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LETTER TO THE EDITOR

SLC19A1 hot spot for MTX plasma concentration

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To the Editor,

We have read with interest the recent study by Wang et al. [1], which has been published in Medical Oncology. In this study, the authors investigated the effects on methotrexate (MTX) plasma concentrations of polymorphism rs1051296 in a miRNA binding site in solute carrier family 19, member 1 (*SLC19A1*), analyzing a group of 131 Chinese children with acute lymphoblastic leukemia (ALL). They concluded that rs1051296 G allele, which is predicted to change the miRNA binding profile of *SLC19A1* in silico, is associated (p value = 0.02) with increased MTX plasma concentration. They suggest that miRNAs might be involved in the post-transcriptional regulation of *SLC19A1*, affecting MTX transport.

We found this result very interesting because in a previous study published by our group [2], we analyzed the association between 14 SNPs in *SLC19A1* and MTX plasma levels in 151 Spanish children diagnosed with ALL. Three SNPs out of 14 showed significant associations with MTX plasma levels. These SNPs were rs1051266, rs3788200, and rs1131596 (p values 0.013, 0.015, and 0.022, respectively). Among them, we can highlight rs1051266 (RFC1 80G>A) since it is a missense variant that changes the protein sequence (His>Arg). It is noteworthy that rs1051266 has been associated with MTX plasma concentration or toxicity in several studies. In our study, this SNP could explain the association with MTX plasma concentration of the other two SNPs as they are in strong linkage disequilibrium ($r^2 = 0.98$ in CEU population) with rs1051266.

Both results support the hypothesis that genetic variants in *SLC19A1* might affect gene function and, consequently, may be relevant for the regulation of MTX transport and, therefore, for MTX plasma concentration. The fact that different SNPs in *SLC19A1* have been found associated with MTX concentration in these two populations may be due to ethnic disparities or to the fact that this gene corresponds to a big haplotype block. The results found by Wang et al. could be due to the fact that SNP rs1051296 is in the same linkage disequilibrium block ($r^2 = 0.8$ in CHB population) as rs1051266. The analysis of the association between this SNP and MTX plasma concentration in Chinese population could be interesting to clarify this point.

Conflict of interest None.

References

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