Steric stabilization of cationic lipid-DNA (CL-DNA) complexes is required for their use in vivo, but PEGylation (PEG; polyethylene glycol) of CL-DNA complexes reduces their efficacy as gene delivery vectors in vitro [1]. One approach to improving gene delivery with PEGylated CL-DNA nanoparticles is to covalently attach a targeting peptide at the distal end of PEG. We have developed PEGylated CL-DNA nanoparticles with an RGD or iRGD motif present at the distal end of the PEG and carried their efficacy of cancer cells in an in vitro environment.

Although neuropilin-1 is known to play a role in the tumor penetration properties of nanoparticles in the intracellular mechanism that allows for tumor penetration is unknown. In order to investigate how iRGD promotes tumor penetration, we performed live cell imaging of fluorescently labeled RGD and iRGD-tagged CL-DNA nanoparticles using GFP-Rab-GTPases, an endosomal membrane bound protein which allows for spatio-temporal tracking of endosomal cargo. We present quantitative analysis using GFP-Rab-5 (7 and 9) which label early and late endosomes and compare the colocalization of RGD and iRGD in these endosomes as a function of time. Finally, we investigated the gene delivery properties of RGD and iRGD-tagged lipid-DNA nanoparticles through the use of gene expression assays. A thorough understanding of the intracellular fate of CL-DNA nanoparticles will allow for optimization of gene delivery vectors. Funded by NIH-GM59288.


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Biomimetic Light Harvesting in Nanoporous Metal Organic Materials
Randy W. Larsen, Lukasz Wojtas, Christi Whittington, Chemistry, University of South Florida, Tampa, FL, USA.

Metal organic framework materials (MOFs) represent a class of solid state materials with a number of properties advantageous for numerous applications ranging from gas storage and separation, heterogeneous catalysis, and controlled drug release to name only a few. Of the plethora of unexplored applications of MOFs, frameworks that can facilitate biomimetic solar photocatalysis are of significant interest. Solar photochemistry applications rely on the ability of the MOF material to undergo facile and directional photon-duced electron transfer, much like biological light harvesting systems. One strategy is to utilize the nanoscopic cavities within the MOF to encapsulate photoactive guests that can participate in directional photo-induced electron transfer reminiscent of biological electron transport chains. Here we discuss two such light harvesting systems. First, photoexcitation of a Zn(II)-trimesic acid based metal organic framework containing co-encapsulated Ru(bpy)32+ and pyridine (Ru(bpy)3 and Co(bpy)3) results in intermolecular electron transfer (ET) between the excited state of Ru(bpy)3 (MLCT) and the ground state Co(bpy)3 The rate of inter-cavity ET, kET, is found to be 3.7x106 s−1. Using the semi-classical Marcus equation and the observed excited state constant, it is determined that ET occurs between Ru(bpy)3 and Co(bpy)3 complexes located in adjacent cavities (~19.6 A). We have also previously demonstrated the ability to specifically encapsulate metalloporphyrins within the octahemicoctahedral cavities of both Cu and Zn HKUST-1. Here the simultaneous encapsulation of both Zn(II) tetraakis(tetraceten-4-sulphonato)porphyrin (Zn4SP) and Fe(III)tetraakis (tetraceten-4-sulphonato)porphyrin (Fe4SP) into a Zn(II)-HKUST-1 metal organic framework is demonstrated. Photo-excitation of the Zn4SP results in intramolecular electron transfer (ET) between the encapsulated Zn4SP and the Fe(III)4SP sites as evident by the reduction in Zn4SP lifetime from 370 μs (τZn = 2.7x10−6 s−1) to 83 μs (τK = 1.2x10−6 s−1) in the presence of Fe4SP giving a kET ≈ 9.1x107 s−1.