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Stable silencing of IGF1R using lentiviral-mediated shRNA and evaluating sensitivity to immunotherapy with monoclonal antibody rituximab in lymphoma cells

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The high expression of insulin-like growth factors and their receptors is a common phenomenon in the process of invasion and metastasis of many malignancies such as lymphoma. Rituximab is the first monoclonal antibody to be approved for the treatment of lymphoma. Epitope complex of rituximab has been determined by co-crystallizing a synthetic peptide mimic of the extracellular loop epitope of CD20 (residues 163–187) in complex with the antigen-binding fragment of rituximab. Genetic mutations in the rituximab epitope can reduce the binding and efficacy of the antibody and these mutations are important causes of failure to treatment. Sequencing and bioinformatics analysis exhibits mutations in CD20 gene indicative of resistance and therefore it seems the synergistic effect of combined therapy with the stable system of lentiviral gene therapy and immunotherapy can provide a promising therapeutic approach for the treatment of lymphoma. We made lentiviruses using six lentiviral cassettes against IGF-IR and used to transduct HEK293T cells. Then we compared them to non-silencing control cassette and the reduction in mRNA and protein expression level was determined using real time PCR and Western Blot techniques. The most effective cassette was selected and used to transduct Raji cells. The expression of IGF-IR and Bcl2 at mRNA and protein level was assessed and the cell growth and cytotoxicity were assessed using MTT assay. We evaluated the role of IGF-1 receptor in growth and proliferation of Raji tumor cells by reducing the expression of IGF-IR. Finally, we detected sensitivity to rituximab- immunotherapy in the lymphoma cells.

Biography

Leila Nasehi received her Master's in Microbiology in 2008 and PhD degree in Molecular Medicine in 2017 from Tehran University of Medical Sciences. Her research activities take place in the field of antibiotic resistance in patient's samples, particularly in the field of resistance genes in microorganisms (ESBL) and genetic manipulation by employing plasmids or lentiviruses vectors for silencing or stable silencing in adherent & suspension cells. She is a faculty member of Zanjan University of Medical Sciences.

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