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CRISPR/Cas9 mediated next generation gene therapy in chronic myeloid leukemia

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Present study, we aimed to manipulate the *BCR::ABL1* fusion gene, which is responsible for the etiopathogenesis of Chronic myeloid leukemia (CML), *in vitro*. Mechanism of this molecular pathogenesis is based on encoding the *BCR::ABL1*^{p210} oncoprotein with excessive and irregular tyrosine kinase activity and eventually causes the CML phenotype. On the other hand, patients developing drug resistance or the side effects of bone marrow transplantation on mortality and morbidity strengthened our hypothesis that CRISPR/Cas9 could be an advance in preclinical studies in this research. Cytogenetic and molecular genetic characterization of K562 cells has been performed. Intronic sequences were detected by sequencing in the translocation of the *BCR::ABL1* fusion gene. Genome editing in CML cells was done by transfection of lipofectamine and electroporation. The efficiency of CRISPR/Cas9 on the *BCR::ABL1*^{p210} was analyzed by qRT-PCR. Gene expression of the *BCR::ABL1*^{p210} fusion before and after CRISPR/Cas9 manipulation, which changed during the culture time, was compared logarithmic over the transcript values in the molecular response. We recorded that *BCR::ABL1*^{p210} manipulation showed an approximately 100-fold decrease in expression as (+1 log) before (-1 log) after CRISPR/Cas9 manipulation. Thus, the *BCR::ABL1*^{p210} fusion gene expression was significantly decreased by mediated CRISPR/Cas9 manipulation. As a result, the effect of the CRISPR/Cas9 genome editing was revealed *via* the knockdown of the *BCR::ABL1*^{p210} in our study. Thus, CRISPR/Cas9 can target the *BCR::ABL1p210* fusion gene due to the interference effect.

Keywords: *BCR::ABL1*^{p210} expression, Gene editing, Molecular response