Supplemental Material

Polymorphisms in *GSTT1*, *GSTZ1*, and *CYP2E1*, Disinfection Byproducts, and Risk of Bladder Cancer in Spain

Kenneth P. Cantor[1,2]
Cristina M. Villanueva[3,4,5]
Debra T. Silverman[1]
Jonine D. Figueroa[1]
Francisco X. Real[4,6,7]
Monserrat Garcia-Closas[1]
Nuria Malats[4,6]
Stephen Chanock[1]
Meredith Yeager[1]
Adonina Tardon[8]
Reina Garcia-Closas[9]
Consol Serra[7,10]
Alfredo Carrato[11]
Gemma Castaño-Vinyals[3,4,5]
Claudine Samanic[1]
Nathaniel Rothman[1]
Manolis Kogevinas[3,4,5,12]

[1]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA; [2]Formerly of the National Cancer Institute, currently: KP Cantor Environmental LLC, Silver Spring, MD, USA; [3]Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; [4]Institut Municipal d'Investigacio Medica (IMIM-Hospital del Mar), Barcelona, Spain; [5]CIBER Epidemiologia y Salud Publica (CIBERESP), Barcelona, Spain; [6]Centro Nacional de Investigaciones Oncológicas, Madrid, Spain; [7]Universidad Pompeu Fabra, Barcelona, Spain; [8]Universidad de Oviedo, Oviedo, Spain; [9]Unidad de Invesigación, Hospital Universitario de Canarias, La Laguna, Spain; [10]Consorci Hospitalari Parc Tauli, Sabadell, Spain; [11]Ramon y Cajal University Hospital, Madrid, Spain; [12]National School of Public Health, Athens, Greece

Table 1. Odds ratios (95% CI) for the combined effects of polymorphic forms of GSTT1 and GSTZ1, restricted to subjects with *CYP2E1* rs2031920 CC. [a,b]

	***GSTT1* null & *GSTZ1* CC**		***GSTT1* present & *GSTZ1* CT/TT**		p (interaction)[c]
Average THM (µg/L)	**Ca/Ctl**	**OR (95% CI)**	**Ca/Ctl**	**OR (95% CI)**	
≤8.0	18/15	1.0 (ref)	31/45	1.0 (ref)	
>8.0-26.0	19/21	0.99 (0.3-2.9)	33/35	2.5 (0.96-6.4)	
>26.0-49.0	20/27	1.3 (0.4-4.2)	56/41	5.3 (1.9-14.5)	
>49.0	16/22	1.9 (0.5-7.3)	58/42	9.3 (2.5-34.0)	
p (trend)		0.32		0.0006	0.010

[a] OR (95% CI) from logistic regression adjusted for age (continuous), sex, smoking status (never/former/current); size of the municipality of longest residence until 18 years of age, education (three strata), geographic area (six strata) and overall quality of interview.

[b] Restricted to subjects with either both *GSTT1* null and *GSTZ1* CC or both *GSTT1* present & *GSTZ1* CT/TT.

[c] p for multiplicative interaction between the average THM level (age 15 to index year) and the indicated genetic characteristic. The calculation uses the median level of average THM within each successive quartile.

Table 2a. ORs (95% CIs) for the combined effects of ever swimming in pools and polymorphic forms of GSTT1.[a]

Swimming in Pools[b]	GSTT1 Null		GSTT1 Present		$p_{interaction}$[c]
	N(cases/controls)	OR (95% CI)	N(cases/controls)	OR (95% CI)	
Never	116/168	1.0 (referent)	500/587	1.3 (0.98-1.7)	
Ever	28/21	2.5 (1.3-4.8)	120/98	1.9 (1.3-2.7)	0.14

Table 2b. ORs (95% CIs) for the combined effects of ever swimming in pools and polymorphic forms of GSTZ1 (rs1046428).[a]

Swimming in Pools[b]	*GSTZ1* rs1046428 CC		*GSTZ1* rs1046428 CT/TT		$p_{interaction}$[c]
	N(cases/controls)	OR (95% CI)	N(cases/controls)	OR (95% CI)	
Never	358/430	1.0 (referent)	228/246	1.2 (0.9-1.5)	
Ever	99/62	1.9 (1.4-2.9)	43/45	1.3 (0.8-2.1)	0.07

[a]OR (95%CI) from logistic regression adjusted for age (continuous), sex, smoking status (never/former/current, size of the municipality of longest residence until 18 years of age, education (three strata) geographic area (six strata), and overall quality of interview. [b]Ever/Never swam in indoor or outdoor pools as an adult. See Villanueva et al. (2007) for additional details on the 'swimming in pools' variable. [c]p-value for multiplicative interaction between ever swimming in pools and the respective polymorphism. [c] p for multiplicative interaction between ever swimming in pools and the indicated genetic characteristic.

NOTE: Data from the test of interaction between swimming in pools and the *CYP2E1* variant for rs2031920 not shown due to statistical instability (5 cases and 7 controls with CT/TT for rs2031920 and who reported ever swimming in pools).