C-terminal mutations of the phosphoprotein nucleophosmin (NPM) are the most frequent genetic aberration detected in adult acute myeloid leukemia (AML). I focused on characterization of type A, B and E of AML-related C-terminal mutations. The plasmids bearing fluorescently labeled wild type or mutated NPM have been constructed to characterize mutation-induced changes in the localization of NPM. Mammalian cell lines HEK293T, HeLa and NIH 3T3 were used for production of the chimeric proteins. The intracellular localization of the mutated forms of NPM was analyzed by immunofluorescence staining and fluorescence microscopy of the living cells. The localization of the mutNPM type A and B was almost identical and predominantly cytoplasmic, while mutNPM type E was detected in nucleolus and cytoplasm simultaneously. However localization of the mutated forms was greatly influenced by the used cell line. It has been demonstrated that the exogenous NPM interacts with the endogenous NPM and that they mutually affect their intracellular localization due to heterooligomer formation.

Detailed analysis of the relationship between the C-terminal mutations and the localization of the mutated NPM improves understanding of specific mutation effect on the formation and progression of AML and also specifies its prognostic meaning. Further investigation of NPM mutations might uncover new possibilities of drug development especially in case of targeted therapy.