Regulation of the expression of zinc finger protein genes by microRNAs enriched within acute lymphoblastic leukemia-derived microvesicles

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ABSTRACT. Microvesicles (MVs) are submicrometric membrane fragments that can “engulf” cytoplasmic contents such as microRNAs (miRNAs) from their cellular origin. The study of miRNAs carried within MVs might provide insights into the roles that miRNAs play in the underlying pathophysiologic processes of acute lymphoblastic leukemia (ALL). We identified numerous dysregulated MV miRNAs in patients with B- and T-cell ALL by using Agilent microarray analysis. Selected miRNAs obtained by microarray profiling were validated using quantitative reverse transcription-polymerase chain reaction. Using bioinformatic tools, we found that 118 and 116 miRNAs from B- and T-ALL MVs, respectively, regulated the expression of zinc finger protein (ZFP) genes. For example, zinc finger protein 238 (ZNF238),...
known as a tumor suppressor, was regulated by miR-20b over-expression. Conversely, ZNF267, a cancer-promoting factor, was mediated by downregulated miR-23a and miR-23b. Considering that miRNAs are generally believed to repress gene expression, antineoplastic ZNF238 was likely inhibited while the level of oncogenic ZNF267 was likely increased by miRNA dysregulation, leading to modification of the ALL microenvironment. In addition, gene ontology and signaling pathway analysis demonstrated that a subset of the ZFP genes targeted by altered MV miRNAs are involved in cellular biological processes including proliferation, differentiation, apoptosis, and cell cycle regulation. These findings indicated that cancer-associated MV miRNAs and their target ZFP genes might be novel pathogenic factors in ALL. However, the specific roles exerted by MV miRNAs and their target ZFP genes on the pathological mechanisms of ALL remain to be further understood.

**Key words:** Microvesicles; MicroRNAs; Zinc finger protein genes; Acute lymphoblastic leukemia