Folic acid-conjugated cross-linked cytochrome c nanoparticles as smart carrier combining triggered release and active targeting for lung cancer therapy

Irivette Domínguez-Martínez and Kai Griebenow

Department of Chemistry, University of Puerto Rico, Rio Piedras Campus, San Juan, PR, 00931

Lung cancer is the most common cause of death due to cancer in both men and women throughout the world. Statistics from the American Cancer Society estimated that in 2019 there will be about 228,150 new cases of lung cancer in the U.S. occurred and over 142,670 deaths were due to the disease. Natural biomolecules, such as proteins, are an attractive alternative as therapeutic agents due to their highly specific biological activities. However, the use of protein as therapeutic agents is hampered by their physical and chemical instabilities during formulation, storage, and delivery. Therefore, it is of great interest to engineer nano-sized drug delivery systems to stabilize protein therapeutics and allow targeted treatment. In our study, we propose a cytochrome c (Cyt c) cross-linked nanoparticle (NP) that was designed for active targeting and stimulus-triggered release of the apoptotic protein Cyt c. This system is composed of a Cyt c NP stabilized by a homobifunctional redox-sensitive cross-linker for smart release and folic acid-polyethylene glycol (FA-PEG) on the surface for receptor-mediated targeting. The NPs were prepared using a nanoprecipitation method in the presence of the crosslinker, dithiobis(succinimidyl propionate) (DSP), then the FA-PEG was added to react overnight. Dynamic Light Scattering (DLS) showed that NPs were created with this method whose diameter is in the approximate range of 200 nm. Preliminary results show that Cyt c NP coated with the FA-PEG polymer induced a significant reduction in the cell viability of the folate receptor positive Lewis Lung Carcinoma cell after 24 h of incubation while not in the non-cancer NIH 3T3 cells used as control.