Note of clarification of data in the paper titled X-ray repair cross-complementing group 1 Arg194Trp polymorphism is associated with increased risk of lung cancer in Chinese Han population

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Received: 29 January 2015 / Accepted: 2 February 2015 / Published online: 11 February 2015
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We read with great interest the paper titled “X-ray repair cross-complementing group 1 Arg194Trp polymorphism is associated with increased risk of lung cancer in Chinese Han population” published in *Tumor Biol.* 2013, 34: 2611–2615 [1]. Wu et al. performed a meta-analysis to investigate the association between X-ray repair cross-complementing group 1 (XRCC1) Arg194Trp polymorphism and lung cancer risk in Chinese Han population on the basis of 12 case-control studies with 4385 cases and 4545 controls. The authors found that XRCC1 Arg194Trp polymorphism was associated with increased risk of lung cancer in Chinese Han population under three main models (allele contrast model, odds ratio (OR)=1.12, 95 % confidence interval (CI) 1.00–1.26, $P=0.049$; homozygote model, OR=1.27, 95 % CI 1.09–1.48, $P=0.003$; recessive model, OR=1.26, 95 % CI 1.09–1.46, $P=0.003$) when all eligible studies were pooled into meta-analysis. It is an interesting study.

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Nevertheless, a careful examination of the data provided by Wu et al. (Fig. 1 in the original text) [1] revealed two key issues that are worth noticing. Firstly, one overlapping paper [2] was not properly excluded from Wu et al.'s study [1]. Secondly, four eligible papers [3–6] published before 2013 were not included in Wu et al.'s study [1]. Therefore, the conclusions by Wu et al. [1] are not entirely reliable. In order to obtain a precise estimation of the relationship between XRCC1 Arg194Trp polymorphism and lung cancer risk in Chinese population, a meta-analysis was re-conducted on the basis of a total of 16 studies with 4591 cases and 4899 controls, which may provide comprehensive evidence for the association of XRCC1 Arg194Trp polymorphism with lung cancer risk in Chinese population.

Table 1 listed the general information of selected studies. Table 2 listed the summary odds ratios of the association between XRCC1 Arg194Trp polymorphism and lung cancer risk in Chinese population. Overall, we observed an increased lung cancer risk in Chinese population among subjects carrying XRCC1 194 Trp/Trp genotype (OR=1.26, 95 % CI 1.09–1.46) comparing with Arg/Arg genotype carriers in total population (Fig. 1a). We did not observe any association of Arg/Trp vs. Arg/Arg and Trp/Trp+Arg/Trp vs. Arg/Arg polymorphisms with lung cancer risk in Chinese population (OR=1.05, 95 % CI 0.90–1.22 and OR=1.12, 95 % CI 0.95–1.31, respectively) (Fig. 1b, c). In the subgroup analysis by a source of control, we observed an increased risk of XRCC1 194 Trp/Trp vs. Arg/Arg polymorphism for lung cancer in a healthy subject-based study (OR=1.34, 95 % CI 1.13–1.59) (Table 2); we did not observe any association between XRCC1 Arg194Trp polymorphism and lung cancer risk in additional subgroup analyses (Table 2). Limiting

Fig. 1 Forest plots for the association between XRCC1 Arg194Trp polymorphism and lung cancer risk in Chinese population **(a)** Trp/Trp vs. Arg/Arg, **(b)** Arg/Trp vs. Arg/Arg, **(c)** Arg/Trp+Trp/Trp vs. Arg/Arg

the analysis to the studies with controls in agreement with Hardy-Weinberg equilibrium (HWE), we did not observe

any association between XRCC1 Arg194Trp polymorphism and lung cancer risk (Table 2).

Table 1 Characteristics of selected papers

Author	Year	Area	Source of control	Number of case	Number of control	HWE
Chan Eunice C [4]	2005	Hong Kong	Healthy subjects	75	162	0.745951
Chen Senqing [7]	2002	Jiangsu	Healthy subjects	103	102	0.546278
Du Yong [8]	2012	Shanghai	Healthy subjects	100	100	0.000012
Du Yong [9]	2014	Shanghai	Healthy subjects	120	120	0.000009
Guo Shujie [10]	2013	Heilongjiang	Hospitalized patients	684	602	0.526784
Hao Bingtao [11]	2006	Beijing	Healthy subjects	1024	1118	0.701669
Hu Zhibin [12]	2005	Jiangsu	Healthy subjects	710	710	0.556829
Li Mingchuan [13]	2008	Liaoning	Hospitalized patients	350	350	0.803017
Ratnasinghe Duminda [3]	2001	Yunnan	Healthy subjects	108	210	0.182984
Shen Min [14]	2005	Yunnan	Healthy subjects	118	112	0.614295
Song Yahui [5]	2004	Jiangsu	Hospitalized patients	100	65	0.797994
Su Jia [15]	2008	Shanxi	Healthy subjects	396	465	0.126621
Wang Na [16]	2012	Henan	Healthy subjects	209	256	0.027626
Yin Jiaoyong [17]	2007	Liaoning	Hospitalized patients	241	249	0.570251
Yu Hongping [6]	2006	Hubei	Healthy subjects	104	121	0.043211
Zhang Wenjuan [18]	2005	Henan	Healthy subjects	149	157	0.356342

