptake	increase of mRNA expression and activity		[178,212]
BGT1, SLC6A12	Physiological condition	Cellular osmolality	Hypotonic environment	primary normal human keratinocytes hyperosmotic exposure	osmolyte efflux	increase of activity		[212]
BGT1, SLC6A12	Experimental condition	Cellular osmolality	Ultraviolet A and B radiation	primary normal human keratinocytes, hyperosmotic exposure	RT-PCR, osmolyte uptake	increase of mRNA expression and activity		[212]
CNT1, SLC28A1	Illness	Infection	HIV-1 viral infection	clinical samples, adipose tissue, adipocytes	RT-PCR	increase of mRNA expression		[94]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
CNT2, SLC28A2	Physiological condition	Hypoxia	Decreased oxygen pressure	HepG2 human hepatocellular carcinoma, Hep3B human hepatocellular carcinoma, Panc-1human pancreatic carcinoma, and A673 human rhabdomyosarcoma cells	RT-PCR	decrease of expression		[180]
CNT3, SLC28A3	Illness	Infection	HIV-1 viral infection	clinical samples, adipose tissue, adipocytes	RT-PCR	increase of mRNA expression		[94]
ENT1, SLC29A1	Demographic factor	Hypoxia	Decreased oxygen pressure	human umbilical vein endothelium (HUVEC), HepG2 human hepatocellular carcinoma, Hep3B human hepatocellular carcinoma, Panc-1human pancreatic carcinoma, and A673 human Rhabdomyosarcoma cells, gas mixture exposure	RT-PCR, Adenosine transport, Western immunoblotting	decrease of mRNA expression, protein level and activity		[179,180]
ENT1, SLC29A1	Physiological condition	Oxidative stress	Reactive oxygen species	human neuroblastoma SH-SY5Y cells transfected with either familial amyotrophic lateral	Glutamate transport	impaired function		[200]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				sclerosis-typical G93A mutant or wild-type copper/zinc superoxide dismutase				
ENT2, SLC29A2	Physiological condition	Hypoxia	Decreased oxygen pressure	clinical samples, HepG2 human hepatocellular carcinoma, Hep3B human hepatocellular carcinoma, Panc-1human pancreatic carcinoma, and A673 human Rhabdomyosarcoma cells	RT-PCR	decrease of expression		[180]
ENT2, SLC29A2	Illness	Infection	HIV-1 viral infection	clinical samples, adipose tissue, adipocytes	RT-PCR	increase of mRNA expression		[94]
ENT3, SLC29A3	Physiological condition	Oxidative stress	Reactive oxygen species	human neuroblastoma SH-SY5Y cells transfected with either familial amyotrophic lateral sclerosis-typical G93A mutant or wild-type copper/zinc superoxide dismutase	Glutamate transport	impaired function		[200]
GLUT1, SLC2A1	Illness	Cancer	Bladder carcinoma	clinical tumor tissue samples, transitional cell carcinoma	immunohistochemistry	increase of protein expression in invasive or extensive disease, not expressed in normal	suggested as a marker of aggressive biologic potential, strongly associated with the neoplastic progression	[108,112,133]

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Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						bladder or benign papilloma samples		
GLUT1, SLC2A1	Illness	Cancer	Brain carcinoma	clinical tumor tissue samples, embryonal neoplasm, cerebellar medulloblastoma, medulloblastoma cell line	Western immunoblotting	expressed in cell membranes of neoplastic cells, not expressed in non-embryonal neoplasm	suggested as useful marker to define the embryonal nature of primitive undifferentiated small cell neoplasm of CNS	[125]
GLUT1, SLC2A1	Illness	Cancer	Brain carcinoma	clinical malignant and normal tissue samples, malignant glial cells, choroid plexus papilloma, meningioma, glioma, ependymoma , and astrocytoma biopsies	immunohistochemistry, autoradiography	increase of mRNA and protein expression, weak to moderate expression in tumor tissue, weak expression in normal tissue, decrease of protein expression in malignant choroid plexus reported	mRNA expression suggested as a marker of aggressive biologic potential and potential targets for future therapy	[113,116,151,155,177]
GLUT1, SLC2A1	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples, tumor and adjacent normal breast tissues samples, benign and malignant cell line, breast cancer cell lines MCF-7, MDA-468, and ZR-75-1	immunohistochemistry, immunoblotting, Deoxyglucose uptake, in situ RT-PCR	increase of mRNA and protein expression in breast cancer cells and cancer tissue compared with the healthy breast tissue, very weak expression in ductal epithelial cells, or not	suggested as a marker of aggressive biologic potential associated with poor survival of patients; increase of mRNA, protein expression and activity by progesterone and estrogen treatment	[88,107,110,114,117, 118,119,157,173,175,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						expressed in normal breast tissue		
GLUT1, SLC2A1	Illness	Cancer	Cervical carcinoma	clinical tumor and normaltissue samples, biopsy samples, cervical squamous carcinoma and normal cervical tissue samples	immunohistochemistry	increase of expression in cancer specimens, no or low expression in normal tissues	absence of Glut-1 significantly increased the likelihood of metastasis-free survival (P = 0.022) but did not significantly effect disease-free or recurrence-free survival, suggested as a prognostic marker for metastases-free survival and related to grade of tumor	[120,153,154]
GLUT1, SLC2A1	Illness	Cancer	Cholangiocarcinoma	clinical tumor tissue samples	immunohistochemistry	increase of expression, not present in normal tissue or benign bile ductule proliferations	suggested as reliable marker for detection of bile duct carcinoma	[160]
GLUT1, SLC2A1	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples, primary colon cancer tissue, colorectal neoplastic endoscopic or surgical tissue samples, normal colon, benign colon adenomas and colorectal carcinoma tissue samples, normal and	immunohistochemistry, RT-PCR, Western immunoblotting, (18)F-FDG uptake, Northern blotting	increase of mRNA and protein expression and activity in cancer tissue and cells, central part of the tumor thought to be relatively hypoxic had stronger expression, not expressed in normal tissue	suggested as a marker for poor prognosis and poor survival of patients, suggested as noninvasive biomarker for advanced tumor indicative of a large hypoxic tumor with deep invasion, associated with poor survival of patients	[88,121,122,123,128, 162,164,173,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				colon cancer cells transplanted in nude mice, invasive tubular carcinoma				
GLUT1, SLC2A1	Illness	Cancer	Cutaneous carcinoma	clinical tumor tissue samples, squamous cell carcinoma samples	immunohistochemistry	increase of expression		[124]
GLUT1, SLC2A1	Illness	Cancer	Esophageal carcinoma	clinical tumor tissue samples, esophageal carcinomas tissue samples, squamous cell carcinoma, adenocarcinoma	immunohistochemistry	increase of mRNA expression in adenocarcinomas and squamous cell carcinomas		[104]
GLUT1, SLC2A1	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples, adenocarcinoma	immunohistochemistry, RT-PCR	increase of mRNA and protein expression with tumor progression, low expression in stomach adenocarcinoma, not expressed in normal tissue	suggested as tumor marker in the diagnosis and prognosis of gastric malignancies, not expressed in normal tissue	[126,127,151,177]
GLUT1, SLC2A1	Illness	Cancer	Head and neck carcinoma	clinical tumor and normal tissue samples, head and neck squamous cell carcinoma, tissue of head and neck tumors,	immunohistochemistry	increase of protein expression, increase of expression in hypoxic regions, expression of mRNA and protein	suggested as reliable marker in the diagnosis of premalignant lesions of the oropharyngeal mucosa and that combination of an antitumor agent with inhibitors of GLUT1 would be	[129,130,131,132]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				adjacent mucosa, and normal mucosa samples, biopsy (FNAB) material			beneficial to the cancer therapy, also high GLUT expression observed in some tumors was not associated with amplification or rearrangement of the corresponding genes, gene expression level and protein expression were correlated with lymph node metastases, poor survival and clinical stage	
GLUT1, SLC2A1	Illness	Cancer	Kidney carcinoma	clinical tumor and normal tissue samples, kidney surgical samples, renal cell carcinoma (RCC), papillary RCC, chromophobe RCC and oncocytoma tumors	RT-PCR, immunohistochemistry	Increase or decrease of mRNA expression in tumor cells, expressed in normal tissue		[161,177]
GLUT1, SLC2A1	Illness	Cancer	Laryngeal carcinoma	clinical tumor tissue samples, biopsy samples of squamous cell carcinoma (SCC) of the larynx	immunohistochemistry, RT-PCR	mRNA expressed	not associated with poor survival of patients	[174]
GLUT1, SLC2A1	Illness	Cancer	Leiomyosarcoma	clinical tumor tissue samples, extrauterine and uterine leiomyosarco	immunohistochemistry	increase of expression, not present in leiomyoma tissues	positivity closely correlated with aggressive biologic behavior	[134]

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Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				ma tissue samples				
GLUT1, SLC2A1	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, liver vascular tumor pathology samples from biopsy, excision, or autopsy tissue samples	immunohistochemistry	increase of expression, not expressed or low level in normal tissue	suggested as specific for proliferating hemangioma, and its expression predicts the typical course of proliferation followed by involution	[159,177]
GLUT1, SLC2A1	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, normal fibroplast and hepatocellular carcinoma (HCC), HepG2 cells injected into the intraportal vein of SCID mice, hepatocellular carcinoma	immunohistochemistry, Western immunoblotting, (18)F-FDG uptake	increase of expression and activity, not expressed in normal tissue		[162,165,177]
