

GOLD NANOPARTICLES CONJUGATED WITH RITUXIMAB FOR THE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA.

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Chronic lymphocytic leukemia (CLL) is a monoclonal disorder that is characterized by a continuous accumulation of malignant lymphocytes. Despite progress in targeted therapy options for CLL, relapse or progression to a Richter syndrome still appears. Thus, a more focused and targeted therapeutic option is

required. This can be achieved by increasing the concentration of a cytostatic drug in the tumor while reducing its' systemic toxicity. In the continuous effort toward the development of more efficient therapeutic approaches for the treatment of CLL, in the current study we report the conjugation of rituximab antibody drug onto spherical gold nanoparticles. Their effective trans-membrane delivery inside CLL cells and their validation as real-potential therapeutics with increased efficacy, in comparison with drug alone.

The efficient formation of drug-nanocarriers was proved by spectroscopic characterization of the particles. The internalization of rituximab-nanocarriers was proved as a result of the strongly scattered light from gold nanoparticles and was correlated with the results obtained by TEM and dark field microscopy. The therapeutic effect of the newly-designed drugs was investigated by several methods including cell counting assay as well as the MTT assay and was found to be superior when compared with the drug alone, data confirmed by state-of-the-art analyses of internalization, cell biology (flow cytometry, apoptosis and autophagy assay), genomics (RT-PCR for MS4A1) and proteomics (confocal microscopy and western blotting for CD20).

Key words: rituximab, gold nanoparticles, chronic lymphocytic leukemia