We read with great interest the article by Rong et al. (1) on the associations of hemochromatosis gene \((HFE)\) polymorphisms (C282Y and H63D) with type 2 diabetes mellitus. The authors stated, “… persons with a D allele may have a moderately increased risk of type 2 diabetes mellitus” (1, p. 461) (additive model (D allele vs. H allele): odds ratio (OR) = 1.20, 95% confidence interval (CI): 1.03, 1.41, \(P = 0.02\); dominant model (DD + HD vs. HH genotype): OR = 1.12, 95% CI: 1.00, 1.25, \(P = 0.04\)). This is a very important investigation because there were conflicting results with regard to these associations in the original studies. However, we would like to draw attention to the following aspects of the article.

**Figure 1.** Forest plot of odds ratios and 95% confidence intervals (CIs) of type 2 diabetes mellitus in an additive model (D allele vs. H allele) from a random-effect meta-analysis. The sizes of the squares show the weighting of included studies. Adapted from Figure 3 of Rong et al.’s paper (1). Reference numbers correspond to those of Rong et al.’s reference list.
First, the data presented by Rong et al. (1) were not in accord with those provided by the original publications. The genotype of HH/HD/DD in cases and controls should be 69/27/3 and 65/31/3 for the study by Campo et al. (2) (reference 29 in Rong et al.’s paper), 498/184/23 and 782/302/24 for the study by Qi et al. (3) (reference 36 in Rong et al.’s paper), and 143/63/24 and 800/240/24 for the study by Florkowski et al. (4) (reference 25 in Rong el al.s paper). When we reanalyzed the data, the association was no longer significant in an additive model (OR = 1.16, 95% CI: 0.99, 1.36; P = 0.07; I² = 26.5%), although a marginally significant association was found in the dominant model (OR = 1.17, 95% CI: 1.01, 1.35; P = 0.05; I² = 39.1%).

Second, considering the inconsistency among different genetic models, Salanti et al. (5) proposed a method for the choice of genetic models based on the ratio of log-scale effect (λ = log(OR_{HD/HH})/log(OR_{DD/HH})), and they suggested that an additive model of inheritance is more plausible for type 2 diabetes mellitus when the inheritance mode is unknown for gene–disease association studies. When using the random-effects logistic regression models treating the multiple genotypes (HH, HD, and DD) as independent variables as proposed by Salanti et al. (5) and Bagos and Nikolopoulos (6), we found that the association was still not significant (log(OR_{HD/HH}) = 0.10, 95% CI: −0.03, 0.22, P = 0.12; log(OR_{DD/HH}) = 0.31, 95% CI: −0.15, 0.77, P = 0.18). When the choice of genetic models was taken into consideration, the results also suggested an additive model (λ = log(OR_{HD/HH})/log(OR_{DD/HH}) = 0.32) instead of a dominant model (λ = 1 indicates a dominant model).

Third, according to the hierarchy for grading the credibility of molecular evidence in complex diseases (7), the effect observed in the study by Rong et al. should be small or very small instead of moderate (very small: OR = 1–1.2; small: OR = >1.2–2; moderate: OR = >2–5; large: OR = >5). All statistical analyses were performed with Stata, version 10.1, software (StataCorp LP, College Station, Texas). All reported probabilities (P values) were 2 sided, with P ≤ 0.05 considered significant.

In our opinion, readers will have a better understanding of the results by Rong et al. (1) if they take into account the above-mentioned data analysis.

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