Nuclear-Export of PU.1 with Mutated NPM1 Impedes Terminal Monocytic Differentiation of Acute Myeloid Leukemia Cells
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BACKGROUND

Nuclear-export plays a crucial role in the terminal differentiation of acute myeloid leukemia (AML) cells. Mutated NPM1 impairs the expression of PU.1, a key transcription factor in monocytic differentiation. The aim of this study was to investigate the role of nuclear-export in PU.1-dependent monocytic differentiation of AML cells.

METHODS

We generated AML cell lines with nuclear-export mutants of NPM1 and examined their effects on PU.1 expression and monocytic differentiation. We used immunofluorescence and Western blotting to analyze PU.1 and NPM1 localization and expression.

RESULTS

We found that nuclear-export of PU.1 in AML cells was impeded by mutant NPM1. Inhibiting nuclear-cytoplasmic export restored nuclear PU.1 in NPM1 mutant cells. ATRA induced monocytic differentiation in NPM1 mutant cells, while inhibiting nuclear-export did not affect monocytic differentiation.

CONCLUSION

Mutant NPM1 impairs nuclear-export of PU.1, which may contribute to AML differentiation arrest.

REFERENCES