GLUT1, SLC2A1	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples, non-small cell lung cancer (NSCLC)	immunohistochemistry, RT-PCR	increase of mRNA, protein expression and activity, not expressed in normal tissue	suggested as a significant poor prognosis indicator in cases of NSCLC, associated with a lower degree of tumor differentiation, not expressed in normal tissue	[109,115,136,137,138,139,151,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
GLUT1, SLC2A1	Illness	Cancer	Lung carcinoma	clinical tumor tissue samples, bronchioloalveolar carcinomas and non-bronchioloalveolar carcinomas;	immunohistochemistry	decrease of expression and activity, significantly lower in bronchioloalveolar carcinomas than in non-bronchioloalveolar carcinomas	associated with poor survival of patients	[135,173]
GLUT1, SLC2A1	Illness	Cancer	Lung carcinoma-Brain metastases	clinical tumor tissue samples, hematogenous metastases brain tissue samples	immunohistochemistry	decrease of expression, significantly lower comparing to endothelial cells of microvessels around the metastases		[140,151]
GLUT1, SLC2A1	Illness	Cancer	Lymphoid carcinoma	clinical tumor tissue samples, Hodgkin's lymphoma biopsies samples	immunohistochemistry	not expressed in tumor tissue		[177]
GLUT1, SLC2A1	Illness	Cancer	Lymphoid carcinoma	clinical tumor tissue samples, Non-Hodgkin's lymphoma biopsies	immunohistochemistry	low expression in tumor tissue		[177]
GLUT1, SLC2A1	Illness	Cancer	Ovarian carcinoma	clinical malignant and normal tissue samples, borderline, benign epithelial tumor	immunohistochemistry	increase of protein expression, progressively more staining in invasive tumors as compared to borderline tumors, not expressed in benign	suggested as clinically useful prognostic information in patients with ovarian carcinoma, associated with a lower degree of tumor differentiation and with poor survival of patients	[141,147,148,173,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						ovarian epithelial tumors and normal tissue		
GLUT1, SLC2A1	Illness	Cancer	Pancreatic carcinoma	clinical tumor and normal tissue samples, transfected pancreatic cancer cell lines MIAPaCa-2, PANC-1, BXPC-3, and CAPAN-2, adenocarcinoma and neuroendocrine tumor biopsies	Northern blotting, RT-PCR, immunohistochemistry, Western immunoblotting	increase of mRNA and protein expression and activity, also low expression in adenocarcinoma, not expressed in normal tissue	suggested as a fruitful target for therapeutic strategies aimed at suppression of tumor glycolysis, promotes pancreatic cellular invasiveness, and its expression is associated with pancreatic cancer invasiveness	[142,151,152,156,158,177]
GLUT1, SLC2A1	Illness	Cancer	Penile carcinoma	clinical malignant tissue samples	immunohistochemistry	increase of protein expression		1 [43]
GLUT1, SLC2A1	Illness	Cancer	Prostate carcinoma	clinical prostate carcinoma tissue samples, prostate cancer cells and cultured prostate cancer cell line LNCaP, C4, C4-2, and C4-2B using primers to amplify GLUT1, benign prostatic hyperplasia	RT-PCR, immunohistochemistry	protein weakly or not expressed in malignant tissue, mRNA and protein expressed in benign prostatic hyperplasia and in carcinoma cell lines, expressed in normal tissue		[176,177]
GLUT1, SLC2A1	Illness	Cancer	Renal carcinoma	clinical tumor tissue samples, tissue samples of renal	immunohistochemistry	increase of expression, not present in normal tissue	strongly associated with the neoplastic progression	[133]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				transitional cell carcinoma and renal clear cell carcinoma				
GLUT1, SLC2A1	Illness	Cancer	Skeletal muscle carcinoma	clinical tumor and normal tissue samples, Rhabdomyosarcoma biopsies	immunohistochemistry	not expressed in tumor or normal tissue		[177]
GLUT1, SLC2A1	Illness	Cancer	Skin carcinoma	clinical tumor and normal tissue samples, melanoma biopsies	immunohistochemistry	not expressed in tumor, low expression in normal tissue		[177]
GLUT1, SLC2A1	Illness	Cancer	Testicular carcinoma	clinical tumor and normal tissue samples, seminoma and embryonal cancer biopsies	immunohistochemistry	expressed as in normal tissue		[177]
GLUT1, SLC2A1	Illness	Cancer	Thyroid carcinoma	clinical tumor and normal tissue samples, papillary carcinoma biopsies	immunohistochemistry, RT-PCR	increase of mRNA and protein expression, not expressed in papillary carcinoma biopsies, not expressed in normal breast tissue	suggested as a prognostic marker for thyroid cancer	[106,144,145,177]
GLUT1, SLC2A1	Illness	Cancer	Uterus carcinoma	clinical tumor and normal tissue samples, endometrial adenocarcino ma, hyperplasia, leimyeoma and normal	immunohistochemistry	**Inconsistent results reported** -increase of protein expression or low expression, not	GLUT1 immunoreactivity in endometrial hyperplasia appears to be a useful indicator of high risk for development of endometrial	[146,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				tissue samples		expressed in all atypical complex hyperplasia, benign endometrial epithelium as well as cystic, complex hyperplasia and normal tissue	carcinoma	
GLUT1, SLC2A1	Illness	Cancer	Vascular carcinoma	clinical tumor tissue samples, surgical tissue samples of postnatal proliferating infantile hemangioma	immunohistochemistry	increase of protein expression, nonprogressive lesions showed complete lack of immunoreactivity		[150]
GLUT1, SLC2A1	Physiological condition	Hypoxia	Decreased oxygen pressure	clinical samples, CoCl(2) induced hypoxia, biopsies samples, cervical squamous carcinoma cells, cultured human cervical cancer cell line HeLa, primary syncytotrophoblast cell, BeWo choriocarcinoma cells and human placental villous tissue	immunohistochemistry, RT-PCR, immunoblotting, Northern blotting	increase of mRNA, protein expression and activity	weak correlation between Glut-1 expression and tumor pO(2) measurements	[120,168,169,170,171,172,173]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				explants				
GLUT1, SLC2A1	Physiological condition	Hypoxia	Decreased oxygen pressure	clinical samples, chronic placental hypoxia, placenta basal membrane fractions and syncytial microvillous from normal term pregnancy	immunoblotting	decrease of expression		[167]
GLUT2, SLC2A2	Illness	Cancer	Brain carcinoma	clinical tumor and normal tissue samples, choroid plexus papilloma, ependymoma	immunohistochemistry	weak to moderate expression, no expression in normal tissue		[177]
GLUT2, SLC2A2	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples, benign and malignant cell line, breast cancer cell lines MCF-7 and MDA-468	immunocytochemistry immunoblotting, Deoxyglucose uptake, Western blotting, immunohistochemistry, *in situ* RT-PCR	**Inconsistent results reported** -expressed in breast cancer cell lines, increase of expression in ductal invasive carcinoma; no increase of mRNA, protein expression and activity by progesterone and estrogen treatment, expressed or not expressed in normal breast tissue	protein levels decreased with invasive potential	[110,107, 157,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
GLUT2, SLC2A2	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples, normal colon, benign colon adenomas and colorectal carcinoma tissue samples, normal and colon cancer cells transplanted in nude mice, invasive tubular carcinoma	RT-PCR, Northern blotting	**Inconsistent results reported** -mRNA expression similar in cancer and normal tissue, also no expression in colon cancer tumors or normal tissue		[128,164,177]
GLUT2, SLC2A2	Illness	Cancer	Gastric carcinoma	clinical tumor tissue samples	immunohistochemistry, RT-PCR	increase of mRNA expression, not expressed in normal tissue		[127,151,177]
GLUT2, SLC2A2	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney surgical samples, renal cell carcinoma (RCC), chromophobe RCC and oncocytoma tumors, clear cell RCC and papillary RCC	RT-PCR	decrease of mRNA expression in tumor cells, or mRNA expression in tumor cells as expressed in normal tissue		[161]
GLUT2, SLC2A2	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, hepatocellular carcinoma	immunohistochemistry, Western immunoblotting, (18)F-FDG uptake	increase of expression and activity, expressed in normal tissue	suggested that combined evaluation of 18F-FDG uptake and expression of Glut-2 might have an important role for	[165,177

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							management of patients	
GLUT2, SLC2A2	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples, mesothielioma	immunohistochemistry	low expression, not expressed in normal tissue		[177]
GLUT2, SLC2A2	Illness	Cancer	Ovarian carcinoma	clinical malignant and normal tissue samples	immunohistochemistry	weak expression or no expression, not expressed in normal tissue		[177]
GLUT2, SLC2A2	Illness	Cancer	Pancreatic carcinoma	clinical malignant and normal tissue samples, adenocarcinoma, insulinomas, glucagonomas and their lymph node metastases, and gastrinoma	Northern blotting, Western immunoblotting, RT-PCR, immunohistochemistry	decrease of mRNA expression comparing to normal islets, expressed in normal human pancreatic islets		[151,152,177]
GLUT2, SLC2A2	Illness	Cancer	Uterus carcinoma	clinical tumor and normal tissue samples, leimyeoma	immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue		[177]
GLUT3, SLC2A3	Illness	Cancer	Brain carcinoma	clinical malignant and normal tissue samples, meningioma, glioma, ependymoma	immunohistochemistry, autoradiography	increase of mRNA and protein expression, no or low expression in normal tissue	mRNA expression suggested as a marker of aggressive biologic potential and major factor in tumor progression, potential targets for future therapy	[113,151,155,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
