results in the French study[1] cannot be ruled out as a reason for the neutral results observed in the meta-analysis. Also, the heterogeneity of the population (ie, *MMR* gene) is not taken into account when a meta-analysis is performed and as shown by Talseth-Palmer *et al*[3] this can drastically affect the observed results.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Reply to Talseth-Palmer *et al*

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Following the publication of our article entitled 'Evaluation of Lynch syndrome modifier genes in 748 MMR mutation carriers'[1] in which we reported that in MMR mutation carriers 8q23.3 and 11q23.1 polymorphic alleles were not significantly associated with an increased colorectal cancer (CRC) risk, Talseth-Palmer *et al*[2] indicated that we did not correctly report their results by indicating: 'During the submission of this study Talseth-Palmer *et al* reported that in *MLH1* carriers, but not in *MSH2* carriers, the 11q23.1 *CC* and 8q23.3 *AC* genotypes were associated with an increased risk, but this significant association detected in 373 Australian mutation carriers was not found in 311 Polish mutation carriers analysed in the same study'. Their study was indeed performed in two distinct samples of MMR mutation carriers, originated from Australian and Polish families, respectively.[2] As indicated in Figure 1C of their article, the variation in CRC risk according to the 11q23.1 *CC* genotype was not statistically significant in the Polish sample cohort, but only a trend was observed (log-rank P=0.1336; Wilcoxon P=0.1109, and tware P=0.117). Moreover, the variation in CRC risk according to the 8q23.1 genotype was significant only in the Australian sample whereas no results are reported for the combined sample or the Polish sample, likely pointing to non-significant results. Therefore, our comment is appropriate. Moreover, the combination of the Australian and Polish MMR mutation carrier performed in their study amounts to a meta-analysis using pooled data from two different populations. Finally, all significant differences reported were restricted to *MLH1* mutation carriers and no results were reported for *MSH2* mutation carriers or for all subjects, which also raises questions on the real impact of the 8q23.3 and 11q23.1 genotypes on the CRC risk in MMR mutation carriers. Therefore, the title of their article 'Colorectal susceptibility loci on chromosome 8q23.3 and 11q23.1 as modifiers for disease expression in Lynch syndrome' appears too broad. We do not agree with their conclusion suggesting that 8q23.3 and 11q23.1 genotyping might have a clinical utility in *MLH1* mutation carriers.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Association study of the single nucleotide polymorphisms of *PARK2* and *PACRG* with leprosy susceptibility in Chinese population

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Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, affecting both the skin and peripheral nerves. It has long

Table 1 Association results between leprosy and the SNPs of the *PARK2/PACRG* region

SNP	*Chromosome*	*Position*	*A1*	*F-A*	*F-U*	*A2*	*CHISQ*[a]	P	*OR*
rs10945859	6	163142602	T	0.37	0.35	C	1.89	0.17	1.11
rs13195186	6	163159187	G	0.21	0.19	A	1.39	0.24	1.12
rs2276201	6	163149497	G	0.19	0.17	A	1.37	0.24	1.12
rs1801474	6	162622197	A	0.48	0.46	G	0.60	0.44	1.06
rs9347684	6	163151824	C	0.49	0.50	T	0.35	0.55	0.96
rs1040079	6	163214027	C	0.16	0.15	T	0.25	0.61	1.05
rs4495257	6	163214110	A	0.16	0.15	C	0.23	0.63	1.05
rs1514343	6	163213083	T	0.16	0.15	C	0.18	0.67	1.04
rs2803104	6	163139180	C	0.31	0.31	A	0.04	0.84	0.98
rs9356058	6	163151399	C	0.31	0.31	T	0.03	0.86	0.99
rs6915128	6	163211789	C	0.33	0.34	T	0.02	0.88	0.99
rs1333955	6	163213454	A	0.33	0.33	G	0.02	0.90	0.99
rs6939278	6	163152600	A	0.31	0.31	C	0.01	0.95	1.00

Abbreviations: OR, odds ratio; SNP, single-nucleotide polymorphism.
[a]χ^2-test.

been thought that the host genetics has an important role in the development of leprosy.[1] Markers in several genes and genomic regions have been reported to be associated with or linked to susceptibility to leprosy, in which the 80-kb block region of *PARK2* and *PACRG* was reported to be as a major risk locus for leprosy susceptibility in Vietnamese and Brazil.[2] Although there is lack of association between polymorphisms of the *PARK2* and *PACRG* genes and leprosy susceptibility in Indian population,[3] which showed the differential effect of these SNPs in regulating genetic susceptibility to leprosy in different populations.

In 2009, we performed the first Genome-Wide Association Study of leprosy using Illumina Human610-Quad BeadChip (San Diego, CA, USA) and identified six host genetic risk factors with genome-wide significant evidence and an additional risk factor with suggestive evidence.[4] And no promising SNPs were observed in the 80-kb shared locus of *PARK2* and *PACRG*. But the pathway analysis showed variants of *PARK2* and *LRRK2* (a suggestive susceptibility locus of leprosy) interact directly, which suggest there may be a suggestive association of *PARK2* with leprosy in Chinese population.

Owing to inadequate coverage of Human610-Quad BeadChip, we selected 13 SNPs associated with Vietnamese and Brazil population,[2] and additional 2 SNPs according to allele frequency in Chinese population in the 80-kb block region of *PARK2* and *PARCG* (all the 15 SNPs selected for replication, only 13 SNPs were designed in one panel). All samples were Chinese Han recruited from northern China (Shandong province) and matched regarding to age, gender and ethnicity. After informed consent, genotyping analyses of the 742 leprosy cases and 734 controls samples were conducted by using the Sequenom MassArray system (San Diego, CA, USA). In each replication sample, we excluded SNPs with a call rate $<95\%$, low minor allele frequency ($P<0.01$) or deviation from Hardy–Weinberg equilibrium proportions ($P<0.01$) in the controls. Cochran–Armitage trend test was used to test the genotype–phenotype association in the validation study using Plink v 1.07 software. Power calculations, carried out using CaTS software (http://www.sph.umich.edu/csg/abecasis/CaTS/), showed that our sample size of 742 patients and 734 controls had $>81\%$ power to detect an odds ratio of 1.61 at a significance level of 0.1%, when the frequency of the allele of interest was >0.10.

Eleven previously indicated risk variants and other two SNPs (rs13195186 and rs1801474, MAF/Minor Allele count in *Homo sapiens*: G=0.447/538; T=0.1407/175, separately), which are all located in the region of *PARK2* and *PACRG*, show no significant association with susceptibility to leprosy *per se* in the Chinese Population (Table 1).

In summary, we confirmed that Chinese population as well as Indian population[3] show no remarkable association with the risk SNPs within the region of *PARK2* and *PACRG* with leprosy *per se*, which gave the general consideration that there may be a suggestive association of these SNPs with the ethnic heterogeneity of leprosy susceptibility. Furthermore, it was valuable to research more ethnic lines to conform the consideration in future.

CONFLICT OF INTEREST

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