Letter regarding Wang et al. entitled “Effects of murine double minute 2 polymorphisms on the risk and survival of osteosarcoma: a systematic review and meta-analysis”

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We have read with interest the article by Wang et al. [1] in a recent issue of *Tumor Biology*. In this study, the authors conducted a systematic review and meta-analysis to assess the effects of two murine double minute 2 (*MDM2*) polymorphisms, rs2274799 and rs160916, on the risk and survival of osteosarcoma. The authors concluded that *MDM2* polymorphisms had effects on the risk but had no effect on the survival of patients with osteosarcoma. In a recent letter to the editor, Liu et al. [2] detected several weaknesses in the meta-analysis. Firstly, they criticize the small number of papers included in the analyses, which could lead to false significant associations. They also point out the lack of information in the methods used to select the studies. Moreover, they comment the absence of Hardy-Weinberg equilibrium analysis in the control population. Finally, they question the quality of the selected studies. In the present letter, we would like to add some other inaccuracies found in the Wang et al. [1] meta-analysis.

According to our analyses, there is no association between *MDM2* rs2279744 and osteosarcoma risk in the population used by Ito et al. [3]. This contradicts the result shown by Wang et al. [1] in their study. When we calculate the odds ratio (OR) value of Ito et al. [3] samples, using the total of benign tumors ($n=37$) as controls, we obtain a different OR value. This contradictory result has been observed in all hereditary models (allele model, OR=1.46, 95 % CI 0.62–3.43; codominant model, OR=1.50, 95 % CI 0.29–7.65; recessive model, OR 1.11, 95 % CI 0.24–5.08; dominant model, OR=1.88, 95 % CI 0.59–6.01). The main problem we detect here is that Wang et al. [1] specify neither the samples nor the genotype frequencies used for the meta-analyses. The only available data in the

Ito et al. [3] paper that can be used as controls come from the benign tumors. When we used these data (osteosarcoma, GG=3, GT=7, TT=7; benign tumors, GG=6, GT=10, TT=21), no significant values were found. In any case, we disagree with the use of benign tumors as controls in a susceptibility study.

Secondly, we also disagree with the results obtained by Wang et al. [1] in relation to the risk association found between *MDM2* rs1690916 and osteosarcoma in the Naumov et al. [4] population. In this case, Wang et al. [1] used the total of bone tumors ($n=68$) instead of the osteosarcoma patients ($n=26$).

Finally, we would like to highlight the relevance of reporting genotype data used for the meta-analysis. In agreement with Liu et al. [2], we also think that further studies with large samples are still needed to assess the effects of *MDM2* polymorphisms on the risk and survival of osteosarcoma.

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Conflict of interest None.

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