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Using an FDA approved nutrition supplement, intralipid, to improve delivery of anti-cancer nanodrugs: Effects on RES clearance and toxicity, EPR and immune modulation

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According to several meta-analysis studies, less than 1% of anti-cancer nanodrugs are delivered to target tumors. The reticuloendothelial system [(RES)/mononuclear phagocytic system (MPS)] is a key factor that affects nanodrug bio distribution and bioavailability by sequestering nanoparticles from the circulation (1). We have developed a method to temporarily blunt the RES by pre- administration of the FDA-approved nutritional supplement, Intralipid® (2-6). We have tested our Intralipid® method (2 g/kg, clinical dose) on the delivery of two different anti-cancer nanodrugs: (i) an experimental anti-cancer nanodrug, dichloro (1,2-diaminocyclohexane) platinum (II)-loaded and hyaluronic acid polymer-coated nanodrug (DACHPt/HANP) and (ii) the FDA-approved anti-cancer nanodrug, Abraxane®. We have found that pre-treatment with Intralipid® can reduce platinum accumulation in the liver, spleen, and kidney of rats by 20.4%, 42.5%, and 31.2%, respectively at 24-hr post DACHPt/HANP administration. Similarly, we have found in a xenograft breast cancer mouse model that pre-treatment with Intralipid® significantly increases the amount of Abraxane® that reaches tumors to promote tumor apoptosis and that the combination of Intralipid® with half the standard dose of Abraxane® can reduce tumor growth as effectively as the standard clinical dose. Intralipid® also promotes the polarization of macrophages to the anti-cancer M1-like phenotype. A recent study from Dr. Hiroshi Maeda and his colleagues showed a more important role of Intralipid® treatment, namely improving tumor blood flow, which is key for nanodrug delivery via the enhanced permeability and retention (EPR) effect (7). Thus, Intralipid® pre-treatment can be a new way to improve the delivery of anti-cancer nanodrugs with reduced off-target side effects and with improved drug efficacy. Our nanodrug delivery method is a general one, since it can apply to any existing nanodrugs as well as to those in development because there is no need to modify the drug and its nanocarrier.

Biography

Li Liu is a research scientist in the Laboratory of Functional and Molecular Imaging, National Institute of Neurological Disorders and Stroke. Her research focus is on the novel delivery strategies of nano-sized therapeutics and imaging agents. She received her Ph.D. degree from the Department of Medicinal Chemistry at the University of Minnesota. She received her postdoctoral training in Dr. Chien Ho's laboratory at the Department of Biological Sciences at the Carnegie Mellon University. In 2010, she was awarded a postdoctoral fellowship from the American Heart Association. Li has authored or co-authored more than 20 research papers, 3 book chapters, and 2 US patent applications.

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