GLUT3, SLC2A3	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples, tumor and adjacent normal breast tissues samples, benign and malignant cell line, breast cancer cell lines MCF-7, MDA-468, and ZR-75-1	immunocytochemistry immunoblotting, Deoxyglucose and Fructose uptake, RT-PCR, Western blotting, immunohistochemistry	expressed mRNA and protein in breast cancer samples, no reactivity reported in cell lines, not expressed in normal mammary tissue, increase of mRNA, protein expression and activity by progesterone and estrogen treatment		[110,107,119,157,173,177]
GLUT3, SLC2A3	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples, normal colon, benign colon adenomas and colorectal carcinoma tissue samples, normal and colon cancer cells transplanted in nude mice, invasive tubular carcinoma	RT-PCR, Northern blotting	**Inconsistent results reported** -mRNA expression similar in cancer and normal tissue, also increase of expression and activity in SNU-C5 tumors, or not expressed in normal tissue		[128,164,177]
GLUT3, SLC2A3	Illness	Cancer	Gastric carcinoma	clinical tumor tissue samples	immunohistochemistry, RT-PCR	increase of mRNA and protein expression		[115,127]
GLUT3, SLC2A3	Illness	Cancer	Head and neck carcinoma	clinical tumor tissue samples, head and neck squamous	immunohistochemistry	expression of mRNA and protein	**Inconsistent results reported** - no association, or high gene expression level associated with	[130,132]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				cell carcinoma, tissue of head and neck tumors, adjacent mucosa, and normal mucosa samples			an increased incidence of lymph node metastases	
GLUT3, SLC2A3	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney surgical samples, clear cell RCC, papillary RCC, chromophobe RCC and oncocytoma tumors	RT-PCR	mRNA expression in tumor cells as expressed in normal tissue		[161]
GLUT3, SLC2A3	Illness	Cancer	Laryngeal carcinoma	clinical tumor tissue samples, biopsy samples of squamous cell carcinoma (SCC) of the larynx	immunohistochemistry	mRNA expressed	associated with poor survival of patients	[174]
GLUT3, SLC2A3	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples, non-small cell lung cancer (NSCLC) tissue samples, adenocarcinoma, mesothielioma	immunohistochemistry, RT-PCR	**Inconsistent results reported** -increase of mRNA, protein expression and activity, also low or no expression reported, not expressed in normal tissue	suggested as a significant poor prognosis indicator in cases of NSCLC	[109,115,136,137,138,139,151, 177]
GLUT3, SLC2A3	Illness	Cancer	Ovarian carcinoma	clinical malignant and normal tissue samples	immunohistochemistry	**Inconsistent results reported** -increase of protein		[115,127]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						expression or no expression, not expressed in normal tissue		
GLUT3, SLC2A3	Illness	Cancer	Pancreatic carcinoma	clinical malignant and normal tissue samples, insulinomas, glucagonomas and their lymph node metastases, gastrinoma, adenocarcinoma	Northern blotting, RT-PCR, immunohistochemistry	**Inconsistent results reported** – mRNA and protein expression, also low expression in tumor tissue and not expressed in normal tissue		[152,177]
GLUT3, SLC2A3	Physiological condition	Hypoxia	Decreased oxygen pressure	clinical samples, primary syncytotrophoblast cells, BeWo choriocarcinoma cells and human placental villous tissue explants	immunoblotting, Northern blotting	increase of mRNA, protein expression and activity	expression may be of prognostic significance for hypoxic tumors	[168,170,172]
GLUT4, SLC2A4	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples, tumor and adjacent normal breast tissues samples, benign and malignant cell line, breast cancer cell lines MCF-7, MDA-468, and ZR-75-1	immunocytochemistry, immunoblotting, Deoxyglucose and Fructose uptake, RT-PCR, Western blotting, immunohistochemistry	expression of mRNA and protein in breast cancer tissue and cell lines, very low expression, increase of mRNA, protein expression and activity by progesterone and estrogen treatment,		[110,119,157,177]

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Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						not expressed in normal breast tissue		
GLUT4, SLC2A4	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples, normal and colon cancer cells transplanted in nude mice, invasive tubular carcinoma	RT-PCR, Northern blotting	very weak or no expression in colon cancer tumors, expressed in invasive tubular carcinoma, not expressed in normal tissue		[164,177]
GLUT4, SLC2A4	Illness	Cancer	Gastric carcinoma	clinical tumor tissue samples	immunohistochemistry, RT-PCR	increase of mRNA expression		[127,151]
GLUT4, SLC2A4	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney surgical samples, renal cell carcinoma (RCC), chromophobe RCC and oncocytoma tumors, papillary RCC, clear cell RCC	RT-PCR	expressed in normal kidney tissue, in chromophobe RCC cells mRNA expression increased, in papillary RCC mRNA expression was as expressed in normal tissue, in clear cell RCC mRNA expression decreased	suggested that high-affinity GLUTs might have a major role in enhanced glucose uptake in kidney tumors	[161]
GLUT4, SLC2A4	Illness	Cancer	Lung carcinoma	clinical tumor tissue samples, non-small cell lung cancer	immunohistochemistry, RT-PCR	low or no expression, not expressed in normal tissue		[138,139,177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				tissue samples				
GLUT4, SLC2A4	Illness	Cancer	Lymphoid carcinoma	clinical tumor and normal tissue samples, Non-Hodgkin's lymphoma biopsies and normal spleen samples	immunohistochemistry	low expression in tumor tissue, not expressed in normal spleen		[177]
GLUT4, SLC2A4	Illness	Cancer	Ovarian carcinoma	clinical malignant and normal tissue samples, borderline, benign epithelial tumor	immunohistochemistry	increase of protein expression or no expression, absent in benign ovarian epithelial tumors, progressively more staining shown in invasive tumors as compared to borderline tumors, not expressed in normal tissue	suggested as clinically useful prognostic information in patients with ovarian carcinoma	[149,177]
GLUT4, SLC2A4	Illness	Cancer	Pancreatic carcinoma	clinical malignant and normal tissue samples	Northern blotting, Western immunoblotting, RT-PCR	decrease of mRNA expression		[142,151]
GLUT4, SLC2A4	Physiological condition	Exercise	Physical exercise	transgenic mice gastrocnemius muscles samples	Northern blotting	increase of mRNA and protein expression		[92]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
GLUT5, SLC2A5	Illness	Cancer	Brain carcinoma	clinical tumor and normal tissue samples, choroid plexus papilloma, ependymoma	immunohistochemistry	weak expression, no expression in normal tissue		[177]
GLUT5, SLC2A5	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples, breast cancer tissues samples, adjacent normal breast tissue, benign and malignant cell line, breast cancer cell lines MCF-7 and MDA-468	immunocytochemistry, immunoblotting, Fructose uptake, in situ RT-PCR	expressed in breast cancer tissues and cell lines, increase of expression in ductal invasive carcinoma, not expressed in normal breast tissue, expressed in myoepithelial cells	suggested to be related to the neoplastic state in breast cancer cell lines MCF-7 and MDA-468, protein levels decreased with invasive potential	[107,119,157,173,177]
GLUT5, SLC2A5	Illness	Cancer	Colorectal carcinoma	clinical tumor tissue samples, invasive tubular carcinoma	RT-PCR, Northern blotting	expressed in colon cancer tumors, expressed in normal tissue		[177]
GLUT5, SLC2A5	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney surgical samples, renal cell carcinoma (RCC), chromophobe RCC and oncocytoma tumors, clear cell RCC and papillary RCC	RT-PCR	**Inconsistent results reported** -mRNA expression in tumor cells as expressed in normal tissue, or decrease of mRNA expression in tumor cells, expressed in normal		[161]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						tissue		
GLUT5, SLC2A5	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, hepatocellular carcinoma (HCC)	immunohistochemistry	weak expression, expressed in normal tissue		[177]
GLUT5, SLC2A5	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples, mesothielioma	immunohistochemistry	low expression, not expressed in normal tissue		[177]
GLUT5, SLC2A5	Illness	Cancer	Uterus carcinoma	clinical tumor and normal tissue samples, leimyeoma	immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue		[177]
GLUT5, SLC2A5	Illness	Diabetes	Diabetes, type II	clinical samples, diabetic muscle cells	RT-PCR, immunoblotting, immunohistochemistry	increase of mRNA expression		[91]
GLUT6, SLC2A6	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples	immunocytochemistry, immunoblotting, Fructose uptake, immunohistochemistry	weak expression in breast cancer tissues, not expressed in normal breast tissue		[177]
GLUT6, SLC2A6	Illness	Cancer	Pancreatic carcinoma	clinical tumor and normal tissue samples, adenocarcinoma	immunohistochemistry	low expression in tumor tissue, not expressed in normal tissue		[177]
GLUT6, SLC2A6	Illness	Cancer	Uterus carcinoma	clinical tumor and normal tissue samples, leimyeoma	immunohistochemistry	expressed in tumor tissue, not expressed in normal tissue		[177]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
GLUT9, SLC2A9	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney surgical samples, renal cell carcinoma (RCC), clear cell RCC, chromophobe RCC and oncocytoma tumors, papillary RCC	RT-PCR	mRNA expression in tumor cells as expressed in normal tissue, decrease of mRNA expression in tumor cells, expressed in normal tissue		[161]
GLUT9, SLC2A9	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, hepatocellular carcinoma (HCC)	immunohistochemistry	weak expression, expressed in normal tissue		[177]
GLUT9, SLC2A9	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples, mesothielioma	immunohistochemistry	low expression, expressed in normal tissue		[177]
GLUT9, SLC2A9	Illness	Cancer	Skin carcinoma	clinical tumor and normal tissue samples, melanoma biopsies	immunohistochemistry	low expression in tumor tissue, not expressed in normal tissue		[177]
