EFFICIENT TRANSPORT AND DELIVERY OF MFN1 BY GEMINI/DOPE NANOVEHICLES IN MFN1-KNOCKOUT FIBROBLASTS

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Mitochondria form a highly dynamic network of organelles which constantly fuse and divide.[1] The balance between these antagonistic processes of fusion and fission is extremely important for normal cellular function.[1],[2] In mammalian cells, there are three central players involved in the mitochondrial fusion: mitofusin 1 and mitofusin 2 (Mfn1/Mfn2) (outer mitochondrial membrane fusion) and OPA1 (inner mitochondrial membrane fusion). Deletion of either the MFN1 or the MFN2 gene in mouse embryonic fibroblasts (MEFs) leads to fragmented mitochondria due to a lack of mitochondrial fusion. More importantly, mutations of any of these putative functional domains impair mitochondrial fusion and lead to mitochondrial diseases (MD), to which there is no cure.[3] Here, we have conceived lipoplexes as efficient therapeutic agents against MD. Lipoplexes consist on a lipid/DNA highly packed complex that transport and efficiently deliver DNA into the cytoplasm. We have tested different mixed lipoplexes made of Gemini/DOPE[4] and a p-MFN1 plasmid coding for the Mitofusin1 protein in eukaryotic cells. Our results show that lipoplexes recover the normal mitochondrial dynamics phenotype in MFN1-Knockout MEFs. Moreover, we show a good viability and high transfection efficiencies as compared with other canonical transfer agents.

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