Disease Markers 31 (2011) 311–316
DOI 10.3233/DMA-2011-0845
IOS Press

Genetic polymorphism of the glutathione S-transferase M1 and T1 genes in three distinct Arab populations

Abdel Halim Salem[a,b,*], Alaeddin Yaqoob[c], Muhalab Ali[d], Shailandra Handu[e], Raouf Fadel[a,b], Marwan Abu-Hijleh[a] and Wassim Almawi[d]

[a]*Department of Anatomy, College of Medicine and Medical Sciences, Arabian Gulf University, Manama, Bahrain*
[b]*Department of Anatomy, Faculty of Medicine, Suez Canal University, Ismailia, Egypt*
[c]*Salmaniya Medical Complex, Ministry of Health, Manama, Bahrain*
[d]*Department of Biochemistry, College of Medicine and Medical Sciences, Arabian Gulf University, Manama, Bahrain*
[e]*Department of Pharmacology and Therapeutics, College of Medicine and Medical Sciences, Arabian Gulf University, Manama, Bahrain*

Abstract. Deletion polymorphisms for the glutathione S-transferase (GST) gene are associated with increased risk of cancer, and are implicated in detoxifying mutagenic electrophilic compounds. GST Polymorphic variants were reported for different populations. The aim of this study was to investigate the frequencies of *GSTM1* and *GSTT1* null genotypes among Bahraini, Lebanese and Tunisian Arabs. GST genotyping was done by multiplex PCR-based methods. Study subjects comprised 167 Bahrainis, 141 Lebanese and 186 Tunisians unrelated healthy individuals. *GSTM1* deletion homozygosity of 49.7%, 52.5% and 63.4% were recorded for Bahraini, Lebanese and Tunisians, respectively. Among Bahrainis, the prevalence of *GSTT1* null homozygotes was 28.7%, while in higher rates were seen in Lebanese (37.6%) and Tunisians (37.1%). Our results indicate that there are no major differences in allelic distribution of *GSTM1* and *GSTT1* genes between the three Arab populations investigated except between Bahrainis and Tunisians regarding the allelic distribution of *GSTM1* gene ($P = 0.013$). Combined analysis of both genes revealed that 14.4% of Bahrainis, 16.3% of Lebanese and 21.0% of Tunisians harbor the deleted genotype of both genes. This is the first study that addresses *GST* gene polymorphism in Bahraini and Lebanese Arabs, and will help genetic studies on the association of *GSTM1* and *GSTT1* polymorphisms with disease risks and drug effects in Arab populations.

Keywords: Glutathione S-transferase, genetic polymorphisms, Arabs

1. Introduction

Drugs differentially affect patients with the same disease, despite the similarity in dosing regimen, and individual variations in response to cancer therapy, and to toxic chemicals are attributed to the genetic differences in the drug metabolizing enzymes. As such, polymorphisms in genes encoding transporters, receptors, DNA repair enzymes, drug targets and genes involved in the metabolism of xenobiotics are the main causes of patient's heterogeneity [1]. Assessment of polymorphisms of these genes in different populations may explain, at least in part, the variation in response to cancer therapy and to toxic chemicals. Most gene products are involved either in metabolic oxidation (phase I), or in detoxification (phase II) of toxic materials.

Glutathione S-transferases (GSTs) are a class of phase II enzymes present in many tissues, and are involved in xenobiotic detoxification, and thus contribute to the protection from broad range of compounds including carcinogens, chemotherapeutic agents, and en-

*Address for correspondence: Dr. Abdel Halim Salem, Department of Anatomy, College of Medicine and Medical Sciences, Arabian Gulf University, 22979 Manama, Kingdom of Bahrain. Tel.: +973 17239650; Fax: +973 17271090; E-mail: ahaleemfd@agu.edu.bh.