GLUT9, SLC2A9	Illness	Cancer	Thyroid carcinoma	clinical tumor and normal tissue samples, thyroid carcinoma, papillary carcinoma biopsies	immunohistochemistry, RT-PCR	expressed in papillary carcinoma biopsies, not expressed in normal breast tissue		[177]
GLUT10 SLC2A10	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney	RT-PCR	decrease of mRNA expression in tumor		[161]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				surgical samples, renal cell carcinoma (RCC), chromophobe RCC and oncocytoma tumors, clear cell RCC and papillary RCC		cells, or mRNA expression in tumor cells as expressed in normal tissue		
GLUT12, SLC2A12	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, breast cancer and benign tumor tissues samples, breast cancer cultured cells	immunohistochemistry, RT-PCR	increase of expression in breast cancer cell lines, low or no expression in benign tumor	suggested as novel method for detection and treatment of breast cancer	[163,173]
GLUT12, SLC2A12	Illness	Cancer	Kidney carcinoma	clinical tumor tissue samples, kidney surgical samples, renal cell carcinoma (RCC), chromophobe RCC and oncocytoma tumors, clear cell RCC and papillary RCC	RT-PCR	decrease of mRNA expression in tumor cells as expressed in normal tissue		[161]
GLUT12, SLC2A12	Illness	Cancer	Prostate carcinoma	clinical prostate carcinoma tissue samples, prostate cancer cells and cultured cancer cell lines LNCaP, C4, C4-2, and C4-2B using primers to amplify GLUT12, benign	RT-PCR, Western immunoblotting, Northern blotting	increase of mRNA and protein expression, expressed in human prostate tumors, low or no expression in normal cells, not expressed in benign prostatic hyperplasia	suggested as novel method for detection and treatment of prostate cancer	[72,173,176]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				prostatic hyperplasia		, mRNA expressed in cancer cell lines		
LAT1, SLC7A5	Illness	Cancer	Bladder carcinoma	clinical tumor tissue samples,T24 human bladder carcinoma cells	RT-PCR, Northern blot, immunofluorescence	increase of mRNA expression, protein level and activity		[97]
LAT1, SLC7A5	Illness	Cancer	Esophageal carcinoma	esophageal adenocarcinoma cell lines, Barrett's adenocarcinoma cell lines, esophageal squamous-cell carcinoma cell lines, esophagus endoscopy tissue samples, non-cancerous esophageal mucosa	RT-PCR, Western immunoblotting, immunohistochemistry	increase of mRNA and protein expression comparing to non-cancerous esophageal mucosa		[103,105]
LAT1, SLC7A5	Illness	Cancer	Head and neck carcinoma	head and neck squamous cell carcinoma cell line, Hep-2	Western immunoblotting	increase of expression	suggested that combination of an antitumor agent with inhibitors of LAT1 would be beneficial to the cancer therapy	[101,102]
LAT1, SLC7A5	Illness	Cancer	Oral carcinoma	KB oral epidermoid carcinoma cells, oral squamous cell carcinoma and its precursor lesions, human osteoblast cells and Saos2 human	RT-PCR, Western immunoblotting, immunohistochemistry	increase of mRNA and protein expression	proposed as more specific indicator of tumor progression, suggested that specific inhibition of LAT1 in tumor cells might be a new rationale for antitumor therapy	[98,99,100]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				osteogenic sarcoma cells				
LAT2, SLC7A8	Illness	Cancer	Osteosarcoma	human osteoblast cells and Saos2 human osteogenic sarcoma cells	RT-PCR, Western immunoblotting	very low mRNA and protein expression		[99]
LRP, VALUT1, MVP	Illness	Cancer	Bladder carcinoma	clinical tumor and normal tissue samples, transitional cell carcinoma	immunohistochemistry, RT-PCR	high mRNA and protein expression, mRNA level was significantly greater in normal bladder tissue	significantly associated with a worse response to neoadjuvant chemotherapy (NACT) and a decreased probability of bladder preservation	[401,421]
LRP, VALUT1, MVP	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, primary breast cancers	immunohistochemistry, RT-PCR	expression of mRNA and protein	**Inconsistent results reported** – suggested that may play a role in anthracycline resistance, expression is significantly associated with nodal metastases, reported not to relate to the relapse or prognosis in patients treated with doxorubicin-based chemotherapy	[344,346,378,398]
LRP, VALUT1, MVP	Illness	Cancer	Gastric carcinoma	clinical stomach tumor and normal tissue samples, primary gastric cardiac adenocarcinoma	immunohistochemistry	increase of protein expression compared to normal tissue	level of expression appears to correlate with the degree of differentiation, well-differentiated carcinomas contained significantly higher level of	[349,350,352]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							expression, expression not associated with the invasion degree and lymph node metastases	
LRP, VALUT1, MVP	Illness	Cancer	Leukemia	clinical tumor tissue samples, acute lymphocytic (lymphoblastic) leukemia (ALL), acute myeloid leukemia (AML), bone marrow samples	RT-PCR, flow cytometric assays, immunohistochemistry	**Inconsistent results reported** – increase of mRNA and protein expression, also no difference in LRP expression levels between initial or relapsed patients	**Inconsistent results reported** – related to worsened eventfree survival with resistance to induction chemotherapy and the relative risk of relapse, might contribute to drug resistance in B-lineage ALL, also no correlation between LRP expression and clinical outcome and drug resistance, suggested lack of clinical significance in AML but that might contribute to drug resistance in children with ALL	[345,354,355,356,357,377,378,379]
LRP, VALUT1, MVP	Illness	Cancer	Liver carcinoma	clinical tumor tissue samples, hepatocellular carcinoma (HCC), HepG2 cell line	RT-PCR, Western immunoblotting	increase of mRNA expression in tumor tissue compared to normal tissue		[397]
LRP, VALUT1, MVP	Illness	Cancer	Lymphoid carcinoma	clinical samples, T/NK-cell lymphomas, nasal NK/T cell lymphoma	immunohistochemistry	expression of protein		[399,400]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
LRP, VALUT1, MVP	Illness	Cancer	Ovarian carcinoma	clinical tumor tissue samples, advanced ovarian carcinoma	immunohistochemistry	increase of mRNA expression	suggested as indicator of poor response to standard chemotherapy	[376,378]
LRP, VALUT1, MVP	Illness	Cancer	Prostate carcinoma	clinical tumor tissues samples	immunohistochemistry	increase of expression in tumor tissue with increased pathology		[315]
LRP, VALUT1, MVP	Illness	Cancer	Tongue carcinoma	clinical tumor tissue samples, squamous cell carcinoma	immunohistochemistry	expression of protein		[351]
LRP, VALUT1, MVP	Illness	Cancer	Wilms' tumor	clinical tumor tissue samples, nephroblastoma	immunohistochemistry, RT-PCR, tissue microarray technique	**Inconsistent results reported** – expression of mRNA and protein, low or no expression in normal tissue, also no expression of protein in tumor samples reported	significant relationships between expression and chemotherapeutic pre-treatment of tumors and tumor stage found, expression proposed as positive indicator	[404,418,420]
LRP, VALUT1, MVP	Physiological condition	Hypoxia	Decreased oxygen pressure	HepG2 human hepatocellular carcinoma cells, gas mixture and CoCl(2) induced hypoxia	RT-PCR, Western immunoblotting	increase of mRNA expression and protein level	proposed as one of the causes for the formation of multidrug resistance in HepG2 human hepatocellular carcinoma cell line	[183]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MCT1, SLC16A1	Illness	Inflammation	Intestinal inflammation	clinical tumor tissue samples, colonic tissues collected from patients with IBD or healthy controls	RT-PCR, Western immunoblotting, immunohistochemistry, Butyrate uptake	decrease of mRNA expression and protein level		[190]
MCT4, SLC16A3	Physiological condition	Hypoxia	Decreased oxygen pressure	HeLa and COS cells, CoCl(2) induced hypoxya	RT-PCR, Western immunoblotting	increase of mRNA expression, increase of protein level		[186]
MDR1, P-glycoprotein, PgP, ABCB1	Demographic factor	Age	Adults, age range 21-27 years and age range 59-68 years	healthy volunteers, CD3-positive leukocytes	[(11)C]-Verapamil (R)- BBB distribution, positron emission tomography	decreased activity during aging		[79]
MDR1, P-glycoprotein, Pgp, ABCB1	Demographic factor	Age	Children, age range 1 to 17 years	clinical samples, duodenal biopsies samples	RT-PCR	no statistical relation with age in mRNA expression		[62]
MDR1, P-glycoprotein, PgP, ABCB1	Illness	Cancer	Adrenal carcinoma	clinical tumor tissue samples, pheochromocytoma, adrenocortical carcinoma, neuroblastoma	immunohistochemistry, Slot Blot Analysis	increase of mRNA expression, high protein level detected, expressed in normal tissue		[313,314,326,364]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Bladder carcinoma	clinical tumor tissue samples, bladder transitional cell carcinomas, tumor cell lines, vincristine-resistant cell line	immunohistochemistry, flow cytometry, RT-PCR	low or high protein expression detected, low expression in normal tissue, increase of mRNA and protein expression	correlated with shorter progression-free survival but not with overall survival	[314,327,328,329,330,401,421]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				T24/VCR		in T24/VCR cells		
MDR1, P-glycoprotein, P-gP ABCB1	Illness	Cancer	Breast carcinoma	clinical tumor and normal tissue samples, breast-cancer cell lines, primary breast cancers tumor tissue samples, invasive breast carcinomas	immunohistochemistry, RT-PCR, Rhl23 dye-efflux assay, Slot Blot Analysis	low or no mRNA and protein expression and activity in primary tumor tissues and breast carcinoma cells, no significant increase of mRNA expressed in tissue samples from patients clinically treated with anthracyclines	**Inconsistent results reported-** no evidence of significant activity of the P-gp pump, no correlation between clinical response and MDRl/P-Gp mRNA expression, also suggests that MDR1 is an important predictor of poor prognosis in breast cancer patients receiving chemotherapy as first-line treatment for recurrent disease, expression is significantly associated with nodal metastases, associated strongly with higher histological grade (grade III), also no association was shown between MDR-1 P-gp expression and survival times	[,313,314,330,342,343,344,346,347,360,367,398]
