Size controlled protein nanoemulsions for cancer therapy

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Albumin nanoemulsions were produced by high pressure homogenization with a tri-block copolymer (Poloxamer 407), which presents a central hydrophobic chain of polyoxypropylene (PPO) and two identical lateral hydrophilic chains of polyethylene glycol (PEG). We observed a linear correlation between tri-block copolymer concentration and size – the use of 5 mg/mL of Poloxamer 407 yields nanoemulsions smaller than 100 nm. Molecular dynamics and fluorescent tagging of the tri-block copolymer highlight their mechanistic role on the size of emulsions. This novel method enables the fabrication of highly stable protein-based emulsions in the nano-size range, highly desirable for controlled drug delivery. Folic Acid (FA)-tagged protein nanoemulsions were shown to promote specific folate receptor (FR)-mediated targeting in FR positive cells. Carbon monoxide releasing molecule-2 (CORM-2) was incorporated in the oil phase of the initial formulation. FA-tagged nanoemulsions loaded with CORM-2 exhibited a considerable antitumor effect and an increased survival of BALB/c mice bearing subcutaneous A20 lymphoma tumors. The developed nanoemulsions also demonstrated to be well tolerated by these immunocompetent mice. The novel strategy presented here enables the construction of size controlled, functionalized protein-based nanoemulsions with excellent characteristics for active targeting in cancer therapy.