ISSN 0278-0240/11/$27.50

vironmental pollutants [1,2]. Five classes of GST enzymes were described in humans: Alpha (α), Mu (μ), Pi (π), Zeta (ζ) and Theta (θ), with one or more genes in each class. Two major polymorphisms of the *GSTM1* gene (chromosome 1p13.3) and *GSTT1* gene (chromosome 22q11.23), result from gene deletion, and are associated with absent enzymatic activity in individuals carrying both deletions (i.e. null genotype) [3,4]. Functionally, the *GSTM1* and *GSTT1* null genotype is associated with differential susceptibility to various forms of cancer [5], resistance to chemotherapy treatment, drug response [6], and disease susceptibility and outcome [7,8].

Varied distribution of *GSTM1* and *GSTT1* null genotypes was reported in different populations [1]. Approximately half of the Caucasian populations are homozygous deleted for *GSTM1* null allele, and hence fail to express the enzyme [1]. The frequencies of homozygous deletions of *GSTM1* gene are higher in Caucasians and Asians than in Africans [9], whereas homozygous deletions of *GSTT1* gene are higher in Asians and Africans than in Caucasians [5]. Comprehensive reports of variations in the frequency of polymorphisms of *GSTM1* and *GSTT1* genes profiled Caucasians, Asians and Africans but not Arabs [10]. Given that gene polymorphism may predispose these populations to certain adverse drug reactions or disease occurrence, here we analyzed the frequency of *GSTM1* and *GSTT1* polymorphisms in three distinct Arab populations.

2. Subjects and methods

2.1. Subjects

Blood was collected in EDTA-containing tubes from 167 unrelated healthy Bahrainis from the Arabian Gulf University, Manama, from 141 unrelated healthy Lebanese from the city of Beirut, and from 186 Tunisians from Sousse (Central Tunisia). A written informed consent was obtained from all participants, and the study was done under institutionally-approved internal review board (IRB) protocols.

2.2. GSTM1 and GSTT1 Genotype analysis

Genomic DNA was isolated from blood samples by phenol-chloroform extraction followed by ethanol precipitation. *GSTM1* and *GSTT1* genotyping were determined by multiplex PCR, using *CYP1A1* gene as control, as previously described [11]. DNA was amplified in a total volume of 25 μl with *GSTM1* forward (5' GAA CTC CCT GAA AAG CTA AAG C 3') and reverse (5' GTT GGG CTC AAA TAT ACG GTG G 3') primers, and *GSTT1* forward (5' TTC CTT ACT GGT CCT CAC ATC TC 3') and *GSTT1* reverse (5' TCA CCG GAT CAT GGC CAG CA 3') primers. As internal control, exon 7 of *CYP1A1* gene was amplified, using the following forward (5' GAA CTG CCA CTT CAG CTG TCT 3') and reverse (5' CAG CTG CAT TTG GAA GTG CTC 3') primers [11]. PCR consisted of an initial denaturation (94°C for 5 min) followed by 32 cycles of denaturation (94°C for 1 min), annealing (59°C for 1 min), and extension (72°C for 1 min). PCR product from co-amplification of *GSTM1* (215 bp) and *GSTT1* (480 bp) were run on 1.5% agarose gel; DNA bands were visualized under UV transillumination. Presence of the particular allele was designated as wild genotype (positive) and homozygous absence or deletion of the allele was designated as null genotype.

2.3. Statistical analysis

Data were expressed as number of alleles/genotypes, and percent of total. Allele frequencies were calculated by direct counting, and were evaluated using the chi square goodness-of-fit test.

3. Results

GSTM1 and GSTT1 genotyping were assessed by multiplex PCR in 167 Bahraini, 141 Lebanese and 186 Tunisian subjects. While this method does not differentiate between wild-type and heterozygous states, it determines the percentages of the homozygous deletion of both GSTM1 and GSTT1 genes. GST genotypes were coded as positive (wild-type homozygotes and deletion heterozygotes), or as null (homozygous deletion). This made direct calculation of Hardy Weinberg Equilibrium impossible.

In the present study, the frequencies of *GSTM1* null genotype were 49.7% in Bahraini, 52.5% in Lebanese and 63.4% in Tunisians. The frequencies of *GSTT1* null genotype were 28.7% in Bahrainis, 37.6% in Lebanese and 37.1% in Tunisians. *GSTM1* and *GSTT1* null genotype frequencies and the combined *GSTM1* null + *GSTT1* null genotype frequencies (double null genotype) was 14.4% in Bahraini, 16.3% in Lebanese, and 21.0% in Tunisians (Table 1).

