Transporters for Thiol-Mediated Uptake

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The delivery of functional substrates into living cells is one of the main challenges in chemistry and biochemistry. In order to address this, we have developed two type of transporters: Cell-penetrating poly(disulfide)s (CPDs) and strained cyclic disulfides.[1] The efficiency of uptake for both methods involves the underestimated thiol-mediated uptake coupled with counterion-mediated uptake for CPDs and ring tension release for strained cyclic disulfides. A large variety of compounds have been delivered by those transporters, from small molecules such as fluorophores[1,2] to giant substrates such as liposomes and polymersomes.[3] Different strategies are now being investigated to broaden the scope of substrates to be delivered such as the streptavidin/biotin technology, side-chain and terminator functionalization for CPDs, and new cyclic molecules for strained-promoted thiol-mediated uptake as presented in Figure 1.

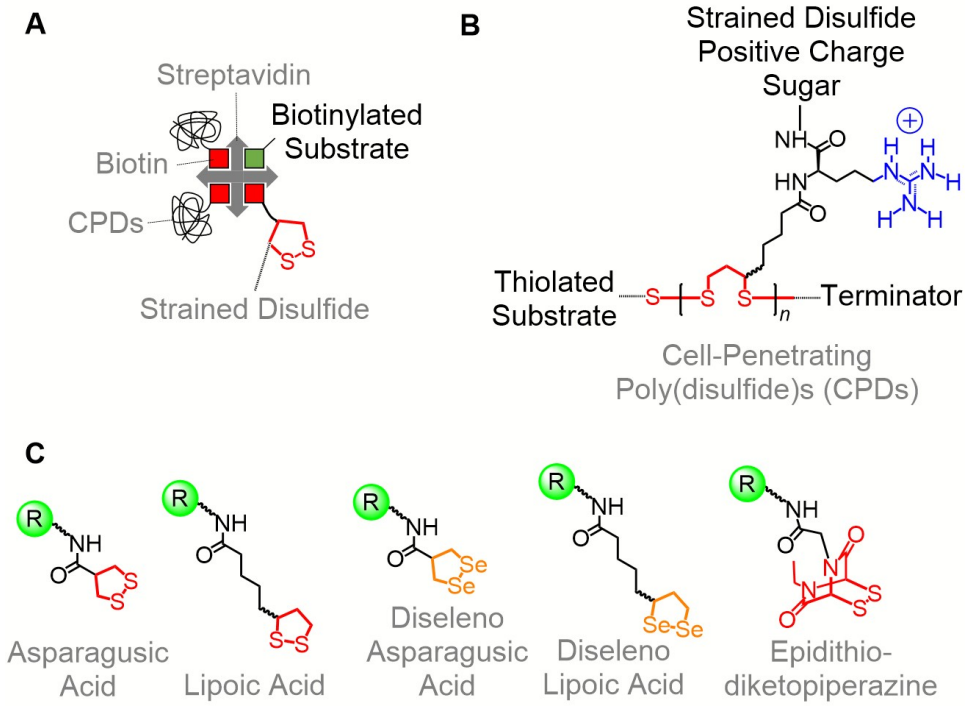

Figure 1. Transporters for thiol-mediated uptake. Streptavidin complexes are formed with a biotinylated substrate and multiple CPDs or strained disulfides (A). The substrate can be directly attached to CPDs (B). Library of compounds for strained cyclic thiol-mediated uptake (C).

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[3] Chuard, N.; Gasparini, G.; Moreau, D.; Lörcher, S.; Palivan, C.; Meier, W.; Sakai, N.; Matile, S. *Angew. Chem. Int. Ed.* **2017**, *54*, 2947-2950.