MDR1, P-glycoprotein, P gP, ABCB1	Illness	Cancer	Childhood carcinoma	clinical tumor tissue samples, neuroepithelioma, Ewing sarcoma, neuroepithelioma	Slot Blot Analysis	low increase of mRNA expression in some samples, low expression in normal tissue		[364]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples, normal colon mucosa, tumor and adjacent non-cancerous tissue samples, tumor cell lines, parental cells and Pgp-overexpressing doxorubicin-resistant SW620R cells from SW620 human colon cancer cells, Human colorectal cancer cells (Caco-2)	immunoblotting, immunohistochemistry, RT-PCR, Slot Blot Analysis	increase of mRNA expression and protein in tumor tissues, decrease of mRNA expression in tumor tissue compared to non-cancerous regions, expressed in normal tissue, expression of mRNA in cell lines	level of expression appears to correlate with the degree of differentiation, well-differentiated carcinomas contained significantly higher level of expression	[,268,314,317,322,326,330,358,364,423]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Eye cancer	clinical tumor tissue samples, retinoblastoma	immunohistochemistry	expression of mRNA and in tumor tissues	no statistically significant relationship between the expressions and tumor differentiation, presence of tumor invasion or treatment with chemotherapy	[371]
MDR1, P-glycoprotein, PgP, ABCB1	Illness	Cancer	Gallbladder carcinoma	Mz-ChA-1 cells derived from gallbladder adenocarcinoma	RT-PCR, immunoblotting, immunofluorescence microscopy	expression of mRNA		[402]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples, gastric cardiac adenocarcinoma,	immunohistochemistry	increase of protein expression compared to normal tissue, low expression in normal tissue	expression was closely related with clinicopathologic staging, the level of expression appears to correlate with the degree of differentiation, well-differentiated colorectal carcinomas contained significantly higher level	[314,349,352,358]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Insulinoma	clinical tumor tissue samples	immunohistochemistry	high protein level detected		[314]
MDR1, P-glycoprotein, PgP, ABCB1	Illness	Cancer	Large intestine tumor	clinical tumor tissue samples	RT-PCR, Western immunoblotting	no difference in mRNA and protein expression between normal and tumor tissue		[63]
MDR1, P-glycoprotein, P-gP ABCB1	Illness	Cancer	Leukemia	clinical tumor and normal tissue samples, acute lymphocytic (lymphoblastic) leukemia (ALL), acute nonlymphocytic leukemia (ANLL), tumor cell lines, lymphoblastic leukemia, acute myeloid leukemia	RT-PCR, flow cytometric assays, Rh l23 and Di(OC)2 efflux assay, Slot Blot Analysis, calcein-AM uptake, MultiDrug Quant assay kit, immunohistochemist	increase of mRNA, protein expression and activity, low or high expression in some samples, low expression of mRNA level in HL6O/DOX cells similar to that of the parent	**Inconsistent results reported** – great variability in mRNA expression in AML patient samples, confirmed the clinical relevance of expression and functional CsA-inhibited drug efflux in AML and in pediatric ALL patients, associated with poor treatment outcome in AML patients, P-gp	[326,330,345,354,355,356,357, 364.377.379,380,381,391,392, 406,408.409.410,411]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				(AML), bone marrow aspirates or peripheral blood were collected from AML patients, HL60 cell line, HL6O/DOX cells, K562/VCR cells	ry, Southern blotting, DOX uptake and efflux, immunobl otting	HL60 cells with no protein detected, expression of mRNA and protein in HHT90 cell lines, expression of protein in PC13, PC13 2-2, HHT90, HL60, and HL60/MRP cell lines	function was a prognostic factor only in AML patients receiving Daunorubicin or Idarubicin, because of diversity of the results it was concluded that clinical importance of P-gp in childhood ALL remains unclear, functional activity is a more sensitive predictor of chemoresistance than P-gp surface expression	
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Lipoma	clinical tumor and normal tissue samples	RT-PCR	increase of mRNA expression in some samples		[330]
MDR1, P-glycoprotein, PgP, ABCB1	Illness	Cancer	Liver carcinoma	clinical tumor and normal tissue samples, hepatocellular carcinoma (HCC)	RT-PCR, Slot Blot Analysis, immunohistochemistry, Western immunobl otting	increase of mRNA expression, or expression as in normal tissue	could be up-regulated by anti-cancer agents *in vitro*	[326,364,396,397]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Lung carcinoma	clinical tumor and normal tissue samples, adenocarcinoma, non-small cell and small cell lung cancer cell lines	immunohistochemistry, RT-PCR, Slot Blot Analysis, Western immunobl otting,	**Inconsistent results reported** - low expression of mRNA and protein in clinical samples, no or expression only in some cell lines, expressed in normal	overexpression related to acquired multidrug resistance *in vivo*	[314,318,320,321,326,320,330,,331,364,368]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
						tissue		
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Lymphoid carcinoma	clinical tumor tissue samples, primary tumors, 44 T-cell lymphomas, indolent non-Hodgkin's lymphoma, resistant leukemia cell sublines, T/NK-cell lymphomas	immunobl otting, immunohi stochemist ry, RT-PCR, Northern blotting, Rh123 dye-efflux assay, Slot Blot Analysis	increase of mRNA, protein expression and activity in leukemic cells, low expression in normal lymphocyte s	concluded that assays tested are suitable for evaluating P-gp expression and function in clinical samples	[287,326,330,341,342,364,399]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Neuroblastoma cancer	clinical tumor tissue samples, primary neuroblastoma, cultured cell lines,	Western immunobl otting, RT-PCR	expression of mRNA and protein	expression demonstrated no prognostic significance	[374,375,414,415]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Ovarian carcinoma	clinical tumor and normal tissue samples, advanced ovarian carcinoma	RT-PCR, Slot Blot Analysis	increase of mRNA expression in some samples, low expression in normal tissue	low-level expression of mRNA correlates with clinical resistance, no association was found between expression and response to chemotherapy and survival	[330,331,364,376]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Pancreatic carcinoma	clinical tumor tissue samples	RT-PCR	increase of mRNA expression in some samples		[326]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Penile carcinoma	penile squamous cell carcinoma	immunohi stochemist ry	expression of protein		[327]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Prostate carcinoma	clinical tumor and normal tissue samples, prostate adenocarcinomas, cancer cell lines	immunohistochemistry Western immunoblotting, Slot Blot Analysis	lower expression of protein in tumor tissue than normal tissue, or no protein expression, low expression in normal tissue		[291,303,315 ,348,364]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Renal carcinoma	clinical tumor tissue samples, renal cell carcinomas (RCC), clear cell type	immunohistochemistry, RT-PCR	increase of mRNA expression, high protein level detected		[314,326,327,361]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Sarcoma	clinical tumor and normal tissue samples, osteosarcoma, chondrosarcoma, soft tissue sarcomas, Ewing's sarcoma	RT-PCR	increase of mRNA expression		[330]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Tongue carcinoma	clinical tumor tissue samples, squamous cell carcinoma	immunohistochemistry	expression of protein, expression ratios in post-chemotherapy cases were higher	relevance with drug resistance	[351]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Cancer	Wilms' tumor	clinical tumor tissue samples, nephroblastoma	immunohistochemistry	no expression of protein		[404]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MDR1, P-glycoprotein, PgP, ABCB1	Demographic factor	Gender	Male, Female	human liver samples	RT-PCR, Western immunoblotting, immunohistochemistry	no significant differences between men and women in mRNA level		[3]
MDR1, P-glycoprotein, PgP, ABCB1	Physiological condition	Hyperthermia	Temperature elevation	ADM-resistant MCF-7 breast cancer cell line	RT-PCR, flow cytometry	decrease of protein level in cell membranes in co-treatment with INF-alpha, and Verapamil	suggested that hyperthermia may be exploited in clinical cancer chemotherapy	[93]
MDR1, P-glycoprotein, Pgp, ABCB1	Physiological condition	Hyperthermia	Temperature elevation	human prostate cancer cell line DU-145, multicellular prostate tumor spheroids	RT-PCR, immunohistochemistry, Doxorubicin uptake, immunoprecipitation	increase of mRNA expression, increase of protein level and activity		[209,211]
MDR1, P-glycoprotein, Pgp, ABCB1	Therapeutic condition	Hypothermia	Temperature decrease	LLC-PK1 and LLC-GA5-COL150 cells	Digoxin, Quinidine, and Tetracycline transport	decrease of activity		[195]
MDR1, P-glycoprotein, Pgp, ABCB1	Physiological condition	Hypoxia	Decreased oxygen pressure	cultured human cervical cancer cell line HeLa, Hepa1 tumor spheroids, human lung adenocarcinoma A549 cells, HepG2 human hepatocellular carcinoma cells, human ovarian cancer cells, gas mixture and CoCl(2)	RT-PCR, Western immunoblotting	increase of mRNA expression and protein level	proposed as one of the causes for the formation of multidrug resistance in HepG2 human hepatocellular carcinoma and human ovarian cancer cells	[181,182,183,184,169]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				induced hypoxia				
