

Single nucleotide polymorphisms in *ABCB1* and *CBR1* can predict toxicity to R-CHOP type regimens in patients with diffuse non-Hodgkin lymphoma

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Supplemental table 1. Selected polymorphisms and role of genes.

Gene	SNP ID	Nucleotide change	Position	Potential role	Reference
ABCB1	rs2229109	C>T	Ser400Asn	Efflux of chemotherapeutic drugs	1
C1QA	rs172378	A>G	Gly92Gly	Activity of rituximab	2, 3
CAT	rs1001179	C>T	5'	Anthracycline-related cardiotoxicity	4, 5, 6
CAT	rs10836235	C>T	Intron 1	Anthracycline-related cardiotoxicity	7
CBR1	rs20572	C>T	Ala209Ala	Anthracycline-related cardiotoxicity	8
CBR1	rs9024	G>A	3'-UTR	Anthracycline-related cardiotoxicity	8
CYP3A4	rs2740574	A>G	5'	Metabolism of chemotherapeutic drugs	9
GSTP1	rs1695	A>G	Ile105Val	Inactivation of alkylating agents	1, 9, 10
SLC22A16	rs12210538	A>G	Met409Thr	Transport of chemotherapeutic drugs	11, 12
SLC22A16	rs714368	T>C	His49Arg	Transport of chemotherapeutic drugs	11, 12
SOD2	rs4880	A>G	Val16Ala	Protection from anthracycline-related cardiotoxicity	13
Gene	SNP ID	Variation	Position	Potential role	
GSTM1	0/1/2/3	Copy number variation		Inactivation of alkylating agents	9
GSTT1	0/1/2/3/4	Copy number variation		Inactivation of alkylating agents	9
UGT1A1	rs8175347	(TA)5/6/7/8	Repeats in promoter	Inactivation of chemotherapeutic drugs	9

1. Rossi D, Rasi S, Franceschetti S, et al. Analysis of the host pharmacogenetic background for prediction of outcome and toxicity in diffuse large B-cell lymphoma treated with R-CHOP21. *Leukemia* 2009;23:1118-1126.
2. Azzato EM, Lee AJ, Teschendorff A, et al. Common germ-line polymorphism of C1QA and breast cancer survival. *Br J Cancer* 2010;102:1294-1299.
3. Racila E, Link BK, Weng WK, et al. A polymorphism in the complement component C1qA correlates with prolonged response following rituximab therapy of follicular lymphoma. *Clin Cancer Res* 2008;14:6697-6703.
4. Ambrosone CB, Ahn J, Singh KK, et al. Polymorphisms in genes related to oxidative stress (MPO, MnSOD, CAT) and survival after treatment for breast cancer. *Cancer Res* 2005;65:1105-1111.
5. Forsberg L, Lyrenas L, de Faire U, Morgenstern R. A common functional C-T substitution polymorphism in the promoter region of the human catalase gene influences transcription factor binding, reporter gene transcription and is correlated to blood catalase levels. *Free Radic Biol Med* 2001;30:500-505.
6. Quick SK, Shields PG, Nie J, et al. Effect modification by catalase genotype suggests a role for oxidative stress in the association of hormone replacement therapy with postmenopausal breast cancer risk. *Cancer Epidemiol Biomarkers Prev* 2008;17:1082-1087.
7. Rajic V, Aplenc R, Debeljak M, et al. Influence of the polymorphism in candidate genes on late cardiac damage in patients treated due to acute leukemia in childhood. *Leuk Lymphoma* 2009;50:1693-1698.
8. Lal S, Sandanaraj E, Wong ZW, et al. CBR1 and CBR3 pharmacogenetics and their influence on doxorubicin disposition in Asian breast cancer patients. *Cancer Sci* 2008;99:2045-2054.
9. Ribrag V, Koscielny S, Casasnovas O, et al. Pharmacogenetic study in Hodgkin lymphomas reveals the impact of UGT1A1 polymorphisms on patient prognosis. *Blood* 2009;113:3307-3313.
10. Ekhart C, Doodeman VD, Rodenhuis S, Smits PH, Beijnen JH, Huitema AD. Influence of polymorphisms of drug metabolizing enzymes (CYP2B6, CYP2C9, CYP2C19, CYP3A4, CYP3A5, GSTA1, GSTP1, ALDH1A1 and ALDH3A1) on the pharmacokinetics of cyclophosphamide and 4-hydroxycyclophosphamide. *Pharmacogenet Genomics* 2008;18:515-523.
11. Bray J, Sludden J, Griffin MJ, et al. Influence of pharmacogenetics on response and toxicity in breast cancer patients treated with doxorubicin and cyclophosphamide. *Br J Cancer* 2010;102:1003-1009.
12. Lal S, Wong ZW, Jada SR, et al. Novel SLC22A16 polymorphisms and influence on doxorubicin pharmacokinetics in Asian breast cancer patients. *Pharmacogenomics* 2007;8:567-575.
13. Charniot JC, Sutton A, Bonnefont-Rousselot D, et al. Manganese superoxide dismutase dimorphism relationship with severity and prognosis in cardiogenic shock due to dilated cardiomyopathy. *Free Radic Res* 2011;45:379-388.