Association of genetic polymorphisms in genes involved in Ara-C metabolic pathway with chemosensitivity and prognosis of adult acute myeloid leukemia (AML)

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Background: Cytarabine arabinoside (Ara-C) has been the core of chemotherapy for adult acute myeloid leukemia (AML) for decades. Ara-C undergoes phosphorylation into the active metabolite Ara-C triphosphosphate (Ara-CTP). Several enzymes are involved directly or indirectly in either the formation or detoxification of Ara-CTP.

Methods: A total of 12 eQTL single nucleotide polymorphisms (SNPs) or tag SNPs in 7 genes involved in Ara-C metabolism were genotyped in 361 non-M3 AML patients. Association of the SNPs with complete remission (CR) rate after Ara-C based induction therapy, relapse-free survival (RFS) and overall survival (OS) were analyzed.

Results: Three SNPs were observed to be associated increased risk of chemoresistance indicated by CR rate (NME2 rs3744660, E2F1 rs3213150, and RRM2 rs1130609). Combined genotypes based on E2F1 rs3213150 and RRM2 rs1130609 polymorphisms further increased the risk of non-CR. The SAMHD1 polymorphism rs6102991 showed decreased risk of non-CR marginally. Three SNPs (NME1 rs3760468 and rs2302254, and NME2 rs3744660) were associated worse RFS, and 3 SNPs (NME1 rs3760468, NME2 rs3744660, and RRM1 rs183484) were associated with worse OS in AML patients.

Conclusion: Data from our study demonstrated that SNPs in Ara-C metabolic pathway predict chemosensitivity and prognosis of AML patients in China.