Table 2 shows null-genotype frequencies for the *GSTM1* and *GSTT1* in various populations of Arabs, Asians, Africans, and Europeans using the Chi square test for goodness of fit.

Table 1
Frequency of GSTs null genotypes in three Arab population

Population	n	Genotype frequency (%)				
		GSTM1		GSTT1		double null
		positive	null	positive	null	
Bahrainis	167	84 (50.3%)	83 (49.7%)	119 (71.3%)	48 (28.7%)	24 (14.4%)
Lebanese	141	67 (47.5%)	74 (52.5%)	88 (62.4%)	53 (37.6%)	23 (16.3%)
Tunisians	186	68 (36.6%)	118 (63.4%)	117 (62.9%)	69 (37.1%)	39 (21%)

n = number of tested individuals.

Table 2
Frequency of GSTs null genotypes in various ethnic groups

Population	n	% GSTM1 null	% GSTT1 null	% double null	Reference
Arabs					
Bahrainis	167	49.7	28.7	14.4	Present study
Lebanese	141	52.5	37.6	16.3	Present study
Tunisians	186	63.4	37.1	21	Present study
Egyptians	200	55.5	29.5	NA	[17]
Saudi	513	54.6	25	17.2	[15]
Asians					
Turkish	133	51.9	17.3	NA	[24]
Iranians	229	44.7	21.2	NA	[25]
Indians	198	20.7	18.2	NA	[29]
Chinese	735	56.5	56.5	31.4	[26]
Japanese	143	44.1	43.4	15.4	[28]
Koreans	1051	53.8	54.3	29.1	[27]
Europeans					
British	373	54	18	NA	[20]
French	1184	53.4	16.8	NA	[10]
German	734	51.6	19.5	NA	[10]
Austrian	166	49	20	NA	[23]
Africans					
Cameroonians	126	27.8	46.8	NA	[32]
Zimbabweans	150	24	26	NA	[30]
Gambians	337	20.2	37.1	NA	[31]
Ivory Coast	133	36.1	33.1	14.3	[33]

n, number of subjects. NA, data not available.

4. Discussion

Although the frequencies of *GSTM1* and *GSTT1* null genotypes have been reported in diverse ethnic groups [10,12], sparse data are available for Arab populations. Here we investigated the polymorphism at GST loci in Bahraini, Lebanese and Tunisian Arabs. While the distribution of *GSTM1* and *GSTT1* null genotypes were described previously for Tunisians [13,14], no data has been published for Bahraini and Lebanese. We found that homozygosity for the *GSTM1* deletion was generally comparable between Bahraini (49.7%) and Lebanese (52.5%) samples tested. Despite the higher frequency of *GSTM1* null genotype in Tunisians (63.4%) compared to Lebanese, no statistically significant differences were found. Statistically significant differences were detected only when we compared Bahrainis and Tunisians ($P = 0.013$), which may be due to ethnic mixture in these two populations. The homozygosity for the *GSTM1* deletion in the three Arab populations were comparable to those reported for Saudi Arabian (54.6%) [15,16] and Egyptian (55.5%) [17] Arabs (Table 2).

GSTM1 null genotype are not uniformly distributed among diverse population, but an ethnic and geographic basis of distribution was suggested [10,18]. The prevalence of individuals not expressing the *GSTM1* enzyme due to a homozygous gene deletion is reportedly higher in Europeans and Asians, as compared to Africans [1]. The *GSTM1* null genotype frequencies vary from 38–67% in Europeans, 33–63% in Asians, and 16–36% in sub-Saharan Africans [10,19]. The prevalence of *GSTM1* homozygous deficiency seen here was comparable for Europeans, including British (54%) [10,20], French (51%) [21], German (52%) [22] and Austrians (49%) [23]. In addition, they were comparable to Asians, such as Turkish (51.9%) [24], Iranians (44.7%) [25], Chinese (56.5%) [26], Koreans

