Rapid kinetics of β-cyclodextrin entering and exiting cells: Implication of its mechanism on reduction of cholesterol accumulation in Niemann–Pick disease type C cells

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**Abstract:** β-Cyclodextrin is a seven-membered sugar ring molecule with hydrophobic inside and hydrophilic outside that is commonly used for dissolving and delivering of hydrophobic compounds. It has been reported that beta-cyclodextrins reduce lysosomal cholesterol accumulation in Niemann–Pick disease type C (NPC). The water-soluble cyclodextrin may enter cells through endocytosis and exit cells by exocytosis. We have employed a bodipy-labeled beta-cyclodextrin to study the kinetics of this molecule movement in cells as well as whether cyclodextrin transports cholesterol molecule out of the cells. We found that cyclodextrins entered the cells rapidly and reached a plateau at ~2 h. The cyclodextrins also leave cells quickly with 90% of labeled cyclodextrin out of cells after a cell wash. These results demonstrated that beta-cyclodextrin enters cells through endocytosis and exit cells by exocytosis. We also found that betacyclodextrin dissolved cholesterols could not be loaded into the NPC1 iPSC differentiated neuronal cells, indicating that cyclodextrins may take the cholesterol molecule out of cells. We are currently studying the effect of beta-cyclodextrin on removing lysosomal accumulated cholesterols and on the mechanism of cyclodextrin for the reduction of autophagosomes. Therefore, we will present new results for the mechanism of action for cyclodextrin on the reduction of lysosomal cholesterol accumulation in NPC cells.