HWE Hardy-Weinberg equilibrium

Publication bias was assessed by funnel plots. The shape of funnel plots seemed to be approximately symmetrical (Fig. 2a–c). The results from Egger's test and Begg's test signified that publication biases might have few effects on this current meta-analysis (Table 2).

Sensitivity analyses were performed to identify the effects of the individual dataset on the summary estimates by sequentially removing each study. The summary effects were not modified when the studies were homogenous for Arg/Trp vs. Arg/Arg and Trp/Trp+Arg/Trp vs. Arg/Arg polymorphisms among total

Table 2 Summary odds ratios of the relation of XRCC1 Arg194Trp polymorphism to lung cancer risk in Chinese population

Genotype	Case/control	Heterogeneity test		Summary OR (95 % CI)	Hypothesis test		df	Begg's test		Egger's test	
		<i>Q</i>	<i>P</i>		<i>Z</i>	<i>P</i>		<i>Z</i>	<i>P</i>	<i>t</i>	<i>P</i>
Total											
Trp/Trp vs. Arg/Arg	2776/2950	23.61	0.05	1.26 (1.09–1.46)	3.12	0.002	14	0.30	0.767	0.85	0.411
Arg/Trp vs. Arg/Arg	4130/4495	36.60	0.001	1.05 (0.90–1.22)	0.63	0.53	15	1.22	0.224	1.47	0.163
Trp/Trp+Arg/Trp vs. Arg/Arg	4591/4899	46.22	<0.0001	1.12 (0.95–1.31)	1.35	0.18	15	1.22	0.224	1.53	0.149
Stratification by HWE											
Yes											
Trp/Trp vs. Arg/Arg	2418/2531	15.25	0.12	1.15 (0.99–1.35)	1.78	0.08	10	0.00	1.000	0.20	0.845
Arg/Trp vs. Arg/Arg	3677/3950	26.38	0.006	0.99 (0.84–1.16)	0.18	0.85	11	0.07	1.000	0.74	0.475
Trp/Trp+Arg/Trp vs. Arg/Arg	4058/4302	30.50	0.001	1.03 (0.87–1.21)	0.30	0.77	11	0.34	0.732	0.81	0.437
Stratification by source of control											
Healthy subject-based control											
Trp/Trp vs. Arg/Arg	1997/2204	19.59	0.05	1.34 (1.13–1.59)	3.38	0.007	11	0.75	0.451	0.53	0.607
Arg/Trp vs. Arg/Arg	2876/3334	18.10	0.08	1.01 (0.91–1.12)	0.22	0.82	11	0.62	0.537	0.37	0.716
Trp/Trp+Arg/Trp vs. Arg/Arg	3216/3633	27.24	0.004	1.10 (0.92–1.30)	1.06	0.29	11	0.48	0.631	0.47	0.646
Hospitalized patient-based control											
Trp/Trp vs. Arg/Arg	799/746	2.05	0.36	1.06 (0.80–1.42)	0.43	0.67	2	0.00	1.000	1.19	0.444
Arg/Trp vs. Arg/Arg	1254/1161	18.66	0.0003	1.29 (0.80–2.07)	1.04	0.30	3	1.02	0.308	2.87	0.103
Trp/Trp+Arg/Trp vs. Arg/Arg	1375/1266	18.97	0.0003	1.30 (0.82–2.06)	1.13	0.26	3	1.02	0.308	3.11	0.090

HWE, Hardy-Weinberg equilibrium

Fig. 2 Funnel plots of the association between XRCC1 Arg194Trp polymorphism and lung cancer risk in Chinese population in the heterozygous model (**a** Trp/Trp vs. Arg/Arg, **b** Arg/Trp vs. Arg/Arg, **c** Arg/Trp+Trp/Trp vs. Arg/Arg)

population by deleting Song et al.'s study and Chan et al.'s study (data not shown).

In conclusion, the findings of the study by Wu et al. [1] should be interpreted with caution. To reach a definitive conclusion, well-designed studies with large sample size are still required to assess the association of XRCC1 Arg194Trp polymorphism with lung cancer risk in Chinese population. We hope that this remark will contribute to more accurate elaboration and substantiation of the results provided by Wu et al. [1].

Conflicts of interest None

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