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Inflammation	Inflammatory bowel disease, Crohn's disease	clinical samples, duodenal biopsies samples	RT-PCR	increase of mRNA expression		[61]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Inflammation	Intestinal inflammation	intestinal mucosal biopsies samples from patients with Crohn's disease, diverticulitis, collagenous colitis and healthy controls	RT-PCR, Western immunoblotting, immunohistochemistry	decrease of mRNA expression and protein level		[189]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Liver disease	Acetaminophen overdoses	injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of protein level		[205]
MDR1, P-glycoprotein, Pgp, ABCB1	Illness	Liver disease	Primary biliary cirrhosis	injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression, increase of protein level		[205]
MDR1, P-glycoprotein, Pgp, ABCB1	Physiological condition	Oxidative stress	Reactive oxygen species	hydrogen peroxide exposure, multicellular prostate tumor spheroids overexpressing the ROS-generating enzyme Nox-1, human	RT-PCR, immunohistochemistry, Doxorubic in uptake	decrease of protein level and activity in large prostate tumor spheroids		[181,202,203,210]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				prostate cancer cell line DU-145, multicellular prostate tumor spheroids with prooxidants				
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Bladder carcinoma	the cisplatin-resistant bladder carcinoma cell lines T24/DDP7 and T24/DDP1O, doxorubicin-resistant T24/ADM-1 and T24/ADM-2 cells	immunohistochemistry, RNase protection assays, Southern blotting	low increase of mRNA and protein expression, expressed in normal tissue, increase of mRNA expression in T24/AD M cells	correlated with a higher response and a higher probability of bladder preservation following neoadjuvant chemotherapy (NACT)	[318,329,362,401,421]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Brain carcinoma	clinical tumor tissue samples, glial cell tumors, astrocytoma, anaplastic astrocytoma, glioblastoma cell line A172	immunohistochemistry, RT-PCR, Northern blotting, RNase protection assay, Western immunoblotting, LTC4 uptake	increase of expression of mRNA and protein in tumor tissue, expression of mRNA and protein in untreated cells, transient increase of mRNA, protein expression and activity in cell treated by ACNU, low expression in normal tissue	suggested to contribute in development of MRP-related multidrug resistance	[316,318,353]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, primary breast cancers,	immunohistochemistry, RT-PCR	**Inconsistent results reported** – low expression of mRNA and protein,	**Inconsistent results reported** – suggested that may play a role in anthracycline resistance, but	[344,359,360,367,393,394,398]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				invasive breast carcinomas, breast cancer cell lines		also protein not detected	not in CMF treated patients, suggested to be of prognostic significance in the subgroups of patients with the more favorable prognosis, i.e. patients with small tumors and node-negative patients, as well as in the setting of adjuvant systemic chemotherapy, also no evidence linking this protein to clinical drug resistance	
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Colorectal carcinoma	clinical tumor tissue samples, tumor and adjacent non-cancerous tissue samples, primary colorectal carcinomas, the cisplatin-resistant colon carcinoma cell lines HCT8/DDP, parental cells and Pgp-overexpressing doxorubicin-resistant SW620R cells from SW620 human colon cancer cells	immunohistochemistry, RT-PCR, RNase protection assays	mRNA of expression in tumor tissue and non-cancerous regions, expressed in normal tissue, low increase of mRNA expression in HCT8 cell lines, expression of mRNA in cancer cells	appear not to be related to the age and sex of the patients, localization of the primary tumor, histological grade, tumor size, lymph node metastases, distant metastases and tumor stage	[317,318,322,363,366]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Eye cancer	clinical tumor tissue samples, retinoblastoma	multilayer immunoperoxidase staining, immunohistochemistry	expression of mRNA in tumor tissues	no statistically significant relationship between expression and tumor differentiation, presence of tumor invasion or treatment with chemotherapy	[370,371]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Gallbladder carcinoma	Mz-ChA-1 cells derived from gallbladder adenocarcinoma	RT-PCR, immunoblotting, immunofluorescence microscopy	expression of mRNA, also mRNA not detected		[402]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Gastric carcinoma	clinical tumor and normal tissue samples, primary gastric cardiac adenocarcinoma	immunohistochemistry, RT-PCR, Southern hybridization	increase of mRNA and protein expression compared to normal tissue	level of expression appears to correlate with the degree of differentiation, well-differentiated carcinomas contained significantly higher level of expression, expression not associated with the invasion degree and lymph node metastases	[350,352,372,373]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Hepatic carcinoma	clinical tumor and corresponding normal liver tissue samples	immunoblotting, RT-PCR, immunohistochemistry immunofluorescence microscopy	low or no expression of mRNA and protein, low or no expression in normal tissue		[323]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Leukemia	clinical tumor tissue samples, acute lymphocytic (lymphoblastic) leukemia (ALL), doxorubicin-resistant sublines of the leukemia cancer cell line HL6O/ADR, parental cells and MRP-overexpressing multidrug-resistant HL60R cells from HL60 human promyelocytic leukemia cells, acute myeloid leukemia (AML), bone marrow aspirates or peripheral blood were collected from AML patients, HL60/DOX cells, K562/VCR cells	immunoblotting, RNase protection assays, immunohistochemistry, RT-PCR, flow cytometric assays, DL-Buthionine (S,R)-Sulfoximine (BSO) efflux assay, effect of Probenecid on calcein efflux, calcein-AM and Rh123 assays, MultiDrug Quant assay kit, Southern blot analysis, DOX uptake and efflux assay, immunoblotting	increase of mRNA and protein expression, not expressed in parenteral cells, increase of mRNA expression in HL60/DOX cells, expression of protein in PC13, PC13 2-2, HL60, and HL60/MRP cell lines	**Inconsistent results reported** - great variability in mRNA expression and suggested lack of clinical significance in AML patient samples, also suggested that it contributes to drug resistance in AML, or that does not seem to play a major role in multidrug resistance in childhood acute ALL, concluded that the activity had no prognostic impact and that did not correlate with prognostically unfavorable immunophenotype, white blood cell count or age, mainly involved in the resistance mechanism of the HL60/DOX cells, relapsed patients showed a higher expression, high expression has an unfavorable prognosis	[45,318,322,345,354, 355,356,357,377,379,380,381, 391,406,408,409,410,411]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Liver carcinoma	clinical tumor tissue samples, hepatocellular carcinoma (HCC), HepG2 cell line	RT-PCR, immunohistochemistry, Western immunoblotting	increase of mRNA expression in tumor tissue compared with normal tissue	may result in an aggressive tumor phenotype	[396,397]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Lung carcinoma	clinical tumor tissue samples, large cell carcinoma, non-small cell (NSCLC) and small cell lung cancer cell lines not selected for drug resistance, non-small cell lung cancer cell lines COR-L231R, and small cell lung cancer cell lines GLC4/ADR, doxorubicin-resistant sublines of the lung adenocarcinoma cell line MOR/R	immunoblotting, RNase protection assays, Western immunoblotting, RT-PCR, Northern blotting	increase of mRNA and protein expression, expressed in normal tissue, expression level of squamous-cell carcinomas was significantly higher than that of adenocarcinoma	suggested as component of the multifactor multidrug resistance phenotype of lung cancer in some squamous-cell carcinomas of the lung, gene expression is related to the histopathology and prognosis in NSCLC,	[318,319,320,321,363,369]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Lymphoid carcinoma	clinical tumor tissue samples, T/NK-cell lymphomas, nasal NK/T cell lymphoma	immunohistochemistry	expression of protein		[399,400]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Neuroblastomacarcinoma	clinical tumor samples, primary neuroblastoma tumors, cultured cell lines,	Western immunoblotting, RT-PCR, Southern blotting, Northern blotting	increase of expression of mRNA and protein	suggested to have role in the malignant, chemoresistant phenotype and to be powerful prognostic indicator for children with neuroblastoma, also suggested that positive MRP1 RNA expression at diagnosis has	[374,375,414,415,416,417]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
							prognostic significance, but high drug resistance is conferred by mechanisms other than MRP1, proposed that inhibition may be a clinically relevant approach to improving patient outcome in this disease	