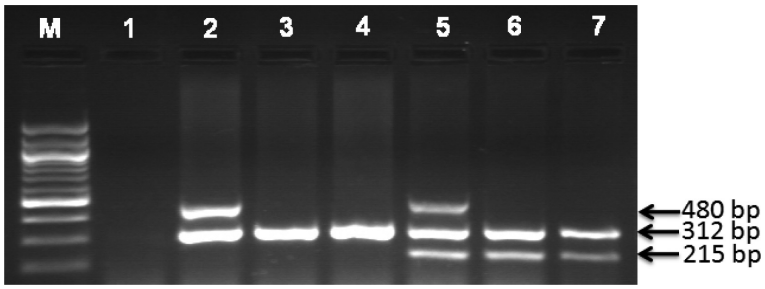

Fig. 1. Multiplex PCR products analyzed on 1.5% agarose gel. The presence or absence of *GSTT1* and *GSTM1* genes was detected by the presence of a band at 480 bp (corresponding to *GSTT1*) and a band at 215 bp (corresponding to *GSTM1*). A band at 312 bp (Corresponding to *CYP1A1* gene) was always present and was used as an internal control to document successful PCR amplification. Lane 1, a negative control. Lane 2, an individual with *GSTT1* present (480 bp) and *GSTM1* null alleles. Lanes 3 and 4: individuals with null alleles for both *GSTT1* and *GSTM1* genes showing only one band at 312 bp corresponding to the internal control (*CYP1A1* gene fragment). Lane 5, an individual with both *GSTT1* and *GSTM1* alleles present. Lanes 6 and 7: individuals harboring *GSTT1* null and *GSTM1* present (215 bp) alleles. M is a DNA molecular marker.

(53%) [27] and Japanese (44%) [28] (Table 2). Significant differences in *GSTM1* null genotype distribution were seen with respect to Indians (20.7%) [29], and Africans, including Zimbabweans (24%) [30], Gambians (20.2%) [31], Cameroonians (27.8%) [32], and Ivory Coast (36.1%) [33] (Table 2).

The prevalence of *GSTT1* null homozygotes was 28.7% in Bahraini, which was lower (though not statistically significant) than the rates seen for (Lebanese 37.6%) and Tunisians (37.1%). In our hands, no differences were seen between the population studied and Saudi (25%) [15,16] and Egyptian (29.5%) [17] Arabs. Worldwide differences in *GSTT1* frequencies were previously documented [10,12], with 20% of Caucasians, 60% of Asians and 40% of Africans not expressing the *GSTT1* enzyme [5]. The frequencies of *GSTT1* deletion in our populations were higher than that described for Europeans, including British (18%) [20], French (16%) [21], German (13%) [22] and Austrian (20%) [23], as well as for other Middle Eastern populations, including Turks (17.3%) [24], and Iranians (21.2%) [25], but was significantly lower than South-East Asians, such as Chinese (56.5%) [26], Koreans (53.8%) [27] and Japanese (44%) [28]. The frequencies of *GSTT1* null genotype in our Arab populations are similar to that of the sub-Saharan Africans: Zimbabweans (26%) [30], Gambians (37.1%) [31], Cameroonians (46.8%) [32] and Ivory Coast (33.1%) [33] (Table 2). The difference of *GTSM1* and *GSTT1* null alleles' frequency between our samples and those of others is attributed to their evolutionary histories, and also to selection arising from varied exposures to toxic substances.

Varied frequencies of *GSTM1* and *GSTT1* null genotypes were previously reported for Tunisians (34.5%, 16.6%, respectively) among 145 subjects [13] and (45.6% and 44.3%, respectively) in 79 subjects [14]. In Tunisian samples, the frequency of *GSTM1* null genotype (63.4%) and comparable frequency of null genotype for *GSTT1* (37.1%), may be explained by the larger number of subjects examined in our study (186) compared with earlier studies. The distribution of *GSTM1* null deletion in Tunisian (63.4%) was higher, but that of the *GSTT1* null genotype (37.1%) was comparable to that of sub-Saharan Africans. This can be explained by the ethnic mixture of the Tunisians, with influence from both sub-Saharan Africans and Arabs. Our data showed that Bahrainis and Lebanese are similar to Europeans and Asians with regards to the frequency of *GSTM1* null genotype, and to Asians and sub-Saharan Africans regarding the distribution of the *GSTT1* null genotype.

