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Bioinformatics prediction and functional verification of micro RNAs involved in the transformation from MDS to AML

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Objective: To explore key microRNAs (miRNAs) involved in transformation from myelodysplastic syndrome (MDS) to acute myeloblastic leukemia (AML).

Methods: Based on Gene Expression Omnibus (GEO) database (GSE15061), a microarray analysis of AML transformation from MDS, RVM t-test, Gene Ontology (GO) and pathway analysis were used to find out crucial miRNAs involved in transformation from MDS to AML. Then target gene verification and functional assay were executed to ensure the bioinformatics prediction.

Results: From 1111 differential genes between MDS to AML, 7 miRNAs (miR-129-5p, miR-520h, miR-200c, miR-181a, hsa-miR-495, miR-590-3p, miR-373) closely related with 15 target genes, 21 GO functions and 15 pathways are screened as candidates involved in pathogenesis of MDS. Real time PCR shows that miR-200c and miR-590-3p are over expressed in CD34+ progenitor cells screened from AML cell lines (HL-60, THP-1) while the other 5 miRNAs are under expressed. After being transfected into CD34+ progenitor cells, miR-520h mimics facilitates clonogenic formation of CFU-E, BFU-E and CFU-GM ($P<0.05$), but not CFU-GEMM ($P>0.05$), miR-495 agomir and miR-181a-5p antagomir promote the propagating of $CD34^+CD38^-$, $CD34^+$ and $CD34^+CD38^+$ ($P<0.05$).

Conclusion: We successfully identified critical miRNAs involved in transformation from MDS to AML, which may be potential targets in prevention and treatment of MDS and AML.

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