Extended Abstract Journal of Cognitive Neuropsychology 2021
Vol.5 No.1

A targeted drug delivery nanosystem to hepatocellular carcinoma

Henrique Faneca
University of Coimbra, Portugal

Introduction:
Hepatocellular Carcinoma (HCC) is one of the major frequent cause of cancer-related mortality worldwide. Combination of different chemotherapeutics drugs may offer advantages for the treatment of HCC. Targeted hepatocellular carcinoma therapy was carried out to improve the efficacy of liver cancer treatment. The purpose of this study was to design an N-acetylgalactosamine (NAcGal) modified and pH sensitive doxorubicin (DOX) prodrug (NAcGal-DOX) for the construction of lipid nanoparticles (LNPs) .Nanotechnology has made exceptional headway, emerging as a revolutionary platform to treat a wide variety of tumors, mainly due to prolonged drug release, as well as increased cell internalization. In this work, we have developed a drug delivery system, a hybrid nanoparticle formulation, which allows the specific delivery into HCC cells. NAcGal-DOX and sorafenib (SOR) co-loaded LNPs were designed and the synergistic effects were evaluated on human hepatic carcinoma (HepG2) cells in vitro and anti-hepatic carcinoma mice model in vivo. The hybrid nanoparticle comprises a core of PLGA coated by a lipidic envelope constituted by 1-palmitoyl- 2-oleoyl-sn-glycero-3-phosphocholine; cholesterol and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N- [methoxy(polyethylene glycol)-2000] (PEG) with a specific ligand (GalNac) covalently attached. The obtained nanosystems were characterized by transmission electron microscopy, dynamic light scattering, zeta potential analysis and differential scanning calorimetry, showing a mean diameter (150 nm) and a surface charge (-25 mv) suitable for in vivo applications. Unfavorable systemic side-effects of chemotherapeutic agents and susceptibility to the degradation of small interfering RNAs (siRNAs), which can knock down a specific gene involved in the disease, have hampered their clinical application. So, it could be beneficial to develop an efficient carrier for the stabilization and specific delivery of drugs and siRNA to cells. Targeted nanoparticles have gained considerable attention as an efficient drug and gene delivery system, which is due to their capability in achieving the highest accumulation of cytotoxic agents in tumor tissue, modifiable drug pharmacokinetic- and bio-distribution, improved effectiveness of treatment, and limited side-effects. Recent studies have shed more light on the advantages of novel drug loaded carrier systems vs free drugs. Most of the animal studies have reported improvement in treatment efficacy and survival rate using novel carrier systems. Targeted delivery may be achieved passively or actively. The hybrid nanoparticle enables the release of two drugs demonstrated through release studies of fluorescent probes and drugs in dialysis. The presence of GalNac (a specific ligand to the asia loglycoprotein receptor that

is overexpressed in HCC) allowed the internalization of the nanosystems and the release of the drugs preferentially in HCC cells, as demonstrated by flow cytometry and confocal microscopy. This new nanosystem represents an added value in the fight against the global scourge of hepatocellular carcinoma.

This work is partly presented at 34th World Congress on Heart Diseases on Jul 27-28, 2020