The significance of the high frequencies of homozygous null deletions at these two loci remains to be seen. Relevant data on the prevalence of various diseases, particularly those related to exposure to toxic substances, in these populations are unavailable. Variable association between various *GSTM1* and *GSTT1* genotypes with senile cataract [34] and bladder cancer [35] among Egyptians, and with thyroid cancer [15] and glaucoma [36] in Saudi population was found. Therefore, it is difficult to ascertain either the causes of variation in the frequencies of these null deletions, or the implications of this variation on epidemiological profiles of diseases. The frequency reported for Tunisians (21%) is the highest frequency described for Arab populations, with Asians having the highest frequencies of double null genotype (20–33%), with Africans and Europeans prevalence rates ranging from 10.4–17.2% [1]. The frequency of the double null genotypes in our popula-

tions was similar to that found in Saudi (17.2%) [15, 16], and to Africans from Ivory Coast (14.3%).

Cancer is an increasing problem in the Arabic countries and it ranks as the fourth leading cause of death among the Arabs [37]. The age standardized incidence (ASR) of all cancers among the Arabs is currently 3 to 4 times lower than in the industrialized countries but is expected to double in the next 15 years [37]. ASR of all cancers per 100.000 in Bahrain is 118 in males and 108 in females [38], in Lebanon is 169 in males and 176 in females [39] and in Tunisia is 114 in males and 78 in females [40]. Associations of *GSTM1* and/or *GSTT1* null genotypes with several types of cancer have been reported and represent an area of intensive research [5,9, 15,19,23,26]. The identification of high frequencies of *GSTM1*and *GSTT1* null alleles in Arabs has its clinical importance as GSTs genes modulate response to cancer treatment associated toxicity. On the other hand, the risk of cancer is modulated by the ethnic background and environmental factors. So, case/control studies that test the potential risk of the GST null alleles in Arabs will contribute in the definition of gene–gene and gene–environment interactions.

In conclusion, this is the first report on the polymorphic distribution of the *GSTM1* and *GSTT1* genotypes in three Arab populations. In this study, we provide a reference database of allelic distribution of the *GSTM1* and *GSTT1* genotypes in these populations. This data will serves as a template for future clinical research associated with cancer and drugs pharmacogenomics in the Arab populations. Further detailed studies of GST variants and other metabolic gene polymorphisms associated with response to chemotherapeutic drugs and susceptibility to cancer could be helpful in understanding their roles as genetic susceptibility markers in Arabs.

Acknowledgment

This work was supported by a grant from the Arabian Gulf University, Grant number 60/2010.

References

[1] G. Ginsberg, S. Smolenski, D. Hattis, et al., Genetic Polymorphism in Glutathione Transferases (GST): Population distribution of GSTM1, T1, and P1 conjugating activity, *J Toxicol Environ Health B Crit Rev* **12** (2009), 389–439.

[2] H.M. Bolt and R. Thier, Relevance of the deletion polymorphisms of the glutathione S-transferases GSTT1 and GSTM1 in pharmacology and toxicology, *Curr Drug Metab* **7** (2006), 613–628.

[3] S. Xu, Y. Wang, B. Roe and W.R. Pearson, Characterization of the human class Mu glutathione S-transferase gene cluster and the GSTM1 deletion, *J Biol Chem* **273** (1998), 3517–3527.

[4] S. Pemble, K.R. Schroeder, S.R. Spencer et al., Human glutathione S-transferase theta (GSTT1): cDNA cloning and the characterization of a genetic polymorphism, *Biochem J* **300** (1994), 271–276.

[5] R.C. Strange and A.A. Fryer, The glutathione S-transferases: influence of polymorphism on cancer susceptibility, *IARC Sci Publ* **148** (1999), 231–249.

[6] J.D. Hayes and D.J. Pulford, The glutathione S-transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer chemoprotection and drug resistance, *Crit Rev Biochem Mol Biol* **30** (1995), 445–600.