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Ovarian carcinoma	clinical tumor tissue samples, the cisplatin-resistant 2008 and the A2780 ovarian carcinoma cell lines, advanced ovarian carcinoma	RNase protection assays, immunohistochemistry	increase of mRNA expression, low expression in normal tissue	no association was found between expression and response to chemotherapy and survival	[318,376]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Pancreatic carcinoma	clinical tumor tissue samples, pancreatic cancer cell lines	reverse-transcriptase (RT)-PCR, RT-PCR, immunohistochemistry	expression of mRNA in cell lines		[395]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Prostate carcinoma	clinical prostate tissues, parental cells and CDDP-resistant P/CDP6 cells derived from PC-3 human prostate cancer cells, cancer cell lines	immunohistochemistry, RT-PCR, Western immunoblotting	increase of mRNA and protein expression in tumor tissue, expressed in normal tissue, expression in cell lines	increase of expression with increased pathology, may play a role in the development of drug resistance	[291,302,315,322,325,348,417]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Renal carcinoma	clinical tumor tissue samples, renal pelvic	Southern blotting, immunohistochemistry	expression of mRNA and protein		[362]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				tumor, renal-cell carcinoma				
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Tongue carcinoma	clinical tumor tissue samples, squamous cell carcinoma	immunohistochemistry	expression of protein, expression ratios in post-chemotherapy cases were higher	relevance with drug resistance	[351]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Ureter carcinoma	clinical tumor tissue samples	Southern blotting, immunohistochemistry	expression of mRNA and protein		[362]
MRP1, MRP, GS-X, ABCC1	Illness	Cancer	Wilms' tumor	clinical tumor tissue samples, nephroblastoma	immunohistochemistry, RT-PCR, tissue microarray technique	**Inconsistent results reported** – expression of mRNA and protein, also observed reduction in expression, high expression in normal tissue	**Inconsistent results reported** - positive expression of MRP1 correlated with a lower probability of survival, but there was no evidence that higher levels of MRP1 at diagnosis conferred a worse prognosis,, higher expression of MRP1 does not always correlate with poor survival, expression proposed also as positive indicator	[404,416,419,420]
MRP1, MRP, GS-X, ABCC1	Physiological condition	Hypoxia	Decreased oxygen pressure	human lung adenocarcinoma A549 cells, HepG2 human hepatocellular carcinoma, human ovarian cancer cells, gas mixture	RT-PCR, Western immunoblotting	increase of mRNA expression, increase of protein level	proposed as one of the causes for the formation of multidrug resistance in HepG2 human hepatocellular carcinoma and human ovarian cancer cells	[182,183,184

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP1, MRP, GS-X, ABCC1	Illness	Infection	Human T cell lymphotropic/leukaemia virus type I, HTLV-I	peripheral blood mononuclear cells, T lymphocytes from infected and control patients	RT-PCR, Western immunoblotting	decrease of mRNA expression, protein level and activity		[95]
MRP1, MRP, GS-X, ABCC1	Illness	Liver disease	Acetaminophen overdoses	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression		[205]
MRP1, MRP, GS-X, ABCC1	Illness	Liver disease	Primary biliary cirrhosis	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression, increase of protein level		[205]
MRP2, cMOAT, ABCC2	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, primary breast cancers tumor tissue samples, breast cancer cell lines	RT-PCR, immunohistochemistry	low expression of mRNA	**Inconsistent results reported** - suggested that may play a role in anthracycline resistance, also no evidence linking this proteins to clinical drug resistance	[344,394]
MRP2, cMOAT, ABCC2	Illness	Cancer	Colorectal carcinoma	clinical tumor tissue samples, tumor and adjacent non-cancerous tissue samples, the cisplatin-resistant colon carcinoma	immunohistochemistry, RT-PCR, Western immunoblotting	increase of mRNA and protein expression in tumor tissues compared to non cancerous regions,		[317,318,322]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				cell lines HCT8/DDP and non-drug-selected cells, parental cells and Pgp-overexpressing doxorubicin-resistant SW620R cells from SW620 human colon cancer cells		increase of mRNA and protein expression in HCT8 cell lines, also no expression in normal tissue		
MRP2, cMOAT, ABCC2	Illness	Cancer	Epidermoid carcinoma	KB-3-1 parental cell lines	RNase protection assays, Western immunoblotting	increase of mRNA and protein expression, no expression in normal tissue		[318]
MRP2, cMOAT, ABCC2	Illness	Cancer	Gallbladder carcinoma	clinical tumor tissue samples, Mz-ChA-1 cells derived from gallbladder adenocarcinoma	RT-PCR, immunoblotting, immunofluorescence microscopy	expression of mRNA in cells and some tumor samples		[402,403]
MRP2, cMOAT, ABCC2	Illness	Cancer	Gastric carcinoma	non-drug-selected cells	immunohistochemistry, RT-PCR, Western immunoblotting	expressed of mRNA and protein, expressed in normal tissue		[317,318,322]
MRP2, cMOAT, ABCC2	Illness	Cancer	Head and neck carcinoma	cisplatin-resistant head and neck cancer KB cell line	fluorescence in situ hybridization	increase of mRNA expression		[322]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP2, cMOAT, ABCC2	Illness	Cancer	Hepatic carcinoma	clinical tumor and corresponding normal tissue samples	immunoblotting, RT-PCR, immunohistochemistry immunofluorescence microscopy	expression of mRNA and protein in tumor and in normal tissue	suggested to contribute to the intrinsic MDR phenotype	[323]
MRP2, cMOAT, ABCC2	Illness	Cancer	Leukemia	parental cells and MRP-overexpressing multidrug-resistant HL60R cells from HL60 human promyelocytic leukemia cells, bone marrow aspirates or peripheral blood were collected from AML patients	immunohistochemistry, RT-PCR, functional drug efflux	expressed of mRNA and protein, expressed in normal tissue, expressed in parenteral cells, expressed of mRNA PC13, PC13 2-2, K562, HL60, and HL60/MRP cell lines	great variability in mRNA expression in AML patient samples, relapsed patients showed a higher mRNA expression, high expression has an unfavorable prognosis	[45,322,377,386,410, 411]
MRP2, cMOAT, ABCC2	Illness	Cancer	Lung carcinoma	non-small cell and small cell lung cancer cell lines not selected for drug resistance, parental lung adenocarcinoma cell line MOR/P, doxorubicin-resistant sublines of the non-small cell lung cancer cell lines SW1573/Sl and non-drug-selected cells	immunohistochemistry, RNase protection assays, Western immunoblotting, RT-PCR	increase of mRNA and protein expression, no expression in normal tissue	little evidence to support or refute a role for the involvement in the drug resistance of lung cancer cells	[318,319,320,322]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP2, cMOAT, ABCC2	Illness	Cancer	Pancreatic carcinoma	clinical tumor tissue samples, pancreatic cancer cell lines	reverse-transcripta se (RT)-PCR, RT-PCR, immunohi stochemist ry	expression of mRNA in cell lines, increase of mRNA and protein tumor tissue samples compared to normal tissue, protein not expressed in normal tissue	may correlate to intrinsic and acquired resistance for CDDP in human pancreatic cancer	[395]
MRP2, cMOAT, ABCC2	Illness	Cancer	Prostate carcinoma	parental cells and CDDP-resistant P/CDP6 cells derived from PC-3 human prostate cancer cells	immunohi stochemist ry, RT-PCR	expressed of mRNA and protein, expressed in normal tissue		[291,322]
MRP2, cMOAT, ABCC2	Illness	Liver disease	Cholecyst cholesterol lithiasis	clinical samples, liver tissue samples	RT-PCR, Western immunobl otting	increase of mRNA and protein expression		[90]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Breast carcinoma	clinical tumor tissue samples, primary breast cancers tumor tissue samples, breast cancer cell lines	RT-PCR, immunohi stochemist ry	expression of mRNA	no evidence linking the protein to clinical drug resistance	[394]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Cholangio carcinoma	clinical tumor tissue samples	RT-PCR, immunobl otting, immunofl uorescenc e microscop y	high expression of mRNA	suggested to contribute to the MDR phenotype,	[402]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Colorectal carcinoma	clinical tumor tissue samples, tumor and adjacent non-cancerous	immunohi stochemist ry, RT-PCR, immunobl otting,	decrease of mRNA of expression in tumor tissues compared to non-		[317,318,365]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
				tissue samples, the cisplatin-resistant colon carcinoma cell lines HCT8/DDP	RNase protection assays, Northern blotting	cancerous regions, high expression in non-cancerous regions, increase of mRNA expression in HCT8 cell lines, expression of mRNA in normal tissue		
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Epidermoid carcinoma	the KB-3-1 epidermoid carcinoma cell line	immunoblotting, RNase protection assays	increase of mRNA expression		[318]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Gallbladder carcinoma	clinical tumor tissue samples, Mz-ChA-1 cells derived from gallbladder adenocarcinoma	RT-PCR, immunoblotting, immunofluorescence microscopy	high expression of mRNA	suggested to contribute to the MDR phenotype,	[402,403]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Head and neck carcinoma	parenteral and cisplatin-resistant head and neck cancer KB cell line	Northern blotting	expression of mRNA		[365]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Hepatic carcinoma	clinical tumor and correspondin g normal tissue samples	immunoblotting, RT-PCR, immunohistochemistry, immunofluorescence microscopy	increase of mRNA and protein expression, low expression in normal tissue	suggested to contribute to the intrinsic MDR phenotype	[323]
MRP3, cMOAT 2, MLP2, MOAT-	Illness	Cancer	Leukemia	clinical tumor tissue samples, childhoodacu	immunohistochemistry, RT-	expressed of mRNA and protein, expressed	great variability in mRNA expression in AML patient	[45,322,377,386,410, 411]

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Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