[7] J. Lear, A. Heagerty, A. Smith et al., Polymorphism in detoxifying enzymes and susceptibility to skin cancer, *Photochem Photobiol* **63** (1996), 424–428.

[8] A.A. Fryer, A. Bianco, M. Hepple et al., Polymorphism at the glutathione S-transferase GSTP1 locus. A new marker for bronchial hyperresponsiveness and asthma, *Am J Respir Crit Care Med* **161** (2000), 1437–1442.

[9] L.R. Bailey, N. Roodi, C.S. Verrier et al., Breast cancer and CYPIA1, GSTM1, and GSTT1 polymorphisms: evidence of a lack of association in Caucasians and African Americans, *Cancer Res* **58** (1998), 65–70.

[10] S. Garte, L. Gaspari, A.K. Alexandrie et al., Metabolic gene polymorphism frequencies in control populations, *Cancer Epidemiol Biomarkers Prev* **10** (2001), 1239–1248.

[11] S.Z. Abdel-Rahman, R.A. el-Zein, W.A. Anwar and W.W. Au, A multiplex PCR procedure for polymorphic analysis of GSTM1 and GSTT1 genes in population studies, *Cancer Lett* **107** (1996), 229–233.

[12] H.H. Nelson, J.K. Wiencke, D.C. Christiani et al., Ethnic differences in the prevalence of the homozygous deleted genotype of glutathione S-transferase theta, *Carcinogenesis* **16** (1995), 1243–1245.

[13] S. Gara, M. Abessi, K. Bendjemena et al., Deletion polymorphism of glutathione s-transferases m1 and t1 in the tunisian population, *Tunis Med* **88** (2010), 700–702.

[14] S. Ouerhani, F. Tebourski, M.R. Slama et al., The role of glutathione transferases M1 and T1 in individual susceptibility to bladder cancer in a Tunisian population, *Ann Hum Biol* **33** (2006), 529–535.

[15] A.K. Siraj, M. Ibrahim, M. Al-Rasheed, et al., Polymorphisms of selected xenobiotic genes contribute to the development of papillary thyroid cancer susceptibility in Middle Eastern population, *BMC Med Genet* **9** (2008), 61.

[16] R. Bu, M.I. Gutierrez, M. Al-Rasheed et al., Variable drug metabolism genes in Arab population, *Pharmacogenomics J* **4** (2004), 260–266.

[17] S.I. Hamdy, M. Hiratsuka, K. Narahara et al., Genotype and allele frequencies of TPMT, NAT2, GST, SULT1A1 and MDR-1 in the Egyptian population, *Br J Clin Pharmacol* **55** (2003), 560–569.

[18] A. Hatagima, C.F. Marques, H. Krieger and M.F. Feitosa, Glutathione S-transferase M1 (GSTM1) and T1 (GSTT1) polymorphisms in a Brazilian mixed population, *Hum Biol* **76** (2004), 937–942.

[19] T.R. Rebbeck, Molecular epidemiology of the human glutathione S-transferase genotypes GSTM1 and GSTT1 in cancer susceptibility, *Cancer Epidemiol Biomarkers Prev* **6** (1997), 733–743.

[20] H. Duncan, C. Swan, J. Green et al., Susceptibility to ulcerative colitis and Crohn's disease: interactions between glutathione

S-transferase GSTM1 and GSTT1 genotypes, *Clin Chim Acta* **240** (1995), 53–61.

[21] N. Jourenkova, M. Reinikanen, C. Bouchardy et al., Effects of glutathione S-transferases GSTM1 and GSTT1 genotypes on lung cancer risk in smokers, *Pharmacogenetics* **7** (1997), 515–518.

[22] V. Jahnke, C. Matthias, A. Fryer and R. Strange, Glutathione S-transferase and cytochrome-P-450 polymorphism as risk factors for squamous cell carcinoma of the larynx, *Am J Surg* **172** (1996), 671–673.

[23] A. Gsur, G. Haidinger, S. Hinteregger et al., Polymorphisms of glutathione-S-transferase genes (GSTP1, GSTM1 and GSTT1) and prostate-cancer risk, *Int J Cancer* **95** (2001), 152–155.

[24] A.O. Ada, S.H. Suzen and M. Iscan, Polymorphisms of cytochrome P450 1A1, glutathione S-transferases M1 and T1 in a Turkish population, *Toxicol Lett* **151** (2004), 311–315.

[25] A. Torkaman-Boutorabi, M. Hoormand, N. Naghdi et al., Genotype and allele frequencies of N-acetyltransferase 2 and glutathione S-transferase in the Iranian population, *Clin Exp Pharmacol Physiol* **34** (2007), 1207–1211.

[26] K.A. Moy, J.M. Yuan, F.L. Chung et al., Isothiocyanates, glutathione S-transferase M1 and T1 polymorphisms and gastric cancer risk: a prospective study of men in Shanghai, China, *Int J Cancer* **125** (2009), 2652–2659.

[27] H.J. Cho, S.Y. Lee, C.S. Ki and J.W. Kim, GSTM1, GSTT1 and GSTP1 polymorphisms in the Korean population, *J Korean Med Sci* **20** (2005), 1089–1092.

[28] A. Morinobu, S. Kanagawa, M. Koshiba et al., Association of the glutathione S-transferase M1 homozygous null genotype with susceptibility to Sjogren's syndrome in Japanese individuals, *Arthritis Rheum* **42** (1999), 2612–2615.

[29] K.M. Girisha, A. Gilmour, S. Mastana et al., T1 and M1 polymorphism in glutathione S-transferase gene and coronary artery disease in North Indian population, *Indian J Med Sci* **58** (2004), 520–526.

[30] C. Dandara, J. Sayi, C.M. Masimirembwa et al., Genetic polymorphism of cytochrome P450 1A1 (Cyp1A1) and glutathione transferases (M1, T1 and P1) among Africans, *Clin Chem Lab Med* **40** (2002), 952–957.

[31] C.P. Wild, F. Yin, P.C. Turner et al., Environmental and genetic determinants of aflatoxin-albumin adducts in the Gambia, *Int J Cancer* **86** (2000), 1–7.

[32] S. Piacentini, R. Polimanti, F. Porreca et al., GSTT1 and GSTM1 gene polymorphisms in European and African populations, *Mol Biol Rep* **38** (2011), 1225–1230.

[33] A. Santovito, C. Burgarello, P. Cervella and M. Delpero, Polymorphisms of cytochrome P450 1A1, glutathione s-transferases M1 and T1 genes in Ouangolodougou (Northern Ivory Coast), *Genetics and Molecular Biology* **33** (2010), 434–437.

[34] A.A. Abdel Azeem, A.A. Mahmoud, M.M. Salaheldine and K. Amr, Implication of glutathione S-transferase M1 and T1 polymorphisms in the development of senile cataract among Egyptians, *Bratisl Lek Listy* **110** (2009), 678–683.

[35] W.A. Anwar, S.Z. Abdel-Rahman, R.A. El-Zein et al., Genetic polymorphism of GSTM1, CYP2E1 and CYP2D6 in Egyptian bladder cancer patients, *Carcinogenesis* **17** (1996), 1923–1929.

[36] K.K. Abu-Amero, J. Morales, G.H. Mohamed et al., Glutathione S-transferase M1 and T1 polymorphisms in Arab glaucoma patients, *Mol Vis* **14** (2008), 425–430.

[37] Revised global burden of disease (GBD) 2002 estimates, Geneva, World Health Organization, (2002), http://www.who.int/healthinfo/bodgbd2002revised/en/index.html.

[38] Cancer incidence report of Gulf Cooperation Council States, Riyadh, Gulf Center for Cancer Registration, 2003.

[39] S.M. Adib and J. Daniel, Cancer in Lebanon, Beirut, Ministry of Health, National Cancer Registry, 2003.

[40] J. Ferlay, F. Bray, P. Pisani and D.M. Parkin, GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide International Agency for Research on Cancer (IARC) CancerBase No. 5, version 2.0., Lyon: IARC Press, 2004.