D, ABCC3				te lymphocytic (lymphoblastic) leukemia (ALL), bone marrow aspirates or peripheral blood were collected from AML patients	PCR, functional drug efflux, immunoblotting	in normal tissue, expressed of and protein in PC13, PC13 2-2, HHT90 and HL60/MRP cell lines	samples, associated with a worse prognosis, suggested to be involved in chemoresistance in AML patients, relapsed patients showed a higher mRNA expression, high expression has an unfavorable prognosis	
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Liver carcinoma	clinical tumor tissue samples, hepatocellular carcinoma (HCC)	RT-PCR, immunohistochemistry	expression of mRNA as in normal tissue		[396]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Lung carcinoma	non-small cell and small cell lung cancer cell lines not selected for drug resistance, parental lung adenocarcinoma cell line MOR/P, doxorubicin-resistant sublines of the non-small cell lung cancer cell lines SW1573/Sl	immunoblotting, RNase protection assays, Western immunoblotting, RT-PCR	increase of mRNA and protein expression, low expression in normal tissue	suggested as component of the multifactor multidrug resistance phenotype of lung cancer	[318,319,320]
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Cancer	Pancreatic carcinoma	clinical tumor tissue samples, pancreatic cancer cell lines	reverse-transcriptase (RT)-PCR, RT-PCR, immunohistochemistry	expression of mRNA in some cell lines		[395]
MRP3, cMOAT 2, MLP2, MOAT-	Illness	Cancer	Prostate carcinoma	parental cells and cisplatin-resistant P/CDP5-R	Northern blotting	expression of mRNA in prostate and normal		[291,365]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
D, ABCC3				cells derived from PC-3 human prostate cancer cells		tissue		
MRP3, cMOAT 2, MLP2, MOAT-D, ABCC3	Illness	Liver disease	Primary biliary cirrhosis	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of protein level		[205]
MRP4, MOAT-B, ABCC4	Illness	Cancer	Leukemia	clinical tumor tissue samples, bone marrow aspirates or peripheral blood were collected from AML patients	RT-PCR	expressed of mRNA, expressed in normal tissue	great variability in mRNA expression in AML patient samples	[45,386]
MRP4, MOAT-B, ABCC4	Illness	Cancer	Lung carcinoma	non-small cell and small cell lung cancer cell lines not selected for drug resistance	RT-PCR	low mRNA expression in cell lines, low expression in normal tissue	no evidence to support involvement in drug resistance	[318,320]
MRP4, MOAT-B, ABCC4	Illness	Liver disease	Acetaminophen overdoses	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression, increase of protein level		[205]
MRP4, MOAT-B, ABCC4	Illness	Liver disease	Primary biliary cirrhosis	clinical samples, injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression, increase of protein level		[205]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP5, SMRP, MOAT-C, ABCC5	Illness	Cancer	Bladder carcinoma	the cisplatin-resistant cell lines T24/DDP1O	RNase protection assays	low increase of mRNA expression, low expression in normal tissue		[318]
MRP5, SMRP, MOAT-C, ABCC5	Illness	Cancer	Colorectal carcinoma	the cisplatin-resistant colon carcinoma cell lines HCT8/DDP	RNase protection assays	low increase of mRNA expression, low expression in normal tissue		[318]
MRP5, SMRP, MOAT-C, ABCC5	Illness	Cancer	Epidermoid carcinoma	the cisplatin-resistant cell lines KCP-4	RNase protection assays	low increase of mRNA expression		[318]
MRP5, SMRP, MOAT-C, ABCC5	Illness	Cancer	Leukemia	clinical tumor tissue samples, bone marrow aspirates or peripheral blood were collected from AML patients, leukemia cell lines	immunohistochemistry, RT-PCR, functional drug efflux, immunoblotting	expressed of mRNA and protein, expressed in normal tissue	great variability in mRNA expression in AML patient samples, relapsed patients showed a higher mRNA expression, high expression has an unfavorable prognosis	[45,386,410,411]
MRP5, SMRP, MOAT-C, ABCC5	Illness	Cancer	Lung carcinoma	non-small cell and small cell lung cancer cell lines not selected for drug resistance, parental lung adenocarcinoma cell line MOR/P	immunoblotting, RNase protection assays, RT-PCR	increase of mRNA expression, low expression in normal tissue	no evidence to support involvement in drug resistance	[318,320]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
MRP5, SMRP, MOAT-C, ABCC5	Illness	Cancer	Ovarian carcinoma	clinical parental ovarian carcinoma cell line 2008	immunoblotting, RNase rotection assays	increase of mRNA expression, low expression in normal tissue		[318]
MRP5, SMRP, MOAT-C, ABCC5	Illness	Liver disease	Primary biliary cirrhosis	clinical injured and normal tissue samples	Western immunoblotting, branched DNA signal amplification assay, immunohistochemistry	increase of mRNA expression, increase of protein level		[205]
MRP6, ARA, MLP1, MOAT-E, ABCC6	Illness	Cancer	Leukemia	clinical tumor tissue samples, bone marrow aspirates or peripheral blood were collected from AML patients	RT-PCR	expression of mRNA, expressed in normal tissue	relapsed patients showed a higher mRNA expression, high expression has an unfavorable prognosis	[45]
NIS, SLC5A5	Illness	Cancer	Gastric carcinoma	clinical tumor and adjacent tissue samples	immunoblotting, immunohistochemistry	decrease of expression	suggested as tumor marker in the diagnosis and prognosis of gastric malignancies	[89]
NIS, SLC5A5	Illness	Cancer	Thyroid carcinoma	clinical tumor tissue samples, thyroid carcinoma tissue samples	RT-PCR	decrease of mRNA expression		[144]
OATP1A2, OATP-A, OATP1, OATP, SLC21A3, SLCO1A2	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples	RT-PCR	decrease of mRNA expression in neoplastic colon tissue		[87]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
OATP1B1, OATP- C, OATP2, LST-1, SLC21A6, SLCO1B1	Illness	Cancer	Colorectal carcinoma	clinical tumor and normal tissue samples	RT-PCR	decrease of mRNA expression in neoplastic colon tissue		[87]
OCTN1, SLC22A4	Illness	Arthritis	Rheumatoid arthritis	human fibroblast-like synoviocyte cell line MH7A derived from RA patients	RT-PCR	increase of mRNA expression		[206]
OCTN1, SLC22A4	Physiological condition	Hypoxia	Decreased oxygen pressure	BeWo cells, CoCl(2) induced hypoxia	RT-PCR, Western immunoblotting, Carnitine transport	increase of mRNA expression, no change of protein level, decreased activity		[187]
PEPT1, SLC15A1	Physiological condition	Oxidative stress	Reactive oxygen species	hydrogen peroxide exposure, human colonic epithelial Caco-2 cells	[^{14}C]glycylsarcosine (Gly-Sar) uptake, Western immunoblotting	decrease of protein level and activity		[201]
SMIT, SLC5A3	Physiological condition	Cellular osmolality	Hypertonic environment	HaCaT keratinocytes, primary normal human keratinocytes, hyperosmotic exposure	RT-PCR, osmolyte uptake	increase of mRNA expression and activity		[178,212]
SMIT, SLC5A3	Physiological condition	Cellular osmolality	Hypotonic environment	primary normal human keratinocytes hyperosmotic exposure	osmolyte efflux	increase of activity		[212]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
SMIT, SLC5A3	Experimental condition	Cellular osmolality	Ultraviolet A and B radiation	primary normal human keratinocytes, hyperosmotic exposure	RT-PCR, osmolyte uptake	increase of mRNA expression and activity		[212]
SMVT, SLC5A6	Food	Dietary habit	Marginal biotin deficiency	leukocytes from human blood of normal subjects on egg-white diet, human hepatoma cell line HepG2	RT-PCR, Western immunoblotting	decrease of mRNA and protein expression		[80,81]
SMVT, SLC5A6	Physiological condition	Growth medium concentration	Biotin deficiency	human-derived renal proximal tubular epithelial HK-2 cells, human intestinal HuTu-80 and Caco-2 cells	RT-PCR, Western immunoblotting	increase of mRNA and protein expression		[82,83]
SVCT2, SLC23A2	Food	Dietary habit	L-Ascorbic acid depletion	platelets from healthy donors	RT-PCR, Western immunoblotting, Vitamin C uptake	increase of mRNA expression, protein level and activity		[193]
System y(+)L, SLC7A7	Food	Dietary habit	Amino acid depletion	platelets from controls and hemodialysis patients	L-arginine transport	decrease of activity		[191]
TAUT, SLC6A6	Physiological condition	Cellular osmolality	Hypertonic environment	HaCaT keratinocytes, primary normal human keratinocytes, hyperosmotic exposure	RT-PCR, osmolyte uptake	high increase of mRNA expression and activity in HaCaT keratinocytes		[178,212]

Transporter	Category	Subcategory	Effectors	Model	Method	Effect	Remarks	References
TAUT, SLC6A6	Physiological condition	Cellular osmolality	Hypotonic environment	primary normal human keratinocytes, hyperosmotic exposure	osmolyte efflux	increase of activity		[212]
TAUT, SLC6A6	Experimental condition	Cellular osmolality	Ultraviolet A and B radiation	primary normal human keratinocytes hyperosmotic exposure	RT-PCR, osmolyte uptake	increase of mRNA expression and activity		[212]
THTR1, SLC19A2	Illness	Cancer	Breast carcinoma	breast cancer cell line HS578T	RT-PCR, Western immunobl otting	no difference in mRNA, protein expression and activity compared to normal tissues		[290]
THTR1, SLC19A2	Food	Dietary habit	Thiamine deficiency	human-derived renal epithelial HEK-293 c	RT-PCR, Western immunobl otting	increase of mRNA expression		[207]
THTR2, SLC19A3	Illness	Cancer	Breast carcinoma	breast cancer cell line HS578T	RT-PCR, Western immunobl otting	decrease of mRNA, protein expression and activity compared to normal tissues	down regulation may be associated with the development of increased resistance to apoptosis in these tumors	[290]
THTR2, SLC19A3	Food	Dietary habit	Marginal biotin deficiency	leukocytes from human blood of normal subjects on egg-white diet	RT-PCR, urinary excretion of biotin	decrease of mRNA and protein expression		[80]
THTR2, SLC19A3	Food	Dietary habit	Thiamine deficiency	human-derived renal epithelial HEK-293 c	RT-PCR, Western immunobl otting	increase of mRNA expression		[207]